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Reducing care time after implementing protocols for acute ischemic stroke: a systematic review

Tempo de atendimento após implementação de protocolos para AVC isquêmico agudo: revisão sistemática

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Abstract

Background The treatment of acute ischemic stroke with cerebral reperfusion therapy requires rapid care and recognition of symptoms.
Objective To analyze the effectiveness of implementing protocols for acute ischemic stroke in reducing care time.
Methods Systematic review, which was performed with primary studies in Portuguese, English, and Spanish published between 2011 and 2020. Inclusion criteria: study population should comprise people with acute ischemic stroke and studies should present results on the effectiveness of using urgent care protocols in reducing care time. The bibliographic search was conducted in June 2020 in the LILACS, MEDLINE, Embase, Scopus, CINAHL, Academic Search Premier, and SocINDEX databases. The articles were selected, and data were extracted by two independent reviewers; the synthesis of the results was performed narratively. The methodological quality of articles was evaluated through specific instruments proposed by the Joanna Briggs Institute.

Keywords
- ► Ischemic Stroke
- ► Acute Disease
- ► Clinical Protocols
- ► Emergency Treatment
- ► Program Evaluation

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Results A total of 11,226 publications were found, of which 35 were included in the study. Only one study reported improvement in the symptoms-onset-to-door time after protocol implementation. The effectiveness of the therapeutic approach protocols for ischemic stroke was identified in improving door-to-image, image-to-needle, door-to-needle and symptoms-onset-to-needle times. The main limitation found in the articles concerned the lack of clarity in relation to the study population.

Conclusions Several advances have been identified in in-hospital care with protocol implementation; however, it is necessary to improve the recognition time of stroke symptoms among those who have the first contact with the person affected by the stroke and among the professionals involved with the prehospital care.

Resumo

Antecedentes O tratamento do acidente vascular cerebral (AVC) isquêmico com terapia de reperfusão requer rápido atendimento e reconhecimento dos sintomas.

Objetivo Analisar a efetividade da implementação de protocolos para AVC isquêmico agudo na redução do tempo de atendimento.

Métodos Revisão sistemática realizada com estudos primários em português, inglês e espanhol publicados entre 2011 e 2020. Critérios de inclusão: a população do estudo foi constituída por pessoas com AVC isquêmico agudo e estudos que apresentassem resultados sobre a efetividade da implantação de protocolos no tempo de atendimento. A pesquisa bibliográfica foi realizada em junho de 2020 nas bases de dados LILACS, MEDLINE, Embase, Scopus, CINAHL, Academic Search Premier e SocINDEX. A seleção dos artigos e a extração dos dados foram feitas por dois revisores independentes; a síntese dos resultados foi feita de forma narrativa. A qualidade metodológica dos artigos foi avaliada por meio de instrumentos do Joanna Briggs Institute.

Resultados Foram encontradas 11.226 publicações, das quais 35 foram incluídas no estudo. Apenas um estudo relatou melhora no tempo início dos sintomas-porta após a implementação do protocolo, no entanto, foi efetiva na melhora dos tempos porta-imagem, imagem-agulha, porta-agulha e início dos sintomas-agulha. A principal limitação encontrada nos artigos diz respeito à falta de clareza quanto à população de estudo.

Conclusões Vários avanços foram identificados no atendimento intra-hospitalar com implantação de protocolo; porém, é necessário melhorar o tempo de reconhecimento dos sintomas do AVC entre aqueles que têm o primeiro contato com a pessoa acometida e entre os profissionais envolvidos com o atendimento pré-hospitalar.

Palavras-chave
- AVC Isquêmico
- Doença Aguda
- Protocolos Clínicos
- Tratamento de Emergência
- Avaliação de Programas e Projetos de Saúde

INTRODUCTION

Epidemiological data on stroke worldwide are extremely important to outline strategies for preventing and managing the disease, incisively impacting political decisions. It is known that approximately 80% of strokes are ischemic and that the burden of the disease goes beyond mortality, since approximately 50% of survivors tend to present some disability or chronic incapacity.[1] Global data from 2019 showed that ischemic strokes occurred in 77.2 million people and caused 3.3 million deaths worldwide.[2] The vast majority of these deaths occurred in countries with medium and low-income per capita, and a 42% decrease in deaths from the disease was observed in high-income countries throughout the last decade.[1,3]

The treatment of acute ischemic stroke with cerebral reperfusion therapy (intravenous thrombolysis and mechanical thrombectomy) requires rapid neuroimaging tests such as cranial computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. Thus, all international guidelines for managing patients with acute stroke recommend developing institutional care protocols for early diagnosis and treatment initiation.[4,5] The speed in treatment initiation for patients with acute ischemic stroke is essential,[6] since thrombolysis within 4.5 hours and mechanical thrombectomy within 24 hours after symptoms onset improves functional outcomes.[7]

In addition to reperfusion therapy, other resources and strategies comprise the approach to stroke, namely: prevention of deep venous thrombosis and aspiration, early mobilization, treatment of seizures, as well as maintaining good glycemic index levels and the need for secondary prevention, which mainly encompasses the use of platelet aggregation inhibitors and oral anticoagulants etc.[4]

In view of the above, acute stroke management is broad and complex, since it requires the combination and coordination of interventions based on implementing guidelines for changes in habits, and for intra- and extra-hospital care. These are necessary to heal, rehabilitate, and provide better quality of life for the affected cases, increasing the country's capacity to cope with strokes. Therefore, this study aims to analyze the knowledge produced about the effectiveness of urgent care protocols for acute ischemic stroke in reducing care times.

METHODS

This is a systematic review, which was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).[8] The steps followed in this review were: elaboration of the question with the use of acronyms; study protocol elaboration; search in databases; selection of studies through inclusion and exclusion criteria; data extraction; narrative synthesis of data; and evaluation of methodological quality.

The Population, Intervention, Comparison, and Outcome (PICO) strategy was used to elaborate the research question, according to the description of the Joanna Briggs Institute (2020).[9] Thus, the study question is: What is the effectiveness of urgent care protocols for acute ischemic stroke in reducing care times? In which: P (population) comprises the patients with acute ischemic stroke; I (intervention), are the urgent care protocols; C (comparison), is the before and after protocol implementation; and O (outcome), is the reduction in care times.

The inclusion criteria for scientific productions were: studies in Portuguese, English, and Spanish; articles with study populations consisting of people who had acute ischemic stroke; and articles which addressed studying the effectiveness of implementing stroke protocols on care times. Articles that did not mention the care time in mean or median and did not present a statistical comparison between the period before and after protocol implementation were excluded. Duplicate articles, technical productions (manuals, protocols), letter to the editor/opinion, research protocols, and secondary studies were also excluded.

The bibliographic search was conducted in June 2020 in the following databases: Embase, Scopus, MEDLINE (accessed by PubMed), and Latin American and Caribbean Health Sciences Literature (accessed by the Regional Portal of the Virtual Health Library). Finally, the searches performed in the Cumulative Index to Nursing and Allied Health Literature (CINAHL), Academic Search Premier, and SocINDEX databases were simultaneously performed through the EBSCO host platform, accessed by the CAPES Periódicos website. This platform automatically deletes duplicates found in these databases.

Vocabularies in Portuguese, English, and Spanish were used in LILACS searches, while only vocabularies in English were used for searches in other databases. The controlled and free vocabularies in searching for the studies included the terms: *stroke and acute or urgent and protocol*. The specific search strategies for each database were limited to articles published after 2011 and are presented in the **Supplementary material (available online).**

After the bibliographic search in the databases, the results were exported to the Rayyan Intelligent Systematic Review of the Qatar Computing Research Institute (2016),[10] which enabled eliminating duplicates and selecting publications by two independent reviewers. The selection was initially made by reading the title and abstract of the articles, and a third reviewer was consulted when there was disagreement between the reviewers' decision. Then, the materials were read in full, and if they were relevant to the review, data were extracted using a specific instrument adapted from Ursi (2005),[11] which included the following items: title of the article, journal name, authors, study location, language and year of publication, objective, study type, population/sample, variables, study duration, statistical analysis, and main results. This last item was used in the narrative data synthesis.

The methodological quality of the articles was evaluated through the use of specific instruments proposed by the Joanna Briggs Institute (JBI).[9] In this case, we used the instrument that evaluates cohort studies (which predicts 11 items), and another that evaluates cross-sectional studies (which predicts 8 items), making it possible to indicate the number of items adequately addressed in the studies, according to the number of items predicted by the instruments. The methodological quality evaluation was not used as a criterion to exclude the studies.

RESULTS

A total of 11,226 publications were retrieved from the databases in the bibliographic search, with 5,218 being excluded due to duplication. Then, after reading the titles and abstracts of 6,008 publications, 5,741 were excluded. Thus, 267 selected materials were considered eligible for full reading, from which 35 were included in the study (►**Figure 1**).

Out of 35 articles included in this review, 34 (97.1%)[12–45] were published in English and one (2.9%)[46] in both English and Spanish. Regarding the origin of the selected studies, 15 (42.9%) studies were performed in the Americas,[13,17,18,21,22,24,26,30,31,37–40,44,45] 10 (28.6%) in Europe,[14,15,20,23,27,29,32,34,35,46] 7 (20.0%) in Asia,[12,19,25,28,33,36,43] and 3 (8.6%) in Oceania.[16,41,42] From the included articles, 15 (42.9%) were performed in the United States of America,[13,17,18,21,22,24,26,30,31,37–40,44,45] 4 (11.4%) in China,[12,25,36,43] 3 (8.6%) in Australia,[16,41,42] 2 (5.7%) in Japan,[19,33] 2 (5.7%) in the Netherlands,[23,34] 2 (5.7%) in Norway,[14,35] and 7 (20.0%) in varying countries[15,20,27–29,32,46] (►**Table 1**).

The objectives and other characteristics of scientific production regarding the systematic review on the effectiveness

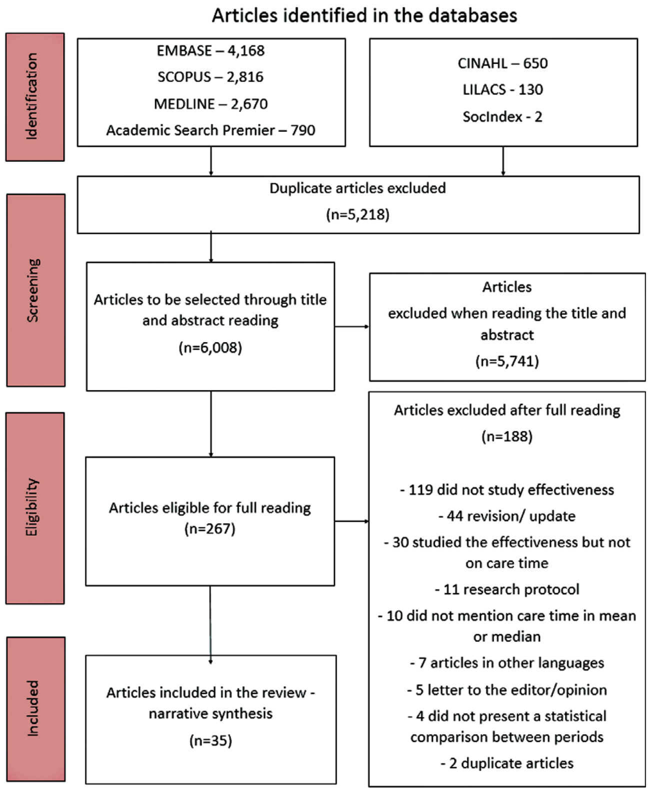

Figure 1 Flowchart of the number of publications analyzed at each stage of the systematic review; regarding the effectiveness of the urgent care protocols for acute ischemic stroke in reducing care times, Ribeirão Preto, São Paulo, Brazil, 2020. Source: Adapted from Moher et al. (2009).[8]

of the use of protocols in the therapeutic approach to acute ischemic stroke are presented in ►**Table 1**. A description of the main results of the articles included in the narrative literature review on the effectiveness of the urgent care protocols for acute ischemic stroke in reducing care times is presented in ►**Table 2**.

Only 1 study[38] reported improvement in the symptoms' onset-to-door time after protocol implementation, out of 14 studies[14,16,23,27,30,36–43,46] that approached this outcome. All (19) studies[13,16,23–25,27,28,30–32,36,38–44,46] that addressed door-to-image time reported improving it. Image-to-needle time improved in 10 studies[15,16,19,23,25,26,30,36,41,46] out of 11[15,16,19,23,25,26,30,32,36,41,46] that assessed it. Door-to-needle time improved in 29 studies[12,13,15–18,20,22–30,32,34–43,45,46] out of 32 studies[12,13,15–18,20–43,45,46] that addressed it. Finally, 12[12,21,23,24,29,36–40,42,46] out of 19 studies[12,17,21,23–26,29,32,33,35–42,46] reported improvement in the symptoms-onset-to-needle time (►**Table 2**).

The main limitation found in the articles regarding the assessment of methodological quality concerned the lack of clarity in relation to the study population,[16,19,21–23,26,28,35–37,39–41,43] and a possible unreliable measurement of exposures and outcomes, since some studies collected data from secondary sources.[13,16,17,19,20,24,26–29,31,34,38,40,41] Additionally, the articles compared two moments (before and after the implantation of the protocol) without the study of cause and effect, so the questions of the instrument related to identification of confounding variables and strategies to minimize follow-up losses did not apply to evaluating the articles included in the review (►**Supplementary Material, available online**).

DISCUSSION

The response time when facing a suspected stroke case was widely addressed in the studies included in this review, being an indicator of the effectiveness of implementing the protocols and of reorganizing services for treating acute ischemic stroke cases. Thus, the response time was stratified into several segments composing a list of indicators, namely: symptoms onset-to-door time, door-to-image time; image-to-needle time; door-to-needle time; and symptoms-onset-to-needle time. In addition to the indicators mentioned above, which were approached in this discussion, it is worth mentioning the existence of other time indicators that were contemplated in articles, but not mentioned in this review.

The symptoms onset-to-door time measures the time elapsed between the onset of symptoms and the patient's arrival at the referral hospital. Only 1 article[38] mentioned the reduction of this time after implementing the stroke protocol, revealing the importance of awareness programs directed to lay people[47,48] and pre-hospital care professionals[47,49–51] to shorten this time. These programs can be provided through campaigns in accordance with community health services and other social sectors. Thus, the effectiveness of implementing protocols when training people to recognize stroke signs is necessary and can lead to an increase in the proportion of suspected cases identified[47,49] and referred to the reference service within the therapeutic time window.

The time between the patient's hospital arrival until the imaging exam (CT or MRI), called door-to-image time, decreased with protocol implementation in all studies that assessed it. It seems that this time was lower in patients who arrived with suspected stroke[16,40,51–53] and in those who arrived at hospitals which had the guideline to immediately direct them to the examination instead of referring it to another department of the hospital,[32,54] or for another exam.[52] Thus, the local health system first needs to have a reference hospital for the care of stroke cases, which has to be warned in advance about the patient's arrival and organize for the direct referral of cases to an imaging exam. To succeed, hospitals have to train the administrative team of hospitals to reduce the time in performing the bureaucracies involved in the admission process of patients.

The image-to-needle time, which corresponds to the time between the imaging exam performance and puncture for thrombolysis or thrombectomy, showed a decrease in 90.9% of the studies that addressed it. It is worth emphasizing the importance of the presence of a neurologist for the exam evaluation, either in person or remotely through telemedicine in places where the reference hospital for the care of stroke cases is already defined, as well as a qualified nursing team, inputs and medicines for the rapid institution of treatment, which must be initiated in the exam room.

Table 1 Description of the articles included in the narrative literature review on the effectiveness of the urgent care protocols for acute ischemic stroke in reducing care times

Authors/Journal/Year/Country	Study design*	Objective(s)	Population(n)
Ye et al.[12]/Stroke Vasc Neurol/2019/ China	Before-after cohort	Evaluate the effectiveness of the Shenzhen stroke emergency map to optimize access to thrombolysis for patients with acute ischemic stroke.	6,843 patients before and 8,268 after; 568 had thrombolysis before and 802 after
Madhok et al.[13]/J Stroke Cerebrovasc Dis/2019/USA	Retrospective cross-sectional	To assess whether the implanted protocol for prehospital and emergency care increases the percentage of patients treated with thrombolysis in a door-to-needle time of up to 45 minutes.	112 patients before and 236 after; 45 patients underwent thrombolysis before and 50 after.
Ajmi et al.[14]/BMJ Qual Saf/2019/ Norway	Cohort	To describe quality improvement project with the objective of reducing door-to-needle time and improving patient results.	446 patients before and 204 after
Vanhoucke et al.[15]/Acta Clin Belg/ 2019/Belgium	Before-after cohort	To evaluate the impact of a stroke code protocol on the door-to-needle time for the use of thrombolysis.	110 patients before and 71 after
Silsby et al.[16]/Intern Med J/2019/ Australia	Retrospective	To assess whether simple and cost-free changes of a protocol could improve treatment time for acute ischemic stroke cases in a tertiary hospital.	143 patients before and 134 after; 30 received thrombolysis before and 14 after
Kansagra et al.[17]/Clin Neurol Neurosurg/2018/USA	Retrospective	To evaluate improvements in the prethrombectomy process in a multihospital network and report the puncture time in patients undergoing mechanical thrombectomy.	104 patients underwent thrombolysis /78 underwent thrombectomy**
Nguyen-Huynh et al.[18]/Stroke/ 2018/USA	Before-after cohort	To present the results of the Kaiser Permanente Northern California stroke protocol, which combines the modified Helsinki protocol and telemedicine, according to the door-to-needle time, use of thrombolysis and symptomatic intracranial hemorrhage rates.	310 patients before and 557 after
Koge et al.[19]/ J Neurol Sci/ 2017/ Japan	Retrospective	To assess the effectiveness and safety of our standardized protocol for intrahospital stroke	25 patients before and 30 after

(*Continued*)

Table 1 (*Continued*)

Authors/Journal/Year/Country	Study design*	Objective(s)	Population(n)
Psychogios et al.[20]/ Stroke/ 2017/ Germany	Retrospective observational	To determine whether centralized treatment can reduce intrahospital treatment times for patients with acute occlusion of large vessels.	44 patients**
Kalnins et al.[21]/ Radiographics/ 2017/ USA	Cohort	To decrease stroke code time to CT for patients with non-prenotified stroke code from a reference mean of 20 minutes to 15 minutes or less.	107 patients before and 298 after
Caputo et al.[22]/ Neurohospitalist/ 2017/ USA	Prospective cohort	To describe the process of developing and implementing a protocol and comparing the door-to-needle times and rates of symptomatic intracranial hemorrhage before and after the implementation of the protocol.	295 patients**
Zinkstok et al.[23]/ PLoS One/ 2016/ Netherlands	Before-after cohort	To reduce the door-to-needle time to 30 minutes or less with the optimization of intrahospital stroke treatment.	373 patients**
Busby et al.[24]/ J Neurointerv Surg/ 2016/ USA	Retrospective	To initiate a quality improvement project called CODE FAST to reduce the door-to-needle time in the institution.	41 patients before and 52 after
Liang et al.[25]/ Australasian Physical and Engineering Sciences in Medicine/ 2016/ China	Prospective	To determine whether the application of lean principles for flow optimization could accelerate the start of thrombolysis.	13 patients before and 20 after
Moran et al.[26]/ Journal of Stroke and Cerebrovascular Diseases/ 2016/ USA	Retrospective Cohort	To assess the impact of the provision of neurocritical nursing care 24 hours a day, 7 days a week, according to the first aid coverage in the "stroke code" on delays in the treatment of patients with acute stroke who received thrombolysis.	44 patients before and 122 after
Marto et al.[27]/ J Stroke Cerebrovasc Dis/ 2016/ Portugal	Retrospective	To evaluate the effect of implementing a regressive timer in the acute stroke emergency room, in the door-to-CT and door-to-needle times.	30 patients before and 41 after

Table 1 (*Continued*)

Authors/Journal/Year/Country	Study design*	Objective(s)	Population(n)
Ibrahim et al.[28]/ J Stroke Cerebrovasc Dis/ 2016/ Qatar	Retrospective	To assess the effect of the acute thrombolysis protocol on "door-to-needle time" and on the prognosis of acute stroke cases.	102 patients before and 102 after
Heikkilä et al.[29]/ Scand J Trauma Resusc Emerg Med/ 2016/ Finland	Retrospective	To describe a new protocol for patients with acute ischemic stroke and thrombolysis administered by emergency physicians in the Emergency Department – the so-called Hämeenlinna model and present preliminary results regarding the door-to-needle and treatment initiation times.	31 patients before and 33 after
Rai et al.[30]/ J Neurointerv Surg/ 2016/ USA	Prospective	To present the results of a quality improvement process aimed at reducing stroke treatment time in a tertiary academic medical center.	64 patients before and 30 after
Zuckerman et al.[31]/ Surg Neurol Int/ 2016/ USA	Retrospective	To describe the process of implementing a new stroke algorithm, compare the pre- and postalgorithm quality improvement metrics, specifically door-to-CT, door-to-neurologist, and door-to-needle times.	Not described**
Kendall et al.[32]/ Emerg Med J/ 2015/ England	Before-after	To describe how the Stroke 90 project was configured and what interventions were implemented, report the results and discuss lessons learned from it.	136 patients before and 215 after
Atsumi et al.[33]/ J Stroke Cerebrovasc Dis/ 2015/ Japan	Prospective	To investigate whether prehospital and hospital thrombolysis indicators improved after using a single prehospital scale in a municipal transport protocol, and examine whether a deleterious effect of admission on weekends was observed.	2,049 patients**

(*Continued*)

Table 1 (*Continued*)

Authors/Journal/Year/Country	Study design*	Objective(s)	Population(n)
Van Schaik et al.[34]/ J Stroke Cerebrovasc Dis/ 2014/ Netherlands	Before-after	To reduce the delay in intrahospital treatment of patients with acute ischemic stroke through the implementation of a standard operating procedure and the creation of a greater and sustained awareness of the importance of this time-oriented protocol among all health professionals involved in the process.	41 patients before and 185 after
Advani et al.[35]/ Cerebrovasc Dis Extra/ 2014/ Norway	Retrospective	To retrospectively evaluate the importance of streamlining the treatment chain for patients with acute ischemic stroke, reviewing and improving the pre- and intrahospital routines around the treatment of these patients in the procedure in relation to the number of patients treated with thrombolysis. The secondary objective of the study was to assess changes in door-to-needle times and onset of symptoms-to-needle resulting from changes in pre- and intrahospital routines.	320 patients**
Chen et al.[36]/ PLoS One/ 2014/ China	Prospective	To investigate the impact of the stroke code on the performance of thrombolytic therapy and functional results for patients with acute ischemic stroke.	91 patients before and 216 after
Fonarow et al.[37]/ JAMA/ 2014/ USA	Before-after	To analyze the time trend of the door-to-needle time for the administration of thrombolysis and determine the proportion of patients with a time of 60 minutes or less before and after the beginning of the program; to evaluate whether improvement in the door-to-needle time was associated with improved clinical results, including hospital mortality, destination of discharge, ambulatory status, the presence of symptomatic intracranial hemorrhage 36 hours after thrombolysis and complications of thrombolysis.	27,319 patients before and 43,850 after

Table 1 (*Continued*)

Authors/Journal/Year/Country	Study design*	Objective(s)	Population(n)
Ruff et al.[38]/ Stroke/ 2014/ USA	Retrospective	To assess whether the incorporation of a stroke protocol into the Target Stroke initiative significantly changed the mean door-to-CT and door-to-needle times.	1,413 patients before and 925 after
Ford et al.[39]/ Stroke/ 2012/ USA	Prospective	The "current state analysis" mapped operations with waste and those that added value. A "future state analysis" removed useless steps and retained value-added steps. An "action plan" was created to implement the simplified protocol and provide feedback for continuous improvement. The efficiency and safety metrics of the protocol were compared before and after implementation.	132 patients before and 87 after
Lin et al.[40]/ Circ Cardiovasc Qual Outcomes/ 2012/ USA	Retrospective	To assess the association of prenotification of the emergency medical service with assessment and treatment of acute ischemic stroke, including door-to-CT and door-to-needle times, symptoms-door onset and thrombolytic treatment rates in eligible patients.	249,197 patients before and 122,791 after
Tai et al.[41]/ Intern Med J/ 2012/ Australia	Retrospective	To perform a comprehensive qualitative analysis of the stroke code service at a Melbourne hospital to determine whether it had resulted in a reduction in door-to-needle and door-to-CT times, and increased the percentage of patients treated with thrombolysis.	96 patients before and 189 after
O'Brien et al.[42]/ J Clin Neurosci/ 2012/ Australia	Prospective cohort pre- and postintervention	To determine whether the introduction of a prehospital notification scheme based on an ambulance stroke service (FASTER) reduces the assessment time for thrombolysis and increases the use of thrombolysis in a health service in the Central Coast area.	42 patients before and 67 after

(*Continued*)

Table 1 (*Continued*)

Authors/Journal/Year/Country	Study design*	Objective(s)	Population(n)
Sung et al.[43]/ Stroke Res Treat/ 2011/ China	Before-after	To determine whether modifying the protocol shortened intrahospital delay and facilitated thrombolytic therapy.	338 patients before and 139 after
Hoegerl et al.[44]/ Journal of the American Osteopathic Association/ 2011/ USA	Prospective	To determine whether implementing a stroke alert protocol, in conjunction with a limited education program, will reduce the arrival time for CT and the treatment time for stroke patients in the emergency department.	132 patients before and 101 after
Kamal et al.[45]/ Circulation/ 2017/ USA	Prospective cohort	To analyze the impact of four specific strategies (a new call activation system; registering the patient with suspected stroke as unknown on admission until laboratory confirmation/image; sending direct patient to CT in emergency services; applying thrombolysis on the CT table scan or imaging) to reduce the door-to-needle time in a single center.	350 patients**
Iglesias Mohedano et al.[46]/ Neurologia/ 2020/ Spain	Before-after cohort	To determine whether a new intrahospital intravenous thrombolysis protocol is effective in reducing the door-to-needle time and correcting previously identified factors associated with delays.	239 patients before and 222 after

Abbreviation: CT, computed tomography. **Notes:** *The study design was noted according to how it was mentioned in the original article. **The authors did not present the study population before or after implementing the protocol.

Table 2 Description of the main results of the articles included in the narrative literature review on the effectiveness of the urgent care protocols for acute ischemic stroke in reducing care times

References / methodological quality appraisal	Symptoms onset-to-door time	Door-to-image time	Image-to-needle time	Door-to-needle time	Symptoms onset-to-needle time
	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value
Ye et al.[12] 8/11	DNM	DNM	DNM	Mdn 71.5–51.5 $p < 0.001$	Mdn 175.5–149.5 $p = 0.039$
Madhok et al.[13] 4/8	DNM	Mdn 19(IQR 14–23)–9(9–11) $p < 0.01$	DNM	Mdn 35(IQR 32–57)–29 (22–36) $p < 0.01$	DNM
Ajmi et al.[14] 8/11	Mdn 38(IQR 27–54)–37 (25–50) $p = 0.2$	DNM	DNM	Mdn 27(IQR 19–41)–13(9–23)*	Mdn 110(IQR 77–168)–96(68–146)*
Vanhoucke et al.[15] 8/11	DNM	DNM	Mdn 24(IQR 13–42)–15 (10–21) $p = 0.009$	Mdn 57 (IQR 43–69)–33 (25–45) $p < 0.001$	DNM
Silsby et al.[16] 5/11	Mdn 90(IQR 65–130)–93 (64–154) $p = 0.66$	Mdn 23(IQR 14–55)–22(9–49) $p = 0.11$ Reduced from Mdn 16 (IQR 9–22) to 8 (4–14) min ($p < 0.01$) in patients pre-notified by the ambulance	Mdn 55 (IQR 39–67)–26 (23–27) $p < 0.01$	76(54–91)–33(27–44) $p < 0.01$	DNM
Kansagra et al.[17] 6/11	DNM	DNM	DNM	Mdn 147–39 minutes $p < 0.001$	Mdn 290–212 $p = 0.05$
Nguyen-Huynh et al.[18] 8/11	DNM	DNM	DNM	Mdn 53.5(IQR 42–73)–34 (26–45) $p < 0.001$	DNM
Koge et al.[19] 5/11	DNM	DNM	Mdn 45(IQR 20–58)–16 (13–40) for thrombolysis $p = 0.02$ Mdn 75(IQR 45–90)–53 (45–73) for thrombectomy $p = 0.08$	DNM	DNM
Psychogios et al.[20] 6/11	DNM	DNM	DNM	M 54.5(95% CI 47–61)–20.5 (95% CI 17–26)	DNM
Kalnins et al.[21] 7/11	DNM	DNM	DNM	M 98–65 $p = 0.08$	M 186–130 $p = 0.02$
Caputo et al.[22] 7/11	DNM	DNM	DNM	Mdn 38–28 $p < 0.001$	DNM
Zinkstok et al.[23] 7/11	Mdn 65(IQR 50–90)–71 (48–120) $p < 0.156$	Mdn 35(IQR 27–47)–6(4–10) $p < 0.001$	Mdn 40(IQR 31–55)–20 (15–28) $p < 0.001$	Mdn 75(IQR 60–105)–28 (20–37) $p < 0.001$	Mdn 158(IQR 135–177)–105(75–160) $p < 0.001$

(*Continued*)

Table 2 (*Continued*)

References / methodological quality appraisal	Symptoms onset-to-door time	Door-to-image time	Image-to-needle time	Door-to-needle time	Symptoms onset-to-needle time
	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value
Busby et al.[24] 6/11	DNM	Mdn 16(IQR 11–25)–8(5–11) $p < 0.0001$	DNM	Mdn 62(IQR 49–77)–25 (18–36) $p < 0.0001$	DNM
Liang et al.[25] 8/11	DNM	Mdn 37(IQR 26–40)–22 (13–27) $p = 0.003$	Mdn 33(IQR 30–47)–25 (18–29) $p < 0.001$	Mdn 90(IQR 60–125)–47 (40–61) $p = 0.004$	Mdn 163(IQR 140–180)–170(133–205) $p = 0.625$
Moran et al.[26] 5/11	DNM	DNM	Mdn 36(IQR 28–64)–21 (16–31) $p < 0.0001$	Mdn 53(IQR 45–43)–45 (35–58) $p = 0.001$	Mdn 118(IQR 96–157)–110(80–141) $p = 0.13$
Marto et al.[27] 6/11	M 91.5(SD 51.6)–90.7(SD 42.8) $p = 0.943$	M 24–16.5 $p = 0.004$	DNM	M 47–39 $p = 0.016$	DNM
Ibrahim et al.[28] 5/11	DNM	M 42.5(SD 42.1)–27.1(SD 26.4) $p < 0.001$	DNM	M 83.3(SD 47.7)–47.1(SD 25.7) $p < 0.001$	DNM
Heikkilä et al.[29] 6/11	DNM	DNM	DNM	Mdn 54–28 $p < 0.001$	Mdn 139–101 $p < 0.001$
Rai et al.[30] 8/11	M 180(SD 128)-183(SD 244) $p = 0.2$	M 40(SD 29)-26(SD 15) $p = 0.008$	M 111–66 for thrombectomy $p < 0.0001$ M 111(SD 49)–67(SD 33) for thombolysis $p < 0.0001$	M 151(SD 51)–93(SD 37) $P < 0.0001$	DNM
Zuckerman et al.[31] 6/11	DNM	M 39.9–12.8 $p < 0.001$	DNM	M 62.5 (SD 44.9)–43.5 (SD 21.5) $p = 0.169$	DNM
Kendall et al.[32] 8/11	DNM	M 32(SD 22.6)–23.5(SD 21.8) $p < 0.001$	M 43.8(SD 27.3)–42.1(SD 26.1) $p = 0.57$	M 76.2(SD 32.3)–65.6(SD 33.7) $p = 0.004$	M 164.9(SD 50.1)–154.1 (SD 51.7) $p = 0.053$
Atsumi et al.[33] 8/11	DNM	DNM	DNM	M 75.3(SD 23.8)–78.1(SD 31.6) $p = 0.457$	M 132.4(SD 27.4)–117.4 (SD 59.0) $p = 0.168$
Van Schaik et al.[34] 8/11	DNM	DNM	DNM	Mdn 60(IQR 41–65)–25 (20–37) $p < 0.001$	DNM
Advani et al.[35] 5/11	DNM	DNM	DNM	Mdn 73–31 $p < 0.001$	Mdn 135–119 minute $p < 0.44$

Table 2 (*Continued*)

References / methodological quality appraisal	Symptoms onset-to-door time	Door-to-image time	Image-to-needle time	Door-to-needle time	Symptoms onset-to-needle time
	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value	Before-After (min) *p*-value
Chen et al.[36] 7/11	Mdn 45(IQR 30–65)–58 (32–94.5) $p = 0.009$	Mdn 24(IQR 19–38.5)–11 (9–13) $p < 0.001$	Mdn 61(IQR 44–79)–40 (32–51) $p < 0.001$	Mdn 88(IQR 67–107)–51 (43–64) $p < 0.001$	Mdn 145(IQR 122–163)–125(90.3–157) $p < 0.001$
Fonarow et al.[37] 7/11	Mdn 50(IQR 35–70)–52 (36–73)*	DNM	DNM	Mdn 77(IQR 60–98)–67 (51–87) $p < 0.001$	Mdn 137(IQR 113–160)–128(103–154) $p < 0.001$
Ruff et al.[38] 6/11	Med 576 (180–2,166)–498 (120–1,578) $p = 0.001$	Med 71 (IQR 37–156)–59 (24–142) $p < 0.001$	DNM	Mdn 70(IQR 56–85)–47 (32–62) $p < 0.001$	Mdn 124(IQR 100–162)–105(75–148) $p = 0.002$
Ford et al.[39] 7/11	Mdn 62(IQR 43–93)–67 (38–91) $p = 0.75$	Mdn 16(IQR 10–22)–1(0–4) $p < 0.001$	DNM	Mdn 60 (IQR 46–73)–39 (28–56) $p < 0.0001$	Mdn 131(IQR 105–165)–11(80–158) $p = 0.0161$
Lin et al.[40] 5/11	Mdn 113(IQR 55–340)–150 (60–445) $p < 0.0001$	Mdn 55(IQR 28–103)–42 (22–83) $p < 0.0001$	DNM	Mdn 80(IQR 60–103)–78 (60–100) $p < 0.0001$	Mdn 145(IQR 116–170)–141(115–169) $p < 0.0001$
Tai et al.[41] 5/11	Mdn 61.5 (IQR 49.0–73.8)–72.0 (56.0–111.5) $p < 0.001$	Mdn 42 (IQR 29–56)–23 (16–39) $p < 0.001$	Mdn 48.5 (IQR 32.8–67.3)–39.0 (25.0–62.0) $p = 0.044$	Mdn 90 (IQR 77.3–111)–72 (50.5–93.5) $p < 0.001$	Mdn 160 (IQR 133–175)–160 (128–195) ($p < 0.339$)
O'Brien et al.[42] 8/11	M 59–76 minutes $p = 0.180$	M 49–19 minutes $p = 0.004$	DNM	M 102–56 minute $p = 0.001$	M 157–125 minutes $p = 0.005$
Sung et al.[43] 7/11	Mdn 65(IQR 34–108)–66 (IQR 36–117) $p = 0.217$	Mdn 29 (IQR 19–50)–20 (13–38) $p < 0.001$	DNM	Mdn 68.5 (IQR 57–83)–58 (54–69) $p = 0.035$	DNM
Hoegerl et al.[44] 8/11	DNM	Mdn 65.5(IQR 41.0–101.0)–54.0(33.1–55.3) ($p < 0.004$)	Mdn 23.0–16.3*	Mdn 85.5–48.9*	DNM
Kamal et al.[45] 8/11	DNM	DNM	DNM	Mdn 53–35 $p = 0.0002$	DNM
Iglesias Mohedano et al.[46] 8/11	Mdn 84(IQR 60–120)–82.5 (57.7–116.2) $p = 0.90$	Mdn 17(IQR 13–24.8)–15 (11.7–20) $p < 0.001$	Mdn 34(IQR 26–47)–18 (13–25) $p < 0.001$	Mdn 52(IQR 43–70)–34 (28–45) $p < 0.001$	Mdn 145(IQR 120–180)–119(93–155.2) $p < 0.001$

Abbreviations: DNM, did not mention; IQR, interquartile range; M, mean; Mdn, median; min, minutes; SD, standard deviation. **Notes:** *Did not present *p*-value.

The door-to-needle time showed a significant decrease in 90.6% of the studies after implementing the stroke protocol. This time is closely related to the structural and operational reorganization to provide adequate and timely care to affected cases in the stroke care units, and can also be reduced if an adequate diagnostic hypothesis is raised for stroke cases by the prehospital urgency and emergency medical services,[40,45,50,54] with the intention of quickly activating the stroke code.[46,50,55]

The symptoms-onset-to-needle time decreased in 63.2% of the studies after implementing the protocol.[12,21,23,24,29,36–40,42,46] Thus, despite the advances in in-hospital care, efforts are required to raise awareness and sensitize people in the community regarding recognition of the urgency of attending a case with signs and symptoms compatible with stroke. In this sense, Primary Health Care services and teams need to be involved in the Stroke Care Network with clear roles and responsibilities to achieve these objectives. Additionally, the availability of a specific algorithm to avoid treatment delays and to prioritize cases when emergency medical services are triggered should be encouraged.

The need to better elucidate the study population should be emphasized in the studies included in the present review, to highlight the similarities between the groups studied, and to provide reliable measures of exposures and outcomes by conducting a prospective data collection.

This review had as a limitation the impossibility of relating the effectiveness of using protocols in stroke care based on their composition and characteristics, since they were not always described in detail in the studies. The systematic review is also limited, as the searches for articles were conducted only by title, abstract, and keywords in most of the databases—no full text search was made. Additionally, meta-analysis and assessment of the quality of the evidence of this systematic review could not be performed.

In conclusion, the importance and relevance of implementing protocols in stroke care and effectiveness in the time elapsed between the onset of symptoms and initiating treatment was identified in this study. Therefore, it is necessary to seek improvement in the recognition time of stroke symptoms among people who have first contact with the person affected by the stroke, as well as prehospital care and hospitalization, making efforts to provide reperfusion therapy. Furthermore, the lack of detailed description of the implemented protocols represents a gap to be investigated in future comparative studies.

Supplementary material is avalilable online.

Authors' Contributions

KFSL, SRS, RLPA, AAM: conceptualization; KFSL, SRS, RLPA, MGBFF: data curation; KFSL, SRS, RLPA, MGBFF, NMS, RAA, ISSI, CEMR, TCSV, OMPN, AAM: formal analysis, writing original draft, writing - review & editing; KFSL, RLPA, AAM: funding acquisition, project administration; KFSL, SRS, RLPA, AAM: methodology.

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Conflict of Interest

The authors have no conflict of interests to declare.

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