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ORIGINAL RESEARCH

The Necessity of Using MRI as an Imaging Modality in Acute Code Stroke in Indonesia

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Purpose: To evaluate the performance and outcomes of the 6-minute magnetic resonance imaging (MRI) protocol in diagnosing stroke within Indonesian healthcare setting compared to computed tomography (CT).

Patients and methods: This retrospective single-center study was conducted at the Universitas Indonesia Hospital in Depok, Indonesia from September 2021 to September 2023. Patients who were diagnosed with acute stroke underwent a clinical evaluation and a 6-minute MRI protocol. The primary objective was to assess the efficiency of the 6-minute MRI protocol in promptly and accurately evaluating acute stroke patients, including determining average MRI time, thrombolysis eligibility, and post-thrombolysis outcomes compared to CT imaging. Exclusions comprised those requiring resuscitation, lack of stroke code activation, or having incomplete documentation.

Results: This study involved 182 stroke patients, 136 of which underwent MRI and 46 had CT scans. Thrombolysis eligibility was similar between the groups (48.9% for MRI vs 47.8% for CT-Scan), but a higher proportion of eligible MRI patients received thrombolysis (70.1% vs 54.5%, p = 0.037). MRI also achieved shorter door-to-imaging times, especially from February to June 2022. Among those treated for ischemic stroke via MRI, 70.3% showed improvement compared to 55% for CT (p=0.016). Door-to-MRI times varied across periods, averaging 88.2 minutes before national healthcare insurance collaboration, 29.1 minutes during transition, and 47.8 minutes afterward.

Conclusion: This study emphasizes the crucial role of the 6-minute MRI protocol for accurately diagnosing stroke types, severity, and determining thrombolysis eligibility. Positive outcomes in thrombolysis patients using this protocol highlight its effectiveness. However, prolonged time-to-MRI indicates the need for further improvement. Optimizing time management and workflow efficiency are critical for improving treatment efficacy and safety.

Keywords: MRI, CT-scan, code stroke, developing country, thrombolysis

Introduction

Stroke remains a substantial global burden, transcending geographical and ethnic boundaries.[1] Globally, stroke is the second leading cause of death, accounting for 11.6% of all deaths in 2019. Ischemic stroke is the most frequent type, accounting for 62.4% of all stroke cases worldwide in 2019.[2] Based on the Indonesia Basic Health Research data, the prevalence of stroke in Indonesia reached 10.9 per 1000 population in 2018 and was the leading cause of death in Indonesia.[3]

Since timely intervention is crucial in minimizing brain damage and improving outcomes, "Code Stroke" is used to trigger a rapid and coordinated response from the emergency team. This response involves rapid assessment to confirm the diagnosis of stroke, brain imaging (CT-scan or MRI) to identify the type of stroke, and administering treatments such as thrombolytic agents. Alteplase (recombinant tissue plasminogen activator, rtPA) is the only approved drug for patients with acute ischemic stroke. It is recommended as an initial treatment within 4.5 hours after stroke onset and also shows

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therapeutic effects in a longer time window in carefully selected patients.[4,5] Due to the short window time period, neuroimaging plays a critical role in evaluating patients with stroke, both for diagnosis and to facilitate the pursuit of the golden period for thrombolysis therapy.[5] The important benchmark to reduce delays in the management of stroke is the door-to-imaging (CT scan or MRI) which refers to the time interval between a patient arriving at the hospital (the "door") and the moment they receive a brain imaging.

Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the two primary imaging modalities for assessing acute stroke. MRI offers several advantages over CT in evaluating the brain parenchyma in individuals with acute ischemic stroke. These benefits include the rapid detection of symptomatic ischemic lesions, the ability to differentiate between stroke mimics, the capacity to identify lesions in the brain stem, the capability to distinguish newly symptomatic from chronic ischemic lesions, and the establishment of prognosis.[6] The utilization of MRI is currently less widespread than CT due to limited availability in medical facilities and the use of MRI in the emergency setting has not been proven to be more effective than CT.[7] Additionally, a study comparing the outcomes of patients with acute ischemic stroke initially imaged with CT alone versus CT plus MRI found that the use of initial CT alone was noninferior to initial CT plus additional MRI in terms of clinical outcome.[8,9]

Indonesia still faces challenges in the management of stroke patients, so thrombolysis therapy is not yet widely performed. Examining the challenges in facility availability, out of the 3.200 hospitals across Indonesia, only 372 hospitals have CT-Scan facilities. Among them, 120 hospitals are capable of performing thrombolysis, but only 69 hospitals actively engage in this practice.[10,11] In 2022, we established a stroke code system at the University of Indonesia Hospital in Indonesia using 6 minutes protocol to diagnose stroke. The purpose of this study was to establish the feasibility and evaluation the performance of the 6-minutes MRI protocol for code stroke. We describe the outcome and present our initial clinical experience using this protocol.

Methods

Patients and Study Design

This retrospective single-center study was conducted at the Universitas Indonesia Hospital, a secondary and educational hospital based in Depok, West Java, Indonesia. The study involved medical records with complete patient information who underwent either MRI or CT-Scan for stroke evaluation admitted from September 2021 to September 2023. Informed consent was obtained through verbal and written consent, while the participants also aware that this health facility is an educational institution. The participants in this study were patients with a clinical presentation of stroke, thus the stroke code should be activated. We excluded patients who required resuscitation (including intubation), arrived with no stroke code activation, and had incomplete documentation.

Patients with a clinical diagnosis of acute stroke were evaluated using the National Institutes of Health Stroke Scale (NIHSS) and underwent a 6-minute MRI brain-based protocol. The observation period would be divided into 3 phases, namely before, during the transition period, and after collaboration with the Indonesia Healthcare Insurance. This collaboration is significant to note, as a substantial proportion of Indonesian patients (nearly 95% coverage, encompassing more than 260 million people) depend on this insurance to cover the costs of accessing healthcare facilities.[12] The primary outcome of this study was to evaluate the use of a 6-minute MRI protocol to rapidly and accurately assess patients with acute stroke by seeking data on the average time to MRI with the 6-Minute MRI Protocol, determine their eligibility for thrombolysis, and assist in the decision to administer thrombolysis.

MR Protocol

The 6-minute MRI protocol includes five MRI sequences: diffusion-weighted imaging (DWI), EPI fluid attenuation inversion recovery imaging (FLAIR), EPI-gradient recalled echo (GRE), Magnetic Resonance Angiography (MRA), and dynamic susceptibility contrast (DSC) perfusion imaging.[13]

Statistical Analysis

The extracted data were reviewed, cleaned, and entered into SPSS version 24.0 software for analysis. Descriptive statistics were used to characterize the frequency and percentage of every variable. The results were presented in the form of texts, diagram and tables. We conducted a case-control study using chi-square statistics to determine the prevalence ratios (PR) with 95% confidence intervals (CI). P-values were calculated to assess associations between variables, particularly in clinical outcomes.

Results

In this study, we compared various parameters between patients undergoing MRI and CT-Scan for stroke evaluation. Among the 182 patients included in the analysis, 136 underwent MRI and 46 underwent CT-Scan. Demographic analysis revealed that patients undergoing MRI were, on average, younger (58.4 ± 13.3 years) compared to those undergoing CT-Scan (62.1 ± 13.3 years) (see Table 1). Gender distribution showed slight variations, with 53.7% males in the MRI group and 56.5% in the CT-Scan group.

Analysis of radiological findings indicated that ischemic stroke was the most common diagnosis in both groups, with a significant higher findings of ischemic stroke observed in the MRI group (72.1% MRI vs 50.0% CT-Scan, p = 0.017).

Table 1 The Demographic and Clinical Characteristics of Study Participants

Variables	MRI (n=136)	CT-Scan (n=46)	p-value*
Age (years old; mean ± SD)	58.4 ± 13.3	62.13 ± 13.3	N/A
Gender (n; %)			
Male	73 (53.7)	26 (56.5)	N/A
Female	63 (46.3)	20 (43.5)	
Diagnosis from Radiological Findings (n; %)			
Ischemic stroke	98 (72.1)	23 (50.0)	0.017
Haemorrhagic stroke	23 (16.9)	16 (34.8)	
Others	15 (11.1)	7 (15.2)	
Door to MRI time (n; %)			
≤ 25 min	48 (35.3)	7 (17.9)	0.01
> 25 min	88 (64.7)	39 (82.1)	
NIHSS in ER admission			
<5	46 (34.1)	9 (19.6)	N/A
5–20	77 (57.0)	27 (60.9)	
>20	12 (8.9)	9 (19.6)	
Eligibility for thrombolysis (n; %)			
Yes	48 (48.9)	11 (47.8)	0.92
No	50 (53.0)	12 (52.2)	
Undergo thrombolysis from eligible (n; %)			
Yes	37 (70.1)	5 (54.5)	0.037
No	11 (29.9)	6 (45.5)	

Note: *significant if p-value <0.05.

Hemorrhagic stroke was the second most frequent diagnosis, followed by other diagnoses. In terms of stroke severity, In the MRI group, the distribution of NIHSS scores revealed that 34.1% of patients had mild strokes (NIHSS < 5), 57.0% had moderate to severe strokes (NIHSS 5–20), and 8.9% had severe strokes (NIHSS > 20). Conversely, in the CT-Scan group, a lower proportion of patients presented with mild strokes (19.6%), while a slightly higher percentage had moderate to severe strokes (60.9%), and a comparable proportion had severe strokes (19.6%).

Thrombolysis eligibility rates were comparable between MRI (48.9%) and CT-Scan (47.8%) groups. However, a higher proportion of eligible patients underwent thrombolysis in the MRI group compared to the CT-Scan group (70.1% and 54.5% respectively, p = 0.037).

The observation period from September 2021 to September 2023 is divided into 3 periods. During these three periods, the analysis reveals a non-linear trend in the door-to-MRI/CT time. Additionally, examination of door-to-imaging time intervals across different periods unveiled substantial variations. Notably, MRI evaluations demonstrated significantly shorter times during the period from February 2022 to June 2022, with a mean of 29.1 minutes (IQR: 14.0–39.7), compared to CT-Scan evaluations during the same period, with a mean of 88.2 minutes (IQR: 49.6–111.5) (see Table 2).

Out of 136 samples, 98 patients were diagnosed with ischemic stroke following a 6-minute MRI examination. Among these patients, 48 met the criteria for thrombolysis therapy. 37 of them received alteplase treatment, while the remaining 11 opted for conservative management. Furthermore, 50 patients were deemed ineligible for thrombolysis due to various clinical factors. As a result, the stroke code was deactivated for these individuals, and they received conservative therapy tailored to their specific clinical conditions (Figure 1). There are 50 patients who were classified as thrombolysis candidates but were deemed ineligible based on neurologist assessment. The list of reasons for patient ineligibility is provided in Table 3 attached.

Among 38 patients categorized as eligible to receive thrombolysis, there were 11 patients who did not receive alteplase therapy due to several reasons. In Table 4, there are a description of the reasons why eligible patients did not undergo thrombolysis.

Out of 37 patients in the MRI group who received thrombolysis therapy, 33 patients (89.19%) showed clinical improvement and a reduction in NIHSS scores following alteplase administration, compared with 3 patients (50%) in the CT-scan group (p = 0.016) (Table 5). Meanwhile, 4 patients (10.81%) in the MRI group and 2 patients (33.3%) in the CT-scan group experienced adverse effects such as bleeding and decrease of consciousness. Of the total deceased patients, some succumbed to other comorbid conditions including cardiopulmonary problems and renal failure.

Discussion

Acute stroke is a medical and surgical emergency, with the outcome of care closely related to time to treatment. However, patients with stroke commonly arrive late to the hospital, and significant delays are frequently observed in the treatment of those with acute stroke, particularly in limited-resource settings, especially in emergency settings.[13,14]

Patients experiencing acute ischemic stroke should be promptly hospitalized and administered thrombolytic therapy within one hour of admission, aligning with the guidelines established by the National Institute of Neurological Disorders and Stroke (NINDS).[15] Therefore, the time-to-treatment window is critical for managing acute ischemic stroke.

We found that acute ischemic stroke was the most prevalent type, consistent with findings from Narayanaswamy et al, who noted its higher frequency in South, East, and Southeast Asia compared to other stroke types.[16] In our study, many MRI evaluations met the recommended 25-minute threshold, while most CT-Scans did not, highlighting the need to enhance CT

Table 2 Average Time to MRI With 6-minute MRI Protocol

Period	Door to MRI Time in Minute (mean, IQR) (n=136)	Door to CT Time in Minute (mean, IQR) (n=46)
September 2021-January 2022	88.2 (19.8–80.9)	61.1 (15.3–89.5)
February 2022 – June 2022	29.1 (14.0–39.7)	87.2 (49.6–111.5)
July 2022 - September 2023	47.8 (22.5–62.9)	63.4 (25.1–104.5)

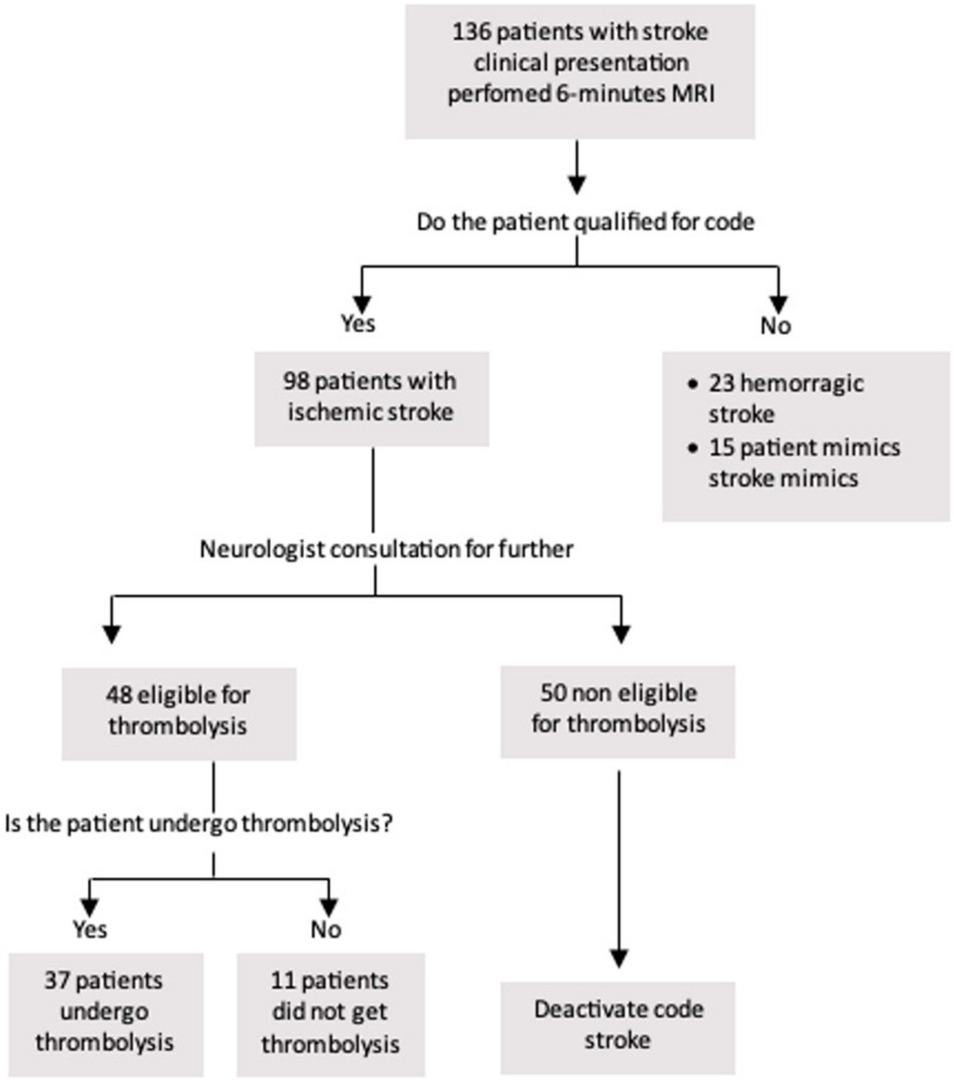

Figure 1 Flowchart of Patients Undergoing 6-Minute MRI.

efficiency to align with American Heart Association standards for stroke management.[17] Comparing these results with previous studies offers additional insights into potential implications, emphasizing that door-to-imaging times are influenced by various factors such as hospital infrastructure, staffing levels, patient volume, and technological advancements.[18–21] In Indonesia, MRI and CT-Scan interpretations are conducted by radiologists, and thrombolysis decisions are approved by

Table 3 List of Ineligible Criteria Based on Clinical Features

Ineligible Criteria	n=50 (n;%)	n=12 (n;%)
Transient ischemic attack	13 (26.0%)	0 (0.0%)
NIHSS < 5	11 (22.0%)	2 (16.7%)
Recurrent stroke	10 (20.0%)	2 (16.7%)
Large Vessel Occlusion	6 (12.0%)	0 (0.0%)

(*Continued*)

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Table 3 (Continued).

Ineligible Criteria	n=50 (n;%)	n=12 (n;%)
Age >65 years old	5 (10.0%)	3 (25.0%)
GI bleeding	3 (6.0%)	2 (16.7)
History of hemorrhagic stroke	2 (4.0%)	0 (0.0%)

Table 4 List of Reasons for Eligible Patients Not Receiving Thrombolysis

Reasons	MRI (n=11)	CT-Scan (n=6)
Stroke onset > 6 hours	6 (54.5%)	3 (50.0%)
Wake-up stroke	1 (9.1%)	0 (0.0%)
Associated with STEMI but refused intervention	1 (9.1%)	1 (16.7%)
Associated with STEMI and bradycardia	1 (9.1%)	0 (0.0%)
Recurrent ischemic stroke with hematuria history	1 (9.1%)	0 (0.0%)
Recurrent central venous thrombosis	1 (9.1%)	0 (0.0%)
Others	0 (0.0%)	2 (33.3%)

Table 5 The Outcomes of Patients Receiving Thrombolysis

Outcome	MRI (n=37)	CT-SCAN (n=6)	p- value*
Improvement based on clinical assessment & decreasing NIHSS score	33 (89.19%)	3 (50%)	0.016
No Improvement	4 (10.81%)	3 (50%)	

Note: * significant if p-value <0.05.

neurologists. Therefore, Emergency General Practitioners (GPs) play a crucial role in acute ischemic stroke treatment.[22,23] Despite not completely meeting our aim, the timing for MRI scans has greatly improved since partnering with Indonesia Healthcare Insurance. The average time has decreased from 88.2 minutes to 47.8 minutes. This advancement shows great potential for further decreasing MRI waiting times in the future.

Thrombolysis using recombinant tissue plasminogen activator (rt-PA) and interventional thrombectomy are proven therapeutic interventions for acute stroke based on evidence.[24] Mechanical thrombectomy is currently available in only a limited number of healthcare facilities in Indonesia; therefore, the broader implementation of thrombolysis is essential for the effective treatment of ischemic stroke across the country. However, certain criteria must be met to ensure patient safety during thrombolysis, as this therapy also carries adverse effects such as allergies and bleeding, which can potentially result in fatalities.[25–27] Our study revealed that 50 out of 98 individuals diagnosed with acute ischemic stroke were deemed unsuitable for thrombolysis treatment. This was frequently owing to worries over their age, despite the fact that being over 65 years old is not officially recognized as a contraindication. Neurologists may exhibit caution due to the possible hazards of bleeding in elderly patients. Recent study indicates that thrombolysis can be advantageous for older people. It has been demonstrated that administering TPA promptly to individuals aged 85 or younger can reduce mortality rates and enhance results.[28] There are even case reports of thrombolysis being administered to a 105-year-

old woman, who experienced clinical improvement post-thrombolysis.[29] Therefore, further studies are needed to explore the perception of neurologists in Indonesia regarding thrombolysis itself.

Our study revealed that out of the 48 MRI patients who were suitable candidates for thrombolysis, 37 had alteplase therapy, while the remaining 11 opted for conservative management due to a variety of reasons. Alteplase therapy for acute ischemic stroke at Universitas Indonesia Hospital is typically optimum and limited to patients without contra-indicating circumstances. Nevertheless, the extent of thrombolysis utilization in Indonesia is still limited, as only a mere 500–1000 stroke patients out of a total of 150,000–200,000 receive this treatment on a yearly basis.[22] The occurrence of this phenomena can be attributed to the difficulties encountered by Indonesian neurologists, such as the restricted opportunities to gain experience in thrombolysis therapy and the lack of consistent training provided by educational institutions between 2010 and 2014. This has resulted in a diverse range of skills among medical professionals, which frequently leads to delays in responding to strokes and extended discussions on the use of thrombolysis. Indonesia need standardized and comprehensive training to enhance the efficiency and uniformity of stroke management. However, this study's significant findings demonstrate that MRI provides a more accurate assessment, enabling neurologists to confidently determine the eligibility of patients for thrombolysis therapy.[11]

Clinical improvement and reduced NIHSS scores were significantly seen in 89.19% of MRI patients and 50% of CT-Scan patients with the p-value of 0.016. This supports Tork et al's findings that intravenous thrombolytic therapy enhances outcomes in acute ischemic stroke patients.[30] However, the limitation of this study includes the disparity in sample sizes, largely because MRI is the preferred initial imaging modality for stroke assessment at the University of Indonesia Hospital, resulting in more MRI evaluations compared to CT-Scans. This study also has limitations such as single-center design and relatively small sample sizes due to the uncommon practice of using MRI as an imaging modality in managing acute stroke.

The study's findings are consistent with the importance of timely and accurate diagnosis in acute stroke management.[31,32] The 6-minute MRI protocol has proven effective in identifying stroke types and severity, and determining thrombolysis eligibility. However, the variable door-to-MRI times indicate a need for more efficient imaging processes. Our study underscores the importance of incorporating clinical and imaging data into acute stroke treatment decisions and highlights the ongoing need to enhance imaging technology use and stroke management.

Conclusion

In conclusion, this study emphasizes the implementation of the 6-minute MRI protocol in Indonesia has been pivotal in determining the type and severity of strokes, as well as evaluating patient suitability for thrombolysis. The outcomes of patients who underwent thrombolysis following the use of the 6-minute MRI imaging protocol in diagnosing acute ischemic stroke also demonstrate positive results, compared to CT-scan. The prolonged time-to-MRI highlights the imperative for further improvement. Moreover, further studies are needed to explore the perception of neurologists in Indonesia regarding thrombolysis itself. Optimization of time management during the complete acute diagnostics and treatment procedure by avoiding specific delays and streamlining universal workflow is of utmost importance regarding the efficiency and safety of treatment.

Data Availability

The datasets generated and/or analysed during the current study are not publicly available due to patients' privacy concerns but are available from the corresponding author on reasonable request.

Ethics Statement

This research complies with the Declaration of Helsinki and has been approved for ethical clearance from the research Ethics Committee of University of Indonesia – Cipto Mangunkusumo Hospital. Approval number: KET −1322/UN2.F1/ETIK/PPM.00.02/2023. The ethics committee has approved the verbal and written informed consent process.

Disclosure

The authors report no conflicts of interest in this work.

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