Ref: Ro J Neurol. 2023;22(4)
DOI: 10.37897/RJN.2023.4.13

Improving stroke care in Indonesia: Integrating CT perfusion for enhanced prognostication and treatment guidance - A case report

Rakhmad Hidayat[1,2], Aruni Cahya Irfannadhira[1], Ramadhanti Salma Ulwanda[1], David Pangeran[1], Reyhan Eddy Yunus[1,2], Taufik Mesiano[1,2], Mohammad Kurniawan[1,2], Al Rasyid[1,2], Salim Harris[1]

[1]Faculty of Medicine, Universitas Indonesia, Jakarta, Indonesia
[2]"Dr. Cipto Mangunkusumo" Hospital, Jakarta, Indonesia

Rakhmad Hidayat **ORCID ID:** 0000-0003-4615-5246
Reyhan Eddy Yunus **ORCID ID:** 0000-0001-9046-6303
Al Rasyid **ORCID ID:** 0000-0002-7568-8124
Salim Harris **ORCID ID:** 0000-0002-4271-2933

ABSTRACT

Background. Over the last three decades, stroke management has witnessed substantial progress, from the introduction of recombinant tissue plasminogen activator (rtPA) in 1995 to the approval of thrombectomy in 2016. Intravenous tissue plasminogen activator (tPA) within 4.5 hours of symptom onset is the standard for eligible acute ischemic stroke patients, dissolving clots and restoring blood flow. Endovascular thrombectomy (EVT) surpasses intravenous thrombolysis for large vessel occlusion cases, typically within 6 to 24 hours based on CT-perfusion criteria. CT perfusion (CTP) provides crucial quantitative data on cerebral blood flow, aiding in ischemia detection, tissue assessment, treatment guidance, and outcome prediction. This case report marks a pivotal moment in Indonesian stroke management, introducing the inaugural use of CTP for diagnostic purposes. By scrutinizing blood flow dynamics and cerebral conditions, CTP augments conventional diagnostics, offering enhanced prognostic value.

Case presentation. The case of a 58-year-old male with notable comorbidities exemplifies this successful integration. He presented with sudden left-sided weakness and dysarthria, without accompanying symptoms. Neurological evaluation revealed a Glasgow Coma Scale score of E3M6V5, 7th cranial nerve paresis, and a positive Babinski reflex on the left side. With a National Institute of Health Stroke Scale (NIHSS) score of 10, a head CT scan rules out cerebral hemorrhage, prompting precise thrombolysis at 0.7 mg/kg. Within one hour post-thrombolysis, the NIHSS score improved to 6, ultimately culminating in an NIHSS score of 2 upon discharge.

Conclusion. This case underscores the efficacy of acute ischemic stroke management, fortified by the strategic integration of CTP, heralding a new era in Indonesian stroke care.

Keywords: stroke, CT perfusion, thrombolytic

List of abbreviations

CBF	– cerebral blood flow	MTT	– mean transit time
CBV	– cerebral blood volume	rtPA	– tissue plasminogen activator
CTP	– CT perfusion	TMM	– time mismatch
EVT	– endovascular thrombectomy	TTP	– time to peak

Corresponding author:
Rakhmad Hidayat
E-mail: rhidayat.md@gmail.com

Article History:
Received: 12 December 2023
Accepted: 28 December 2023

INTRODUCTION

There is already a massive development of stroke management throughout the last 30 years. Starting from the use of recombinant tissue plasminogen activator (rtPA) in 1995 to the approval of thrombectomy in 2015 [1,2]. The choice of definitive therapy for stroke depends on the type of stroke, ischemic or hemorrhagic, and the time window available for intervention. The administration of tissue plasminogen activator (tPA) within the first 4.5 hours of symptom onset is the standard of care for eligible patients with acute ischemic stroke. tPA helps dissolve the blood clot causing the blockage and restore blood flow [3]. For selected patients with large vessel occlusion, endovascular thrombectomy, involving mechanical removal of the clot using specialized devices, has shown superior efficacy compared to intravenous thrombolysis [4]. It is typically performed within 6 to 24 hours after symptom onset, depending on specific criteria based on CT-perfusion. The quality development of imaging plays an important role in management of stroke. Starting from CT scan to MRI and CT perfusion that has been widely used in the world [5].

CT perfusion (CTP) is a specialized imaging technique used in the evaluation and management of stroke patients. It provides quantitative information about cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time to peak (TTP) of contrast agent passage through the brain. CTP can help identify areas of ischemia, assess the extent of tissue at risk, guide treatment decisions, and predict patient outcomes [6,7]. There is now strong evidence for thrombolytic treatment of patients with a Time mismatch (TMM) profile up to 9 hours and for clot removal in patients with a TMM up to 24 hours after last seen well [8].

In Indonesia, there has not been a report of the use of CT perfusion to evaluate stroke patients. This case report will be the first case in Indonesia in which CT perfusion is being used as a diagnostic tool. We will also discuss the use of CT perfusion to predict prognostication in acute ischemic stroke and enable identification of patients with treatment targets well beyond the conventional time windows for intravenous thrombolysis or EVT.

CASE REPORT

A 58-year-old male patient was admitted into the Emergency Room, "Dr. Cipto Mangunkusumo" General Hospital, Jakarta. The patient had sudden weakness on his left side an hour before admitted to hospital. There was a sign of dysarthria but no sign of headache, seizure, nausea, or vomiting. He had a history of type 2 diabetes mellitus for 2 years, hypertension for 5 years, and recent intestinal tuberculosis. General examination showed hemodynamically stable and neurological status showed Glasgow Coma Scale of E3M6V5, with paresis of 7th cranial nerve, dysarthria, and left side hemiparesis. Physiological reflexes were within normal range and Babinski pathological reflex was positive on the left side. The National Institute of Health Stroke Scale (NIHSS) was 10. Cerebral hemorrhage was ruled out by head CT scan; thus, thrombolysis was conducted with dosage of 0,7 mg/kg. One hour after thrombolysis, the NIHSS score decreased by four points into 6. The patient was hospitalized for 8 days, and was discharged with a NIHSS score of 2.

TABLE 1. CTP conclusion

	Case
Conclusion	There are heightened levels of CBF, CBV, MTT, and Tmax in the remaining infarcted area, suggesting potential vasodilatation in the subacute phase of the infarct. No reductions in CBF/CBV were observed in the right cerebral hemispheres. A chronic infarction was identified in the left occipital region.

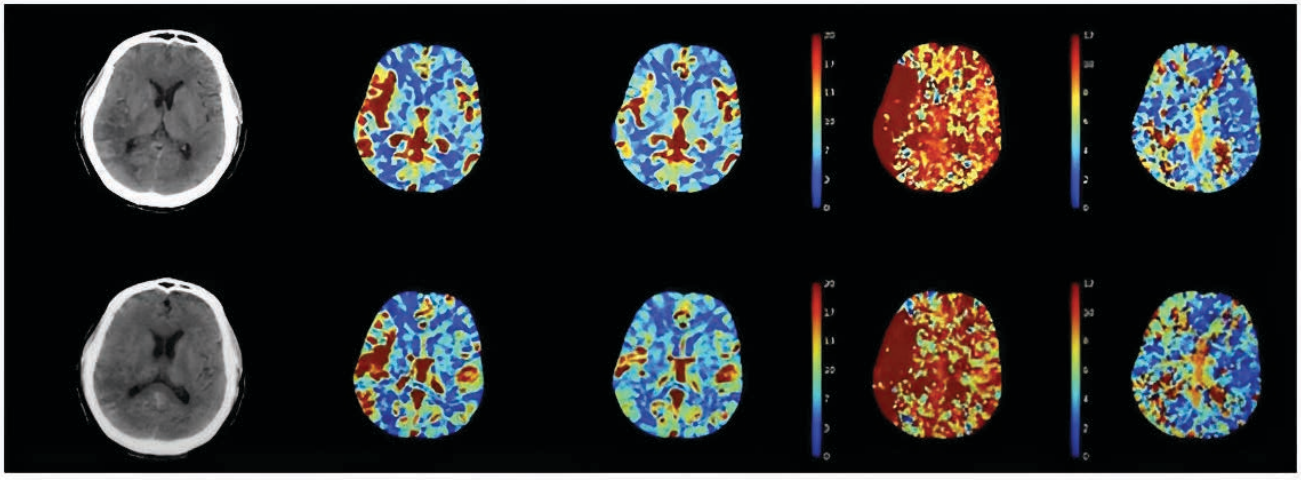

FIGURE 1. CTP image

DISCUSSION

We present a case of ischemic stroke admitted to the hospital within the golden time period of stroke with initial NIHSS >4. The case fulfilled the eligibility of thrombolysis, thus the treatment was conducted. ASA recommends the use of intravenous alteplase as thrombolytic agent with dose of 0.9 mg/kg with maximum dose of 90 mg to be administered within the first 3 hours of symptoms onset [9]. In Indonesia, rTPA is recommended to be given within < 4.5 hours after initial onset or within < 6 hours in anterior circulation stroke, using recommended dose of 0.6-0.9 mg/kg [10]. The dose used in this patient is 0.7 mg/kg and maximum dose of alteplase used is 50 mg.

The goals of radiological imaging are to diagnose and assess both the spared and irreversible tissue damage. Initial imaging using noncontrast CT or MRI is preferred to rule out intracerebral hemorrhage (ICH) before administering IV alteplase. Another advanced neuroimaging technique used for strokes is CT perfusion (CTP). In the realm of acute stroke management, advanced imaging techniques such as CTP have proven to be instrumental. Studies like ECASS 4-EXTEND and EPITHET have delved into the impact of intravenous thrombolysis guided by perfusion imaging, effectively extending the treatment window up to 4.5-9 hours after stroke onset. These trials demonstrated notable improvements in clinical outcomes for patients meeting specific imaging criteria. CTP identifies low perfusion in the brain parenchyma and distinguishes between the penumbra area (CBF<40 mL/100 g/minute) and the infarct core (CBF<20 mL/100 g/minute). The total hypoperfusion area is defined as an area with prolonged Tmax>6 seconds, and the ischemic core has reduced CBF<30% of the contralateral area [8].

CT perfusion (CTP) imaging marks a paradigm shift in stroke care, particularly for wake-up strokes or those with delayed presentations, offering a critical extension of the treatment window up to 9 hours post-symptom onset. By pinpointing key criteria such as rCBF <30% and Tmax >6s, indicating areas of significant hypoperfusion, CTP provides a precise map for thrombolytic therapy eligibility, ensuring tailored treatment decisions [11-13]. This individualized approach, integrating clinical profiles with CTP findings, strikes the right balance between benefits and risks, allowing prioritized interventions for cases with severe functional impairment [12]. With its ability to delineate viable tissue with precision, CTP expands the horizons of treatment possibilities, ultimately leading to improved outcomes for cases that were once considered beyond the scope of intervention [11-13]. However, it's important to note that a higher incidence of intracranial hemorrhages was observed in some of the treatment groups [12,13].

The hypoperfusion area in our case indicates an extensive penumbra area that needs to be addressed. Considering the extent of this, it is likely due to an occlusion of the MCA M1 and possibly a small chance of reperfusion. The CT perfusion data was obtained after the patient underwent thrombolysis and showed clinical improvement, so the decision to proceed with thrombectomy was not made based on the CT perfusion results. From this, we can take note that CT perfusion is important for understanding the ischemic imaging data, but the primary consideration remains the patient's clinical condition. CT perfusion provides a picture of salvageable penumbra, which increases confidence in pursuing management and physiotherapy.

Mechanical thrombectomy, as demonstrated in the DEFUSE 3 and DAWN studies, has proven its effectiveness within a 6-24 hour time frame post-stroke onset. In these studies, automated CTP analysis was utilized to identify patients with occlusions in the middle cerebral or internal carotid arteries. Those meeting specific perfusion criteria in the intervention group exhibited significantly higher rates of reperfusion and improved functional outcomes, as evidenced by a reduction in mortality and an increase in favorable outcomes (mRS 0-2) compared to medical management [14,15].

CTP plays a crucial role in predicting stroke outcomes by revealing the extent of the penumbra in radiological images. This information is invaluable in guiding treatment decisions and secondary stroke prevention. While radiological imaging is essential, it's important to note that any additional imaging should not delay the administration of IV alteplase [16]. These findings underscore the significance of combining CTP with mechanical thrombectomy in stroke care, especially for patients outside the conventional time window. DEFUSE 3 and DAWN studies emphasized the precision of perfusion-based patient selection, resulting in improved reperfusion rates, favorable outcomes, and reduced mortality. This approach sets these studies apart from those without perfusion assessments beyond the initial hours after stroke onset [17,18]. DAWN further reinforces the benefits of mechanical thrombectomy within an extended treatment window, highlighting its potential to transform stroke management [19].

Furthermore, CTP has emerged as a critical tool in distinguishing between true strokes and stroke mimics. Various conditions, such as migraine, epilepsy, and others, can manifest with stroke-like symptoms. CTP boasts a remarkable sensitivity of 82% and specificity of 96% in diagnosing ischemic strokes. By facilitating the exclusion of stroke mimics and guiding treatment decisions, CTP significantly contributes to a more accurate prognosis, ultimately enhancing the quality of stroke care [20].

However, there are some CTP limitations, such as utility in acute ischemic posterior circulation stroke (PCS), lacunar strokes with 50% false negative cases and small cortical and subcortical strokes with a size of infarction under 3 cm^2 with low sensitivity of CTP

(29%) [21]. Another disadvantages that may occur from using CTP was exposure to ionizing radiation and the use of iodinated contrast. The lack of standardized guidelines of CTP also make it more difficult to utilize it while making the decision of performing reperfusion therapy. At the end, the availability of stroke physicians with a combination of multimodal CT examination can further improve the rates of correct diagnosis and treatment.

CONCLUSION

This case underscores the transformative potential of CT perfusion (CTP) in Indonesian stroke management. The integration of CTP augments diagnostics and prognostics, particularly for patients like the 58-year-old male with complex comorbidities presented here. Over the past three decades, stroke care has evolved, from rtPA introduction in 1995 to thrombectomy endorsement in 2016. tPA within 4.5 hours remains standard, with EVT increasingly favored for specific cases. CTP's quantitative data on cerebral blood flow proves invaluable for ischemia detection and outcome prediction. This report pioneers CTP's diagnostic role in Indonesia, extending the therapeutic window and enhancing prognostic accuracy. While CTP holds promise, factors like radiation exposure and standardized protocols merit careful consideration. Prehospital care and teleconsultation potential are crucial in ensuring accurate and timely diagnosis, thereby optimizing stroke care.

Patient consent:
Verbal and written informed consents were given by the patient for the publication of this case.

Competing interests:
I undersign, certificate that I do not have any financial or personal relationships that might bias the content of this work.

Funding:
No funding for this case report.

Authors' contributions:
All authors attest that they meet the current ICMJE criteria for authorship. RH and AC conceptualized and designed the study. RS and AC drafted the initial manuscript. RH, RS, DP, TM and RE reviewed and revised the manuscript, final editing of the manuscript. RH, MK, AR, and SH critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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