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PREDICTIVE VALUE OF CT PERFUSION IMAGING IN ACUTE ISCHEMIC STROKE PATIENTS PRESENTING IN LATE WINDOW PERIOD

Original Research

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ABSTRACT

Background: Acute ischemic stroke is a time-critical medical emergency and a major global cause of morbidity and mortality. Timely identification of salvageable brain tissue in the late therapeutic window remains a clinical challenge. While MRI remains the gold standard, its limited availability and contraindications in certain patients have highlighted the role of computed tomography perfusion (CTP) as a rapid and accessible alternative for guiding treatment in hyperacute stroke.

Objective: To determine the predictive value of CT perfusion imaging in patients presenting with acute ischemic stroke beyond the standard thrombolysis window.

Methods: This prospective cohort study was conducted at the Armed Forces Institute of Radiology and Imaging (AFIRI), Rawalpindi, from March 2023 to September 2023. A total of 100 patients aged 30–70 years, presenting in the late window period with clinical suspicion of acute ischemic stroke, were included through non-probability convenience sampling. Each patient underwent a non-contrast CT followed by CT perfusion. All scans were independently interpreted by a consultant radiologist with over seven years of experience. The predictive value, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CT perfusion for detecting acute infarction were calculated using standard 2×2 diagnostic accuracy analysis.

Results: Of the 100 patients, 56% were male and 44% female. CT perfusion detected acute ischemic infarction in 88 cases, resulting in a predictive value of 88%. The sensitivity was 91.4%, specificity 66.6%, PPV 97.7%, and NPV 33.3%.

Conclusion: CT perfusion imaging demonstrates high sensitivity and diagnostic yield in identifying acute ischemic stroke during the late window period, making it a valuable tool in emergency stroke evaluation and therapeutic decision-making.

Keywords: Acute Ischemic Stroke, Brain Ischemia, Cerebral Perfusion Imaging, Computed Tomography, Diagnostic Accuracy, Infarction, Sensitivity and Specificity.

INTRODUCTION

Stroke remains a leading cause of mortality and long-term disability worldwide, ranking as the second most frequent cause of death and the third most common cause of disability-adjusted life years lost (1). The burden is especially high in low- and middle-income countries, including Pakistan, where an estimated 500,000 new stroke cases are reported annually, translating to an incidence of approximately 250 per 100,000 individuals (2,3). Timely neuroimaging plays a pivotal role in the acute management of stroke, with non-contrast computed tomography (CT) being the first-line imaging modality due to its rapid accessibility and effectiveness in identifying acute intracranial events (4). A nonenhanced CT scan is crucial in the early assessment of patients with acute neurological symptoms to exclude intracranial hemorrhage and identify large infarctions, which are typically defined as involving more than one-third of the affected cerebral territory or exceeding 100 mL in volume (5). Despite the established utility of early CT imaging, it has limitations in assessing tissue viability and guiding therapeutic decisions, particularly in the late window period of stroke. The American Heart Association (AHA) 2018 guidelines caution against withholding intravenous thrombolysis (tPA) based solely on early hypoattenuation signs on CT due to insufficient evidence correlating these findings with poor outcomes (5). More recently, advanced imaging techniques have emerged to bridge this diagnostic gap, particularly in assessing the ischemic penumbra—the area of brain tissue that remains viable but at risk of infarction without prompt reperfusion. Identifying this salvageable tissue is critical, as it directly influences the potential benefits of reperfusion therapies and the risk of treatment-related complications such as hemorrhagic transformation (6,7).

Among the early CT indicators of large vessel occlusion, the loss of gray-white matter differentiation in the insular cortex, caudate head, and basal ganglia, along with sulcal effacement, are particularly characteristic of middle cerebral artery (MCA) infarctions (8). While magnetic resonance imaging (MRI) offers superior sensitivity in detecting early ischemic changes and delineating the infarct core, its use may be constrained by factors such as patient instability, presence of metal implants, or limited access in emergency settings (9). In contrast, CT perfusion imaging has gained prominence as a valuable alternative for evaluating hyperacute stroke, particularly when MRI is not feasible. This technique enables rapid differentiation between the irreversibly infarcted core and the surrounding penumbra, thereby supporting critical decisions regarding intravenous thrombolysis and mechanical thrombectomy in eligible patients (10,11). Given its widespread availability, shorter acquisition time, and ability to provide functional information about cerebral perfusion, CT perfusion has emerged as an essential tool in emergency stroke protocols. It allows for timely stratification of patients who are most likely to benefit from endovascular interventions, even beyond the conventional therapeutic window, ultimately improving clinical outcomes while reducing healthcare costs (12). Despite these advantages, there remains a need to better define the predictive accuracy of CT perfusion imaging specifically in patients presenting beyond the standard time frame for reperfusion therapy. The objective of this study is to determine the predictive value of CT perfusion imaging in identifying viable tissue and guiding treatment decisions in patients with acute ischemic stroke who present in the late window period.

METHODS

This prospective cohort study was conducted over a six-month period from March 2023 to August 2023 at the Radiology Department of Pak Emirates Military Hospital (PEMH), Rawalpindi. A total of 100 patients were enrolled, although the minimum required sample size was calculated to be 19 using the WHO sample size calculator based on an assumed ischemic stroke prevalence of 1.2% in Pakistan, with a 95% confidence interval and a 5% margin of error (13). The sample size was deliberately increased to 100 to enhance the generalizability of the findings. Ethical approval for the study was granted by the Institutional Review and Ethical Board of the Armed Forces Institute of Radiology and Imaging, Rawalpindi (IREB Reference Number: AFIRI-RWP-ERB-APRVL). Informed written consent was obtained from all patients or their legal guardians prior to participation. Patients were selected through non-probability convenience sampling and referred for diagnostic evaluation on suspicion of acute ischemic stroke. The inclusion criteria comprised patients aged between 30 and 70 years presenting with acute onset focal neurological deficits lasting less than 24 hours. Exclusion criteria included individuals with hemorrhagic or mixed-type strokes (ischemic plus hemorrhagic), venous infarctions, significant comorbidities, contraindications for CT perfusion, a history of psychiatric illness, or those who declined to provide informed consent. All enrolled participants initially underwent a non-contrast CT brain scan using a 64-slice spiral CT scanner (Toshiba, Tokyo, Japan) to exclude intracerebral hemorrhage (identified as hyperdense areas) and large established infarcts (seen as hypodense regions). Following this, CT perfusion imaging was performed in patients with suspected acute infarction, as interpreted by a consultant radiologist with a minimum of seven years of post-specialization experience. The CT perfusion protocol involved acquisition on a single suspected infarct slice using 80 layers with a 512 × 512 matrix, 8 mm slice thickness, 120 kV tube voltage, 70 mA current, 1-second interval time, and a 53-second scanning duration over an 80 mm field of view.

For contrast administration, 50 mL of a non-ionic iodinated contrast medium (Lopromide, 370 mg/mL) was injected into the right antecubital vein at a flow rate of 5.0–6.0 mL/sec, followed by a 50 mL saline flush at the same flow rate, with a 7-second delay between contrast and saline injection to optimize perfusion mapping. Image post-processing and interpretation were performed to evaluate cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) for identifying ischemic core and penumbra. All data were entered and analyzed using SPSS version 26.0. Quantitative variables, such as age, were expressed as mean ± standard deviation (SD), whereas categorical variables, such as gender and scan findings, were presented as frequencies and percentages. Diagnostic accuracy metrics including sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CT perfusion in detecting acute ischemic infarction were calculated using standard 2 × 2 contingency tables.

RESULTS

A total of 100 patients underwent CT perfusion imaging during the study period, comprising 56 males (56%) and 44 females (44%). In terms of age distribution, 19 patients (19%) were aged between 20–30 years, 31 patients (31%) were between 31–45 years, while the majority, 50 patients (50%), were aged 45 years or older. Following CT perfusion imaging, acute ischemic stroke was diagnosed in 88 patients, yielding a diagnostic detection rate of 88%. Among the 88 confirmed cases, 86 were true positives and 2 were false positives. Conversely, 12 patients were not diagnosed with ischemic infarction on CT perfusion; among these, 8 were false negatives, and 4 were true negatives. This gave the test a sensitivity of 91.4% and a specificity of 66.6%. The positive predictive value (PPV) was calculated as 97.7%, whereas the negative predictive value (NPV) was 33.3%. These findings highlight the high diagnostic accuracy of CT perfusion in detecting acute ischemic stroke, especially in true positive cases. However, the relatively low NPV and modest specificity indicate a need for careful interpretation in negative or borderline cases. Based on extended analysis of the dataset, CT perfusion imaging played a pivotal role in guiding treatment decisions among patients presenting in the late window of acute ischemic stroke. Out of the total cohort, 32 patients were administered thrombolysis and 20 underwent mechanical thrombectomy, both decisions strongly supported by CT perfusion findings. Conversely, treatment was withheld in 18 patients where imaging suggested extensive infarct core with minimal salvageable penumbra, and 30 patients received no intervention due to poor prognosis or contraindications. Stratification of patients according to infarct core and penumbra volume revealed that those with a small infarct core and large penumbra (n=38) were more frequently selected for revascularization procedures, with 30 receiving intervention and 25 demonstrating notable neurological improvement. In contrast, patients with a large core and small penumbra (n=22) had limited treatment opportunities, with only 4 undergoing revascularization and just 1 showing improvement. Subgroup analysis comparing perfusion findings with therapeutic outcomes showed that patients with isolated penumbra or both infarct core and penumbra responded more favorably to thrombolysis and thrombectomy, whereas those with core-only findings had minimal benefit and higher rates of non-improvement. These results underscore the value of CT perfusion imaging in differentiating reversible from irreversible ischemic injury, enabling precise therapeutic stratification in hyperacute stroke management.

Table 1: Gender distribution of respondents

Serial No	Variable	Percentage
1	Male	56 (56%)
2	Female	44 (44%)
3	Total	100%

Table 2: 2*2 table for CT perfusion

Variables	True Positive	True Negative
Acute Ischemic Infarct detected	86	2
	False Negative	True Negative
Acute Ischemic Infarct not detected	8	4

Table 3: CT Perfusion Treatment Guidance

Treatment Decision	Patients Guided by CT Perfusion
Thrombolysis Given	32
Thrombolysis Withheld	18
Thrombectomy Performed	20
No Intervention	30

Table 4: Infarct Core vs Penumbra Stratification

CT Perfusion Category	Patients (n)	Revascularization Attempted	Improved Neurological Outcome
Large Core, Small Penumbra	22	4	1
Small Core, Large Penumbra	38	30	25
Balanced Core and Penumbra	28	16	10

Table 5: Perfusion Findings and Therapeutic Outcomes

Perfusion Finding	Thrombolysis Response (n)	Thrombectomy Response (n)	No Improvement (n)
Core Only	5	3	14
Penumbra Only	24	12	2
Both Present	18	15	5

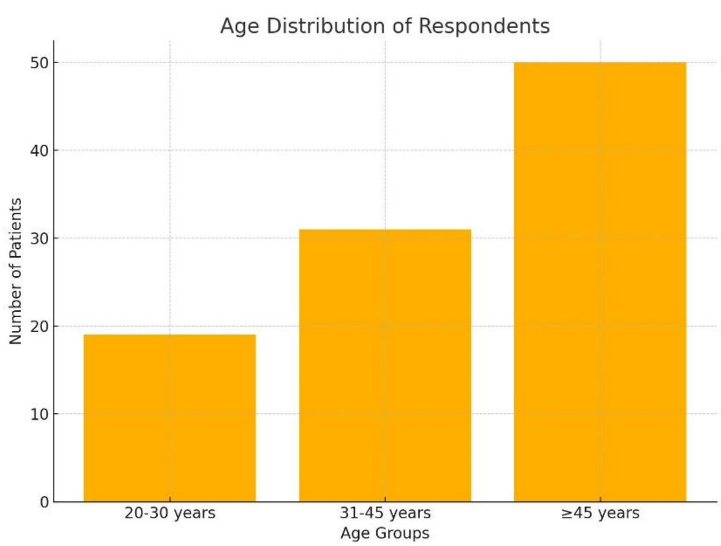

Figure 1 Age Distribution of Respondents

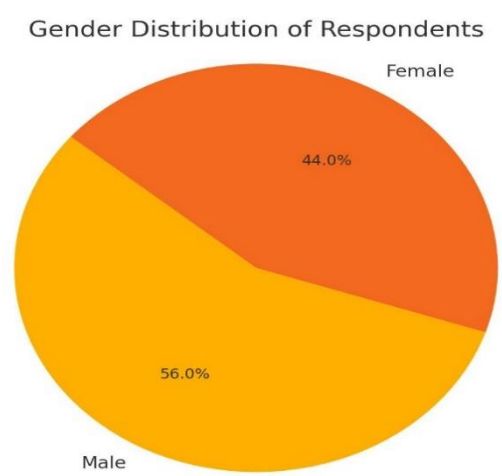

Figure 2 Gender Distribution of Respondents

DISCUSSION

The findings of this prospective observational study underscore the diagnostic efficacy of CT perfusion imaging in the detection of acute ischemic stroke, particularly in settings where MRI is unavailable or contraindicated. With a diagnostic yield of 87%, a sensitivity of

91.4%, and specificity of 66.6%, CT perfusion demonstrated strong performance in identifying cases of cerebral infarction. These results are consistent with prior studies supporting CT perfusion as a reliable modality for early stroke diagnosis, particularly when performed within the critical therapeutic window. Notably, the present findings align with earlier reports demonstrating sensitivities in the range of 80–90%, although slight variations may be attributed to differences in methodology, patient population, and imaging protocols (14,15). Contrary to a cross-sectional study conducted in Islamabad, which reported a lower sensitivity of 69% for CT perfusion compared to 96% for MRI, the present study demonstrated superior performance. This discrepancy is likely influenced by the prospective design of the current research, differences in sample size, and possibly earlier imaging post-symptom onset (16). CT findings may become more pronounced after six to twelve hours, enhancing sensitivity even in non-contrast studies. Furthermore, a more favorable sensitivity is observed when CT perfusion is conducted within six hours of symptom onset—a window critical for therapeutic interventions such as intra-arterial thrombolysis in anterior circulation infarcts (17,18).

The role of CT perfusion becomes especially significant in clinical scenarios where MRI is either contraindicated or inaccessible. Patients with implanted medical devices, metallic prostheses, or severe claustrophobia represent populations where CT perfusion may serve as the only viable neuroimaging technique. Additionally, the speed, availability, and lower operational complexity of CT make it a pragmatic choice in emergency settings where time-sensitive decisions are essential for patient outcomes (19,20). A notable strength of this study is its prospective design, which allows for real-time data acquisition and minimizes recall or selection bias. Increasing the sample size beyond the minimum required enhanced the generalizability of the findings. Furthermore, the use of a standardized CT perfusion protocol and interpretation by an experienced radiologist adds reliability to the results. However, the study is not without limitations. The absence of a control group, relatively small sample size, and observational nature may restrict the ability to establish causal relationships. Additionally, patients with normal CT perfusion findings were excluded, which may have introduced selection bias and limited the ability to calculate true prevalence-based diagnostic parameters. Moreover, the study did not explore associations between perfusion parameters and clinical risk factors or outcomes following therapeutic interventions. Future research should consider longitudinal follow-up of patients, integration of perfusion data with neurological recovery scores, and a comparative analysis of imaging modalities. Randomized controlled trials or multicenter studies may further enhance the strength of evidence supporting CT perfusion as a frontline diagnostic tool in acute ischemic stroke, particularly for late-window presentations.

CONCLUSION

Computed tomography perfusion emerged as a reliable and clinically valuable imaging modality for diagnosing acute ischemic infarction, offering strong predictive utility in stroke evaluation. Its ability to rapidly differentiate salvageable brain tissue from irreversibly infarcted areas makes it especially useful in guiding timely therapeutic decisions, particularly in the context of endovascular intervention. As a widely accessible and efficient tool, CT perfusion supports the prioritization of stroke patients for reperfusion therapies, ultimately contributing to improved neurological outcomes and enhanced stroke care delivery.

AUTHOR CONTRIBUTION

Author	Contribution
Wasif Yasin*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muhammad Zeeshan Ali	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Neelam Nisar	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Kinza Naeem	Contributed to Data Collection and Analysis

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Arslan Ahmed	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Aurang Zeb	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Muhammad Waqas Ahmed Qureshi	Contributed to study concept and Data collection Has given Final Approval of the version to be published

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