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Original Research Article

# Determining the Role of CT Perfusion in Patients with Acute Ischemic Stroke: A Prospective Study

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**Abstract**

**Aim:** The aim of the present study was to determine the role of CT perfusion in patients with acute ischemic stroke in the patients of less than 12 hrs of acute stroke symptoms.

**Methods:** The present study was a prospective study to determine the value of CT in evaluation of cerebral perfusion by use of a bolus of iodinated contrast medium in 50 patients with acute stroke, carried out in the Department of Radiology, Katihar Medical College and Hospital, Katihar, Bihar, India. All the patients enrolled in study were evaluating in period of 18 months.

**Results:** Majority of subjects in the study were in the age group 61 to 70 yrs. (34%). Mean age of subjects was 61.9 ± 14.26 yrs. Majority of subjects in the study i.e., 56% were males and 44% were females. 48% of lesions were on Right side, 34% of them on Left side, 14% on Midline and 4% on both cerebral hemispheres. Majority of subjects (94%) presented with Weakness as symptom. 68% of subjects presented with duration of <6 hrs and 32% presented with duration >6 hrs. Non contrast CT showed that 26 patients had Loss of Gray Matter Interface, 14 patients had Loss of Insular Ribbon, 10 patients had hyper dense MCA and none of them had hyper dense Basilar. On CT perfusion 7 patients had ACA involvement, 20 patients had LCS of MCA involvement, 15 patients had M1 of MCA involvement, 26 patients had M2 of MCA involvement and 18 patients had M3 of MCA involvement and 2 patients had PCA involvement.

**Conclusion:** PS elevation more than 5ml/min/100gm appears to be a promising marker for predicting the risk of HT in acute stroke patients. More importantly, a small PCT lesion (<100 mL) identifies patients who will have a small final infarct and good clinical outcome. A large PCT lesion (>100ml) identifies patients who will have a large final infarct and poor clinical outcome. PCT can play an important role in guiding acute stroke treatment.

**Keywords:** PCT, infarct, PS elevation, stroke



## Introduction

Stroke is the second leading cause of death and the third leading cause of disability in the world. [1,2] In 2010, there were 16.9 million incident stroke cases, 33.0 million prevalent stroke cases, 5.9 million deaths attributed to stroke, and 102.2 million lost DALYs. [3,4] According to a report from the American Heart Association, approximately 87% of all strokes were ischemic strokes. [5] An accurate and timely diagnosis of ischemic stroke is crucial for establishing an appropriate patient treatment. Non-enhanced computed tomography (NCCT) is widely used in acute ischemic stroke imaging due to its rapid performance, high tolerance, and high reliability. [6]

However, NCCT has difficulty in detecting early infarct signs and is influenced by the size of the infarct and severity of ischemia. CT perfusion (CTP) is performed for physiological evaluation of the brain parenchyma, which allows better detection of ischemia. However, the accuracy of CTP in detecting acute ischemic stroke (AIS) was still uncertain. To the best of our knowledge, there were two systematic reviews to evaluate the diagnostic value of CTP for AIS. A systematic review which based on 15 studies showed that the sensitivity and specificity of CTP were 80% and 95% respectively; however, another systematic review which based on 11 studies reported that the sensitivity and specificity of CTP were 69.9% and 87.7%. [7,8]

Perfusion imaging uses an intravascular tracer and serial imaging to quantify blood flow through the brain parenchyma. In acute ischemic stroke, perfusion imaging may increase diagnostic accuracy, aid treatment target identification, and provide prognostic information about functional outcome. [9] Moreover, perfusion imaging can identify patients who benefit from reperfusion beyond the conventional time window or in whom time of symptom onset is unknown. [10-12] Implementation of perfusion imaging in routine acute stroke care allows individualized treatment of stroke patients based on brain tissue status, rather than time-based treatment on the group level.

CTP provides absolute and relative information about brain perfusion parameters, namely cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time to peak (TTP). MTT is the time between the arterial in flow and the venous out flow. TTP refers to the time taken by the contrast to achieve maximum enhancement (HU value) in the selected region of interest (ROI) before its value starts decreasing. CBV is the volume of blood available per unit of brain tissue and is usually measured as milli litres per 100 gm of blood. Change in CTP parameters in ischemic brain with decrease in CBF due to any cause, cerebral auto regulation ensures adequate CBV by causing capillary dilatation which, in effect, causes increase in MTT and CBV. This continues till the decrease in CBF reaches a critical level (usually 20% of its normal value), at which point auto regulation fails and there is reduction in CBV and CBF. CTP, by measuring these values, tries to identify how much area of the brain is ischemic and/or infarcted. In general, if CTP shows a decrease in CBF with a stable or increased CBV, it signifies reversible ischemia; if both CBF and CBV fall below a critical level, it signifies irreversible infarction. [13-16]

The aim of the present study was to determine the role of CT perfusion in patients with acute ischemic stroke in the patients of less than 12 hrs of acute stroke symptoms.

## Materials and methods

The present study was a prospective study to determine the value of CT in evaluation of cerebral perfusion by use of a bolus of iodinated contrast medium in 50 patients with acute stroke, carried out in the Department of Radiology, Katihar Medical College and Hospital, Katihar, Bihar, India. All the patients enrolled in study were evaluating in period of 18 months.

### Inclusion Criteria

All Patients with obvious acute stroke symptoms such as hemiparesis, aphasia, or hemianopia of less than 12 hours duration.

### Exclusion Criteria

1. Brain stem symptoms.

2. Haemorrhage in NCCT scan.

3. Contraindications to I.V iodinated contrast like previous allergic reaction or deranged renal function.

### Methodology

After obtaining the informed consent the patient's personal identification information was recorded. e.g., name, age, sex, address, contact number. The signs and symptoms of acute stroke such as hemiparesis, aphasia, or hemianopia of less than 12 hours duration with any other systemic illness such as HT, DM at the time of presentation were noted.

Basic Equipment Used to Carry Out the Procedure

Ingenuity 128 slice CT Machine, Phillips

Perfusion CT software - Ingenuity 128 slice CT scanner, Phillips Iohexol Contrast media

Perfusion Imaging

The main principle of our method of perfusion imaging was based on the analysis of plain and contrast-enhanced CT scans obtained at admission. Most important was a sharp bolus of contrast medium resulting from rapid injection (5 mL/s). The software used the maximal slope of the time-density curve (Perfusion CT software; ingenuity 128 slice CT scanner, Phillips) to measure cerebral blood perfusion from dynamically enhanced cerebral CT scans, as described previously. The parameters chosen for evaluating cerebral perfusion are CBF, cerebral blood volume (CBV), time to peak (TTP), mean transit time (MTT), permeability surface area (PS).

Perfusion Imaging Procedure and Follow-up Examinations

Conventional plain CT of 5mm-thick whole brain sections was obtained. Patient was injected with an intravenous bolus of iodinated contrast, typically 50ml (350 mg of iodine per ml) at a rate of 4-5ml/sec. A two- phase CT perfusion/permeability examination was performed.

The first phase involved a 45-second continuous (cine) acquisition of scans reconstructed at 0.5-second intervals to produce a series of 90 sequential images of each of eight sections encompassing a total of 40 mm of selected area of interest depend on the findings of plain scan.

In the second phase of the CT permeability examination, images encompassing the same five to six sections were collected at 30-second intervals for an additional 150- 180 seconds immediately after the first phase.

The scanning parameters for both phases were 80 kVp, 120 mA, 8 × 5-mm collimation, and a gantry speed of 1 second per rotation. The images obtained from the ―cine model acquisition are used to generate time attenuation curves for an arterial region of interest (ROI), for the whole image on a pixel by pixel basis employing mathematical techniques. A number of perfusion parameters can be obtained from the two-phase perfusion study.

**Data Analysis**

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. Bar diagram and Pie charts were used to represent the data graphically. Chi-square or Fischer Exact* Test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test or Mann Whitney U test was used as test of significance to identify the mean difference between two groups. Paired t test or Wilcoxon Signed Ranks Test was as the test of significance for paired data such as before and after. p value <0.05 was considered as statistically significant.

**Results**

**Table 1: Demographic details**

| Age | Frequency | Percentage |
|---|---|---|
| < 50 yrs | 8 | 16 |
| 51 to 60 yrs | 16 | 32 |
| 61 to 70 yrs | 17 | 34 |
| > 70 yrs | 9 | 18 |
| **Gender** | | |
| Female | 22 | 44 |
| Male | 28 | 56 |
| **Side** | | |
| Right | 24 | 48 |
| Left | 17 | 34 |
| Midline | 7 | 14 |
| Both Side | 2 | 4 |
| **Symptoms** | | |
| Weakness | 47 | 94 |
| Slurring of speech | 12 | 24 |
| Deviation of Angle of Mouth | 8 | 16 |
| Giddiness | 3 | 6 |
| Duration of Stroke | | |
| <6 hrs | 34 | 68 |
| > 6 hrs | 16 | 32 |

Majority of subjects in the study were in the age group 61 to 70 yrs. (34%). Mean age of subjects was 61.9 ± 14.26 yrs. Majority of subjects in the study i.e., 56% were males and 44% were females. 48% of lesions were on Right side, 34% of them on Left side, 14% on Midline and 4% on both cerebral hemispheres. Majority of subjects (94%) presented with Weakness as symptom. 68% of subjects presented with duration of <6 hrs and 32% presented with duration >6 hrs.

**Table 2: Distribution of Non-contrast CT & CT perfusion findings**

| Non-Contrast CT Findings | Present | Absent |
|---|---|---|
| Loss of Gray Matter Interface | 26 | 24 |
| Loss of Insular Ribbon | 14 | 36 |
| Hyper dense MCA | 10 | 40 |
| Hyper dense Basilar | 0 | 50 |
| **CT Perfusion findings** | | |
| ACA | 7 | 43 |
| LCS of MCA | 20 | 30 |
| M1 of MCA | 15 | 35 |
| M2 of MCA | 26 | 24 |
| M3 of MCA | 18 | 32 |
| PCA | 2 | 48 |

Non contrast CT showed that 26 patients had Loss of Gray Matter Interface, 14 patients had Loss of Insular Ribbon, 10 patients had hyper dense MCA and none of them had hyper dense Basilar. On CT perfusion 7 patients had ACA involvement, 20 patients had LCS of MCA involvement, 15 patients had M1 of MCA involvement, 26 patients had M2 of MCA involvement and 18 patients had M3 of MCA involvement and 2 patients had PCA involvement.

**Table 3: Mean difference of CBV, CBF and PS values of Core infarct and Penumbra**

| | | Hemorrhagic transformation (HT) | | | | P value |
|---|---|---|---|---|---|---|
| | | Absent | | Present | | |
| | | Mean | SD | Mean | SD | |
| Core Infarct | CBV | 1.98 | 0.66 | 1.48 | 0.62 | 0.148 |
| | CBF | 10.04 | 6.16 | 10.14 | 4.12 | 0.943 |
| | PS | 3.08 | 2.42 | 8.38 | 6.14 | 0.007 |
| Penumbra | CBV | 3.48 | 1.08 | 2.94 | 1.36 | 0.316 |
| | CBF | 26.94 | 12.00 | 15.75 | 4.02 | 0.056 |
| | PS | 2.46 | 2.34 | 6.84 | 6.76 | 0.032 |

Evaluation of CBV, CBF and PS values in two patient groups, Patients with hemorrhagic transformation and patients without hemorrhagic transformation shows no significant co relation of CBV and CBF values. However, PS value has significant co-relation with hemorrhagic transformation.

**Table 4: Association between PS value and haemorrhagic transformation**

| | | Hemorrhagic transformation | | P value |
|---|---|---|---|---|
| | | Present | Absent | |
| | | Count | Count | |
| PS Core infarct | <5 | 2 | 20 | 0.0122 |
| | >5 | 3 | 4 | |
| PS penumbra | <5 | 3 | 18 | 0.165 |
| | >5 | 2 | 4 | |

No significant association was observed between PS value of Penumbra and HT.

**Table 5: Association between Infarct Volume and Predicted Modified Rankin Score**

| | | Infarct volume | | | |
|---|---|---|---|---|---|
| | | <100ml | >100ml | Total | P value |
| | | Count | Count | Count | |
| Predicted | < 3 | 32 | 0 | 32 | <0.001 |
| | > 3 | 0 | 9 | 8 | |
| | Total | 32 | 8 | 40 | |

It was observed that there was significant association between Infarct volume and Predicted Modified Rankin Score.

## Discussion

According to the World Health Organization (WHO), stroke is the world leading cause of long-term morbidity, and the third leading cause of death in developed countries. [17] Stroke is defined as a rapidly progressive focal or global brain dysfunction of vascular origin lasting more than 24 hours or leading to death within 24 hours.[13] As one of the leading contributors to death and disability worldwide, the burden of stroke is felt physically, socially, economically and emotionally on patients, their families and health care services.[17] Within stroke, several subtypes exist with ischemic stroke representing the majority, accounting for between 67 and 80 % of stroke cases reported in epidemiological studies. [17] Ischemic stroke is more often disabling rather than fatal but remains the most common life-threatening neurological disorder. [14] 10 % of patients with ischemic stroke will die within 30 days of stroke onset, while half of those who survive have persistent disability 6 months later. [15] The remaining 20% of stroke cases are due to intracerebral or subarachnoid haemorrhages which are also potentially devastating conditions with 30-day mortality of primary intracerebral haemorrhage approaching 50 %. [16,18,19]

Majority of subjects in the study were in the age group 61 to 70 yrs. (34%). Mean age of subjects was 61.9 ± 14.26 yrs. Majority of subjects in the study

i.e., 56% were males and 44% were females. 48% of lesions were on Right side, 34% of them on Left side, 14% on Midline and 4% on both cerebral hemispheres. Majority of subjects (94%) presented with Weakness as symptom. 68% of subjects presented with duration of <6 hrs and 32% presented with duration >6 hrs. Non contrast CT showed that 26 patients had Loss of Gray Matter Interface, 14 patients had Loss of Insular Ribbon, 10 patients had hyper dense MCA and none of them had hyper dense Basilar. On CT perfusion 7 patients had ACA involvement, 20 patients had LCS of MCA involvement, 15 patients had M1 of MCA involvement, 26 patients had M2 of MCA involvement and 18 patients had M3 of MCA involvement and 2 patients had PCA involvement. The NCCT lesion volumes, once visually evident, are strongly associated with irreversible infarction. [20] Although we obtained quantitative PCT lesion volumes using image segmentation; we were forced to estimate the degree of mismatch by direct visual comparison between the abnormal NCCT and PCT regions. Quantitative NCCT lesion volumes could not be reliably measured because of the indistinct margins and limited visual conspicuity typical of acute ischemic NCCT hypodensity. The attenuation differences between normal and oedematous tissue on the initial NCCT images are typically only in the 1– to 3–Hounsfield unit range. Despite our careful use of optimal window width and center level display settings during NCCT image interpretation [21], our preliminary attempts to segment hypo dense NCCT regions were characterized by marked intra observer and inter observer variability. Indeed, many portions of the abnormal, hypodense brain tissue present on the admission NCCT images were detected only retrospectively during careful review of the NCCT scans alongside co registered PCT images.

Evaluation of CBV, CBF and PS values in two patient groups, Patients with hemorrhagic transformation and patients without hemorrhagic transformation shows no significant co relation of CBV and CBF values. However, PS value has significant co-relation with hemorrhagic transformation. No significant association was observed between PS value of Penumbra and HT. It was observed that there was significant association between Infarct volume and Predicted Modified Rankin Score. A potentially important role of PCT imaging in acute stroke may be to improve detection of subtle NCCT findings of ischemia, a frequent problem in stroke clinical trials. It is noteworthy that in our study a PCT lesion volume of 100 mL identified patients with a ―poor‖ clinical outcome, because 100 mL is approximately equal to one third the brain volume supplied by an MCA. [22] This result is consistent with the European data indicating that intravenous thrombolytic therapy within 6 hours of stroke onset results in poor outcome in patients with initial NCCT lesion volumes greater than one third that of the MCA territory. [23,24]

## Conclusion

PS elevation more than 5ml/min/100gm appears to be a promising marker for predicting the risk of HT in acute stroke patients. More importantly, a small PCT lesion (<100 mL) identifies patients who will have a small final infarct and good clinical outcome. A large PCT lesion (>100ml) identifies patients who will have a large final infarct and poor clinical outcome. PCT can play an important role in guiding acute stroke treatment.

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