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Feasibility of CT Head Perfusion for The Evaluation of Acute Lacunar Ischemic Infarcts in The Subcortical Gray Matter

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Abstract

Background: *Acute thalamic and basal ganglionic lacunar infarcts are common and can result in significant neurological manifestations. They are easily overlooked in the initial evaluation in patients suspected of stroke. Our purpose was to evaluate the efficacy and accuracy of CT head perfusion in the detection of acute ischemic strokes in the subcortical gray matter i.e., thalamus and basal ganglia.*

Methods: *An IRB-approved retrospective study included 89 patients (47 females and 42 males) who presented to our institute with symptoms of acute stroke. Patients who underwent CT head perfusion, followed by MRI brain were included. Patients with other diagnoses e.g., intraparenchymal hemorrhage were excluded. Subjective evaluation of CT head perfusion in different maps i.e., CBF, CBV, MTT, T max was performed. The results were correlated with the findings of DWI and ADC with quantitative measurement of ADC value. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated. ROC curve and AUC were plotted to graphically represent the sensitivity of CT head perfusion compared to DWI-MR images.*

Results: *Our cohort included 89 patients (60 with acute ischemic infarcts in the subcortical gray matter and 29 normal individuals). The patient's average age was 67 years (± 13.61 years, ranging from 29 - 94 years). CT head perfusion yielded true positive (n = 42), false positive (n = 3), true negative (n = 27), and false negative (n = 17). The specificity of CT head perfusion was 90% with a positive predictive value of 93.3%. However, the sensitivity was lower at 71.19% and overall accuracy of 77.53%. There was a statistically significant AUC = 0.806 with a p-value of < 0.001.*

Conclusion: *CT head perfusion can detect acute lacunar ischemic infarcts in the subcortical gray matter with good specificity and positive predictive value compared to DWI-MR imaging, which allows for early diagnosis and prompt management with improved patients' outcomes.*

Keywords: *CT perfusion, Subcortical gray matter, acute infarct, Thalamus, Basal ganglia.*

Introduction

Acute stroke is the 5th leading cause of mortality and the leading cause of long-term adult disability in the US. Stroke is subclassified into ischemic or hemorrhagic with 80% of cases being ischemic.[1] Lacunar infarcts result from occlusion of a single small perforating artery and can affect the internal capsule, corona radiata, thalamus or basal ganglia.[2] Acute ischemic lacunar infarcts within the subcortical gray matter i.e., thalamus and basal ganglia are common (accounting for 30-40%) due to lack of good collateral blood supply compared to cortex.[3, 4] Basal ganglionic stroke results in severe neurological manifestations such faciobrachiocrural hemiparesis, aphasia and ataxia which could be the result of disconnection between basal ganglia and prefrontal, temporal, and parietal cortices.[5] Thalamic strokes can present with abulia, apathy, amnesia, ipsilateral paresthesia or hemiparesis.[6]

Subcortical gray matter infarcts are usually small and associated with good outcome in 75% of cases.[3] These strokes result from occlusion of the middle cerebral artery or isolated occlusion of lenticulostriate arteries.[3,7] Reperfusion therapy with intravenous tissue plasminogen activator (tPA) within 4.5 hours of symptom onset is the most effective treatment of ischemic stroke as it can prevent propagation of necrosis.[8] Delayed treatment results in faster and more frequent progression to infarction or hemorrhagic transformation even after successful reperfusion.[3, 9, 10] The narrow window of treatment puts a lot of emphasis on prompt detection and diagnosis of these strokes with early management.

Computed Tomography Perfusion (CTP) of the head is a rapid and effective tool for diagnosing ischemic stroke in large cortical infarcts such as middle cerebral artery (MCA) occlusion.[11-16] Small ischemic strokes may not be as obvious as large cortical infarcts.[17] These infarcts affect subcortical gray matter and central white matter tracts and can cause severe neurological manifestations. They can be easily missed as they require high level of attention.[18] Core ischemic infarct appears on CTP with matched reduction of cerebral blood flow (CBF), and cerebral blood volume (CBV) maps in affected areas and prolonged mean transit time (MTT), and time-to-maximum (T max).[19] MTT and Tmax maps show the total area of ischemia while the mismatched area of MTT/T max and CBV represent the salvageable penumbra.[14, 18, 20]

The purpose of our study is to evaluate the efficacy and accuracy of CTP in early detection of acute ischemic lacunar infarcts in the subcortical gray matter i.e., the thalamus and basal ganglia. To the best of our knowledge, our study is the first study to focus only on utilizing CTP for early diagnosis of deep subcortical gray matter acute lacunar ischemic infarcts.

Methods

Patients:

A retrospective study of 89 patients (47 females and 42 males) who presented to our hospital with symptoms of acute stroke. Only patients who underwent CT perfusion followed by MRI brain were included in the study. Patients with other diagnoses such as intracranial hemorrhage or brain tumors were excluded.

Image acquisition:

- **CT perfusion protocol:**

In our cohort, all patients have undergone evaluation of suspected stroke with non-contrast CT head, CT head perfusion and CT angiography of the head and neck. The patients with negative results for acute infarct within the large vascular territories and/or large vessel occlusion, have undergone further evaluation with MRI brain. All CT studies were conducted on 128 and 64-slice multi-row detector CT scanners (SOMATOM Definition Flash and Drive, Siemens Healthineers, Erlangen, Germany). The non-contrast CT head scans were acquired with an average 120 kVp, 150-317 mA, and matrix of 512 x 512 x 16. Then, the images were reformatted into axial, coronal, and sagittal planes with 5mm slice thickness. After acquisition of CT angiography images, a 60s delay to acquire CT perfusion was permitted to avoid venous contamination of CTA images. With 18–20 gauge IV placed in the right antecubital vein, 35 ml of preheated to body temperature contrast medium (Omnipaque/Iohexol, 350mg, Guerbet, France) was injected with a rate of 5 ml/s followed by 20-30 ml saline with the same flow rate. Time resolved dynamic acquisition of the contrast bolus through the brain was acquired for a continuous 45s.

- **Post-processing of CT perfusion raw data:**

The raw data was sent into the perfusion software package (SyngoVia VB50A, Siemens Healthineers, Erlangen, Germany). Automatic calculation of the perfusion data provides the parametric perfusion maps i.e., cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), and time-to-maximum (T max). Then, images have been checked for correct placement of ROI at arterial input function (AIF), and venous output function (VOP). Studies with extensive motion artifacts have been excluded, through check of graph simulation of patient motions. Positive findings for acute stroke include reduction of CBF and CBV with prolonged MTT, and T max. Reversible ischemic tissues (penumbra) has been defined as the mismatch between CBF and CBV maps.

- **Magnetic resonance imaging:**

MRI is the gold standard for detection and diagnosis of acute brain infarction. For patients with persistent clinical symptoms concerning for acute stroke and negative or inconclusive CT perfusion findings, MRI brain has been acquired. The MRI sequences included T2, FLAIR, DWI, SWI and 3D T1 MPRAGE and 3D FLAIR. The diffusion weighted imaging was acquired using different b values (0, and 1000) with the following parameters: TE/TR (83/4400ms); slice thickness 5mm; flip angle 90°, and 260 x 260 x 16 matrix. Apparent diffusion coefficient (ADC), and exponential apparent diffusion coefficient (eADC) maps were automatically generated. The acute infarct manifest as hyperintense signal on b1000 images with corresponding hypointense signal on ADC.

Image analysis:

A qualitative analysis of all CTP maps (i.e., CBF, CBV, MTT and T max) for every patient were evaluated to determine positive and negative cases. Two ABR-certified neuroradiologists (C.L, and HA) with 7-, and 12-year experience evaluated the CT perfusion images and DW-MRI. A more senior neuroradiologist (JC) with > 15-year experience was consulted in case of disagreement between the neuroradiologists. Positive cases i.e., cases of deep subcortical gray matter infarctions, had prolonged T max and MTT and reduced CBF and CBV within the thalami and basal ganglia. Given the high probability of artifacts within the thalami and basal ganglia, suspected infarcts appear as asymmetry on the color-coded CTP parametric maps (Fig. 1, 2). Negative cases had normal CBV, CBF, MTT and T max. Then, the results were correlated with the findings of DWI, and ADC with quantitative measurement of ADC value. Positive cases on MRI appear hyperintense on b1000 images, and hypointense on ADC images (Fig. 1, 2). Each CTP parametric map was also correlated with MRI findings to investigate which parameter would have the best accuracy for detection of acute infarcts.

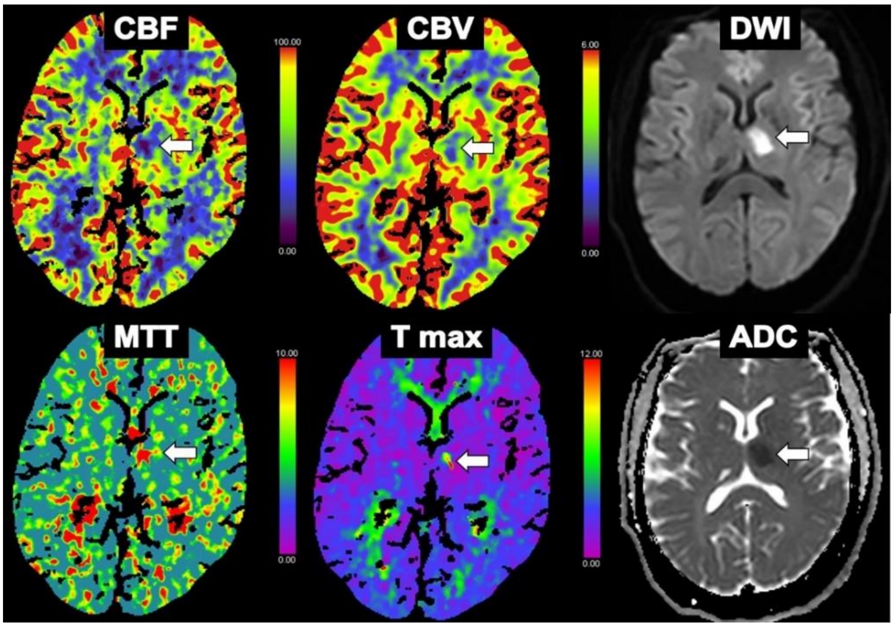

Figure 1: Left thalamic acute lacunar infarct in a 57-year-old female presented with right sided weakness. CT perfusion demonstrates focal area of asymmetric decreased CBF and CBV with prolonged MTT and T max (arrows). Corresponding diffusion-weighted imaging shows focal area of restricted diffusion within the ventromedial thalamus.

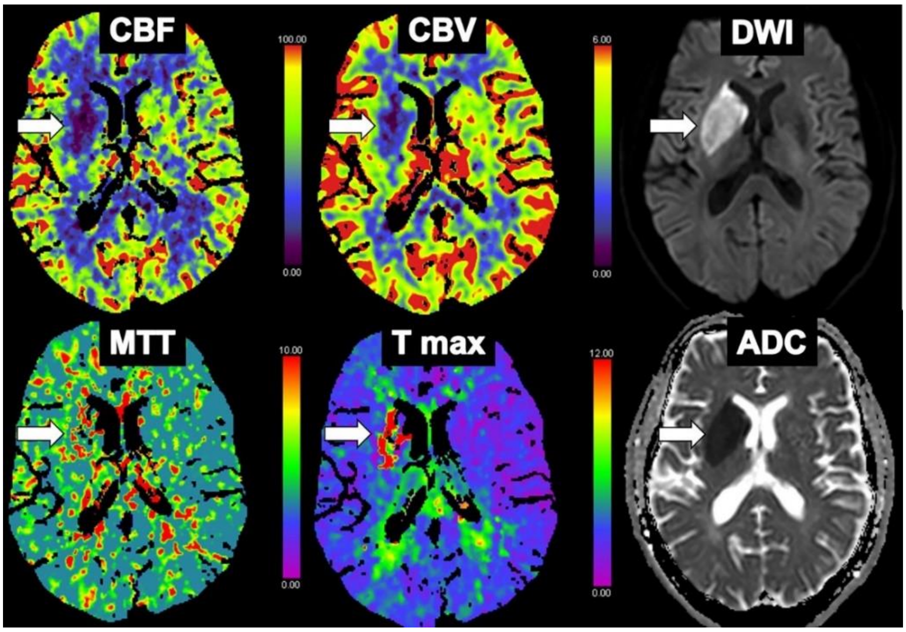

Figure 2: Acute lacunar infarct within the right striatum in a 65-year-old male presented with left side weakness. CT perfusion demonstrates area of decreased CBF and CBV with prolonged MTT and T max (arrows). Diffusion-weighted imaging shows a corresponding area of restricted diffusion within the right striatum.

Statistical analysis:

The data was tested for normality using a standard software package. Chi square test was used for categorical data (i.e., qualitative assessment of CTP maps for each patient). The categorical data were summarized as percentages and ratios and continuous data such as ADC values were represented as the mean and SD. The sensitivity, specificity, positive predictive value, and negative predictive value were calculated for each parameter. **Receiver operating characteristic** (ROC) curve and the area under the curve (AUC) plotted to graphically represent the sensitivity of CT perfusion compared to DWI-MR images. Microsoft Excel and IBM SPSS software were used for analysis of the data and P value <.05 was considered statistically significant.

Results

Our cohort included 89 patients (60 with MRI-confirmed acute lacunar ischemic infarcts within thalami/basal ganglia and 29 normal individuals). The patient's average age was 67 years (± 13.61 years, ranging from 29 - 94 years) (Table. 1).

Table 1: Summary of epidemiologic and imaging findings.

	Mean±SD	***P-value***
Age	67±13.61	<0.001
Gender		<0.001
Female	47 (52.8%)	
Male	42 (47.2%)	
Side		<0.001
Normal	29 (32.6%)	
Right	29 (32.6%)	
Left	31 (34.8%)	
Size	21±13.7 mm	<0.001
ADC value	653.19±206.15 x 10^{-3} mm/s	<0.001

CT head perfusion yielded true positive (n = 42), false positive (n = 3), true negative (n = 27), and false negative (n = 17). The specificity of CT head perfusion was 90% with a positive predictive value of 93.3%. However, the sensitivity was lower at 71.2%, negative predictive value was 61.4% and overall accuracy was 77.53%. The receiver operating characteristics curve showed an area under curve (AUC) = 0.806 with a p-value of <0.001 (Fig. 3).

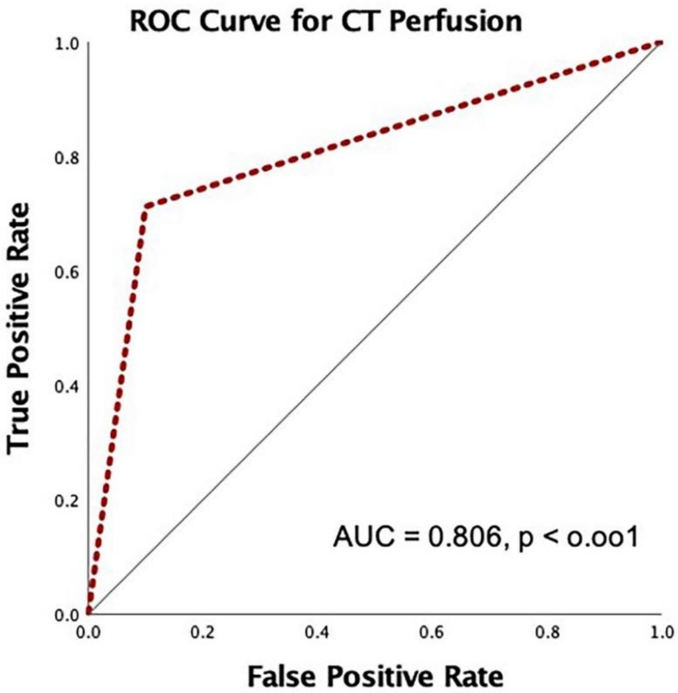

Figure 3: Receiver Operating Characteristics curve of CT perfusion for detection of acute lacunar infarcts.

When investigating each parameter for predicting acute lacunar infarcts, CBV was the most accurate in correlation to DWI findings. CBV had an accuracy of 77.53%, specificity of 90%, sensitivity of 77.53%, positive predictive value of 93.3% and negative predictive value of 61.4%. The remaining parameters had less specificity, sensitivity, and overall accuracy. When compared to ADC values, CT perfusion was found more positive with cases had lower ADC values. There was weak negative correlation between the CT perfusion finding and ADC value (Spearman rho = -0.388, 2-tailed p-value < 0.001). There was no statistically significant difference in CT perfusion between different gender, ages, or infarct sizes.

Discussion

CT perfusion is an established imaging technique to detect acute cerebral ischemic changes and differentiate between reversible and irreversible ischemic tissue. Hence, the patients can be triaged accordingly for the reperfusion therapy with extended time window beyond 4.5 hours or time of onset is unknown.[8, 21-24] Acute lacunar infarcts within the thalami and basal ganglia can lead into significant neurological manifestations due to difficult detection on CTP with delayed management. Owing to the low spatial resolution of CTP, small lacunar ischemic strokes within the deep grey matter may be overlooked.[17] Delayed treatment can cause hemorrhagic transformation.[10, 25]

Our results showed a good positive predictive value of CT perfusion in early detection of acute lacunar infarcts within the basal ganglia and thalami. A systematic review of 50 studies with total of 1,107 patients with both cortical and lacunar strokes showed that CTP has high sensitivity (80%) and very high specificity (95%).[26] There was no difference between retrospective and prospective studies. Most false negatives were due to small lacunar infarcts.[26] Rudilosso et al. investigated CTP for detection of lacunar infarct. Their results demonstrated an accuracy of 62.5% with increased sensitivity for supratentorial than infratentorial lacunar infarct.[27] Benson et al.

found high specificity (98%) and very low sensitivity (19-50%) of CTP to detect lacunar infarcts with the lowest sensitivity in the thalamus and basal ganglia (0%).[28] Cao et al has investigated the accuracy of CTP in detection of lacunar infarctions in 32 patients and found a sensitivity of 72.2% for detection of striatal lacunar infarcts versus 35.7% for other locations. [29] MTT had the best sensitivity among CTP maps (56%) and the overall sensitivity was 56%, specificity was 100%, positive predictive value was 100% and negative predictive value was 68%.[29]

Diffusion weighted imaging is the gold standard for accurate detection of acute cerebral stroke; however many institutes opt in utilizing CTP as the primary imaging study in the evaluation of ischemic stroke as it is cheaper, widely available, well-tolerated by patients and takes less time to complete compared to MRI.[15, 20] Nevertheless, CTP has low spatial resolution and is susceptible to artifacts. The quality of the images can be affected by patient motion which could result in an inaccurate estimation of stroke size.[3] Head angulation and chin tilting during image acquisition can give false results due to asymmetry and incorporation of non-brain tissue e.g., skull.[30, 31] CTP requires repeated scanning which causes increased exposure to radiation unlike DW-MRI. CT protocols should use the lowest possible dose of radiation however it can result in a higher amount of noise.[18, 32] Using thick slices or reduced matrix reconstruction can decrease the noise but it comes at the cost of lowering the spatial resolution.[33]

These pitfalls are more apparent in subcortical gray matter strokes because of their small size which makes the diagnosis more challenging. Despite these possible limitations, our study results showed that CTP is a rapid and effective method of detecting ischemic lacunar infarcts within thalami and basal ganglia. Though image noise and low resolution of CTP, careful attention for any asymmetry on parametric CTP maps can be helpful to suggest lacunar infarct. High index of suspicion, careful evaluation and awareness of possible artifacts within the thalami and basal ganglia regions on CT perfusion can help early diagnosis.[18] It is of great importance for early detection to prevent propagation of ischemia and preserve reversible ischemic tissues (penumbra).[34, 35]

Conclusion

Subcortical gray matter structures should be carefully evaluated on CTP for early detection of ischemic changes as they are very subtle and often overlooked. CTP is an efficient method for detecting small infarcts within these areas. CTP can help prompt patient management and avoid treatment delay which is of paramount importance.

Disclosures:
None

Conflict of interest statement – The corresponding author A.N is a PI on an industry funded clinical trial by Bayer Corporation for testing a new GBCA (Gadoquatrane), however all authors declare no conflict of interest regarding this project.

Author contributions: Conceptualization, A.N. and C.LS.; methodology, A.N.; software, F.H, A.N.; validation, A.N., E.M. and C.LS.; formal analysis, A.N.; investigation, E.M.; resources, E.M.; data curation, H.A.; writing original draft preparation, E.M, F.H, A.N.; writing—review and editing, A.N, E.M, C.J, C.LS; visualization, E.M.; supervision, A.N, C.J. All authors have read and agreed to the published version of the manuscript.

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