ORIGINAL ARTICLE

Degree of Agreement between Perfusion CT and Delayed CT in Early Detection of Cerebral Ischemia in Patients with Clinical Signs of Stroke

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ABSTRACT

Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries.[1] A comprehensive evaluation of stroke may be performed with a combination of Computed Tomography (CT) or Magnetic Resonance (MR) Imaging techniques. Unenhanced CT (NECT) can be performed quickly, can help identify early signs of stroke and can rule out hemorrhage. CT angiography and CT perfusion imaging, respectively, can depict intravascular thrombi and salvageable tissue indicated by a penumbra. The present study highlights the importance of utilization of CT perfusion imaging technique in the detection of stroke at a time when plain CT is less likely to be helpful and urgent medical treatment can significantly alter the course of this catastrophic event.

Objectives: *The aim of this study was to determine the degree of agreement between perfusion CT and delayed CT in early detection of cerebral ischemia in patients with clinical signs of stroke having negative early NECT scan.*

Results: *This study was conducted on 150 patients with clinical suspicion of stroke but having no or early signs of infarction on NECT scan during a period of six months from August 2013 to February 2014. The age of patients ranged from 29 to 90 years with mean age 63.80 ± 13.62 years with maximum number of patients aged between 71 – 80 years i.e. 61 (40.7%) and Minimum number of patients aged between 20 – 30 years i.e. 4 (2.7%). 74 patients (49.3%) out of total number of patients included in the study had signs of infarct on NECT while 76 patients (50.7%) had no signs of infarct on NE CT. 138 patients (92.0%) showed signs of infarct on perfusion CT while 12 patients (8.0%) had no signs of infarct on perfusion CT. Out of the 138 patients positive on perfusion CT, 131 proved to be positive on follow up CT and were thus true positive while 7 patients were false positive. Cohen $\acute{k}$ coefficients were calculated to determine the agreement between NECT and perfusion CT. A value of .607 was derived for $\acute{k}$ with standard error of ± .113 which shows substantial agreement between perfusion CT and delayed CT.*

Conclusion: *Because CT is still the primary imaging modality in patients with acute stroke, perfusion CT evaluation improves the rate of detection of infarction in comparison with NECT alone. The use of multi-detector row CT demonstrated improved detection rate of perfusion deficit, particularly in patients with minor neurologic symptoms. We believe multimodal CT evaluation can aid decision making for treatment of patients suspected of having a stroke.*

Key Words: *Brain, CT Brain, Infarction, Cerebral blood vessels, Computed tomography (CT), Perfusion study.*

INTRODUCTION

Stroke is the third most common cause of death and the first leading cause of disability in developed and developing countries.[1] There are no sizeable community based epidemiologic studies on stroke from Pakistan. Contrary to decline in the incidence of the disease in the Western population, the burden of the disease in South Asian countries (India, Pakistan, Bangladesh, and Sri Lanka) has inclined and is expected to rise.[2]

A comprehensive evaluation of stroke may be performed with a combination of Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) techniques. NECT can be performed quickly, can help identify early signs of stroke, and can help rule out hemorrhage. CT angiography and CT perfusion imaging, respectively, can depict intravascular thrombi and salvageable tissue indicated by a penumbra. The information obtained by combining various imaging techniques may help differentiate patients who do not need intravenous or intra arterial therapy from those who do, and may alter clinical outcomes.[3]

But before we embark upon the original study, it will be helpful to have a brief recall of stroke and medical terminology used in this study.

ANATOMY

Blood is supplied to the brain, face, and scalp via two major sets of vessels: the right and left common carotid arteries and the right and left vertebral arteries.

The common carotid arteries have two divisions. The external carotid arteries supply the face and scalp. The internal carotid arteries supply blood to the anterior three – fifths of cerebrum, except for parts of the temporal and occipital lobes. The vertebrobasilar arteries supply the posterior two – fifths of the cerebrum, part of the cerebellum and the brain stem.

At the base of the brain, the carotid and vertebrobasilar arteries form a circle of communicating arteries known as the Circle of Willis. From this circle, other arteries — the anterior cerebral artery (ACA), the middle cerebral artery (MCA), the posterior cerebral artery (PCA) — arise and travel to all parts of the brain.

Anterior cerebral artery supplies the frontal lobes, the parts of the brain that control logical thought, personality, and voluntary movement, especially of the legs. The middle cerebral artery is the largest branch of the internal carotid and is the artery most often occluded in stroke.

The posterior arteries supply the temporal and occipital lobes of the left as well as right cerebral hemispheres. When infarction occurs in the territory of the posterior cerebral artery, it is usually secondary to embolism from lower segments of the vertebrobasilar system or heart.

Small, deep penetrating arteries known as the lenticulostriate arteries branch from the middle cerebral artery. Occlusions of these vessels, penetrating branches of the Circle of Willis or vertebral / basilar arteries are referred to as lacunar strokes.

Pathophysiology of Ischemic Stroke

The two major mechanisms causing brain damage in stroke are ischemia and hemorrhage. In ischemic stroke, which represents about 80% of all strokes, decreased or absent circulating blood deprives neurons of necessary substrates. The effects of ischemia are fairly rapid because the brain does not store glucose, the chief energy substrate, and is incapable of anaerobic metabolism.

A thrombus or an embolus can occlude a cerebral artery and cause ischemia in the affected vascular territory. The impact of ischemic injury is greatly influenced by the state of collateral circulation in the affected area of the brain and a good collateral circulation is associated with a better outcome.

Cerebral Blood Flow

Normal cerebral blood flow (CBF) is approximately 50 – to 60 ml / 100 g / min and varies in different parts of the brain. In response to ischemia, the cerebral autoregulatory mechanisms compensate for a reduction in CBF. However, when the CBF is reduced to below 20 ml / 100 g / min, an electrical silence ensues and synaptic activity is greatly diminished in an attempt to pre-serve energy stores. CBF of less than 10 ml/ 100 g/ min results in irreversible neuronal injury.

Ischemic Penumbra (IP)

Within an hour of hypoxic- ischemic insult, there is a core of infarction surrounded by an oligemic zone called the ischemic penumbra (IP) where auto regulation is ineffective. The critical time period during which this volume of brain tissue is at risk is referred to as the "window of opportunity" since the neurological deficits created by ischemia can be partly or completely reversed by reperfusing the ischemic yet viable brain tissue within a critical time period (2 to 4 hours).

IP is characterized by some preservation of energy metabolism because the CBF in this area is 25% to 50% of normal. Cellular integrity and function are preserved in this area of limited ischemia for variable periods of time.

Imaging of Stroke

Role of CT in Acute Stroke Evaluation

The use of computed tomography (CT) for stroke evaluation has progressively increased since magnetic resonance (MR) imaging is less widely available than CT outside major stroke centers and is much more limited by patient contraindications or intolerance.[6]

In recent years, the amount of information provided by the radiologist has increased owing to the use of additional CT techniques such as perfusion CT and CT angiography. Multimodal CT evaluation that combines NECT, perfusion CT, and CT angiography has been shown to improve detection of acute infarction;[7-8] permit assessment of the site of vascular occlusion, the infarct core, and salvageable brain tissue; and help assess the degree of collateral circulation.[9] This multimodal approach requires only 10 – 15 minutes more than NECT alone.[10]

Perfusion CT delineates the ischemic tissue (penumbra) by showing increased mean transit time with decreased cerebral blood flow (CBF) and normal or increased cerebral blood volume (CBV), whereas infracted tissue manifests with markedly decreased CBF and decreased CBV. CT angiography can depict the occlusion site, help grade collateral blood flow, and help characterize carotid atherosclerotic disease. A complete CT study (NECT, perfusion CT, and CT angiography) may be performed and analyzed rapidly and easily by general radiologists using a simple standardized protocol and may even facilitate diagnosis by less experienced radiologists in affected patients.

Unenhanced CT

NECT is widely available, can be performed quickly, and does not involve the administration of intravenous contrast material. It not only can help identify a hemorrhage (a contraindication to thrombolytic therapy), but it also can help detect early – stage acute ischemia by depicting features such as the hyperdense vessel sign, the insular ribbon sign, and obscuration of the lentiform nucleus within 2 hours after the onset of a stroke.[11]

CT Angiography

CT angiography is a widely available technique for assessment of both the intracranial and extracranial circulation. Its utility in acute stroke lies in its capabilities for demonstrating thrombi within intracranial vessels and for evaluating the carotid and vertebral arteries in the neck.[24]

CT Perfusion Imaging

In 1979, just 8 years after introduction of CT, Leon Axel proposed a method for determining tissue perfusion from dynamic contrast enhanced CT data.[16] Due to the requirement for rapid image acquisition and processing, CT perfusion measurements were largely confined to research studies of renal or myocardial blood flow using electron beam CT systems.[17-18] However, the advent of spiral CT systems in the 1990s enabled perfusion CT to be performed with conventional CT systems, thereby broadening the technique's availability.[19-20]

More recently, clinical use of CT perfusion imaging has been facilitated by the release of commercial software packages from a range of CT manufacturers. CT perfusion imaging can be used to measure the following perfusion parameters.

Cerebral Blood Flow (CBF)

Cerebral blood flow is the most important parameter and it is measured in ml blood / 100 g brain tissue / min. Normal values for CBF are between 50 and 80 ml of blood per 100 g of brain tissue per minute.

Below a CBF of 20 ml / 100 g / min, the synaptic function of the nerve cells is retarded due to the lack of energy, i.e. there is neurological failure. This loss may, however, be completely reversible if blood flow is normalized again. Below a CBF of 10 – 15 ml / 100 g / min the metabolism of the nerve cells can no longer be maintained. If CBF remains below this so called ischemia threshold for 2 – 10 minutes, the result is irreversible cell damage. In ischemic cerebral infarcts around an irreversibly damaged infarct core with CBF values below 10 – 15 ml / 100 g / min, there is frequently a margin of brain tissue in which the CBF is maintained by collateral vessels at 10 to 20 ml / 100 g/ min. The cells of this area known as an infarct penumbra are not neurologically functional, but they are not yet ireversibly damaged.

Cerebral Blood Volume (CBV)

Cerebral blood volume (CBV) is defined as the percentage of blood vessels in a specific volume of tissue. This is very helpful in diagnosing strokes: areas showing reduced CBV in the acute stage of ischemia are as a rule irreversibly damaged.

Parameters for Describing Delay in Perfusion (TTP, MTT)

The most common of the parameters indicating retarded perfusion are mean transit time (MTT) and time –

to – peak (TTP).[21] There is a direct correlation between them and cerebral perfusion pressure. In clinical studies on strokes the MTT and TTP were found to be very sensitive to disruption in regional perfusion of the brain.[22-23]

Penumbra

In acute stroke, there is a central, irreversibly infarcted tissue core surrounded by a peripheral region of stunned cells called the penumbra that receives a collateral blood supply from uninjured arterial and leptomeningeal territories. The cells in the penumbra are potentially salvageable with early recanalization.[3] Perfusion CT can help distinguish the penumbra from infarcted tissue in acute stroke patients. CBF and normal or mildly increased CBV (secondary to autoregulatory mechanisms in the early stage of ischemia), whereas infarcted tissue shows markedly decreased CBF and increased MTT with markedly decreased CBV.[8] Hence, the salvageable brain tissue is equivalent to CBF – CBV.

Perfusion CT Technique

Perfusion CT is performed by monitoring only the first pass of an iodinated contrast agent bolus through the cerebral circulation.[24] It involves continuous cine imaging for 45 seconds over the same slab of tissue (1 – 32 sections) during the dynamic administration of a small (50 – mL), high – flow contrast material bolus (injection rate, 4 – 5 mL / sec).

Color – coded perfusion maps showing CBV, mean transit time (MTT), and CBF are obtained.[24-25] The quantification of these parameters is based on the equation CBF = CBV / MTT. MTT is calculated by performing a mathematical technique called deconvolution on the regional time – attenuation curve of each pixel with respect to the arterial curve (arterial input function).[26-27] CBV is calculated by dividing the area under the curve in a parenchymal pixel by the area under the curve in an arterial pixel.

The accuracy of perfusion CT has been validated with other standard perfusion techniques such as positron emission tomography and stable xenon CT.[28]

The study Objectives

The aim of this study was to determine the degree of agreement between perfusion CT and delayed CT in early detection of cerebral ischemia in patients with clinical signs of stroke having negative early NECT scan.

MATERIALS AND METHODS

It was a Cross Sectional Study conducted in the Department of Diagnostic Radiology, PGMI, Lahore General Hospital and continued for six months from August 2013 till February 2014. The calculated sample size came out to be 150 cases with 95% confidence level, 9% margin of error, taking expected percentage of agreement between Perfusion CT and delayed CT to be 78%. Non probability Purposive Sampling was used to select sample patients.

All the patients presented to medical emergency of Lahore General Hospital Lahore with clinical signs of ischemic stroke having no radiological signs of stroke on NECT were included in study. Informed consent was taken and Dynamic perfusion CT data was obtained at the level of the basal ganglia. This section includes the vascular territories most frequently affected by an acute stroke, namely the middle cerebral artery territory.

Data Analysis Procedure

Data was entered and analyzed by using computer software SPSS 13. For quantitative data i.e. age, mean and standard deviation were calculated. For qualitative data i.e. gender, diagnosis and presence or absence of infarct on NECT or perfusion CT, frequencies and percentages were calculated.

RESULTS

This study was conducted on 150 patients with clinical suspicion of stroke but having no or early signs of infarction on NECT scan.

The age of patients ranged from 29 to 90 years with mean age 63.80 ± 13.62 years. The highest number of patients was aged between 71 – 80 years i.e. 61 (40.7%). Minimum number of patients was aged between 20 – 30 years i.e. 4 (2.7%). Out of 150 patients, 93 patients (62.0%) were males and 57 patients (38.0%) were females.

74 patients (49.3%) out of total number of patients included in the study had signs of infarct on NECT while 76 patients (50.7%) had no signs of infarct on NECT.

138 patients (92.0%) showed signs of infarct on perfusion CT while 12 patients (8.0%) had no signs of infarct on perfusion CT.

Out of these 138 patients which were positive on perfusion CT, 131 proved to be positive on follow up CT and were thus true positive while 7 patients were negative on follow up CT and thus were false positive.

Cohen ḱ coefficients were calculated to determine the agreement between NECT and perfusion CT. These were determined for both the presence and absence of abnormalities on non enhanced CT and Perfusion CT.

A value of .607 was derived for ḱ with standard error of ± .113 which shows substantial agreement between perfusion CT and delayed CT.

DISCUSSION

The ability to rapidly and accurately depict the location and extent of acute brain ischemia is of major clinical importance. NECT, especially in patients with acute stroke, is known to have some uncertainty in terms of depiction of early signs of infarction and quantification of affected tissue.

We found an excellent agreement between location of critically ischemic tissue defined by acute CT perfusion mapping and delayed un enhanced CT scan which is in line with the previous studies.[29]

This finding is also within the range of findings of previous studies which have correlated results of dynamic CT mapping with postmortem size of infarction. Lo et al[30] compared the results of CT-derived maps of relative bolus delay of contrast material and relative blood volume with TTC staining in a rabbit model of focal cerebral ischemia.

Moreover, the large number of patients with minor complaints in our study has to be taken into consideration, as a greater portion of transient ischemic attacks or small infarctions can be presumed to exist in this subgroup on the basis of the presented clinical findings. Accordingly, this subgroup revealed that NECT had less sensitivity for infarction. The estimated extension of infarction calculated according to the ASPECT score correlated poorly with the final size of infarction at the follow-up examination.

CBF and TTP maps showed more agreement for perfusion disturbances than were CBV maps. Thus, the use of multi-detector row CT with two sections and a total coverage of 20 mm seem to improve the detection rate compared with that of a single – section technique.

In contrast with NECT alone, the detection rate could be increased with the use of multimodal CT in our examined patients.

Other imaging techniques, such as diffusion – and perfusion – weighted MR imaging, offer excellent information about ischemic brain tissue[31-34] and are in use since some time. However clinical condition of patients with acute stroke can make MR imaging difficult or impossible as usually stroke patients are restless and administration of hypnotic agents is not recommended to reduce movement during scanning. Thus, further studies with larger numbers of patients are needed to confirm the superiority of MR imaging. It may be recommended that comparative studies of perfusion CT with MR imaging may be carried out to be employed in those tertiary care settings where both modalities are available round the clock.

CONCLUSION

In conclusion, because CT is still the primary imaging modality in patients with acute stroke, perfusion CT evaluation improves the rate of detection of infarction in comparison with NECT alone. Small brain ischemia, however, particularly lacunar infarction outside of the perfusion CT section levels, can be missed.

CBF maps derived from the dynamic perfusion CT study show a good correlation with the final size of infarction. The use of multi–detector row CT demonstrated improved detection rate of perfusion deficit, particularly in patients with minor neurologic symptom. We believe multimodal CT evaluation can aid decision making for treatment of patients suspected of having a stroke and as such should become a routine in all such cases.

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