Original Article

A study of effectiveness of initial NECT versus combined NECT plus ct perfusion in detection of cerebral ischemia

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Abstract

Background: Acute ischemic stroke (AIS) is a common cause of mortality and morbidity all over the world. Cerebral ischemia is a pathology that stems from a decrease in cerebral perfusion. Computed Tomography Perfusion (CTP) is an additional method to the conventional non-enhanced CT (NECT) that could be performed by using developed softwares, in a short period of time and with a low risk of complications. CT angiography is highly sensitive in detection of arterial anatomy and occlusion of intracranial vessels. CT angiography can be used for initial imaging of patients with suspected stroke as screening test for internal carotid artery stenosis. In the present study an effort has been made to study the effectiveness of initial NECT versus combined NECT plus CT Perfusion in detection of cerebral ischemia. **Material and Methods:** A total of 1325 patients clinically suspected of having stroke were included in the study. Among 1325 cases, 55 patients with hemispheric symptoms of ischemic stroke were enrolled and subjected to non enhanced CT followed by perfusion analysis (n=25) or CT angiography. **Results:** Sensitivity and specificity of initial NECT as a modality in detecting ischemia are 55.56% and 100% respectively. Whereas, sensitivity and specificities of CT perfusion in detecting ischemia are 83.33% and 100% respectively. The ability to diagnose hyper acute stroke is superior with CT perfusion as compared to initial NECT. **Discussion:** We actually recommend that the imaging protocol for stroke patients should combine all three which can include plain CT, CT perfusion and CT angiography at one sitting if possible than including Doppler and MRI.

Keywords: Cerebral ischemia, Non-enhanced Computed tomography, CT perfusion, CT angiography.

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INTRODUCTION

Acute ischemic stroke (AIS) is a common cause of mortality and morbidity all over the world. Researches show that acute ischemic stroke is on the third place amongst causes of death[1]. Stroke is defined according to the World Health Organization (WHO) criteria as rapidly developing signs of focal or global disturbance of cerebral function, lasting more than 24 hours or leading to death, with no apparent cause other than vascular[2]. The four major types of stroke are cerebral infarction, intracerebral haemorrhage (ICH), primary subarachnoid haemorrhage (SAH) and venous occlusion. Evaluation of stroke patients must be done to by diagnostic procedure to demonstrate lesion in the tissue, detect vascular lesion responsible for attack and assessment of pathophysiological changes that might indicate the course and prognosis of event. The diagnosis of many of the subtypes such as cardio-embolic and athero-thrombotic stroke require detailed clinical, radiological and laboratory evaluation. For further management and initiation of appropriate treatment, it is essential to differentiate strokes from non-ischemic strokes i.e.,

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intracerebral haemorrhage, subarachnoid haemorrhage and venous thrombosis. In addition, radiographic imaging techniques are helpful in classifying subtypes of ischemic strokes due to emboli, stenosis or thrombosis of large vessels, small vessel disease, or other pathological conditions. Computerized tomography (CT) scan is a widely available, affordable, non- invasive and relatively accurate investigation in patients with stroke and is the modality of choice as an initial investigation in patients with stroke. The purpose of CT is to differentiate ischaemic stroke from ICH and to rule out other pathological processes such as tumour, which may present as stroke. In majority of patients of ischemic stroke imaged in the first 6 hour, CT is either normal or demonstrates subtle abnormalities that are not picked up easily[3]. The Perfusion CT data can positively identify patients with non-hemorrhagic stroke in the presence of a normal conventional CT, provide an indication as to prognosis and potentially select those patients for whom thrombolysis is appropriate. As thrombolysis may only be effective if administered within 3 h to 6 h of ictus, the time saved by avoiding additional imaging modalities will be of great value[4]. CT angiography is highly sensitive in detection of arterial anatomy and occlusion of intracranial vessels. CT angiography can be used for initial imaging of patients with suspected stroke as screening test for internal carotid artery stenosis. Advances in technology contribute to diagnostics and treatment of AIS. The fact that early imaging and accurate diagnosis increase the success in treatment has made the neuroradiologist's role in diagnostics and treatment of AIS more important[5]. The present study was undertaken to study the Effectiveness of Initial Non-enhancing CT scan (NECT) versus Combined NECT plus CT Perfusion in Detection of Cerebral Ischemia.

MATERIAL AND METHODS

In this prospective study 1325 patients with complaints of ischemic stroke with varied presentation admitted to the emergency ward, from August 2008 to September 2010 were included. The subjects belonged to a mixed ethnic and predominantly lower socioeconomic group. Besides detailed medical history and clinical examination, routine laboratory work-up and electrocardiogram was done in all patients. Cranial CT Scan (plain) was done in all the cases in emergency hours immediately. Adults of more than 18 years' age with hemispheric symptoms such as, hemiplegia, aphasia, hemianopia and with acute stroke of less than 12 hours' duration for CTP and more than 12 hours' duration for CT angiography were included in the study. Patients with signs of intracranial hemorrhage on plain CT, excessive movements, history of an allergic reaction to contrast dye or iodine allergy and evidence of renal insufficiency as determined by a measured serum creatinine level >1.5 mg/dl and pregnant females were excluded from the study. As per the inclusion and exclusion criteria of the study only 25 patients were eligible and hence selected for the perfusion data. Of the rest of the patients, those who could be convinced and where the clinician agreed a CT angiography were done. 55 patients with hemispheric symptoms of ischemic stroke were subjected to non enhanced CT followed by perfusion analysis (n=25) or CT angiography (n=30). Of them 25 presented within 12 hrs duration were subjected to CT Perfusion and in them follow-up imaging was performed with NECT (n=25) within 2-7 days (mean, 2.32 days) of admission. Rest (n=30) presented after 12 hr were subjected to CT angiography. The CT examination of these patients was carried out with commercially available Tossiba Aquilion 64 multislice CT scanner equipped with Perfusion CT software (SVD and SVD+), COW post processing angio software and a Medrad pressure injector which was used to inject 50 mL of concentrated nonionic contrast medium (Iohexol USP 350, Omnipaque) for CT Perfusion and 80 mL for CT angiography. Once the injection is started, the bolus tracking software measures attenuation values within arch of aorta (ICA), and the spiral scan is automatically started as soon as a threshold of 100 HU is exceeded.

RESULTS

A total of 1325 patients clinically suspected of having stroke were included in the study. Among 1325 cases, 55 patients with hemispheric symptoms of ischemic stroke were enrolled and subjected to non enhanced CT followed by perfusion analysis (n=25) or CT angiography (n=30). Out of 55 cases 43 (78.1%) were males and 12 (21.8%) were females. Twenty-one males and four females underwent perfusion CT and 22 males and eight females underwent CT angiography. A total of 23 (41.8%) patients were within 31-50 yrs age group; whereas 20 (36.3%) patients were in 51-70 yrs age group. Nine (16.3%) and three (5.4%) were within 10-30 yrs and 71-90 yrs age group respectively. Clinical presentations of cases were hemiplegia, facial nerve palsy, headache, aphasia, loss of consciousness and hemianopia as the most common, seen in 51 (92.7%), 7 (12.7%), 8 (14.5%), 6 (10.9%), 5 (9%) and 2 (3.6%) of patients respectively. Follow up CT has been considered as gold standard for infarct. Results of initial NECT and CTP were compared with follow up. A total of 10 were abnormal on initial NECT, whereas on perfusion CT 15 were abnormal. Eighteen were abnormal on follow up CT and 7 were normal on follow up with NECT. Sensitivity and specificity of Perfusion CT as a modality in detecting ischemia is given in Table 1. Sensitivity and specificities

of CT perfusion in detecting ischemia are 83.33% and 100% respectively.

Table 1: Sensitivity and specificities of CT perfusion

Ischemia on follow up NECT / Perfusion CT	Present	Absent	Total
Positive	15	00	15
Negative	03	07	10
Total	**18**	**07**	**25**

Sensitivity and specificity of initial NECT as a modality in detecting ischemia are given IN Table 2. Sensitivity and specificity of initial NECT as a modality in detecting ischemia are 55.56% and 100% respectively.

Table 2: Sensitivity and specificities of initial NECT

Ischemia on follow up NECT / Initial NECT	Present	Absent	Total
Positive	10	00	10
Negative	08	07	15
Total	**18**	**07**	**25**

As (p=0.012; less than 0.05); the observed difference between CT perfusion and initial NECT is significant that means the ability to diagnose hyper acute stroke is superior with CT perfusion as compared to initial NECT.

Figure 1 A: Plain CT

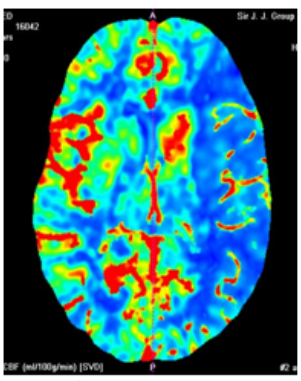

Figure 1 b: CBF

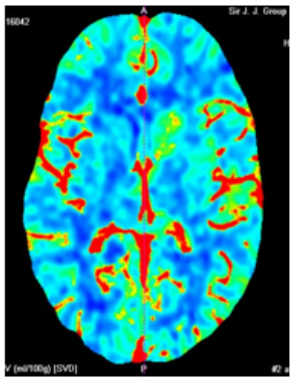

Figure 1 c: CBV

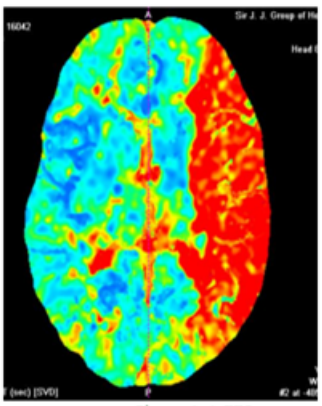

Figure 1 d: TTP

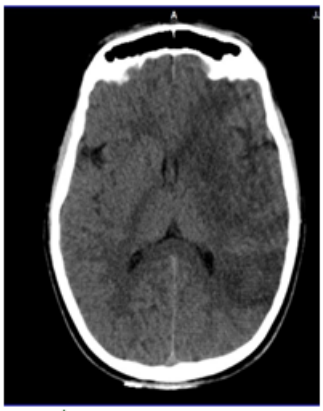

Figure 1 e: Follow-up CT

Figure 1: CT Brain images of 18 yrs male with upper motor neuron facial paralysis, aphasia and right upper and lower limb hemiparesis. a. NECT showed obscuration of left lentiform and caudate nucleus with subtle hypodensity. b, c, d. Perfusion CT images showed a CBF-CBV mismatch and delay in TTP in the posterior parietal and temporo-occipital territory of MCA. e. Follow up NECT showed infarct almost equal to mismatch. (CBF=Cerebral blood flow; CBV=Cerebral blood volume; TTP=Time to peak)

Considering of both components (initial NECT and CTP) of the CT evaluation, 16 of 18 patients had true-positive results with infarction at the follow-up examination, resulting in a sensitivity of 88.89%. In one of these patients, signs of ischemia were found only on the initial unenhanced CT scan, whereas the result of perfusion CT was unremarkable. Sensitivity and specificity of combined initial NECT and CT perfusion as a modality in detecting ischemia are 88.89% and 100% respectively (Table 3).

Table 3: Sensitivity and specificity of combined initial NECT and CT perfusion

Ischemia on follow up NECT / Initial NECT and/or Perfusion CT	Present	Absent	Total
Positive	16	00	16
Negative	02	07	09
Total	**18**	**07**	**25**

This study suggests that angiographic abnormality was found in the 18 cases (i.e. 60%). Significant stenosis was found in more than half (55.56%) of them and insignificant stenosis was seen in less than half (44.44%). Angiography was normal in 12 cases (40%). Overall sensitivity of angiography to detect cause of stroke in all patients with presented with acute ischemic stroke was 60%. In our two cases we observed that even with insignificant angiographic stenosis (<50%) large territorial infarct were seen. In both of them there were ulcerated soft atherosclerotic plaque with lipid core (HU value between -40 to 50) in carotid bulb causing <50% stenosis. In our three cases we observed that even with significant angiographic stenosis (>50%), no infarct was seen. All three cases were presented with transient ischemic attack and recovered completely. The sensitivity and specificity of CT angio as a modality in detecting atherosclerotic disease in ischemia (established infarct on initial NECT) are 77.78% and 85.71% respectively. (Chi-square = 8.750 with 1 degree of freedom; P = 0.003 - highly significant). In our 9 cases with infarct on plain CT significant angiographic stenosis was seen in about 7 patients (sensitivity=77.78%). Remaining two patient showed ulcerated soft plaque in carotid bulb causing insignificant stenosis (<50%). These findings suggested that cause of ischemia was detected in around 100% of established infarct. This justifies the use of CT angiography in all patients with established infarct on initial CT. In our 15 cases presented with TIA we observed that angiographic abnormality was noted in only 6 cases of which 4 had insignificant stenosis and only 2 had significant stenosis. Hence CT angio should be used judiciously in patients with TIA but no obvious infarct as a aggressive primary modality to search for a cause.

DISCUSSION

Acute stroke is usually diagnosed by neurological examination or Plain CT only. Although clinical symptoms are very sensitive to cerebral ischemia, they are nonspecific. Perfusion CT for the diagnosis of acute stroke is a rapidly emerging adjunct to conventional CT studies; the advent of possible therapeutic strategies for acute stroke has increased the need for a simple, quick, reliable and effective method of assessing cerebral blood flow that is practicable in any hospital admitting patients with acute stroke[6]. In our study Perfusion CT was used as an adjunct to conventional CT in 25 patients with hemispheric symptoms of acute stroke within 12 hrs of symptom onset the mean age of the patients was 47.12 years. The most commonly affected age group was between 31-50 years. We compared NECT, CT perfusion and combined NECT and CT perfusion with follow up CT (at mean 2.32 day). We found that overall sensitivity of NECT, CT perfusion and combined NECT and CT perfusion were 55.56%, 83.33% and 88.89% respectively. Results were well comparable with Kloska *et al*. study[7] which demonstrated that sensitivity of NECT, CT perfusion and multimodality (NECT, CT perfusion and CT angiography) were55.53%, 76.3% and 78.9% respectively. On comparison between initial NECT and CT perfusion for detection ischemia in <12 hours, we found as p value is less than 0.05 (0.012 by a Pearson Chi-Square test or 0.018 Fisher's Exact Test) suggesting the observed difference between CT perfusion and initial NECT is significant. This suggests that the ability to diagnose hyper acute stroke is superior with CT perfusion as compared to initial NECT. We did not directly compare the performances of Perfusion CT and DW imaging in the early detection of brain ischemia. Instead we found Perfusion CT, has a overall sensitivity of 83.33%, which can be compared with the 86% reported for DW imaging[8,9]. Our study also showed that combined used of NECT and Perfusion CT has high sensitivity (up to 88.89%), specificity (100%), in the depiction of stroke extent. In our study, 55.56 % of all hyper acute infarct (<12 hrs) were detected in NECT. Early CT signs of stroke were not picked up on non-contrast CT in 44.44% cases. This finding is within the range of findings of previous studies with reported sensitivities between 45% and 88%[7] depending on the time of examination. In the second part of the European Cooperative Acute Stroke Study (ECASS II), specially trained neuroradiologic experts evaluated the extent of early signs within the 1st 6 hours after the onset of ischemic symptoms. The accuracy of predicting the exact volume of affected brain tissue was only 76%[10]. However, We found that signs of salvageable hyper acute infarct were seen in 38% patient's as compared to 100 % patients in CTP. So sensitivity of NECT early infarct signs for detection of salvageable hyper acute infarct is 38% and however specificity of 100%. Which was comparable with Leys *et al* study, specificity of hyper dense MCA sign is nearly 100%, but its sensitivity is only about 30%[6]. Our finding that CT angiography added to information obtained on plain CT outlining exact site block or stenosis was expected finding. It has already been documented by S. A. Josephson, MD, S. O. Bryant[11] and many others[11-13] in their study. Furthermore none of the patients included in our study experienced any side effects or discomfort during this procedure despite the rapid rate of contrast infusion. The sensitivity and specificity of CT angiography as a modality in detecting atherosclerotic disease in ischemia (established infarct on initial NECT) are 77.78% and 85.71 % respectively. (Chi-square P = 0.003- highly significant). In our 9 cases with infarct on plain CT significant angiographic stenosis was seen in

about 7 patients (sensitivity=77.78%). Remaining two patient showed ulcerated soft plaque with lipid core in carotid bulb causing insignificant stenosis (<50%). These findings suggested that cause of ischemia was detected in around 100% of cases with established infarct on plain CT. This justifies the use of CT angiography in all patients with established infarct on initial CT. A single time investigation which can include plain CT,CT perfusion and CT angiography can go a long way to complete evaluation of the patient for all the possible causes at one go with marginal increase in cost and radiation to conduct the study. Also as multiple modalities are not involved much time is saved which is crucial in such patients. We actually recommend that the imaging protocol for stroke patients should combine all three which can include plain CT, CT perfusion and CT angiography at one sitting if possible than including Doppler and MRI as this saves time and give information of intra and intracranial vessels with precession at the same sitting.

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