Comparison of ability of ASPECTS on non-contrast CT and CT angiography source images to predict the final size of infarct in a 256-slice CT scanner

THESIS

SUBMITTED IN PARTIAL FULFILLMENT FOR DEGREE
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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY,
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CERTIFICATE

This is to certify that the work incorporated in this thesis titled ***"Comparison of ability of ASPECTS on non-contrast CT and CT angiography source images to predict the final size of infarct in a 256-slice CT scanner"*** *for the degree for DM (NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY) has been carried out by Dr. Amritendu Mukherjee under guidance of Dr Chandrasekharan Kesavadas (Professor, Dept. of IS & IR) and Dr. Sylaja P. N. (Additional Professor, Dept. of Neurology). I am satisfied that he has carried out the work with sincerity. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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DECLARATION

I hereby declare that this thesis titled ***"Comparison of ability of ASPECTS on non-contrast CT and CT angiography source images to predict the final size of infarct in a 256-slice CT scanner"*** *has been prepared by me under the supervision and guidance of Dr Chandrasekharan Kesavadas (Professor, Dept. of IS & IR) and Dr. Sylaja P. N. (Additional Professor, Dept. of Neurology), Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.*

While undertaking the study, voluntary informed consent was taken from each patient/ close relative in writing and full confidentiality of the patients have been retained.

I further declare that this is an original study and no part of this study has been previously published or submitted to any university.

Date: 03/10/2015 *(Dr Amritendu Mukherjee)*

Place: Thiruvananthapuram

ACKNOWLEDGEMENT

This section of the thesis will remain inadequate whatever the efforts.

I am deeply indebted to my honourable teachers and guides Dr Chandrasekharan Kesavadas and Dr Sylaja PN for their constant support, encouragement, helpful criticism, expert supervision and guidance throughout this study which assisted largely in bringing this study to fruition.

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Institutional Ethics Committee (IEC)
(IEC Regn No. ECR/189/Inst/KL/2013)

SCT / IEC- 489/ JULY-2013

29-07-2013

Dr. Amritendu Mukherjee
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Dear Dr. Amritendu Mukherjee

The Institutional Ethics Committee reviewed and discussed your application to conduct the clinical trial entitled "COMPARISON OF ABILITY OF ASPECTS ON NON-CONTRAST CT AND CT ANGIOGRAPHY SOURCE IMAGES TO PREDICT THE FINAL SIZE OF INFARCT IN A 256-SLICE CT SCANNER" IEC/ 489 on 20th July, 2013.

The following documents were reviewed:

1. *Covering letter dated 24.5.2013*
2. *IEC application form*
3. *TAC form*
4. *Proposal for study*
5. *Consent forms (English and Malayalam)*
6. *Short CVs*
7. *Proforma*
8. *TAC Approval Letter*

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The following members of the Ethics Committee were present at the meeting held on 20th July, 2013 at Conference Room, Director's Office.

Sl. No	Member Name	Highest Degree	Gender	Scientific / Non-scientific	Affiliation with Institution (s)
1.	Justice M.R. Hariharan Nair.	MA BL	Male	Legal Expert (Chairperson)	No
2.	Dr. J. M. Tharakan	MD	Male	Clinician (Cardiologist)	Yes
3.	Dr. K. A. Kumar	MD	Male	Clinician (Psychiatrist)	No
4.	Dr. Rema M. N	MD	Female	Pharmacologist	No
5.	Dr. Meenu Hariharan	DM	Female	Clinician (Gastro Enterologist)	No
6.	Dr. S. N. Pal	PhD	Male	Basic Scientist (Biomaterials Expert)	No
7.	Dr. C. P. Sharma	FBAO, FBSE	Male	Basic Scientist (Biomaterials)	Yes
8.	Smt. Lalithambika IAS	MBA	Female	Lay Person (Administrator)	No
9.	Dr. M. D. Gupte	MD DPH	Male	Epidemiology/Public Health	No
10.	Dr. Premila P.G.	MD	Female	Clinician (Paediatrician)	No
11.	Dr. Anoopkumar Thekkuveettil	PhD	Male	Basic Scientist (Molecular Biology) /Ethicist (Member Secretary)	Yes

IEC Decision

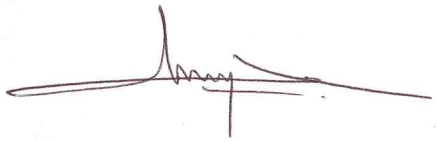
PI should make sure that the study follows the standard procedures.
Approved the conduct of the study in the present form

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Yours Sincerely



Dr. Anoopkumar Thekkuveettil
Member Secretary, Ethics Committee.

CONTENTS

Introduction

Acute ischaemic stroke is a debilitating disease and is often associated with mortality and significant morbidity. Imaging plays a significant role in directing management of acute ischaemic stroke. However, choice of modality of imaging and their proper usage is vital in this setting as time is the most crucial factor in determining the outcome of acute ischaemic stroke.

Computed tomography (CT) is presently the imaging modality of choice for evaluation of acute stroke patients. The European Cooperative Acute Stroke Study (ECASS) trials established the importance of evaluating early CT changes in acute ischaemic stroke to foresee the benefit from intravenous (IV) thrombolysis(1,2). In both of these trials, the randomization was decided on whether more or less than one third of the territory of the middle cerebral artery (MCA) was involved. However, subsequent studies have shown that even veteran stroke physicians and radiologists have issue reckoning and quantifying these findings(3–7).

The Alberta stroke program early CT score (ASPECTS) is a reproducible grading system developed to offer the utility and steadfastness of a standard CT examination to assess early ischemic changes in acute ischemic stroke of the anterior

circulation(8). This CT score is simple and consistent and recognizes stroke patients not likely to make an independent recovery despite thrombolytic treatment. ASPECTS has become a widely popular scoring system and is being widely used worldwide these days.

Several studies have shown that ASPECTS using CT angiography source images (CTA-SI) have better correlation with final infarct size than non- contrast CT (NCCT) ASPECTS(9–13). However, most of these studies were conducted in last decade and the use of multislice CT scanner in these studies were limited maximally up to 16 slices. With progress of technology, multislice CT scanner of higher slices (64 slices, 128 slices, 256 slices etc.) have become commonplace now-a-days. These machines can scan very fast and can complete a CT angiography (CTA) from aortic arch to cranial vault within seconds. Undoubtedly, speed is a benefit of these machines. However, these trendy rapid scanners may be too fast to achieve steady-state of arterial and tissue contrast and resulting image may be cerebral blood flow (CBF) weighted rather than cerebral blood volume (CBV) weighted. This phenomenon was previously reported with 64-slice CT scanner(14).

Hence, CTA-SI ASPECTS in these fast scanners may actually reflect CBF rather than CBV. In other words, CTA-SI in a fast scanner tend to overestimate the infarct.

Introduction

Our institute uses a 256-slice CT scanner for imaging of acute stroke. Imaging protocol of our institute for acute stroke includes NCCT and CTA in all acute ischaemic stroke cases and CT perfusion (CTP) and diffusion weighted imaging (DWI) in selected cases. This study aims to determine whether the ASPECTS of CTA-SI in a 256-slice CT overestimates the final infarct size as it will have implications on management. To our knowledge, no such study has been performed until date on a 256-slice CT scanner.

Aims & Objectives

This study involves determining the ability of the ASPECTS derived from Non-contrast CT and CT angiography source images in a 256-slice CT scanner of patients presenting with acute ischaemic stroke (within 8 hours of symptom onset) to predict final size of infarct.

Aim:

1. To compare the ability of ASPECTS derived from NCCT and CTA-SI to predict the final size of infarct in patients of acute stroke in a 256-slice CT scanner.
2. To correlate the NCCT and CTA-SI with perfusion parametric maps in a subgroup analysis.

Hypothesis:

1. **PRIMARY:** CTA-SI overestimates the final size of infarct as compared to NCCT in a 256-slice CT scanner.
2. **SECONDARY:** NCCT correlates with infarct core and CTA-SI correlates with the penumbra of acute stroke in a 256- slice CT.

Review of Literature

Stroke is a clinical syndrome characterized by acute clinical signs of focal (or global in coma) disturbance of brain function persisting over 24 hours or causing death with no ostensible cause other than a vascular etiology.(15,16) Stroke is the second most common cause of demise globally.

The objective of prompt brain imaging is to exclude intracranial haemorrhage (ICH), recognize early ischaemic change and exclude stroke mimics. Imaging also permits vessel assessment and gives information about cerebral perfusion, delineating the infarct core and ischaemic penumbra (potentially salvageable brain parenchyma), the detection of which may help to determine management strategies.

Stroke can be classified into two major categories: ischaemic (~80%) and haemorrhagic (20%). Ischaemic stroke comprises manifold etiologies including arterial thrombosis, arterial embolism, venous thrombosis and systemic hypoperfusion. Recombinant tissue plasminogen activator (rtPA) is the treatment of choice for ischaemic stroke within 3 hours of symptom onset, if there is no contraindication including exclusion of ICH by NCCT. NINDS trial (17) showed

efficacy of IV thrombolysis within 3 hours of symptom onset. However, due to a narrow time window, <10% of patients with acute stroke actually receive rtPA.

The earlier acute ischaemic stroke is diagnosed and thrombolysis treatment prompted (if indicated), the better is the clinical outcome. (15) Much of the studies reports approved use of rtPA within 3 hour of symptom onset; though European Cooperative Acute Stroke Study III (ECASS III) shows that extension of the treatment window to 4.5 hours is beneficial in a large subgroup of patients. (18,19)

Non-contrast CT Imaging

Initial assessment of acute stroke is preferably done by NCCT as it is usually at hand even in peripheral units and permits quick evaluation. Multidetector technology acquires images within seconds and at sub-millimeter resolution. (20) The most important role of NCCT in acute stroke is that it detects ICH promptly with high sensitivity. It also rules out stroke mimics and of course detects early parenchymal ischaemic change.

Most of the existing guidelines on thrombolysis consider NCCT the key to decision making about the indication of thrombolysis.

Approximately three fourth of all ischaemic infarcts occur within the middle cerebral artery (MCA) territory. Picking up early ischaemic change (EIC) on NCCT can be challenging as most of the initial radiological features are subtle. A systematic review (21) assessed inter-observer consistency in spotting these early radiological

signs and reported a mean sensitivity of 66% and specificity of 87% for detection of early signs of acute ischaemic stroke; lesion detection improving with observer experience. These early NCCT signs imply the cellular sequelae of acute infarction and also early thrombus in vessels. (21) Acute ischaemic infarct causes cerebral hypoperfusion which result in abrupt dysfunction of cellular potassium pump causing fluid shift from extracellular to intracellular space. The result is cytotoxic edema.

This fluid shift is reflected in NCCT as focal mass effect with gyral swelling and sulcal effacement with loss of the grey-white matter interface. These changes along with hypodensity are usually seen in MCA territory- lentiform nucleus, (22) insular ribbon,(23) cerebral cortex and basal ganglia. Sensitivity of picking up early ischaemic change in NCCT can be increased by viewing the images with variable window width and level maximizing parenchymal contrast.(24) It is not uncommon to find the NCCT normal in hyperacute plase, and, as such, earlier appearance of these parenchymal changes indicates more severe degree of ischaemia.(20)

An additional important sign in NCCT is vessel occlusion, evident as hyperdense vessels such as the ‘hyperdense/ dense MCA sign’ which is seen as linear hyperdensity in proximal M1 MCA or ‘MCA dot sign’ which is seen as hyperdense ‘dot’ in distal MCA within sylvian fissure.(20,25) Hyperdensity can be detected within any occluded vessel such as internal carotid artery (ICA) or basilar

artery (BA). This sign is either due to the thrombus itself or flow stasis distal to the thrombus.

The one-third MCA rule

EIC on admission NCCT predicts patient outcome and the risk of hemorrhagic transformation. (1,26,27) The ECASS-1 study (1) reported increased mortality with thrombolysis in patients with EIC involving more than one third MCA territory within 6 hours. This finding made a notion against thrombolysis had more than one-third MCA territory infarction been detected in NCCT.

Result of ECASS-2 trial, however, could not support this notion. (2) One-third MCA rule failed to prove to have any significant effect on treatment decisions. It also had poor inter-observer reliability.(7,28,29) Present guidelines does not contraindicate rtPA for more than one-third MCA territory EIC.(30)

Failure of one-third MCA rule raised the necessity of a simple but systematic and reliable approach to assess EIC in MCA territory. Alberta Stroke Program Early CT Score (ASPECTS) was developed out of that necessity. (31)

The ASPECTS

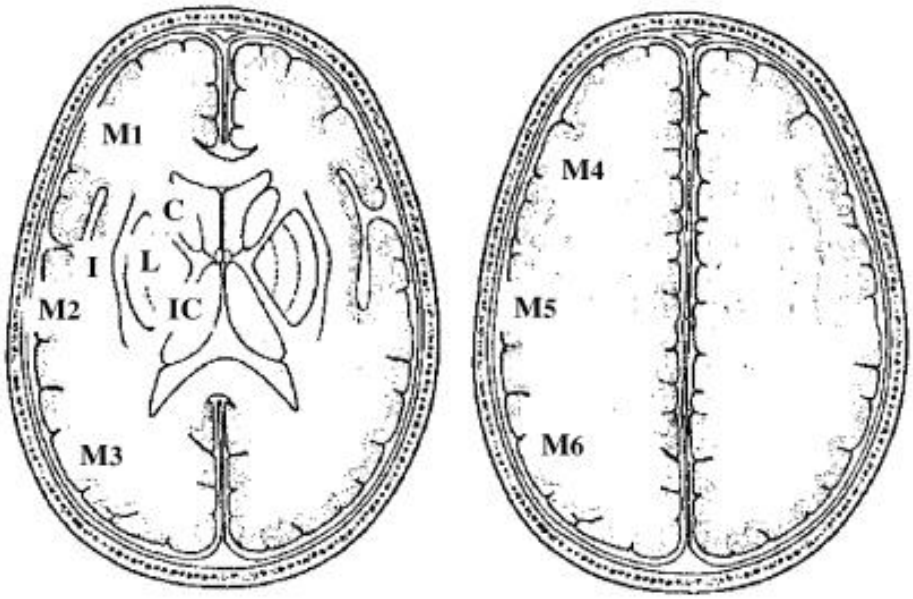
The ASPECTS is a topographic and quantitative scoring system. MCA territory is divided into 10 discrete regions in this system based on functional importance rather than extent. Equal weighting is given to smaller but vital structures

such as internal capsule, lentiform nucleus, insula and caudate, as is given to bigger lobar structures (M1 –M6).

Contrary to the one-third MCA territory rule, ASPECT scoring does not involve estimation of infarct volume from two dimensional images.

For ASPECT scoring MCA territory is evaluated at two levels: (1) basal ganglia level in which thalamus, basal ganglia, and caudate are seen together, and (2) supraganglionic level including both corona radiata and centrum semiovale. These two levels are demarcated by caudate head. All cuts in these two levels are to be evaluated to exclude involvement of these areas. For 5-mm axial sections, involvement of at least two consecutive sections are to be seen to determine a true abnormality rather than a volume averaging effect.

Figure 1



For the scoring, one point is deducted from a total score of 10 for involvement of one of the defined areas (M1–M6, IC = internal capsule, L = lentiform, I = insula and C = caudate). [Figure 1] The highest possible score is 10 and indicates no evidence of MCA territory EIC, whereas a score 0 indicates involvement of all the ASPECT defined areas, i.e. involvement of whole MCA territory. (32)

An EIC may be a parenchymal hypoattenuation or a focal brain swelling. Parenchymal hypoattenuation is abnormal hypodensity of brain parenchyma as compared to similar part of opposite hemisphere. Focal brain swelling indicates any focal CSF space (cortical sulci, brain cisterns, ventricles) narrowing due to compression by adjacent structures.

ASPECTS and outcome prediction

Using ASPECTS to quantify EIC, previous researchers could predict functional outcome and the chance of symptomatic hemorrhagic transformation in rtPA–treated patients.(31) ASPECTS were shown to be superior to one third MCA rule in this study.

Later Canadian Activase for Strokes Effectiveness Study corroborated these findings. The ASPECTS predicted strongly the functional outcome in this study and low ASPECT score correlated with poor outcome. (33)

Later ASPECT scoring has been elaborated in detail with methods to read and difficulties faced by interpreters.(34) Clinical expertise and experience has shown to

improve the reading with better correlation with outcome.(35) With experienced readers, EIC of NCCT correlates well with diffusion weighted imaging (DWI) ASPECTS values. Experience, careful reading and methodical approach improves NCCT ASPECT scoring and gives information as good as DWI imaging.

The ASPECTS is also the foremost way of EIC detection that has a role to play in clinical decision making. Clear interaction was detected upon re-evalutation of NCCTs of Prourokinase Acute Cerebral Infarct Trial–II (PROACT-II) using ASPECTS. PROACT-II represented a homogeneous cohort of patients with proximal MCA occlusion, 50% of which received intra-arterial rtPA therapy within a mean of 5.3 hours after symptom onset. The re-evalutation using ASPECTS demonstrated better outcome in the patients receiving intra-arterial treatment only when their initial ASPECTS were >7. (36) This finding may be of value in selection of patients of intra-arterial therapy in patient with 3-6 hour time period.

Researchers also found that a good ASPECTS (> 7) were associated with improved functional outcome and less mortality in < 3 hour time period also. However, ASPECTS = 3–7 still benefited from rtPA. Overall, there was not enough evidence to show that ASPECTS = 3–7 group should not receive thrombolytic therapy. Only did the ASPECTS < 3 group not show any survival benefit on thrombolytic treatment, though that < 3 % of study population, without much statistical significance. (37) Contrary to NINDS rtPA stroke study, PROACT-II

preselected only MCA occlusions ensuring presence of perfusion defect and ischemic penumbra in most of the study population. (38)

An ASPECTS of 10 (normal NCCT) is seen only in 15% acute stroke cases; hence, these subgroup of patients may not be ideal candidate for rtPA (no penumbra). On other hand, ASPECTS ≤ 5 was associated with intracranial occlusion in all cases. (39) However, these normal NCCT group may also benefit from rtPA if any vessels occlusion can be demonstrated, in other words, if ischemic penumbra can be identified. This was the case with the patients with good ASPECTS in PROACT-II study population. Most of them benefited from thrombolysis because of existence of a significant ischemic penumbra.

Again, the relevance of EIC increases with time; more time means more chance of irreversible injury. NINDS patients received thrombolysis earlier; at least 50% of them received treatment within 90 minutes. On the contrary, PROACT-II patients received treatment later. (38) SO NCCT EIC might be more relevant in decision making in the 3-6 hour time period, as shown in the PROACT-II and ECASS-1 results. The importance of EIC may be superseded by the time factor.(40,41)

The significance of the individual components of EIC (parenchymal hypoattenuation, sulcal effacement and loss of gray-white matter differentiation) has also been seen skeptically. These subtle signs may not always be representative of

irreversible brain damage.(42) The areas of brain which show attenuation lower than normal white matter are likely to be permanently damaged; but the physiological significance of these subtle ischemic changes are not proven beyond doubt.(43)

Alternatively, isolated cortical sulcal effacement on initial NCCT are frequently reversible. Recent study suggested that isolated sulcal effacement in absence of parenchymal hypoattenuation may represent raised cerebral blood volume (CBV) and increased tissue perfusion rather than an irreversible brain damage. Follow up imaging did not always reveal actual infarct in these areas. (44,45) These findings may warrant modification of ASPECTS technique to ignore these sulcal effacements.

Finally poor outcome is also noted in patients with high admission ASPECTS in NCCT. The reasons may be that ASPECTS disregards infarcts in other territories like anterior cerebral artery (ACA) or posterior cerebral artery (PCA). Infarcts in these territories may also cause significant disability. NCCT ASPECTS do not also provide information about ischemic penumbra which may progress into infarct later. Use of newer CT techniques like blood pool imaging in CT angiography or CT perfusion may provide these information.

ASPECTS on CTA-SI

It was universally accepted till few years back that admission CTA improves EIC detection and delineation as compared to NCCT. (46) Thin-cut reconstruction

from CTA source data (CTASI) is a useful tool for imaging assessment of acute stroke, particularly when DWI is not available. (12,46–48) CTA-SI conveniently covers whole brain as opposed to CT perfusion (9) and requires minimal post-processing.(20) CTA-SI have been reported to be more sensitive (70%) as compared to NCCT (48%) in picking up EIC. (10) However, there is pathophysiological difference between hypoattenuation in NCCT and CTASI. NCCT hypodensity reflects more severe injury in terms of reduced proton diffusion/ cytotoxic edema which are irreversible. (49,50) On the other hand CTA-SI hypoattenuation is representative of decrease of blood distribution in the affected territory seen as decreased contrast distribution. (11)

Historically Erica C. S. Camargo et al demonstrated that CTASI compared with NCCT scans, are more sensitive in detecting early irreversible ischemia and more accurate in predicting final infarct volume in 51 patients using 8 slice and 16 slice CT scanners. (10)

Rohit Bhatia et al did a retrospective case analysis of 261 patients from a CTA database at a comprehensive stroke center in Canada (which used MDCT, slice not mentioned). They concluded that CTASI ASPECTS correlates better with baseline stroke severity, predicts final infarct extension better, and independently predicts neurological outcome than non-contrast CT ASPECTS. (51)

Shelagh B. Coutts et al prospectively studied 39 patients with acute ischaemic

stroke with NCCT and CTA-SI ASPECTS and concluded CTA-SI ASPECTS provides extra information to predict final infarct size. They used a multislice CT scanner - slice not mentioned. (11)

Several other studies suggested that CTASI images are volume weighted. A study of 28 patients demonstrated that NCCT, CTA-SI, and CBV maps detect irreversibly damaged brain tissue whether or not having reperfusion. (9) Lev et al (48) showed CTASI had good correlation with final infarct volume even in after early recanalization. Even American Heart Association Guidelines mentioned that CTASI represents a qualitative CBV map giving information about infarct core. (20)

CTA-SI in MDCT- volume weighted or flow –weighted?

As discussed above, CTA-SI ASPECT score on earlier generation CT scanners correlated better than NCCT with the final infarct size (infarct size on follow-up NCCT/ DWI). Extent of abnormality in baseline CTA-SI was shown to reflect final infarct size even after a successful recanalization. (48) Based on these studies CTA-SI was recommended for less experienced interpreters to determine final infarct size when DWI was not available. (10,11,47,52,53)

CTASI changes in acute ischemic stroke were said to reflect CBV,(11) not cytotoxic edema which was the basis of NCCT changes.(47) It is a consensus now-a-days that NCCT, CBV and CTASI changes are irreversible.(9) However, stroke neurologists and neuroradiologists often observed in clinical practice that the extent

of abnormality in CTASI is more than CBV changes and almost like CBF abnormality.

M. Sharma et al (14) retrospectively studied Sixty-four consecutive patients with anterior circulation stroke symptoms on a 64-section CT scanner (Lightspeed VCT; GE Healthcare, Waukesha, Wisconsin) to correlate Plain CT and CTASI abnormalities with CBF and CBV maps. Based on their hypothesis CTASI would reflect CBF rather than CBV in a 64-slice CT. These investigators found strong correlation between plain CT and CBV and CTASI and CBF. Positive outliers of CTASI in this analysis had severe infarct with poor ASPECTS in most of the cases. These findings were important because if CTASI was used to represent infarct core in modern scanners, infarct core might have been overestimated. This might have resulted in some patient not receiving thrombolysis who were otherwise eligible for it.

The reason of CTASI reflecting CBV was mentioned by earlier studies was a steady state between arterial and tissue contrast achieved at the time of the scan.(54–56) Longer scanning time, slower contrast injection and more prep delay facilitated more blood volume weighting.(56) But the steady-state theory does not apply to latest faster multislice CTA protocols. Newer faster MDCT scanners using a contrast injection rate of 5-7 mL/sec and prep delay of 15-20 sec make CTASI images more flow -weighted.(57)

Yoo et al studied 48 AIS patients within 9 hours of symptom onset. They used a faster acquisition protocol in an MDCT machine (slice not mentioned). CTASI significantly overestimated the infarct core as compared to concurrent DWI in ~25% of cases. NIHSS score >14 and Reduced collaterals predicted major CTASI overestimation. They suggested further studies to determine whether CTASI becomes CBF weighted using a faster scan protocol. (58)

Pulli et al analyzed CTASI in 100 patients with acute ischemic stroke using 2 different acquisition protocols with close follow-up DWI. Initially in their institution patients underwent CTA in a 4 or 16 slice CT with fixed delay after contrast injection. After new protocol of bolus tracking was introduced, subsequent patients underwent CTA using faster scan protocol in 64 slice CT. They found that in CTA using older protocol CTA-SI infarct volume correlated well with DWI restriction volume. Later faster acquisition protocol using 64 slice CT caused significant overestimation of concurrent DWI volumes. (59)

Clot burden and Collateral Score in CTA

CTA provides vital information about presence, location and extent of thrombus in intracranial vasculature, presence of vessel pathologies like stenosis, occlusion, dissection or other vessel anomalies and also the amount of collateralization. These information are extremely important in determining the outcome of acute ischemic stroke.

The clot burden score is a 10-point scoring system introduced by Tan et al to define the location and extent of thrombus in proximal anterior circulation. From a total score of 10, 2 points are deducted if thrombus is located in each of the supraclinoid ICA, proximal and distal half of MCA trunk. A score of 1 is deducted in case of thrombus in infraclinoid ICA, ACA and for each of M2 branch. A score 10 means no clot while a score 0 means complete vessel occlusion involving multiple segments. (60)

The collateral score, also devised by Tan et al, is given on a scale of 0–3, 0 indicating no collateral supply in the occluded MCA territory; 1 indicating collaterals filling <50% but >0% of the occluded MCA territory; 2 indicating >50% but <100% collateral supply and 3 indicating 100% collateral supply of the occluded MCA territory. Later other collateral scoring systems have been suggested but aforementioned scoring is the simplest one and easy to use in clinical practice.(60)

CT perfusion Imaging

CTP in acute stroke imaging was first used by Axel in 1980 (61); however, the old generation CT scan was not fast enough to provide images that would have practical implication. Later the technique was developed with advent of newer machines and automatic injectors.

CT perfusion imaging attempts to detect capillary level blood flow. It has several parameters, including cerebral blood flow (CBF), cerebral blood volume (CBV), mean transit time (MTT), Time to peak (TTP), arterial time delay, T_{max} etc.

CBV is defined as the total volume of blood in a given volume of brain tissue, with units of mL of blood per 100 g of brain tissue. CBF is defined as the amount of blood flowing through a given volume of brain tissue per unit time, with units of mL of blood per 100 g of brain tissue per minute. MTT is defined as the average transit time of blood through a given volume of brain tissue, measured in seconds. MTT can be represented by the following equation: $MTT = CBV / CBF$. TTP is defined as the time required from the beginning of contrast injection to achieve maximal enhancement measured in seconds. T_{max} is usually obtained by deconvolution analysis of the CTP source data. (57)

Infarct "Core" is defined as the CBV lesion volume, and "penumbra," as the MTT or CBF lesion volume.(62) "Mismatch" is defined as the difference between CBV-CBF or CBV-MTT.

In acute infarction, irreversibly damaged tissue show matched areas of reduced CBF and CBV with raised MTT. This configuration suggests irreversible brain damage or infarct core. (63)

In several studies correlating CTP with DWI, severe decreases in CBV are particularly sensitive and specific for defining the extent of unsalvageable

core.(12,64–66) Again, areas that show decreased CBF with maintained CBV indicate potentially salvageable tissue or penumbra. Such areas may also show prolonged MTT.(67,68) Window for intravascular therapy can be extended with the identification of substantial penumbra. (64,69–71) Sometimes there is another area usually outside penumbra which shows maintained CBV, normal or slightly reduced CBF, slightly increased MTT and TTP. This type of tissue recovers even without therapy and thereby is of not much clinical importance. This type of finding is known as benign oligemia.

So core means the area that is destined to die, penumbra can be saved by therapeutic intervention whereas benign oligemia is destined to recover.

Perfusion CT increases diagnostic accuracy in the setting of AIS by both experienced and inexperienced readers. In a study, review of CTP caused a 4-fold increase in diagnostic accuracy of acute stroke among inexperienced readers. (72)

Perfusion CT is not free of caveats requiring attention: extra radiation dose, extra contrast dose, extra expenditure and most precious time required for image acquisition, processing, and interpretation.

MRI in Acute Stroke

MRI can be used to complement NCCT, particularly in detection of early ischaemic change and identification of small infarcts when CT is normal and to detect infarcts in posterior fossa as evaluation is restricted in NCCT due to beam

hardening artefact. MRI has the advantage of better anatomic detail and no ionizing radiation. However, it is expensive, not readily available and more time-consuming.

The most important MRI sequence in the imaging of acute stroke is diffusion-weighted imaging (DWI).(73,74) Improved sensitivity of DWI over NCCT have been previously reported by Fiebach et al.(75) Another study (76) compared NCCT and DWI ASPECT scores to detect early ischaemic changes in patients with acute stroke of less than 6 hours' duration. They found NCCT and DWI to be comparable for detecting and quantifying these early changes. However ASPECT scores with DWI found to be lower indicating DWI more sensitive than NCCT.

DWI measures of Brownian motion of water molecules. The rapid disruption of the NA^+/K^+ pump and intracellular water molecule influx causing cytotoxic edema results in a restriction in hydrogen (H^+) ion diffusion and thereby a low apparent diffusion coefficient (ADC), seen as dark area on the ADC map and bright area on DWI map.(77,78) DWI acquisition time is less than 1 min on most 1.5 Tesla MR systems.(79) However, Diffusion restriction can also be seen in other conditions including haemorrhage, encephalitis, cerebral abscess, highly cellular tumors such as lymphoma or medulloblastoma, sometimes in active demyelination and in post-ictal phase. Clinical history review and lack of conformation to a vascular territory clinches the diagnosis.

Other MR sequences can provide useful additional information. T2 and fluid attenuation inversion recovery (FLAIR) images offer increased sensitivity and specificity to detect the same early changes as detected on the NCCT.(80) Cytotoxic edema results in T2 hyperintensity and loss of grey matter/ white matter differentiation. Thrombus in the arteries as well as flow stagnation distal to the clot are seen as loss of normal arterial flow voids or hyperintense vessels in FLAIR.(80) However, T2 hyperintensity usually develops after several hours and cannot be relied upon in acute setting. Changes in FLAIR images are seen much earlier (even within 3 hours) than in T2 images. (81,82)

Gradient-refocused echo (GRE) imaging is highly sensitive for identifying microscopic and macroscopic hemorrhage because of its susceptibility to paramagnetic effect of deoxyhemoglobin.(83) However, calcification and bleed cannot be distinguished by GRE. Susceptibility weighted imaging (SWI) allows differentiation of hemorrhage and calcification by PHASE images with high sensitivity and specificity to detect foci of micro and macro- hemorrhages. Clot within the artery produces blooming in SWI with apparent increase in diameter of the artery (Susceptibility sign/ susceptibility vessel sign).(84)

Magnetic resonance angiography (MRA) allows noninvasive vessel assessment. Two principal techniques at our disposal are time-of-flight (TOF) and contrast-enhanced MRA (CEMRA).(20) TOF-MRA is usually adequate to delineate

large-vessel occlusion. However, because of its lower spatial resolution, depiction of distal vessels is inferior as compared to CTA. A fairly good assessment of neck vessels is also possible. Commonly done sequences for acute stroke are axial FLAIR, DWI, SWI/ GRE and MRA. MRI is fairly accurate to detect cervical dissection and findings include visualization of an intimal flap, absence of normal flow void, intraluminal T1 hyperintensity due to stasis, and classical flame shaped tapering of the vessel on MRA.(85)

Importance of the Current Study

From the above discussion it is evident that multiple imaging modalities are available for evaluation of acute ischemic stroke. CT scan is definitely the first line investigation and a number of techniques are available for CT interpretation. ASPECTS is the most useful technique in terms of clinical utility. So it is very important to know how the ASPECTS behave in modern CT scanners which are abundant now-a-days. Our study aimed to determine the ability of CTASI in a 256-slice CT to predict final infarct size as compared to NCCT. This study is expected to have a significant impact on the traditional imaging practice of acute ischemic stroke.

Materials & Methods

STUDY DESIGN:

Prospective observational study.

STUDY PERIOD:

2 years (August 2013 to August 2015).

STUDY POPULATION:

Total 105 consecutive cases were included in the study within the above time period.

PARTICIPANT SELECTION:

All consecutive acute ischemic stroke patients who presented within 8 hours of symptom onset and underwent NCCT and CT angiography as per clinical necessity, were included in the study.

Informed consent were taken from the close relative of the patient as per routine departmental practice for CT in acute stroke patients, as most of these patients were not able to give consents themselves due to their condition.

Data from 105 consecutive patients were collected throughout the data collection period and analyzed.

Consecutive patients who fulfilled inclusion criteria were recruited, irrespective of their age or sex.

Inclusion and exclusion criteria were as follows:

Inclusion criteria:

Admission to the emergency department with signs and symptoms suggesting acute anterior circulation stroke within 8 hours of symptom onset.

Exclusion criteria:

1) Evidence of intracerebral hemorrhage on the admission NCCT.
2) Conditions which would contra-indicate the routine use of CT contrast agent eg. Allergy, renal failure etc.
3) Poor quality CT scan due to patient movement or other technical factors.
4) Anterior cerebral artery (ACA) territory strokes.
5) Patient who could not undergo follow up imaging between 24-48 hours due to various reasons.

PROCEDURE:

Once the Informed Consent process was completed, the principal investigator collected, stored, and analyzed the data according to the following procedure:

- Informed Consent
- CT scanning were performed on a Philips 256-section iCT scanner (as per routine departmental protocol in these cases).

NCCT protocol- NCCT were performed with a multislice CT scanner using following parameters:

- 120 kV, 350 mAs.
- 5-mm slice thickness.
- Coverage is from skull base to vertex with contiguous axial slices parallel to the inferior orbitomeatal line.

CTA Protocol-

- Scanned from arch of aorta to vertex.
- 50 mL of nonionic contrast into an antecubital vein (18 G cannula) @ 5 mL/s followed by 40 mL saline chaser at 5mL /s.
- Bolus tracking technique is used, with tracker in the proximal DTA, threshold of 150HU and pre scan delay of 5 sec after attainment of threshold.

- Parameters used are 120 kV, 400 mAs; 0.9mm thickness and 0.45 mm increment, gantry rotation time 0.5sec, pitch <1

CT Perfusion Protocol-

- 50 mL nonionic contrast @ 5 mL/s → saline chaser 20 mL @5 mL/s.
- At 5 seconds into the injection, start cine scan.
- 80 kV, 100–120mA, 40 cycles x1.5sec= 60sec .
- After the initial 60 second cine scan, 6 more cycles with cycle time 30sec, for an additional 180 sec.
- Total acquisition time of 240 sec.

Radiation dose-

- NCCT: 953 mGy cm ~ 2.2mSv
- CT Angio: 25O2 mGy cm ~5.8mSv
- CT Perfusion: 1151 mGy cm ~ 2.6mSv
- Total: ~11 mSv
- Clinical management of patients and treatment algorithms were not affected by the study.
- For all patients presenting with the time period of 0-8 hours, NCCT and CTA were performed and ASPECTS will be calculated.
- CT perfusion study were performed in selected cases as per institute protocol

(clinical and radiological consensus on which patients require CT perfusion). CT perfusion parametric maps were obtained.

- Follow up MR/CT were done to look for final infarct size between 24-48 hours (again as per institute protocol). FU DWI were done in a Siemens 1.5T MRI machine.
- All images were interpreted separately by two radiologists (one having 7 years and other having 8 years of experience) who were blinded to the clinical data apart from the side of involvement. Both the radiologists had 1.5 years of experience in dedicated stroke imaging.
- Images from NCCT, CTA-SI and follow up imaging of each patient were interpreted at an interval of at least one week in between images, with randomization of images for interpretation done by a CT technologist who was part of the study group.

DATA ANALYSIS:

Data were not analyzed to understand gender, caste, class, ethnicity, race differentials, but merely to see the applicability of the proposed method to future cases of acute stroke.

ASPECTS of NCCT and CTA-SI were compared with ASPECTS of 24-48 hour CT/DWI. The study population were divided into two groups- those receiving

therapy and those not receiving therapy. Data analyses were done separately in these two groups. In a subgroup analysis, correlation studies were done between NCCT, CTA-SI and CT perfusion parameters.

i. Patient data were filed in separate cabinets and were never disclosed outside of the clinician's necessitation for treatment and follow-up.
ii. Since the data analyzed were same as which is routinely collected for clinical purposes, its use were limited to the same.

STATISTICAL ANALYSIS:

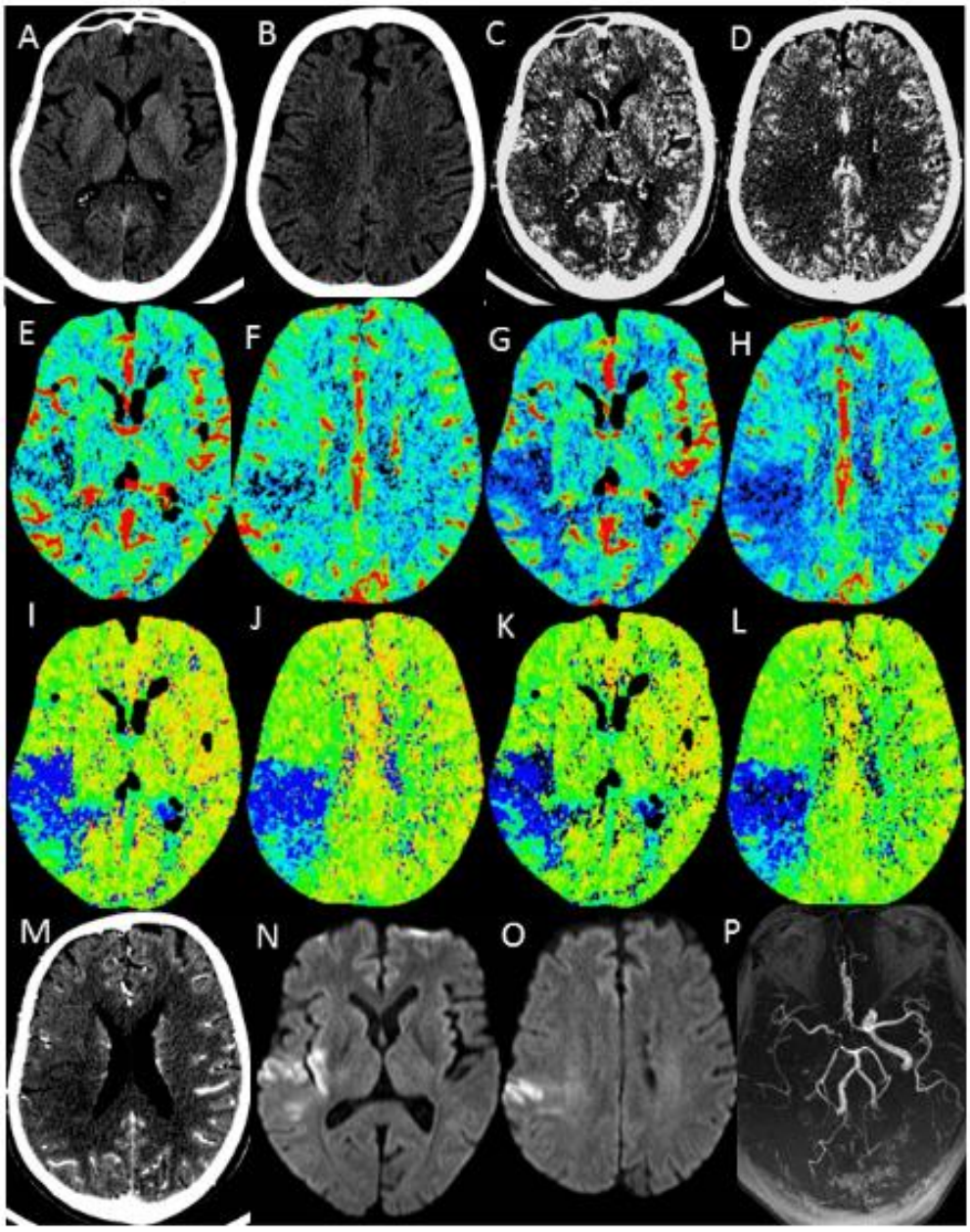
Statistical analyses were done in consultation with two professional statisticians who have experience in statistical analysis of clinical studies. SPSS version 22 was used for all statistical analyses.

- Patients' clinical data were represented using percentages, mean± 2SD, median values and percentiles.
- Wilcoxon Signed Ranks test was performed to find whether any statistically significant difference existed between the ASPECT scores of the two raters.
- Two raters' scores were also correlated using Spearman Rank Correlation.
- Once it was found that two raters' observation had good correlation and no statistically significant difference, unified ASPECT scores were created for each study accepting the lesser score of two raters.

- Spearman Rank Correlation and simple linear regression analyses were performed between NCCT and FU ASPECTS and CTASI and FU ASPECTS.
- Among 25 patients who underwent CT perfusion, Spearman Rank Correlation analyses were done between NCCT and CTP parameters and CTASI and CTP parameters.
- Patients were divided into two subgroups according to who did and did not receive thrombolysis and Spearman Rank Correlation analyses of NCCT with FU ASPECTS and CTASI with FU ASPECTS were done separately in these two groups.
- Correlation and regression analyses were done separately for subgroups according to time of CT scan after symptom onset.

Representative Cases

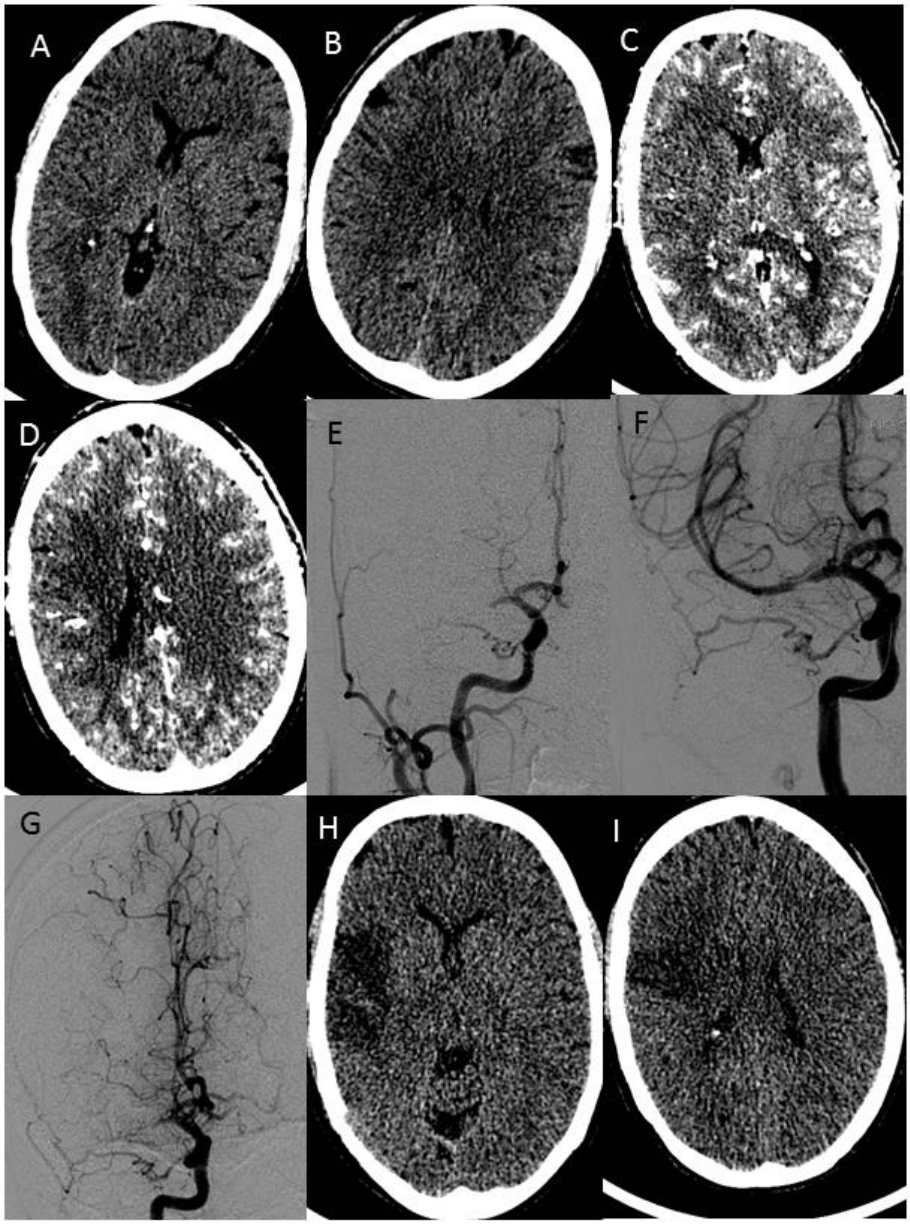
Case 1



A 68-year-old male patient presented with left sided weakness, facial deviation and dysarthria within 2 hours of symptom onset (wake up). NIHSS on admission was 7 and MRS was 4. NCCT (A & B) showed right MCA infarct with

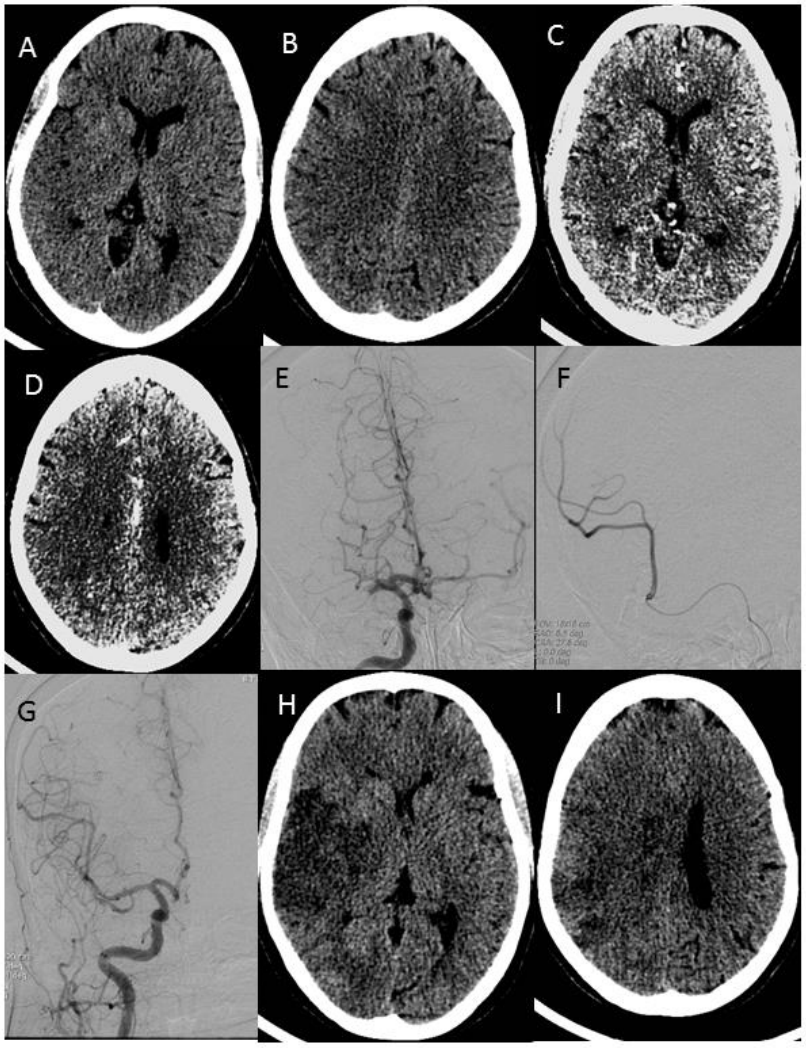
ASPECTS 8 (Insula and M5 involved). CTASI (C & D) showed ASPECTS 5 (M2, M3, M5, M6 and insula). CBV (E & F) ASPECTS was 7 (M2, M5 and insula), CBF (G & H), MTT (I & J) and TTP (K & L) ASPECTS were 5 (M1, M3, M5, M6 and insula). MIP image (M) showed a collateral score of 1 (<50%). Follow up DWI after 24 hours showed involvement of M2, M5 and insula which correlated with CBV (ASPECTS 7). CTASI overestimated the infarct and correlated with CBF, MTT and TTP. TOF MRA (P) showed right ICA occlusion. Patient did not undergo thrombolysis because of wake up stroke.

Case 2



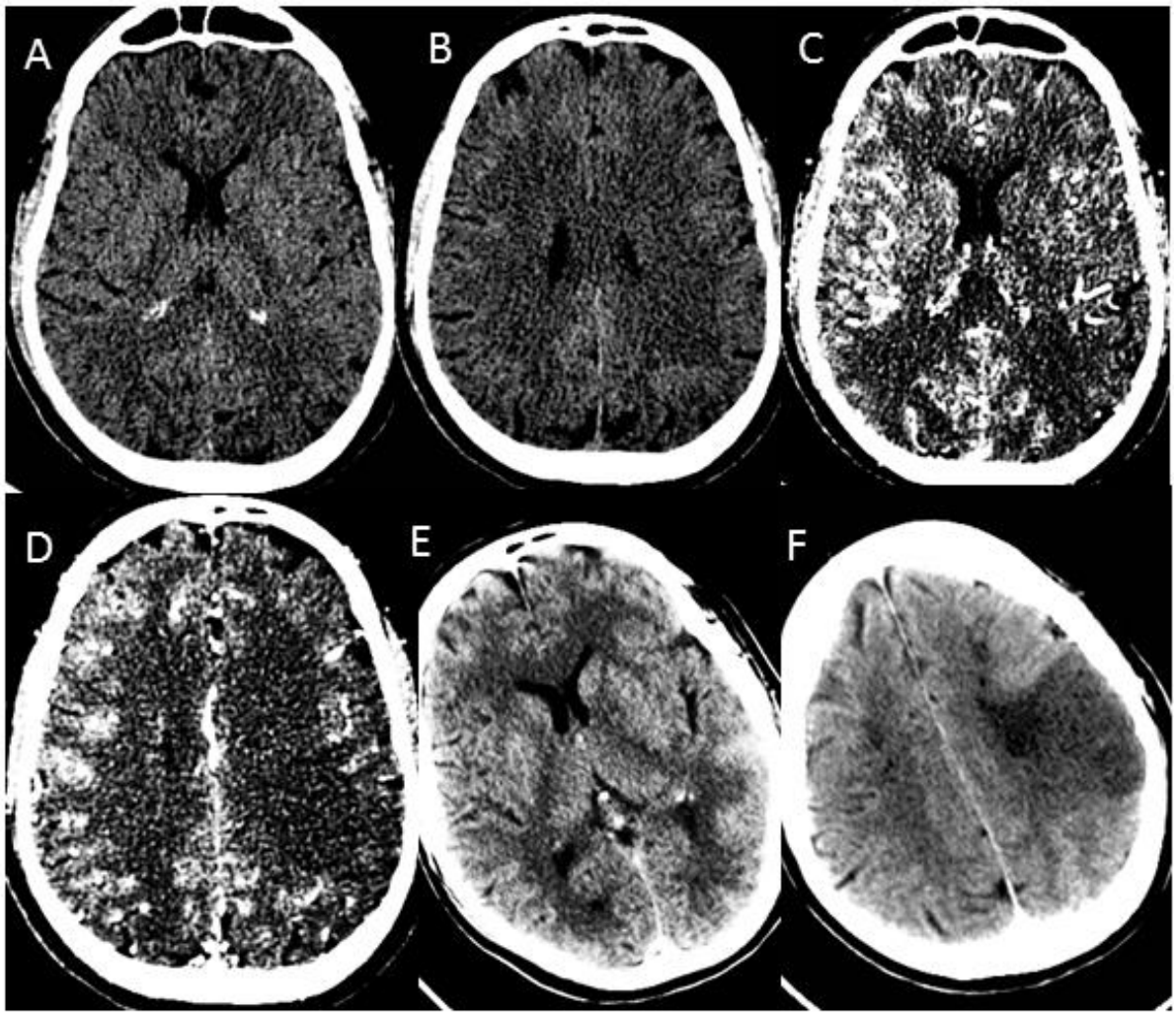
A 29-year-old female patient with history of rheumatic heart disease presented with left sided weakness, facial deviation and dysarthria within 3 hours of symptom onset. NIHSS on admission was 5 and MRS was 2. NCCT (A & B) showed right MCA infarct with ASPECTS 8 (Insula and M2 involved). CTASI (C & D) showed ASPECTS 3 (M2, M4, M5, caudate, lentiform, internal capsule and insula). As patient was on anticoagulation, she was taken for mechanical thrombectomy directly without bridging thrombolysis. DSA revealed right M1 MCA occlusion (E). Solitaire FR stentriever was deployed across the thrombus (F). However, post-procedure angiogram revealed TICI0 recanalization (G). Follow up CT after 24 hours (H & I) revealed infarct in M2, M5 and insula (ASPECTS 7). Significant overestimation of the infarct was seen by the initial CTASI.

Case 3



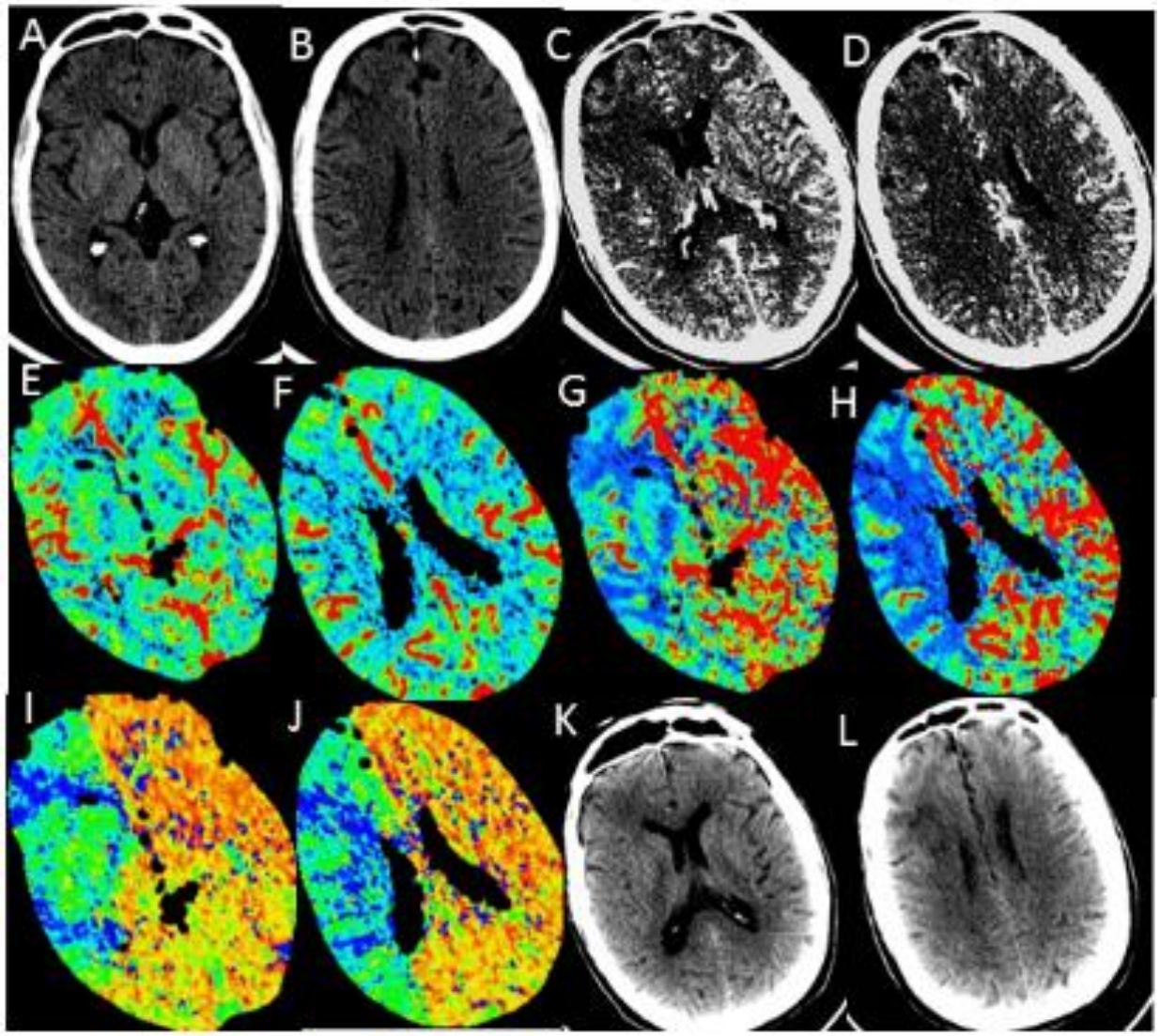
A 44-year-old female patient presented with left hemiparesis, hemisensory loss, hemianopia, dysarthria and facial deviation within 3 hours of symptom onset. NIHSS on admission was 14 and MRS was 4. NCCT (A & B) showed right MCA infarct with ASPECTS 5 (M2, M5, lentiform, internal capsule and Insula). CTASI (C & D) showed similar areas of involvement, ASPECTS 5. Patient underwent bridging thrombolysis followed by mechanical thrombectomy. DSA revealed right M1 MCA occlusion (E). Lesion was crossed with Rebar microcatheter (F) and Solitaire FR stentriever was deployed across the thrombus. Post-procedure angiogram revealed TICI3 recanalization (G). Follow up CT after 24 hours (H & I) revealed infarct in similar areas as initial NCCT and CTASI (ASPECTS 5). No overestimation was noted by CTASI in this case.

Case 4



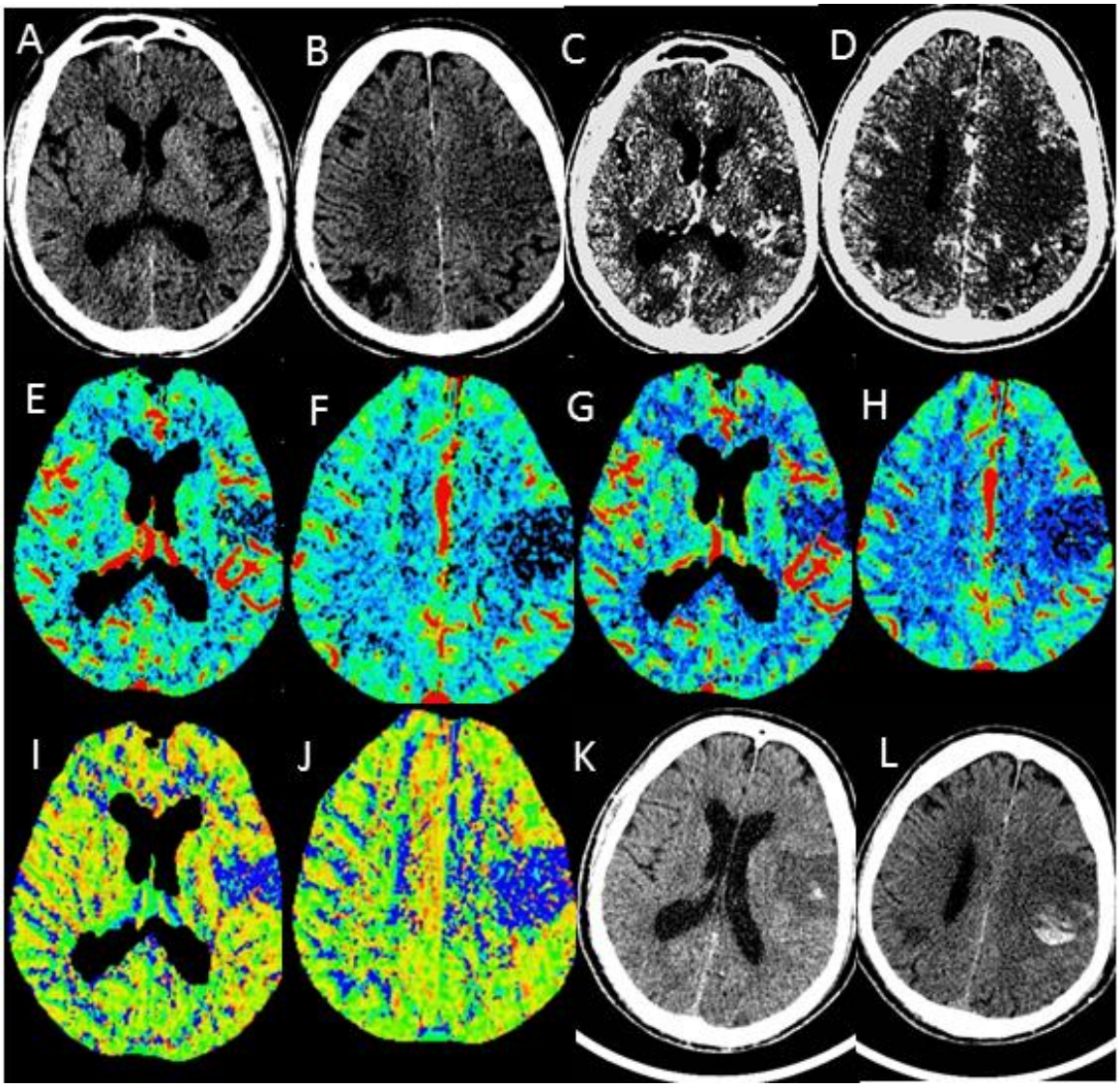
A 57-year-old male patient presented with right hemiparesis, hemisensory loss, hemianopia, dysarthria and facial deviation within 3 hours of symptom onset. NIHSS on admission was 9 and MRS was 4. NCCT (A & B) showed no evidence of infarct in left hemisphere (ASPECTS 10). CTASI (C & D) global decrease in enhancement in left MCA territory, ASPECTS 0. Patient underwent IV thrombolysis 200 minutes after symptom onset. Follow up CT after 24 hours (E & F) revealed infarct in left M5 and M6 areas (ASPECTS 8) with HI1 hemorrhagic transformation. Gross overestimation of infarct size was noted by initial CTASI in this case.

Case 5



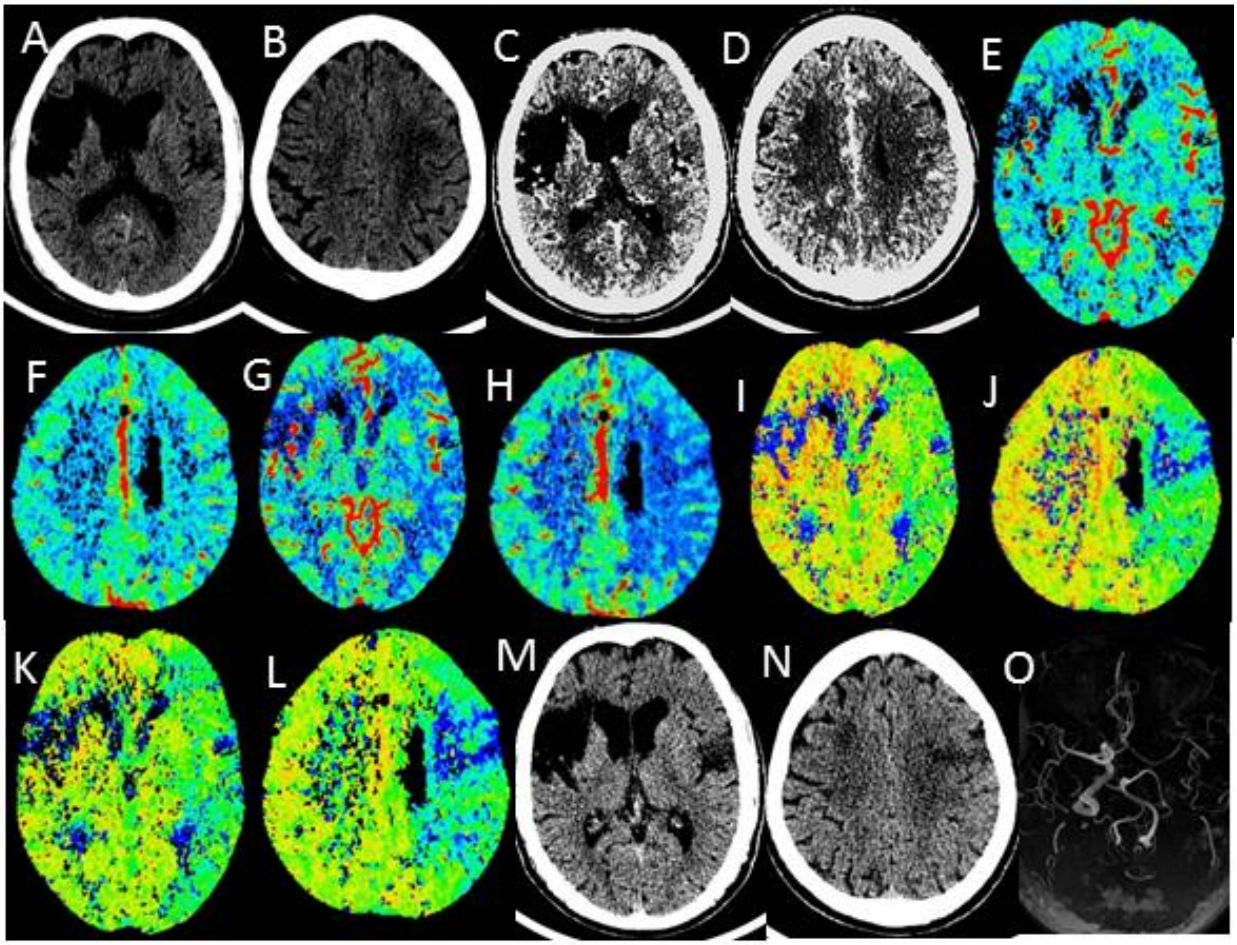
A 55-year-old male patient with history of rheumatic heart disease presented with left sided weakness, hemianopia, facial deviation and dysarthria within 3 hours of symptom onset (wake up). NIHSS on admission was 10 and MRS was 4. NCCT (A & B) showed right MCA infarct with ASPECTS 9 (M4 involved). CTASI (C & D) showed ASPECTS 1 (only M3 spared). CBV (E & F) ASPECTS was 9 (M4 involved), CBF (G & H), MTT (I & J) and TTP (not shown) ASPECTS were 1 like CTASI (M3 spared). Follow up CT after 24 hours (K & L) showed involvement of right M4 only (ASPECTS 9). CTASI overestimated the infarct and correlated with CBF, MTT and TTP. Patient did not undergo thrombolysis because of wake up stroke.

Case 6



A 69-year-old male patient presented with right sided weakness, aphasia and facial deviation 5 hours after symptom onset. NIHSS on admission was 21 and MRS was 5. NCCT (A & B) showed left MCA infarct with ASPECTS 6 (M2, M5, insula, lentiform). CTASI (C & D) showed ASPECTS 6 with involvement of similar areas. CBV (E & F), CBF (G & H), MTT (I & J) and TTP (not shown) ASPECTS were 6 (M2, M5, insula, lentiform) with no mismatch. Patient did not undergo thrombolysis as patient came outside window period for IV thrombolysis. Follow up CT after 24 hours (K & L) showed infarct in right M2, M5, lentiform and insula with PH1 hemorrhagic transformation. In this case both NCCT and CTASI correlated with final infarct size and there was no penumbra as per CT perfusion.

Case 7



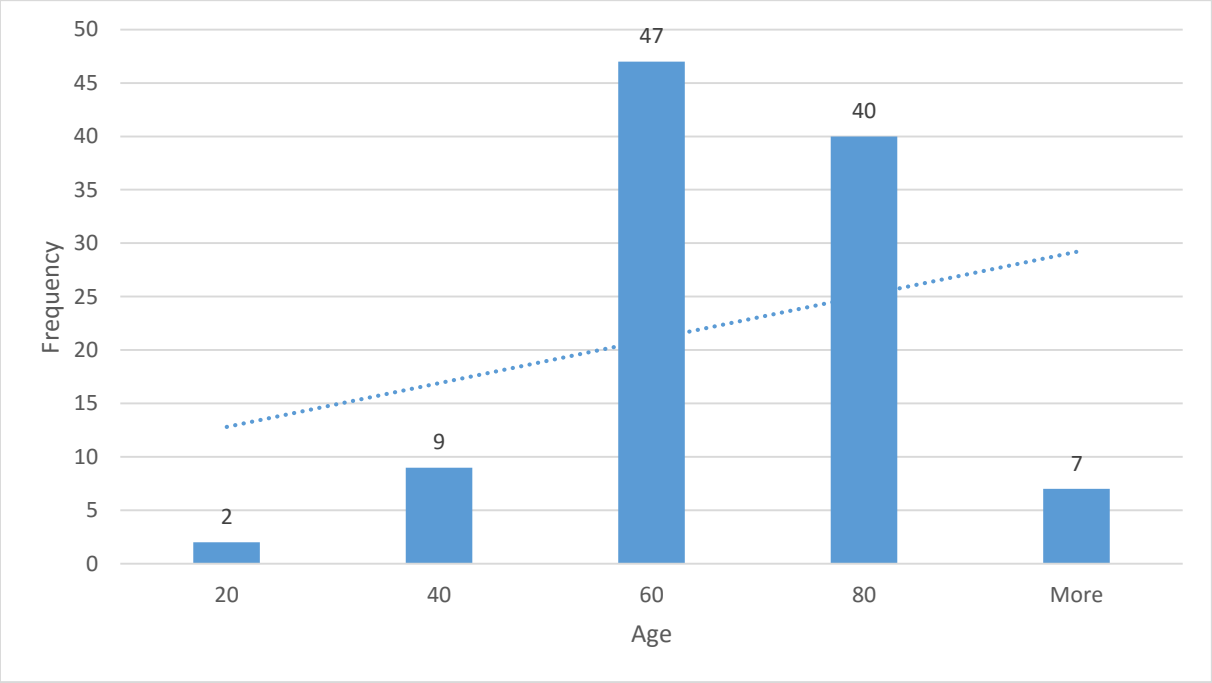
A 68-year-old male patient presented with right sided weakness, hemianopia, aphasia and facial deviation 3 hours after symptom onset (wake up). NIHSS on admission was 12 and MRS was 4. NCCT (A & B) showed left MCA infarct with ASPECTS 8 (M2 & M5). CTASI (C & D) showed similar ASPECTS (8) as NCCT with involvement of similar areas. CT perfusion showed CBV (E & F) ASPECTS of 8 similar to NCCT and CTASI. However CBF (G & H) ASPECTS was 3 (Internal capsule, caudate and lentiform spared); MTT (I & J) and TTP (K & L) ASPECTS were 2 (only internal capsule and caudate spared). Patient did not undergo thrombolysis because of wake up stroke. Follow up CT after 24 hours (M & N) showed infarct in left M2 and M5 only (ASPECTS 8) correlating with NCCT, CTASI and CBV. However, CBF, MTT and TTP maps showed larger areas of abnormality. Careful observation revealed only left M2 and M5 areas show significant drop of CBF and significant rise of MTT and TTP (blue areas in the maps) whereas rest of the abnormal areas showed only mild reduction of CBF and mild increase in MTT and TTP (green areas in the map). So these areas might represent benign oligemia creating CTASI- CBF/ MTT/ TTP mismatch. MRA (O) showed left ICA occlusion. Incidentally old right MCA infarct was noted.

Results

A total of 105 consecutive patients presenting with acute ischaemic stroke involving MCA territory were prospectively included in the study over a period of two years.

Clinical Data

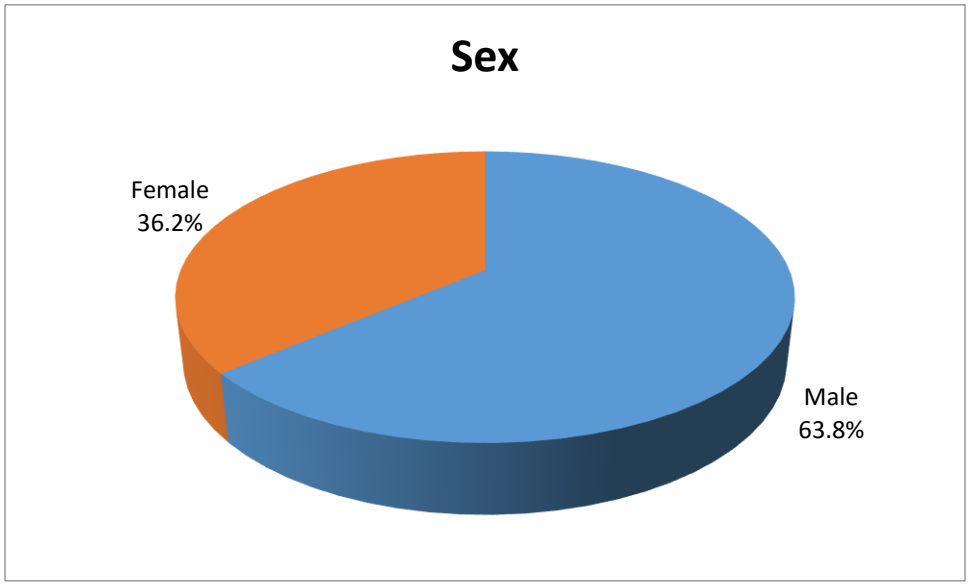
Age distribution:



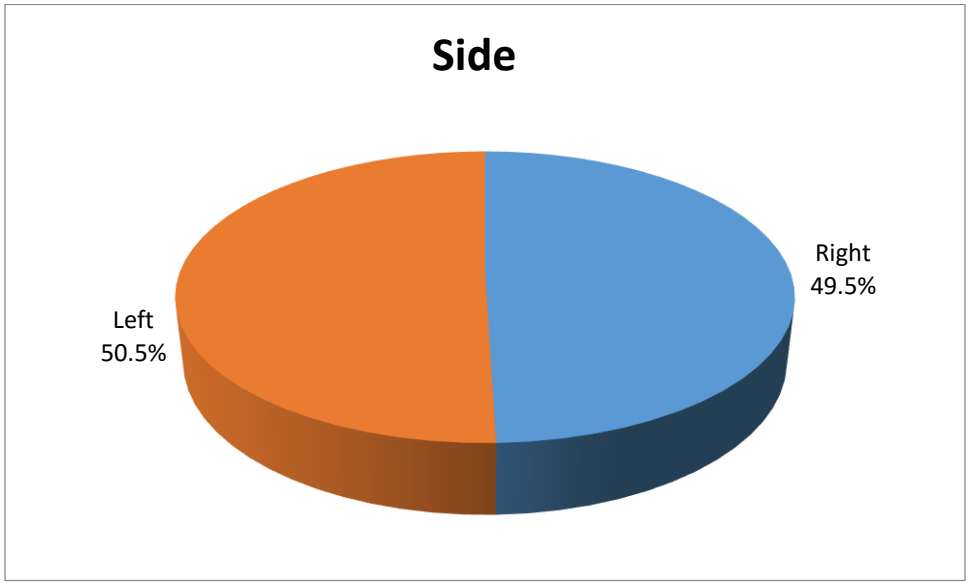
44.8% patients were in 40-60 years age group and 38.1 % patients were in 60-80 years age group. Incidence of young stroke (<40 years) was 10.5%.

Sex Distribution:

There was a male predominance among our study population.



Side of Involvement:

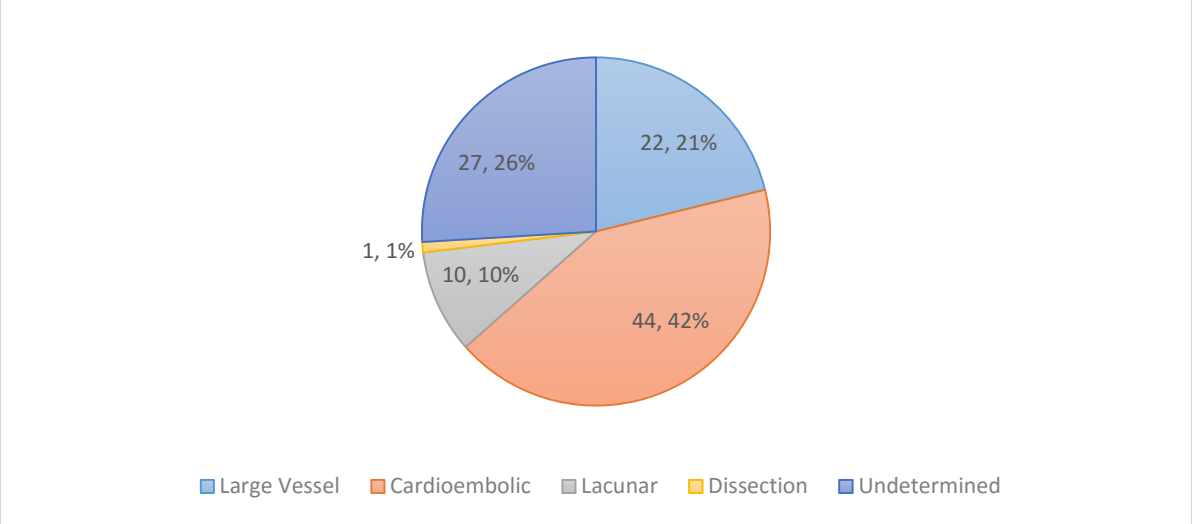


There was an equal distribution among right and left hemispheric strokes.

Clinical Presentation:

There was a considerable overlap of clinical symptoms among our patients. Most of them presented with multiple symptoms. Most common clinical presentation in this cohort was weakness (97%) followed by facial deviation (87%). Next common symptoms were dysarthria (57%), hemianopia (55%) and aphasia (46%) in descending order. Only 28% patients presented with sensory symptoms.

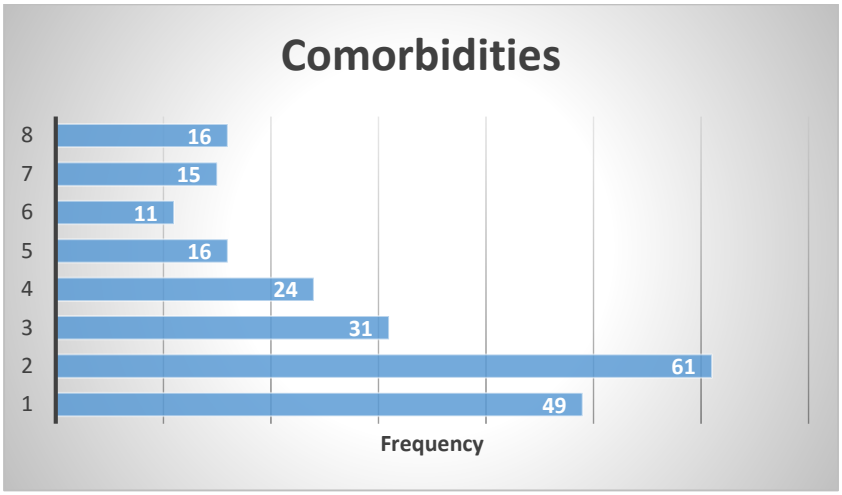
Stroke Subtype:



Most of the patients were having cardioembolic stroke (44.2%). Next most common etiology was large vessel atherosclerosis (22.2%). In 27.3 % cases stroke etiology was undetermined. 10.1 % patients presented with lacunar stroke. Only one patient presented with ICA dissection.

Comorbidities:

Most common associated comorbidity was found to be hypertension (58%) followed by diabetes mellitus (47%). 29.5% patients were having associated coronary artery disease.

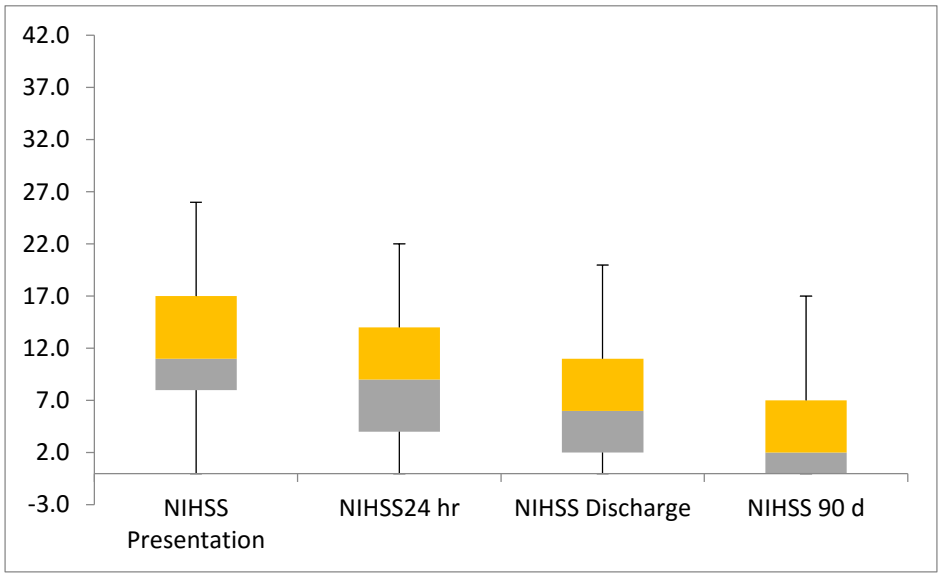


Legend: 1- Diabetes Mellitus, 2- Hypertension, 3- Coronary artery disease, 4- Smoking, 5- Prior Stroke, 6- Transient ischaemic attack, 7- Valvular heart disease, 8- Atrial fibrillation

NIHSS Score:

	NIHSS Presentation	NIHSS24 hours	NIHSS Discharge	NIHSS 90 days
N	103	101	99	84
Mean	12.5	9.1	6.8	4.3
SD	5.4	6.0	5.4	5.0
Minimum	0.0	0.0	0.0	0.0
25th percentile	8.0	4.0	2.0	0.0
Median	11.0	9.0	6.0	2.0
75th percentile	17.0	14.0	11.0	7.0
Maximum	26.0	22.0	20.0	17.0

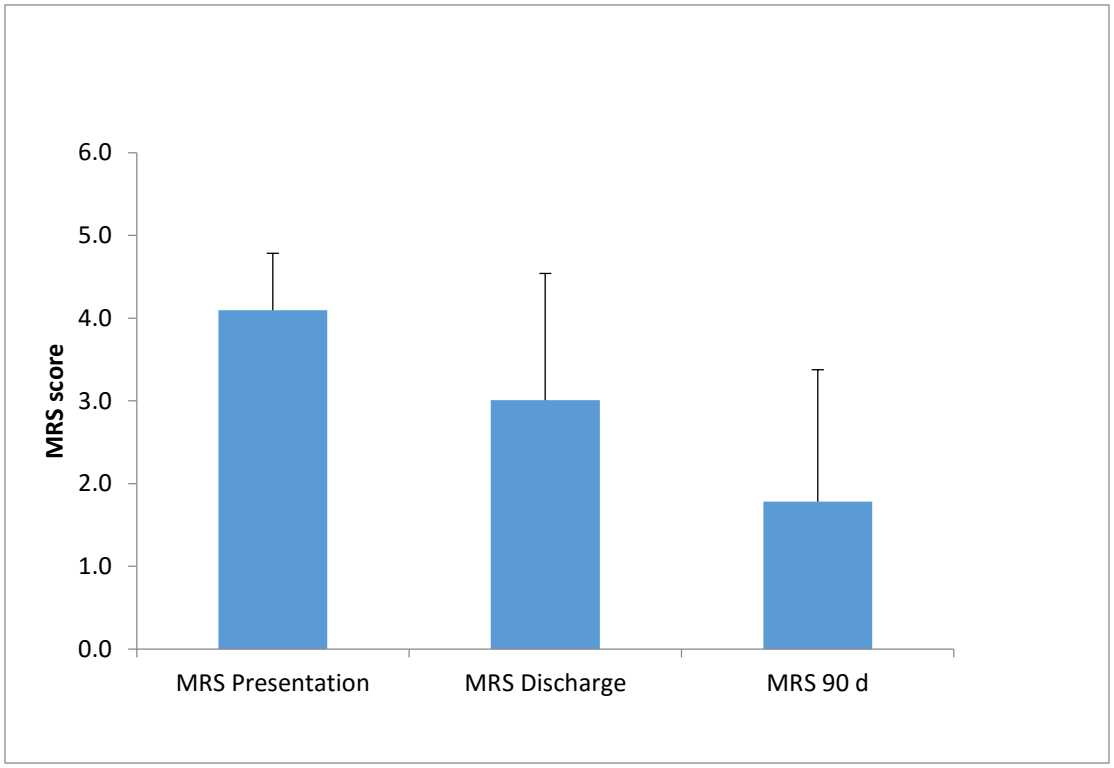
The median NIHSS score at presentation was 11, at 24 hours was 9, at discharge was 6 and at 90 days was 2. Follow up NIHSS at 90 days was available only in 84 patients. Rest of the patients did not appear for follow up/ died (5 patients). The data is represented below in a box plot.



MRS Score:

	MRS Presentation	MRS Discharge	MRS 90 days
N	104	104	83
Mean	4.1	3.0	1.8
SD	0.7	1.5	1.6
Minimum	0.0	0.0	0.0
25th percentile	4.0	2.0	0.0
Median	4.0	3.0	2.0
75th percentile	4.0	4.0	3.0
Maximum	5.0	6.0	4.0

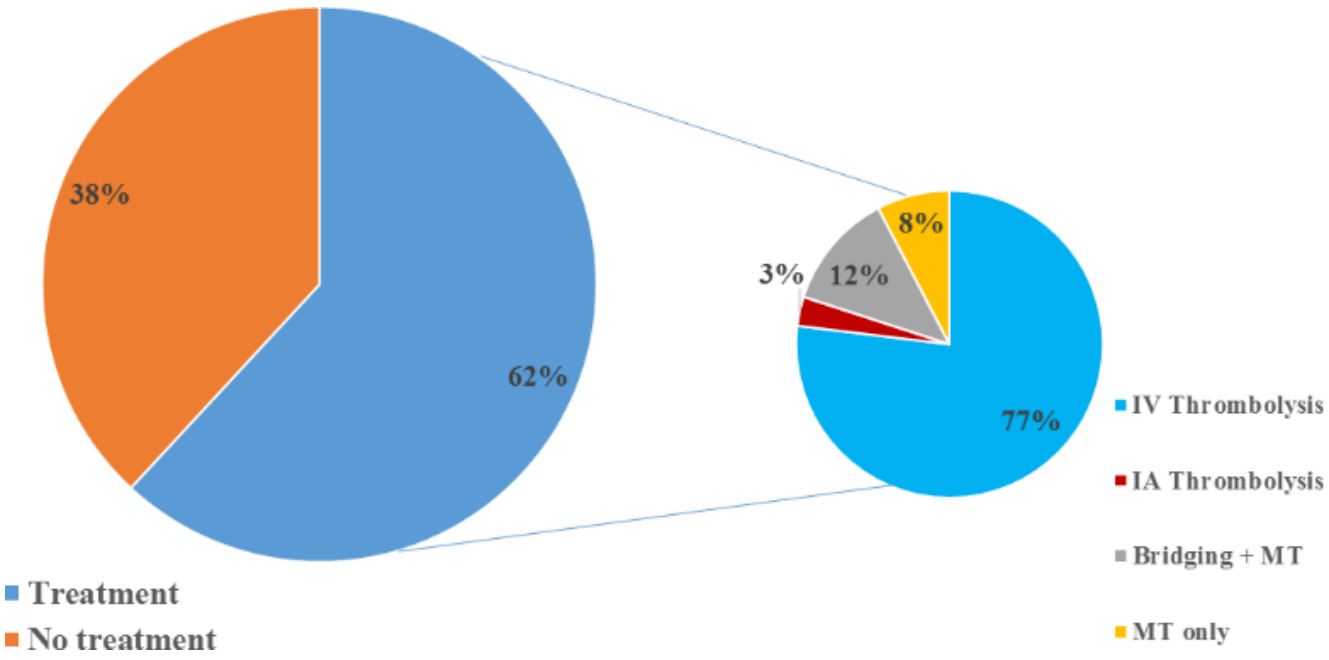
The median MRS score at presentation was 4, at discharge was 3 and at 90 days was 2.



Treatment:

65 (62%) out of 105 patients were offered some form of treatment for recanalization (IV/IA thrombolysis/ Mechanical thrombectomy ± Bridging thrombolysis). Recanalization treatment was not offered in rest of the 40 patients due to lack of indication/ presence of contraindication. Out of these 65 patients receiving treatment, 50 (77%) underwent IV thrombolysis; 2 (3%) patients received IA thrombolysis; 8 (12%) patients received bridging thrombolysis followed by mechanical thrombectomy and 5 (8%) patients received mechanical thrombectomy

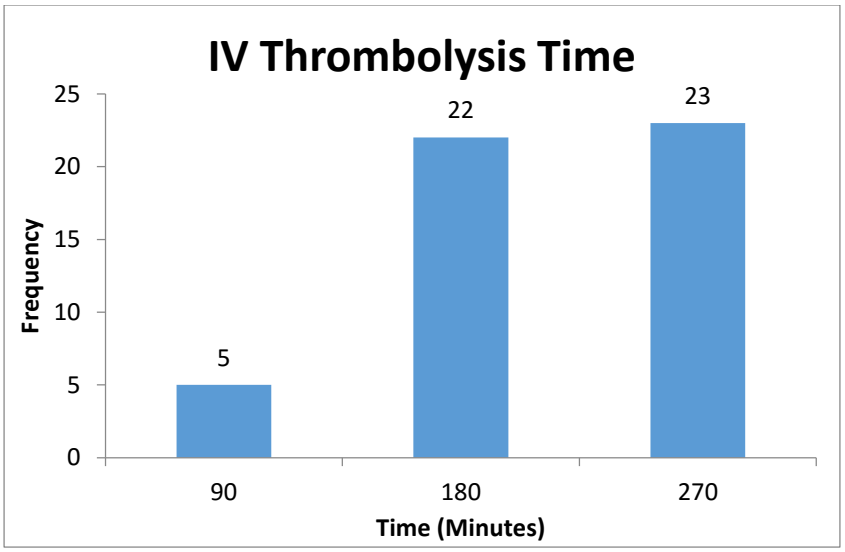
alone. Mechanical thrombectomy was done in solitaire stentriever in 10 cases, Trevo followed by solitaire stentriever in 1 case and Revive stentriever in 2 cases.



Of these 13 cases, TICI 3 recanalization was obtained in 5 cases, TICI 2b in 4 cases, TICI 2a in 1 case and TICI 1 in 1 case. In 2 cases, recanalization could not be achieved (TICI 0).

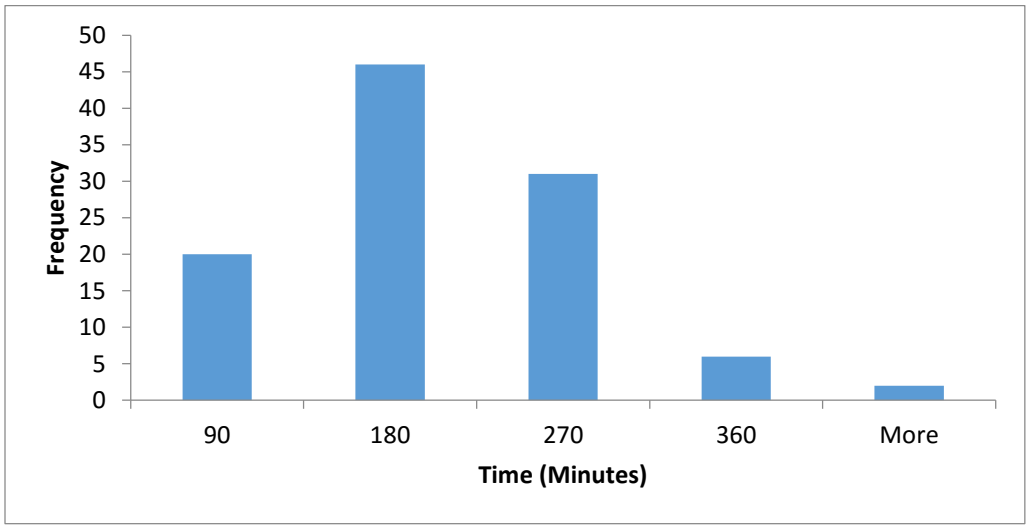
Thrombolysis Time:

Only 5 patients received IV thrombolysis within 1.5 hours of symptom onset, 22 patients received between 1.5- 3 hours. 23 patients received IV thrombolysis in the extended window period (3-4.5 hours).



Imaging Data

Time from symptom onset to CT scan:



CT time (min)	Frequency	Percent
<90	19	18.1
90-180	45	42.9
180-270	32	30.5
270-360	6	5.7
>360	3	2.9
Total	105	100.0

In most (73.4%) of the patients CT scans were obtained within 90-270 minute time period. Only 19 (18.1%) patients had very early CT scan (<90 minutes) whereas 9 (8.6%) patients had delayed (>270 minutes) CT scan.

Vessel occlusion in CT scan:

Plain CT findings of vessel occlusion were detected in total 60 cases (57%). Dense MCA sign was detected in 30.5% cases. An MCA dot sign was detected in 18.1 % of all the cases, whereas only 8.6% cases showed dense ICA sign. Some patients had overlap of these signs.

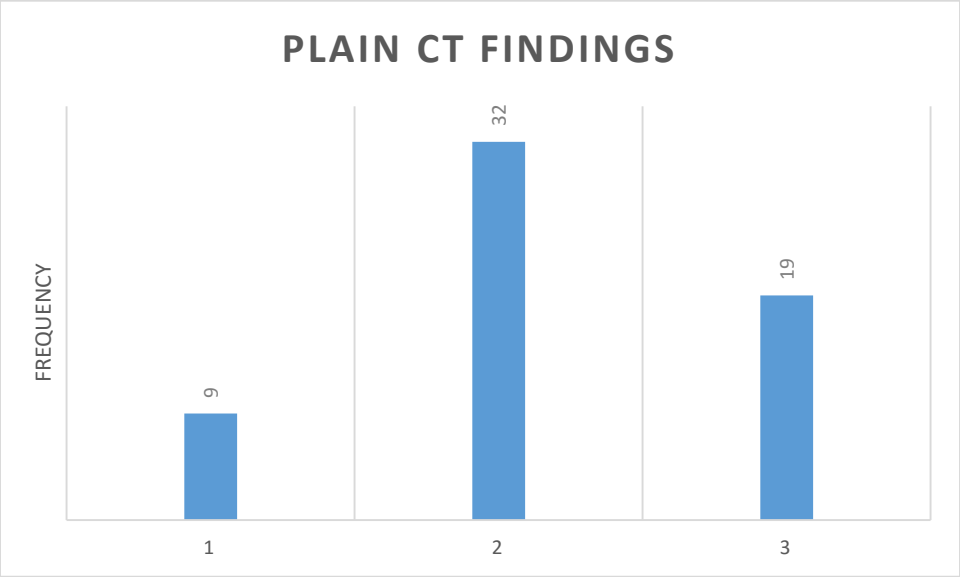
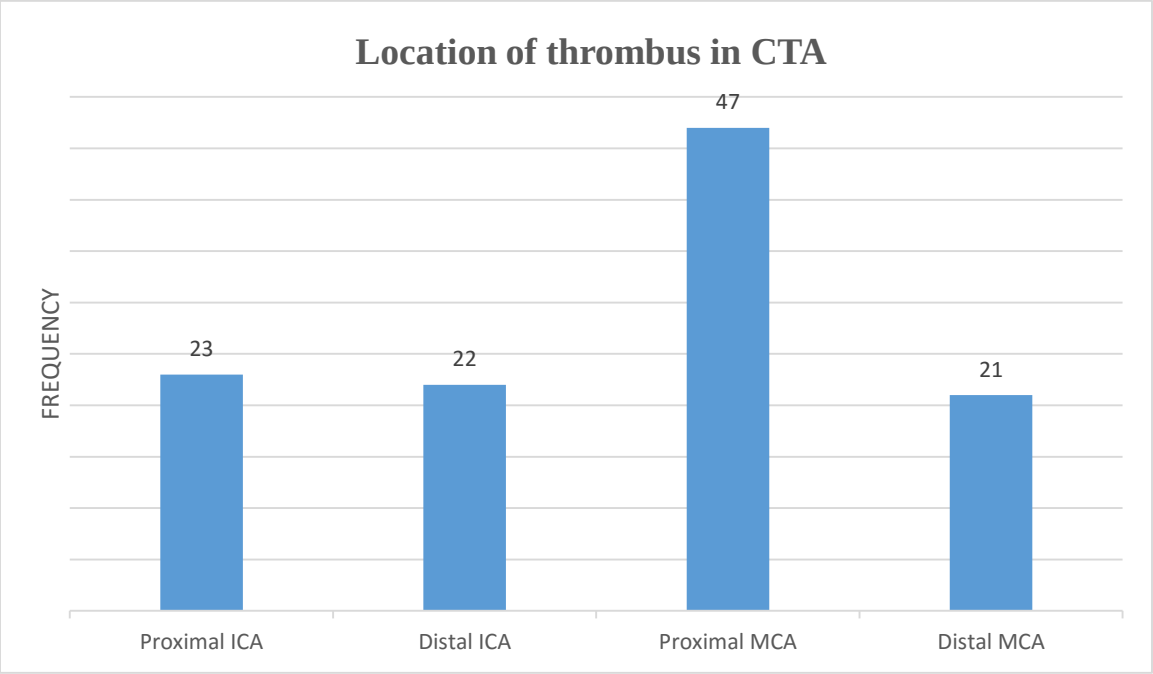


Table legend: 1- Dense ICA, 2- Dense MCA, 3- MCA dot sign.

Vessel occlusion in CT angiogram:

Total 69 (66%) patients were found as having thrombotic vessel occlusion on CTA. 23 (22%) patients had proximal ICA thrombus, 22 (21%) had distal ICA thrombus, 47 (45%) had M1 MCA thrombus and only 21 (20%) patients had

thrombus in M2 MCA and beyond. Many of these patients were having thrombus involving both ICA and MCA at multiple segments.



Correlation of ASPECTS between initial and follow up images

ASPECT scoring of NCCT, CTASI and FU CT/ DWI was done in all the 105 cases by two raters independently. All follow up imaging were done between 24-48 hours after symptom onset. In 90 patients follow up CT was done, whereas DWI was done in rest of the 15 cases. Cerebral perfusion study was done in 25 cases.

Inter-observer variation between rater 1 and rater 2:

To determine whether any statistically significant difference between the scores of two observers exists, we performed a Wilcoxon Signed Ranks Test.

Paired comparison of test score between Rater 1 and Rater 2 (Wilcoxon Signed Ranks Test):	Z	p
NCCT - Rater 1 and Rater 2	0.792	0.428
CTA-SI- Rater 1 and Rater 2	0.582	0.561
CBV- Rater 1 and Rater 2	0.816	0.414
CBF- Rater 1 and Rater 2	0.447	0.655
MTT- Rater 1 and Rater 2	0.816	0.414
TTP- Rater 1 and Rater 2	0.816	0.414
FU- Rater 1 and Rater 2	0.316	0.752

The test revealed that the difference in scoring of the two raters is not statistically significant.

Then we did Spearman Rank Correlation between the scores of the two raters for NCCT, CTASI, CBV, CBF, MTT, TTP and FU ASPECTS.

Correlation between the scores of Rater 1 and Rater 2 (Spearman rank correlation):	Spearman's rho - ρ	p
NCCT - Rater 1 and Rater 2	0.902	<0.001
CTA-SI- Rater 1 and Rater 2	0.935	<0.001
CBV- Rater 1 and Rater 2	0.985	<0.001
CBF- Rater 1 and Rater 2	0.986	<0.001
MTT- Rater 1 and Rater 2	0.986	<0.001
TTP- Rater 1 and Rater 2	0.986	<0.001
FU- Rater 1 and Rater 2	0.960	<0.001

It was seen that the scorings of the two raters correlated very well for all these parameters.

Once it was seen that there is no significant difference in observation among the two raters, lower scores between the two raters were accepted for final analysis for each of the parameters.

Correlation (Spearman) between NCCT and CTASI with FU CT/ DWI:

We performed Spearman rank correlation analysis between NCCT and FU CT/ DWI ASPECTS and CTASI and FU CT/ DWI ASPECTS of all the 105 cases.

Correlation between initial CT and FU CT/ DWI (Spearman rank correlation):	Spearman's rho - ρ	p
NCCT - FU	0.849	<0.001
CTA-SI- FU	0.785	<0.001

NCCT ASPECTS was found to have a better correlation with FU ASPECTS. This indicated that NCCT correlated better with final infarct size that CTASI.

Linear regression between NCCT and FUCT

Then we performed a simple linear regression analysis between NCCT (independent) and FU (dependent) ASPECTS to find the strength of this correlation. The results are summarized in table and plot.

Model Summary:

R	R Square	Adjusted R Square	Std. Error of the Estimate
.857[a]	.735	.732	1.459

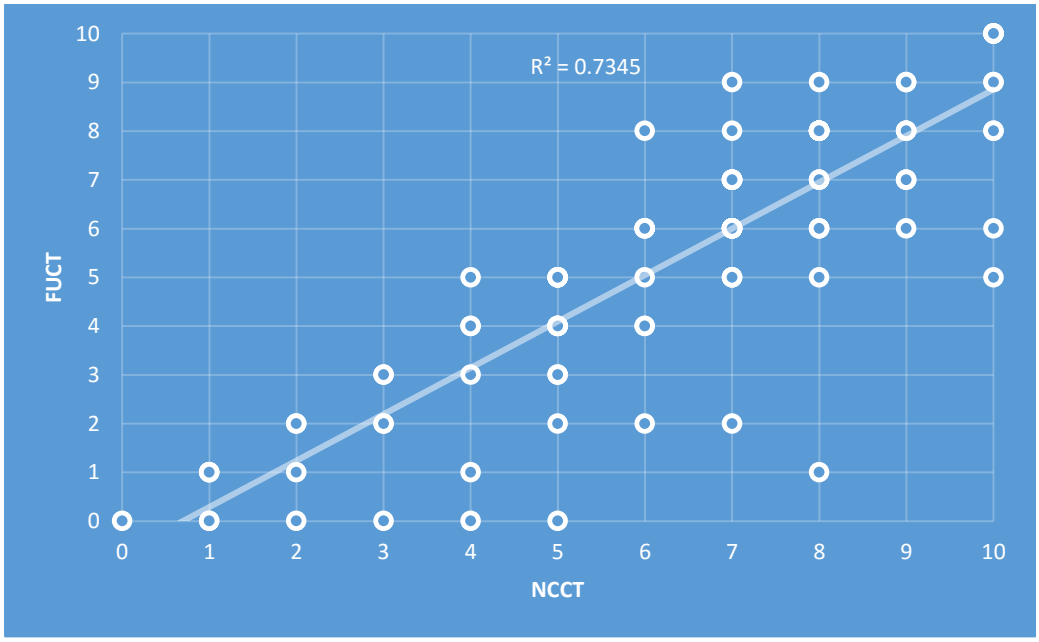
a. Predictors: (Constant), NCCT

b. Dependent Variable: FU

Coefficients[a]

	Unstandardized Coefficients		Standardized Coefficients		
	B	Std. Error	Beta	t	Sig.
(Constant)	-.659	.391		-1.683	.095
NCCT	.952	.056	.857	16.881	.000

a. Dependent Variable: FU



An R^2 value of 0.735 was obtained from the regression analysis.

Linear regression between CTASI and FUCT

Then another simple linear regression analysis was performed between CTASI (independent) and FU (dependent) ASPECTS to find the strength of their correlation. The results are summarized in table and plot.

Model Summary:

R	R Square	Adjusted R Square	Std. Error of the Estimate
.782[a]	.611	.607	1.766

a. Predictors: (Constant), CTASI

b. Dependent Variable: FU

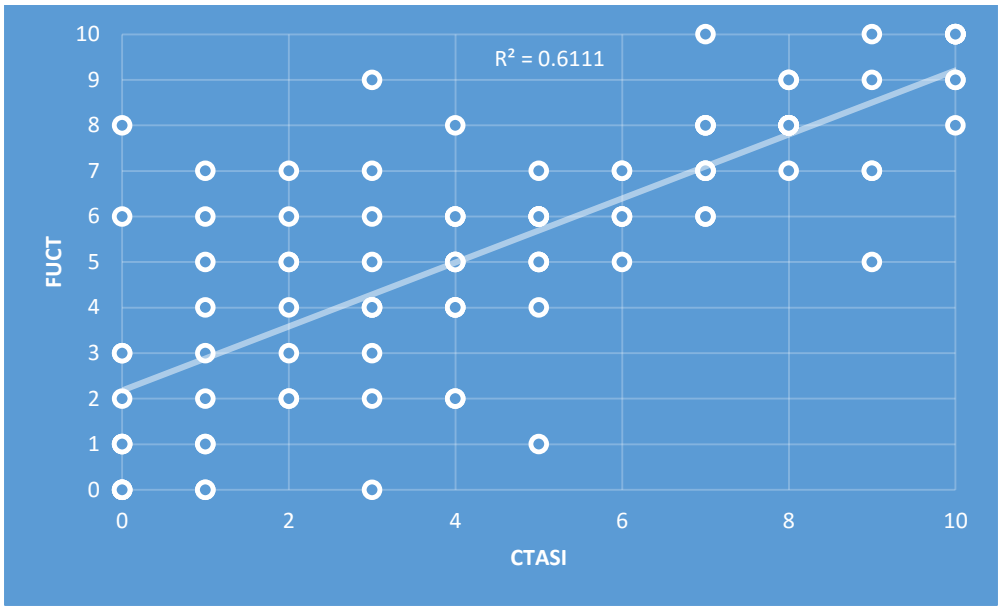
Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	2.184	.312		6.996	.000
	CTASI	.702	.055	.782	12.722	.000

a. Dependent Variable: FU

An R^2 value of 0.611 was obtained from the regression analysis. So NCCT-FU had a greater R^2 value than CTASI-FU, indicating more strength of correlation between NCCT and final infarct size than between CTASI and final infarct size.

The reason for less correlation between CTASI and FU imaging was found to be overestimation of the infarct size by CTASI in 50 (47.6%) out of 105 cases.



Correlation between NCCT, CTASI and perfusion data:

In a subgroup of 25 patients who underwent CT perfusion, we correlated CBV, CBF, MTT and TTP ASPECTS with NCCT and CTASI ASPECTS.

Correlation between the scores of NCCT/CTASI with CTP (Spearman rank correlation):	Spearman's rho - ρ	p
NCCT - CBV	0.933	<0.001
CTA-SI- CBV	0.840	<0.001
NCCT - CBF	0.801	<0.001
CTA-SI- CBF	0.868	<0.001
NCCT - MTT	0.809	<0.001
CTA-SI- MTT	0.854	<0.001
NCCT - TTP	0.809	<0.001
CTA-SI- TTP	0.854	<0.001

NCCT was found to have a very good correlation with CBV whereas correlation of CTASI with CBV was relatively less, though still good. CTASI correlated better with CBF, MTT and TTP than NCCT. However, the difference in correlation indices was not very significant. All of these correlation analyses were statistically significant with p value <0.001 instead of small sample size in the subgroup.

Separate analysis for patient receiving and not receiving thrombolysis (IV/IA/ Bridging):

Separate analysis was done between NCCT and CTASI with FU imaging for patients who did and did not receive thrombolysis (IV/IA/Bridging). Patients receiving only mechanical thrombectomy (5 patients) were excluded from this analysis.

Thrombolysis	Correlation between the scores of NCCT/CTASI with FU (Spearman rank correlation):	Spearman's rho - ρ	p
Yes	NCCT - FU	0.757	<0.001
	CTA-SI- FU	0.703	<0.001
No	NCCT- FU	0.923	<0.001
	CTA-SI- FU	0.879	<0.001

Both NCCT and CTASI had relatively less correlation with final infarct size in patients receiving any form of thrombolysis. However, NCCT remained to have better correlation with final infarct size than CTASI in both the groups.

Regression analysis for CTASI with FUCT for different time of CT:

We wanted to determine if time of CT scan from symptom onset has any significant effect on ASPECTS on CTA-SI. So we divided the study population into three groups according to time of CT scan from symptom onset (<90 minutes, 90-180 minutes, >180 minutes) and did the correlation and regression analysis between CTASI and FU CT/DWI in these three groups separately. We also determined the median CT time (152 minutes) and did separate analysis for patients who underwent CT at greater and lesser than median time.

Correlation (Spearman):

CT Time (Minutes)	Number	Correlation between the scores of CTASI with FU (Spearman rank correlation):	Spearman's rho - ρ	p
<90	19	CTA-SI- FU	0.796	<0.001
90-180	45	CTA-SI- FU	0.767	<0.001
>180	41	CTA-SI- FU	0.774	<0.001

No significant difference was found among these three groups. Slightly higher correlation was found in < 90 minutes' group followed by >180 minutes' group.

Linear Regression:

CTtime	R	R Square	Adjusted R Square	Std. Error of the Estimate
<90	.815[a]	.664	.645	1.758
90-180	.771[a]	.595	.586	1.782
>180	.781[a]	.609	.599	1.816

a. Predictors: (Constant), CTASI

Coefficients[a]

CTtime3		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	t	Sig.
<90	(Constant)	1.666	.725		2.298	.034
	CTASI	.829	.143	.815	5.800	.000
90-180	(Constant)	2.132	.499		4.271	.000
	CTASI	.709	.089	.771	7.947	.000
>180	(Constant)	2.429	.502		4.839	.000
	CTASI	.656	.084	.781	7.797	.000

a. Dependent Variable: FU

Regression analysis also showed highest R^2 value in < 90 minutes' group followed by >180 minutes' group. Least value was obtained in 90-180 minutes' group, though the difference in R^2 values among these three groups was not much.

Correlation (Spearman):

CT Time Median (Minutes)	Number	Correlation between the scores of CTASI with FU (Spearman rank correlation):	Spearman's rho - ρ	p
<152	53	CTA-SI- FU	0.768	<0.001
.>152	52	CTA-SI- FU	0.790	<0.001

Linear Regression:

CT time Median	R	R Square	Adjusted R Square	Std. Error of the Estimate
<152	.779[a]	.607	.599	1.820
>152	.784[a]	.615	.607	1.723

b. Predictors: (Constant), CTASI

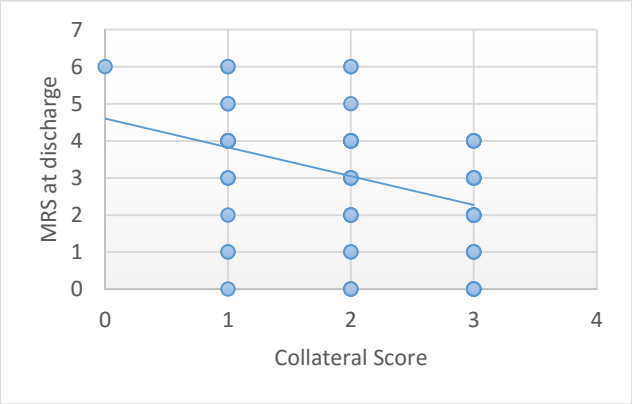
Coefficients[a]

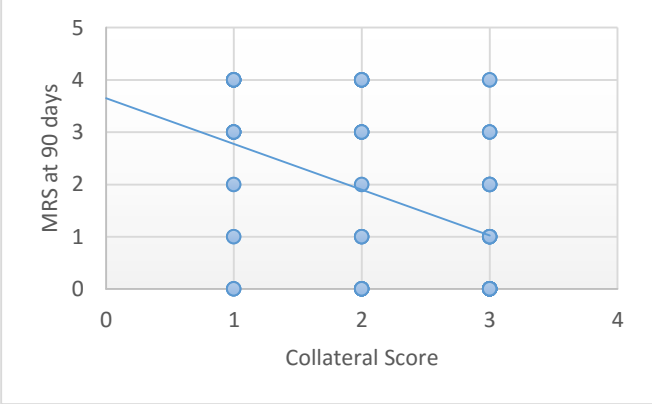
CTtimeMedian		Unstandardized Coefficients		Standardized Coefficients		
		B	Std. Error	Beta	t	Sig.
<152	(Constant)	1.835	.452		4.063	.000
	CTASI	.759	.086	.779	8.869	.000
>152	(Constant)	2.548	.438		5.822	.000
	CTASI	.651	.073	.784	8.939	.000

a. Dependent Variable: FU

When the analysis was done between more and less than median time groups, >152 minutes group showed slightly higher values in both correlation and regression analysis, though the difference was very small.

Correlation between initial collateral score with clinical outcome:



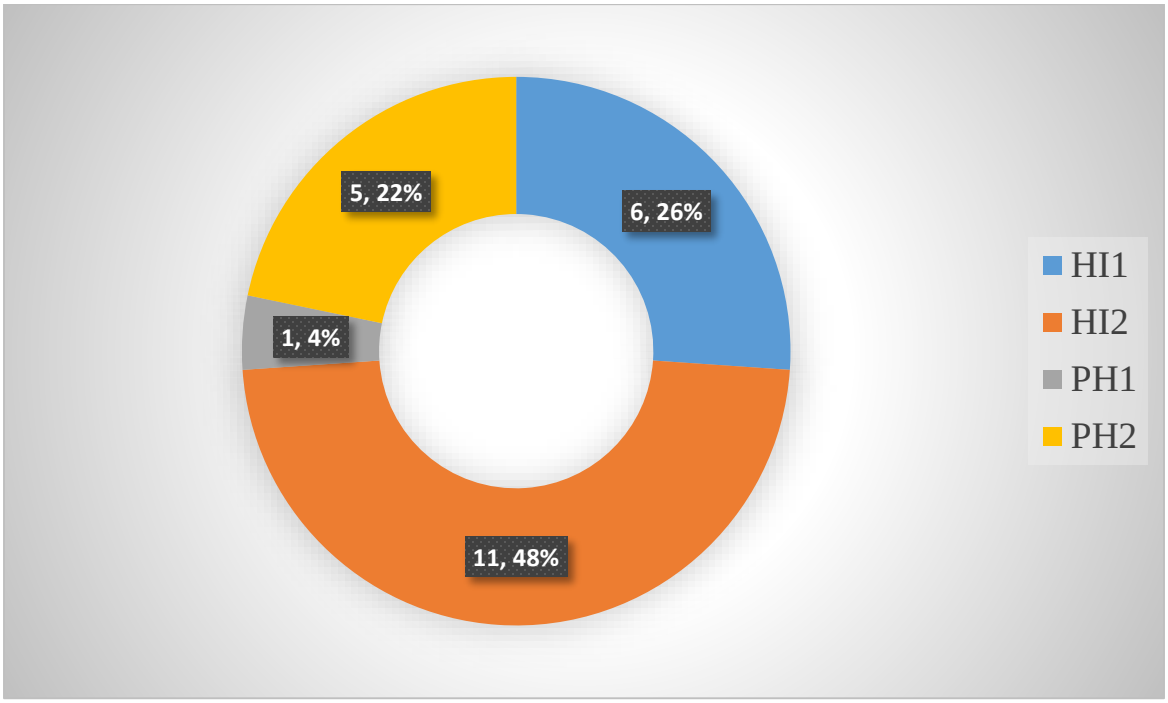


We correlated the patients' clinical outcome (MRS at discharge and at 90 days) with the collateral score (Tan et al) in initial CTA. An inverse relation was found between collateral score and follow up MRS (at discharge and 90 days). It

indicated that patients having a poor collateral score had a poor clinical outcome irrespective of the treatment received.

Hemorrhagic Transformation on follow up imaging:

Total 23 patients were found to have hemorrhagic transformation of the infarct on follow up imaging (24-48 hours). 6 patients had HI1 hemorrhagic transformation, 11 had HI2, 1 had PH1 and 5 patients had PH2 hemorrhagic transformation.



17 of these 23 patients had received thrombolysis. Out of these 17 patients who also received thrombolysis, 6 had HI1 hemorrhagic transformation, 8 had HI2, only 1 had PH1 and 2 had PH2 hemorrhagic transformation.

Discussion

Most neurologists and neuroradiologists use NCCT ASPECTS for initial evaluation of acute ischaemic stroke. However, previous studies showed that it has relatively poor inter-observer correlation and interpreters with less experience tend to miss the early ischaemic changes. CTASI is easier to use particularly for less experienced readers and has a better inter-rater correlation. The EIC is picked up more easily because of non-enhancement of the tissue in these areas.(10) However, our study shows that CTASI is to be interpreted with caution in newer generation multislice CT scanners.

The efficiency of the reader in NCCT can be increased by several means. First, the use of stroke window (window level-40, window width-40) makes the contrast between the grey and white matter favorable for picking up any loss of grey-white differentiation and hypodensity. Secondly, scans are often obtained asymmetrically as the patients tend to rotate head to one side because of hemineglect. Attempt to interpret ASPECTS in these asymmetrical scans decreases reader efficiency and creates confusion. These images need to be corrected in the workstation making them symmetrical before interpretation. Thirdly, ASPECTS is about picking up very

subtle findings in the NCCT. So training and practice definitely improves interpreter efficiency.

We got a very good inter-rater correlation for both NCCT (ρ – 0.902) and CTASI (ρ – 0.935) quite contrary to the previous studies (35). The reason behind this are the meticulous steps taken by us two minimize inter-observer difference. Both the raters discussed several old cases (not from the study population) sitting together before starting interpretation of the images of the study population. Then the observers attempted to interpret a few random cases (not from the study population) independently and cases where inter-observer variation existed, the reasons for difference in scoring were discussed and a consensus was reached. After a reasonable period of training and practice, the observers started interpreting the cases from the study population independently. The images were randomized by a technician, but both the interpreters were made aware of the side of the involvement (clinically). All images were interpreted in same window for both NCCT and CTASI (window level- 40, window width- 40). Same type of monitors and same lighting condition were used for interpretation of all the images. Observers interpreted not more than twenty images per day to maintain good level of concentration. Images were always interpreted after working hours to prevent interruption in between. These meticulous steps paid dividends in the form of no statistically significant difference between the scores given by the two observers. However, interobserver

correlation was seen to be slightly better in CTASI than NCCT, similar to what had been seen in previous studies. CT perfusion maps had very good inter-observer correlation because of ease of interpretation of the color maps.

Once it was seen that there was no statistically significant difference among two raters, we used the lesser score (meaning more infarct) of the two for each patient for each of the parameters. We found NCCT score to have a better correlation with final infarct size than CTASI in both Spearman rank correlation and linear regression analysis. Earlier studies (10,11,51) which had shown CTASI to have a better correlation with final infarct size were done in 16 slice or less CT scanners. The reason for CTASI to have better correlation with final infarct in these studies was ease of interpretation of CTASI because of good contrast between enhancing and non-enhancing areas, an advantage which was not available in NCCT. Moreover, findings in NCCT (hypodensity, loss of grey-white differentiation, swelling) which reflect cytotoxic edema may appear later than non-enhancement in CTASI. So CTASI in these studies actually reflected CBV, in other words the infarct core. We also found slightly better correlation among the two raters in interpreting CTASI images than NCCT images. So the reason for less correlation of CTASI with final infarct size in our study was entirely different.

To find the reason we looked at the individual cases and found that CTASI overestimated the final infarct size in 47.6% cases. The reason for this

overestimation could be CTASI reflecting CBF rather than CBV due to fast scanning in a 256-slice CT scanner. We did a subgroup analysis among the 25 patients who underwent CT perfusion study and found NCCT correlated better with CBV whereas CTASI correlated better with CBF, MTT and TTP. Though the difference in correlation indices were not great, all these correlations were significant at p value <0.001. These findings were in accord with our hypothesis. When we reviewed the cases undergoing CT perfusion, we found that CTASI overestimated the final infarct size only in those cases where significant penumbra existed. In other words, CTASI reflected the ischemic penumbra in these cases rather than the infarct core.

In two cases (one depicted in case 7) CTASI did not correlate with CBF (CTASI-CBF mismatch), MTT and TTP and correlated more with NCCT, CBV and final infarct size. Review of these two cases revealed there was only mild reduction of CBF and mild increase in MTT and TTP. So these are as could represent benign oligemia (tissue that is destined to recover) rather than the ischemic penumbra. In some other cases also we found small areas of slightly increased MTT and TTP surrounding the ischaemic penumbra, not large enough to change the ASPECT score. These areas might be benign oligemia which recovers even without treatment. One of the two cases presenting with CTASI-CBF mismatch did not undergo any recanalization treatment but still did not develop any infarct in the areas of mismatch, supporting our assumption that these areas might represent benign oligemia rather

than ischaemic penumbra. So we could deduce CTASI though reflects penumbra in a 256-slice CT, the drop of CBF has to be significant to be detected in CTASI. In other words, CTASI shows the ischemic penumbra but not the benign oligemia in a 256-slice CT.

We also did separate analysis for patients who received and did not receive thrombolysis (IV/ IA/ Bridging). We found that both NCCT and CTASI correlated to a lesser degree with final infarct size in the thrombolysis group as compared to no thrombolysis group. This indicated that thrombolysis definitely changed final infarct size, a fact which is already proven by previous studies. If CTASI reflected penumbra in a 256-slice CT, difference in CTASI ASPECTS after thrombolysis is natural to occur. However, the difference in NCCT ASPECTS after thrombolysis eluded explanation. It is yet to be proved whether some of the early ischemic changes seen in NCCT are reversible, which may explain this finding. However, present literature suggests that NCCT changes are irreversible. Some other confounding factors could also affected the NCCT ASPECTS in these two groups. Patients who underwent thrombolysis might have undergone CT in earlier time period when image interpretation is more difficult resulting in over-rating. Unfortunately we got recanalization data only in a few patients (either in patients who underwent follow up MRA or who underwent bridging thrombolysis followed by mechanical

thrombectomy). However, in both thrombolysis and no thrombolysis groups NCCT continued to have a better correlation with final infarct size as compared to CTASI.

We also studied whether time of CT scan after symptom onset can affect the CTASI ASPECT scoring. As ischemic penumbra is supposed to be more in early time period, we speculated that overestimation by CTASI will be more if the CT scan is done early. So we divided the study population into three groups according to CT time (<90 minutes, 90-180 minutes and >180 minutes) and did separate correlation and regression analysis between CTASI and FU ASPECTS. Median CT time after symptom onset was also determined and separate correlation and regression analysis was done for patients who underwent CT scan more and less than median time. However, both the correlation indices (ρ) and regression values (R^2) revealed only minor differences among these groups. In the former analysis, lowest ρ and R^2 values were found in 90-180 minutes group. Indices were slightly more in >180 minute group indicating slightly more correlation, a finding which goes along our speculation. However, <90 minutes group showed highest ρ and R^2 values which could not be explained. Probably less number of patients (n=19) in this group and various other confounding factors might have affected the indices. In the later analysis slightly higher ρ and R^2 values were found in more than median time group as compared to less than median time group which was expected, though the difference was minimal. Size of penumbra depends on lot of other factors like

collateral score, site of thrombus etc. which might have affected the final correlation and regression values in these subgroups.

We also tried to find out relation between collateral score (Tan et al)(60) and the clinical outcome (MRS at discharge and 90 days). We found that a poor collateral score in initial CTA resulted in a poor outcome independent of the treatment received. Patient who had poor collateral score had more MRS both at discharge and 90 days indicating the importance of collateral score in initial CTA predicting the clinical outcome.

Finally we found hemorrhagic transformation in 23 patients, 17 of whom underwent thrombolysis. 14 out of these 17 patients had only HI1 or HI2 hemorrhagic conversion indicating reperfusion injury rather than spontaneous hemorrhagic conversion where more severe hemorrhage (PH1 and PH2) is common.(86)

The strength of our study lies in the fairly large study population and the prospective data collection. We randomized the images to avoid interpreter's bias but at the same time took several meticulous steps to reduce interobserver disagreement. We could include strokes of various etiologies in our study population as our hospital has a high volume stroke center. We also got follow up data of most of the patients resulting in good statistical significance of the analyses.

However, our study is not free from limitations. Firstly we could do CT perfusion study only in a limited number of cases, mainly due to lack of indication as per our institute's protocol. Some CTP data had to be rejected because of significant patient movement producing images unsuitable for analysis. Secondly among the patients who underwent thrombolysis, we got recanalization data in very few cases. Finally, though all of our patients had presented within 8 hours of symptom onset, we included 16 wake up stroke cases in the study population and these cases were not excluded while doing the statistical analysis. However, 9 out of these 16 patients underwent CT perfusion study to determine presence of ischemic penumbra. In rest of the wake up stroke cases, CTP was not indicated as per institute protocol (very poor ASPECTS/ presence of contraindication for thrombolysis).

With the technical advancement in the field of CT, use of higher slice CT scanner has become more common. In this background, our study results will definitely shake the popular notion that CTASI correlates better with final infarct size than NCCT in the setting of acute ischaemic stroke. Future studies should be directed to correlate the CTASI with the CTP data (CBV, CBF, MTT and TTP) in modern CT scanners in larger number of patients to get stronger evidence on our second hypothesis that CTASI reflects ischemic penumbra in a modern multislice CT scanner. Once that is proved beyond doubt, we can even think of replacing CTP with CTASI for assessing penumbra in cases of acute ischemic stroke to save time

which is priceless in this setting. Till then it is better to exercise caution to use CTASI to predict final infarct size in a modern multislice CT scanner.

Conclusion

1. ASPECTS in CT angiogram source images tend to overestimate final infarct size in a 256-slice CT scanner. So CTASI should be interpreted with caution in this scanner.
2. Non-contrast CT correlates better with the final infarct size in a 256-slice CT scanner as compared to CTASI.
3. NCCT correlates better with infarct core (CBV) whereas CTASI correlates better with ischaemic penumbra (CBF) in a 256-slice CT scanner. However, further evidence is required to confirm this finding.
4. Fairly good inter-observer agreement can be achieved in ASPECT scoring of both NCCT and CTASI by training, experience, use of identical workstation and interpretation of the images in stroke window.
5. Thrombolysis significantly reduces the correlation between initial CT ASPECTS and final infarct size. This indicates thrombolysis significantly affects final infarct size.
6. CT time does not significantly change the correlation between CTASI ASPECTS and final infarct size, though there is a trend to overestimate by

CTASI in early CT scan. Ischemic penumbra depends on a number of confounding factors. To find the relation between CTASI ASPECTS and CT time, these confounding factors (number of patients, collateral score, location of thrombus etc.) needs to be eliminated in a larger study population.

7. Finally, collateral score in initial CTA is an independent predictor of clinical outcome.

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ANNEXURE I
PROFORMA

[Index No]

PERSONAL DETAILS

NAME AGE SEX HOSP NO

ADDRESS

Ph No

CLINICAL HISTORY

Presenting symptoms	: Weakness-	Yes □ No □	Ataxia-	Yes □ No □
	Sensory-	Yes □ No □	Aphasia-	Yes □ No □
	Hemianopia-	Yes □ No □	FD-	Yes □ No □
	Dysarthria-	Yes □ No □	Others-	

Date of stroke onset :

Time of stroke onset :

Time of patient reaching SCTIMST :

Time of CT scan :

Duration of symptoms :

Stroke subtype* :

NIHSS score at presentation :

NIHSS at 24 hrs :

NIHSS at discharge :

MRS at discharge :

MRS at 9O days :

NIHSS at 9O days :

Presenting symptoms	: DM-	Yes □ No □	Prior stroke-	Yes □ No □
	HTN-	Yes □ No □	TIA-	Yes □ No □
	CAD-	Yes □ No □	VHD-	Yes □ No □
	Smoking-	Yes □ No □	AF-	Yes □ No □

**: stroke subtype classified as: 1. Large vessel, 2. Cardioembolic, 3. Lacunar, 4. Specific cause, 5. Undetermined.*

Imaging

MODALITY	ASPECTS REGIONS INVOLVED				ASPECTS SCORE	Image quality*
NCCT ASPECTS • Date: • Time:	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6		☐ IC ☐ C ☐ L ☐ I		Rater 1 Rater 2	Rater 1 Rater 2
CTA-SI ASPECTS • Date: • Time:	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6		☐ IC ☐ C ☐ L ☐ I		Rater 1 Rater 2	Rater 1 Rater 2
CTP ASPECTS • Date: • Time:	CBV ASPECTS	CBF ASPECTS	MTT ASPECTS	TTP ASPECTS		
	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6 ☐ IC ☐ C ☐ L ☐ I	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6 ☐ IC ☐ C ☐ L ☐ I	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6 ☐ IC ☐ C ☐ L ☐ I	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6 ☐ IC ☐ C ☐ L ☐ I	Rater 1 Rater 2	Rater 1 Rater 2
F/U ASPECTS: • Date: • Time after initial CT: • NCCT/DWI:	☐ M1 ☐ M2 ☐ M3 ☐ M4 ☐ M5 ☐ M6 ☐ IC ☐ C ☐ L ☐ I				Rater 1 Rater 2	Rater 1 Rater 2

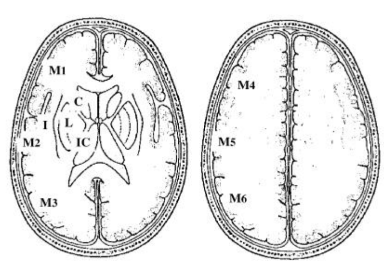

**Image quality is classified as: 1.Excellent, 2. Adequate for interpretation, 3. Poor but partially interpretable, 4. Poor and uninterpretable.*

VESSEL OCCLUSION

- Hyperdense ICA sign :
- Dense MCA sign :
- MCA dot sign :
- Thrombus on CTA [Y/N] :
- Site of thrombus :
- Collateral score :

THROMBOLYSIS

- Thrombolysis done[Y/N] :
- Time of tPA given :
- IV/IA/bridging :
- Time from symptom onset :
- Recanalization data [Y/N/NA] :
- TICI :

MECHANICAL THROMBECTOMY

- Thrombectomy done[Y/N] :
- Device used :
- Time :
- Recanalization data [Y/N/NA] :
- TICI :

HEMORRHAGIC TRANSFORMATION

- Present[Y/N] :
- Grading[HI1/HI2/PH1/PH2] :

Total radiation dose: :

Total contrast dose [ml] :

ANNEXURE II

SREE CHITHRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY – TRIVANDRUM

STUDY CONSENT FORM FOR ADVANCED NEUROIMAGING

TITLE OF THE STUDY: ***Comparison of ability of ASPECTS on non-contrast CT and CT angiography source images to predict the final size of infarct in a 256-slice CT scanner.***

Study number:
You are being requested to participate in a study to see how much CT scan can help in the management decision of acute stroke. It is clinically suspected that you have an acute stroke, for which you will be undergoing advanced neuroimaging as a part of clinical evaluation of your disease to plan the treatment. CT is an advanced imaging technique which uses ionizing radiation to image body part. There will be administration of contrast during the study. We hope to include about 100 people from this hospital in this study.

How will CT scan help you?
CT scan can show which part of your brain is affected by stroke and the treatment will change accordingly.

Does CT scan have any side effects?
We shall be injecting iodinated contrast during the study. Some patients may develop contrast reactions. Minor contrast reactions are allergy, skin rashes, shivering, mild breathlessness, local pain etc. These conditions are self-limiting and do not require any treatment. Rarely may it cause reactions like severe breathlessness, severe allergy etc. for which active treatment will be required. Life threatening contrast reactions are extremely rare. If you have any previous history of allergy, we shall take necessary precautions. If your kidneys are not healthy, contrast agent can cause further damage to them. So your serum creatinine value will be checked before contrast administration and decision will be made accordingly. The radiation dose which is used in CT does not usually cause any adverse reaction. However, there is theoretical possibility of adverse effect including genetic disorders and even cancers in the long run. If done in a pregnant woman, this investigation may harm the fetus.

If you take part what will you have to do?
You have to undergo plain CT scan and CT angiography during you admission. You may also have to undergo CT perfusion study if your doctor considers that it will benefit your treatment. Contrast will be injected for CT angiography and CT perfusion study separately. After 24 hours you shall have to undergo another plain CT scan (without contrast).

Can you withdraw from this study after it starts?
Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

If you do not take part or withdraw from the study, will if affect your treatment?
Participation in this study is absolutely voluntary and it will not influence your treatment. The neuroimaging is being done as a part of clinical evaluation of your disease; however certain data from this study will be used for research purpose. So if you don't take part or withdraw yourself from the study, still you will receive the same treatment.

Will your personal details be kept confidential?
The results of this study will be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr. Amritendu Mukherjee, Senior Resident, Dept. of IS & IR SCTIMST. (Telephone-828165556) or email: amrit@sctimst.ac.in
Participant's name: Date of Birth / Age (in years):
I_____ _____, son/daughter of _____ (Please tick boxes)
• Declare that I have read the above information provided to me regarding the study: ***Comparison of ability of ASPECTS on non-contrast CT and CT angiography source images to predict the final size of infarct in a 256-slice CT scanner*** and have clarified any doubts that I had. [ ]
• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]
• I also understand that I do not have to pay any extra amount for the sake of study and whatever I pay for will be part of my management. [ ]
• I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]
• I understand that my identity will not be revealed in any information released to third parties or published [ ]
• I voluntarily agree to take part in this study [ ]
• I received a copy of this signed consent form [ ]
Name:
Signature:
Date:
Name of witness:
Relation to participant:
Date:
(Person Obtaining Consent) I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____
Name and Signature of Person Obtaining Consent

ശ്രീ ചിത്തിരു തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ മെഡിക്കൽ സയൻസസ് ആന്റ് ടെക്നോളജി തിരുവനന്തപുരം

ആധുനികമായ ന്യൂറോ ഇമേജിംഗിനുള്ള സമ്മതപത്രം

വൈദ്യ പരിശോധനയിൽ ഗുരുതരമായ പക്ഷാഘാതം സംശയിക്കുന്നതിനാൽ താങ്കളുടെ ചികിത്സ ആസൂത്രണം ചെയ്യാൻ വേണ്ടുന്ന വൈദ്യ വിശകലനത്തിന്റെ ഭാഗമായി താങ്കൾ ആധുനികമായ ന്യൂറോ ഇമേജിംഗിന് വിധേയമാവുകയാണ്. എക്സ് കിരണങ്ങൾ ഉപയോഗിച്ച് ചിത്രങ്ങളെടുക്കുന്ന ആധുനിക ഇമേജിംഗ് ടെക്നോളജിയാണ് സി.റ്റി.സ്കാനറുകളുടേത്. പരിശോധനാ സംബന്ധമായി കോൺട്രാസ്റ്റ് രോഗിയുടെ ശരീരത്തിൽ കുത്തിവെയ്ക്കേണ്ടി വന്നേക്കാം. ഈ ആശുപത്രിയിൽ നിന്നും ഏകദേശം നൂറോളം രോഗികളെ ഈ പഠനത്തിൽ ഉൾപ്പെടുത്തണമെന്നാണ് ഞങ്ങൾ പ്രതീക്ഷിക്കുന്നത്.

സി.റ്റി.സ്കാനറുകൾ താങ്കളെ എങ്ങനെ സഹായിക്കും?

താങ്കളുടെ ബ്രെയിനിന്റെ ഏതു ഭാഗത്തായാണ് പക്ഷാഘാതം സംഭവിച്ചിരിക്കുന്നത് എന്ന് സി.റ്റി.സ്കാനറുകൾക്ക് കാണിച്ചുതരുവാനും അതിനനുസരിച്ച് ചികിത്സ മുന്നോട്ട് കൊണ്ടുപോകാനും സാധിക്കും.

സി.റ്റി.സ്കാനിംഗിന് പ്രത്യാഘാതങ്ങളുണ്ടോ?

പരിശോധനക്കായി കോൺട്രാസ്റ്റ് ശരീരത്തിൽ കുത്തിവയ്ക്കേണ്ടി വന്നോക്കാം. ചില രോഗികളിൽ ഇതിന്റെ പ്രത്യാഘാതങ്ങളുണ്ടായേക്കാം. കുറഞ്ഞ പ്രത്യാഘാതങ്ങളിൽ അലർജി, ചൊറിഞ്ഞു തടിക്കൽ, വിറയൽ. ചെറിയ ശ്വാസംമുട്ട് എന്നിവയുണ്ടായേക്കാം. ഇവയെല്ലാം തന്നെ ചികിത്സ കൂടാതെ ശരിയാവുന്നവയാണ്. അപൂർവ്വമായി വലിയരീതിയിലുള്ള ശ്വാസംമുട്ടലും, അലർജിയും ഉണ്ടായേക്കാം. ഇതിന് ഉടനടി തന്നെ ചികിത്സ ആവശ്യമാണ്. ജീവാപായം വരുത്തുന്ന പ്രത്യാഘാതങ്ങൾ വളരെ അപൂർവ്വമാണ്. മുൻകാലത്ത് എതെങ്കിലും രീതിയിലുള്ള അലർജി ഉണ്ട് എന്ന് അറിയിച്ചാൽ വേണ്ട മുൻകരുതലെടുക്കുവാൻ ഞങ്ങൾക്ക് സാധിക്കും. താങ്കളുടെ വൃക്കകൾ പൂർണ്ണ ആരോഗ്യമുള്ളവ അല്ലാ എങ്കിൽ അവയ്ക്ക് തകരാർ സംഭവിച്ചേക്കാം. അതിനാൽ ക്രിയാറ്റിനിൻ എന്ന പരിശോധന നടത്തി വിലയിരുത്തിയ ശേഷം മാത്രമേ കോൺട്രാസ്റ്റ് വേണമോ എന്ന തീരുമാനത്തിലെത്തുകയുള്ളു. സി.റ്റി.സ്കാനിംഗിലൂടെ റേഡിയേഷൻ ഡോസ് സാധാരണ കുഴപ്പങ്ങ

ളൊന്നുമുള്ളതല്ല. എന്നിരുന്നാലും ജനിതക തകരാറോ, കാൻസറോ, പോലുള്ള അസുഖങ്ങൾ ഇതിന്റെ പ്രത്യാഘാതമായി വളരെ കാലങ്ങൾക്കു ശേഷം സംഭവിച്ചേക്കാം. ഗർഭാവസ്ഥയിൽ സി.റ്റി.സ്കാനിംഗ് നടത്തിയാൽ ഗർഭസ്ഥ ശിശുവിന് ഇത് ദോഷമായി സംഭവിച്ചേക്കാം.

ഇതിൽ പങ്കെടുത്താൽ താങ്കൾ എന്താണ് ചെയ്യേണ്ടത്?

ഇതിൽ കോൺട്രാസ്റ്റ് ഉപയോഗിക്കാതെയും ഉപയോഗിച്ചുമുള്ള സ്കാനിംഗുകൾക്ക് താങ്കൾ വിധേയനാകേണ്ടിവരും ഡോക്ടർക്ക് ചികിത്സയ്ക്ക് ആവശ്യമെങ്കിൽ ചിലപ്പോൾ പെർഫ്യൂഷൻ എന്ന പഠനത്തിനും വിധേയനാകേണ്ടി വരും. രണ്ടു പഠനങ്ങൾക്കും കോൺട്രാസ്റ്റ് വെവ്വേറെ ആയിരിക്കും കുത്തി വയ്ക്കുക. 24 മണിക്കൂറുകൾക്കു ശേഷം കോൺട്രാസ്റ്റ് ആവശ്യമില്ലാത്ത ഒരു സി.റ്റി.സ്കാൻ കൂടി താങ്കൾക്ക് നടത്തേണ്ടി വരും.

ഒരിക്കൽ തുടങ്ങി വച്ചാൽ താങ്കൾക്ക് ഈ പഠനത്തിൽ നിന്നും പിൻമാറാൻ സാധിക്കുമോ?

താങ്കൾക്ക് ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം പൂർണ്ണമായും നിയന്ത്രിതമാണ്. എപ്പോൾ വേണമെങ്കിലും താങ്കളുടെ സമ്മതം പിൻവലിക്കാവുന്നതുമാണ്. അങ്ങനെ ചെയ്താലും ഈ ആശുപത്രിയിൽ സാധാരണഗതിയിൽ താങ്കൾക്കു ലഭിക്കേണ്ട ചികിത്സയ്ക്കു ഒരു രീതിയിലുള്ള തടസ്സങ്ങളും ഉണ്ടാകുകയില്ല.

താങ്കൾ ഇതിൽ പങ്കെടുക്കാതിരിക്കുകയോ സമ്മതം പിൻവലിക്കുകയോ ചെയ്താൽ താങ്കളുടെ ചികിത്സയെ ബാധിക്കുമോ?

ഈ പഠനത്തിലെ താങ്കളുടെ പങ്കാളിത്തം പൂർണ്ണമായും നിയന്ത്രിതമാണ് ഇത് താങ്കളുടെ ചികിത്സയെ ബാധിക്കുകയില്ല. ന്യൂറോ ഇമേജിംഗ് താങ്കളുടെ വൈദ്യപരിശോധനയുടെ ഭാഗമായി നടത്തുന്നതാണ് എന്നിരുന്നാലും ചില വിവരങ്ങൾ ഗവേഷണത്തിനായി ഉപയോഗിക്കുന്നു. അതുകൊണ്ട് താങ്കൾ ഈ പഠനത്തിൽ പങ്കെടുത്തില്ലെങ്കിലും പിൻവാങ്ങിയാലും താങ്കൾക്ക് ഒരേ ചികിത്സ തന്നെയായിരിക്കും ലഭിക്കുക.

താങ്കൾ ഈ പഠനത്തിനായി പണം അടക്കേണ്ടതുണ്ടോ?

ഈ പഠനസംബന്ധമായി താങ്കൾ പണമൊന്നും അടക്കേണ്ടതില്ല. സി. റ്റി.സ്കാൻ താങ്കളുടെ വൈദ്യപരിശോധനയിൽ ഉൾപ്പെടുന്നതായതിനാൽ അതിന്റെയും താങ്കൾക്ക് ചികിത്സക്കാവശ്യമായതുമായ പണം മാത്രമായിരിക്കും താങ്കൾ അടയ്ക്കേണ്ടി വിരിക.

താങ്കളുടെ വ്യക്തിപരമായ രേഖകൾ രഹസ്യമായി സൂക്ഷിക്കുമോ?

താങ്കൾ ഈ പഠനത്തിൽ പങ്കാളിയാകാൻ തീരുമാനിച്ചാൽ ഈ പഠനത്തിലൂടെ ശേഖരിച്ച ഫലങ്ങൾ വൈദ്യ പ്രസിദ്ധീകരണങ്ങളിൽ ഉൾപ്പെടുത്തുന്നതാണ്. പക്ഷേ പേരുവിവരങ്ങൾ ഒന്നും തന്നെ ഉൾപ്പെടുത്തുന്നതായിരിക്കില്ല. എന്നിരുന്നാലും, താങ്കളുടെ വൈദ്യ രേഖകൾ പഠനത്തിലൂൾപ്പെട്ടിരിക്കുന്ന ആളുകൾ താങ്കളുടെ അനുവാദമില്ലാതെ തന്നെ വിലയിരുത്തുന്നതായിരിക്കും.

തുടർന്നുള്ള അന്വേഷണങ്ങൾക്കായി ഡോ.അമൃതേന്ദു മുഖർജി, സീനിയർ റസിഡന്റ്, ഐ.എസ്. & ഐ.ആർ, എസ്. സി. റ്റി. ഐ.എം.എസ്.റ്റി.(ഫോൺ 8281655561) ബന്ധപ്പെടുക

പങ്കെടുക്കുന്ന ആളുടെ പേര് **ജനന തീയതി** **വയസ്സ്**

ഞാൻ .....മകൻ/മകൾ

പിതാവിന്റെ പേര് .....

- 256 Slice സ്കാനറിൽ കോൺട്രാസ്റ്റ് ഉപയോഗിക്കാതെ എടുക്കുന്ന സി.റ്റി.സ്കാനും കോൺട്രാസ്റ്റ് ഉപയോഗിച്ചുള്ള സി.റ്റി.ആൺജിയോ ഗ്രാഫിയും തമ്മിൽ താരതമ്യം ചെയ്ത് പക്ഷാഘാതത്തിന്റെ വലുപ്പം നിർണ്ണയിക്കുന്ന ഈ പഠനത്തെപ്പറ്റിയുള്ള മുകളിൽ പറഞ്ഞിരിക്കുന്ന വിവരങ്ങൾ വായിച്ച് മനസ്സിലാക്കുകയും എനിക്കുണ്ടായിരുന്ന എല്ലാ സംശയങ്ങളും നിവാരണം ചെയ്യുകയും ചെയ്തു. ☐

- നിയമപരമായ എല്ലാ അവകാശങ്ങളോടും കൂടി തന്നെ എന്റെ ചികിത്സയെ ബാധിക്കാതെ ഏതു സമയത്തും എന്റെ സമ്മതം പിൻവലിക്കാവുന്നതാണെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. ☐

- ഞാൻ ഇതിൽ നിന്നു പിൻമാറിയാലും എന്റെ ആരോഗ്യ രേഖകൾ പഠനത്തിലുൾപ്പെട്ടിരിക്കുന്ന സ്റ്റാഫുകൾക്കും, ഇൻസ്റ്റിറ്റ്യൂഷനൽ എത്തിക്സ് കമ്മിറ്റിക്കും എന്റെ അധികാരമില്ലാതെ തന്നെ പരിശോധിക്കുവാനുള്ള അധികാരമുണ്ടായിരിക്കുമെന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. ☐

- എന്റെ ചികിത്ക്കാവശ്യമായതല്ലാതെ ഈ പഠനത്തിനായി പണമൊന്നും തന്നെ അടയ്ക്കേണ്ടി വരില്ല എന്നു ഞാൻ മനസ്സിലാക്കുന്നു. ☐

- മറ്റൊരാൾക്കും എന്റെ വ്യക്തിപരമായ രേഖകൾ കൈമാറ്റം ചെയ്യപ്പെടുകയില്ല എന്ന് ഞാൻ മനസ്സിലാക്കുന്നു. ☐

- ഞാൻ പൂർണ്ണമായും ഈ പഠനത്തിൽ പങ്കെടുക്കുവാൻ സമ്മതിക്കുന്നു ☐
- ഞാൻ ഒപ്പിട്ട ഈ സമ്മതപത്രത്തിന്റെ ഒരു പതിപ്പ് കൈപ്പറ്റിയിരിക്കുന്നു. ☐

പേര് :

ഒപ്പ് :

തീയതി :

സാക്ഷിയുടെ പേര്:

രോഗിയുമായുള്ള ബന്ധം :

തീയതി:

വൈദ്യ ഗവേഷണ പഠനത്തിന്റെ ആവശ്യകതയെപ്പറ്റി അറിയിച്ചുകൊ
ണ്ടുള്ള ഈ സമ്മതപത്രം തൃപ്തികരമാണെന്ന് ഞാൻ വിലയിരുത്തുന്നു.
ഗവേഷണ പഠനത്തെപ്പറ്റി ഈ സമ്മത പത്രത്തിലുൾപ്പെട്ടിരിക്കുന്ന കാര്യ
ങ്ങൾ പങ്കെടുക്കുന്ന വ്യക്തിയോട് വിശദീകരിച്ചിട്ടുണ്ട്. ഉണ്ടാകാനിടയുള്ള
അപവാദങ്ങളെപ്പറ്റിയും, പ്രത്യാഘാതങ്ങളെപ്പറ്റിയും ഞാൻ വിശദമായി
പ്രതിപാദിച്ചിട്ടുണ്ട്. തുടർന്നും പങ്കെടുക്കുന്ന വ്യക്തിയെ ചോദ്യങ്ങളും
സംശയങ്ങളും ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും അവയ്ക്കെല്ലാം ഉത്തരം
നല്കുകയും ചെയ്തിട്ടുണ്ട്.

സമ്മതപത്രം ഒപ്പിട്ടു വാങ്ങിയ ആളുടെ പേരും ഒപ്പും.

ANNEXURE III

Plagiarism Check report

Thesis_Amritendu.docx

ORIGINALITY REPORT

12%

SIMILARITY INDEX

PAPER ID 19679905

ANNEXURE IV
Master Chart

No.	Age	Sex	Weakness	Sensory	Hemianopia	Dysarthria	Ataxia	Aphasia	FD	onset to CT	Wake up	Subtype	Presentation NIHSS	NIHSS 24 hr	NIHSS Discharge	NIHSS 90 d	Presentation MRS	MRS Discharge	MRS 90 d	DM	HTN	CAD	Smoking	Prior stroke	TIA	VHD	AF	Side	NCCT	CTASI	CBV	CBF	MTT	TTP	FU	CT/DwI	Dense ICA	Dense MCA	MCA dot	Thrombus on CTA	Prox ICA	Dist ICA	Prox MCA	Dist MCA	Collateral Score	Thrombolysis	Time from onset	IV	IA	Bridging
1	82	1	1	2	1	1	2	2	1	84	2	1	11	14	14	11	4	4	4	1	1	1	2	2	2	2	2	1	8	5					5	1	2	2	1	1	1	1	2	1	2	1	115	1	2	2
2	70	2	1	1	1	1	2	2	1	130	2	5	17	15	13	13	4	4	4	1	1	2	2	2	2	2	2	1	5	3					3	1	2	1	2	1	2	2	1	2	1	1	158	2	2	1
3	37	2	1	2	2	1	2	2	1	205	2	2	11	0	0	0	4	0	0	2	2	2	2	2	2	2	2	1	8	8					8	1	2	1	2	1	2	2	1	2	3	1	250	1	2	2
4	34	2	1	1	1	1	2	2	1	203	2	2	9	9	9	0	4	4	0	2	2	2	2	2	2	1	2	1	7	5	6	1	1	1	6	1	2	1	2	1	2	2	1	2	2	1	243	2	2	1
5	46	1	1	2	1	2	2	1	1	260	2	1	23	19	18	16	5	4	4	1	1	2	2	2	2	2	2	2	4	2					4	1	2	1	1	1	2	2	1	2	1	2		2	2	2
6	58	1	1	2	2	2	2	1	1	140	2	5	21	18	18	11	5	4	3	1	1	2	2	2	2	2	2	2	6	3	5	3	3	3	4	1	2	1	2	1	2	2	1	2	1	2		2	2	2
7	41	2	1	1	1	2	2	1	2	250	1	5	21	19			5	6		2	2	2	2	2	2	2	2	2	5	4					5	1	2	2	1	1	2	2	2	1	2	2		2	2	2
8	63	1	1	2	2	2	2	1	1	75	2	1	7	6	7	4	3	3	3	1	2	1	1	1	1	2	2	2	4	4					5	1	2	2	2	2	2	2	2	2	3	1	115	1	2	2
9	67	2	1	1	2	1	2	2	1	236	2	2	9	8	7	2	4	4	2	1	1	2	2	2	2	2	2	2	7	7					7	1	2	2	2	2	2	2	2	2	3	1	260	1	2	2
10	75	2	1	1	1	1	2	2	1	56	2	2	15	6	2	0	4	1	0	2	1	2	2	2	2	2	1	1	8	5					6	1	2	2	2	2	2	2	2	2	1	1	80	1	2	2
11	60	1	1	1	1	1	2	2	1	141	2	2	16	9	6	3	4	4	2	1	1	2	1	2	2	2	2	1	0	0	0	0	0	0	0	1	2	2	2	1	2	2	1	2	1	2		2	2	2
12	65	1	1	2	1	1	2	1	1	178	1	2	18	18	14	4	4	4	3	1	1	1	2	2	2	2	2	2	8	8	8	8	8	8	8	1	2	2	2	2	2	2	2	2	2	2		2	2	2
13	68	1	1	2	2	1	2	2	1	109	1	1	7	3	3	0	4	3	0	2	1	2	2	2	2	2	2	1	8	5	7	5	5	5	6	1	2	2	2	1	1	1	2	2	1	2		2	2	2
14	65	2	1	2	1	1	2	2	1	270	2	2	10	5	4	0	4	2	0	2	1	2	2	2	2	2	1	1	5	2	6	2	2	2	5	1	2	1	2	1	2	2	1	2	2	1	330	2	1	2
15	63	1	1	2	1	1	1	2	1	20	2	2	9	7	9	6	4	4	4	1	1	1	2	2	2	1	2	1	5	4	4	4	4	4	4	1	2	2	1	1	2	2	2	1	2	1	60	1	2	2
16	70	2	1	1	1	1	2	2	1	120	2	2	16	18	14	10	4	5	4	2	1	2	2	2	2	2	1	1	3	2	3	0	0	0	2	1	2	1	2	1	2	2	1	2	1	2		2	2	2
17	53	1	1	2	2	1	2	1	1	113	2	3	7	0	0	0	4	0	0	2	1	2	2	2	2	2	2	2	8	8					8	1	2	2	2	2	2	2	2	2	3	1	130	1	2	2
18	60	1	1	2	1	2	2	1	1	137	2	2	21	10	7	7	4	4		2	1	1	1	1	1	2	2	2	6	1					6	1	2	2	2	1	1	1	2	2	1	1	195	1	2	2
19	23	1	1	1	1	1	2	2	1	119	2	2	13	2	1	1	4	1	1	2	2	2	2	2	2	1	1	1	7	7					7	1	2	1	2	1	2	2	1	2	3	1	150	1	2	2
20	75	1	1	1	2	2	1	2	2	194	2	3	5	2	2	1	4	4	1	2	1	2	1	2	2	2	2	2	10	10					9	2	2	2	2	2	2	2	2	2	3	2		2	2	2
21	52	2	1	2	2	2	2	1	1	158	2	5	10	12	12	7	4	4	3	1	1	2	2	2	2	2	2	2	5	5					5	1	2	2	2	1	2	2	1	2	1	2		2	2	2
22	47	1	1	2	1	2	2	1	1	383	2	4	22	22	17	17	5	4	4	2	1	2	2	2	2	2	2	2	2	0					2	1	1	1	1	1	1	1	1	2	1	2		2	2	2
23	41	2	1	2	1	1	2	1	1	100	1	2	12	12	10	9	4	4	4	2	2	2	2	2	2	1	1	1	4	3	4	3	3	3	4	1	2	1	1	1	2	2	1	1	1	2		2	2	2
24	61	1	1	2	1	1	2	2	1	210	2	2	10	9	8	0	4	4	1	1	2	1	2	2	2	2	2	1	7	3					6	1	2	1	2	1	2	2	1	2	2	1	235	1	2	2
25	54	1	1	2	2	2	2	1	1	119	1	5	19	17	15	6	5	4	3	2	2	2	1	2	2	2	2	2	1	0					0	1	2	2	2	1	2	2	1	1	1	2		2	2	2

No.	Age	Sex	Weakness	Sensory	Hemianopia	Dysarthria	Ataxia	Aphasia	FD	onset to CT	Wake up	Subtype	Presenting NIHSS	NIHSS 24 hr	NIHSS Discharge	NIHSS 90d	MRS Presentation	MRS Discharge	MRS 90d	DM	HTN	CAD	Smoking	Prior stroke	TIA	VHD	AF	Side	NCCT	CTASI	CBV	CBF	MTT	TTP	FU	CT/DWI	Dense ICA	Dense MCA	MCA dot	Thrombus on CTA	Prox ICA	Dist ICA	Prox MCA	Dist MCA	Collateral Score	Thrombolysis	Time from onset	IV	IA	Bridging
26	31	1	1	1	1	2	2	1	1	89	2	2	16	12	11	2	4	3	1	1	1	2	2	2	2	2	2	2	6	5					6	1	2	2	1	1	2	2	2	1	2	1	180	1	2	2
27	33	1	1	2	1	1	2	2	1	35	2	2	14	4	0	0	4	0	0	2	2	2	2	2	2	1	2	2	9	5					7	1	2	2	2	1	2	2	1	2	2	2		2	2	2
28	67	1	1	2	2	1	2	2	1	46	2	2	5	4	2	1	4	2	1	1	2	2	2	2	2	2	2	2	8	8					8	1	2	2	2	2	2	2	2	2	3	1	85	1	2	2
29	61	1	1	2	1	1	2	2	1	102	2	2	11	10	6	3	4	2	2	1	1	1	2	2	2	2	2	1	5	4					4	1	2	2	1	1	2	2	2	1	2	2		2	2	2
30	60	1	1	2	2	1	2	2	1	151	2	5	9	4	0	0	4	0	0	2	2	2	1	2	1	2	2	1	8	8					8	1	2	2	2	1	2	2	2	1	3	1	200	1	2	2
31	49	2	1	2	2	2	2	1	1	217	2	2	11	12	10	1	5	4	0	1	1	1	2	2	2	2	2	2	10	9					10	1	2	2	2	2	2	2	2	2	3	1	250	1	2	2
32	48	1	1	2	2	1	2	2	1	360	2	5	4	2	5	4	3	3	3	1	1	2	2	2	2	2	2	1	10	10					8	1	2	2	2	2	2	2	2	2	3	2		2	2	2
33	46	2	1	2	2	1	2	1	1	240	2	5	8	4	3	0	4	2	0	2	2	2	2	2	2	2	2	2	7	7					6	1	2	2	2	2	2	2	2	2	3	1	265	1	2	2
34	75	1	1	2	2	2	2	1	1	265	2	2	18	14	13	12	5	4	4	2	1	1	2	2	2	2	1	2	5	3					4	1	2	1	2	1	2	2	1	2	2	2		2	2	2
35	60	2	1	2	1	1	2	2	1	165	2	2	8	6	2	1	4	2	1	2	2	2	2	2	2	1	2	1	5	4					5	1	2	2	1	1	2	2	2	1	2	2		2	2	2
36	82	1	1	1	1	1	2	2	1	208	2	5	7	0	0	0	3	0	0	1	1	2	2	2	2	2	2	1	9	4	7	5	5	5	8	1	2	2	2	1	2	2	1	2	2	1	235	2	2	1
37	52	1	1	2	2	2	2	1	1	85	2	2	11	9	7	5	4	3	2	1	1	1	1	1	2	2	2	2	5	2					5	1	2	2	1	1	2	2	2	1	2	1	105	1	2	2
38	68	1	1	1	1	1	2	2	2	120	2	2	12	5	2	0	4	3	0	2	1	1	2	2	2	2	1	1	7	5					5	1	2	2	2	2	2	2	2	2	2	1	150	1	2	2
39	35	1	1	2	1	2	2	2	2	110	2	5	15	20	10	16	5	4	4	2	2	1	1	1	2	2	2	1	6	4					6	1	2	1	1	1	2	2	1	1	2	1	150	1	2	2
40	74	1	1	2	1	2	2	1	1	71	2	1	13	3	2	1	4	2	1	1	2	2	2	2	2	2	2	2	8	2					6	1	2	2	2	1	1	1	2	2	2	1	100	1	2	2
41	63	1	1	2	2	1	1	2	2	125	2	3	7	5	4	0	4	4	0	1	1	2	2	2	1	2	2	1	10	10					10	2	2	2	2	2	2	2	2	2	3	1	160	1	2	2
42	60	1	1	2	2	2	2	1	1	133	2	5	11	16	8	7	4	4	3	2	1	1	1	2	1	2	2	2	8	5					1	2	2	2	2	2	2	2	2	2	2	1	160	1	2	2
43	84	2	1	2	1	2	2	1	1	116	2	1	23	18	18		5	5		1	1	1	2	2	2	2	2	2	1	0					1	1	1	1	2	1	1	1	1	2	1	1	150	1	2	2
44	60	2	1	2	2	1	2	2	1	224	2	2	2	0	0	0	2	0	0	2	2	2	2	2	2	1	2	1	7	7					8	1	2	2	1	1	2	2	2	1	2	1	270	1	2	2
45	68	1	1	2	1	2	2	1	2	145	1	5	10	3	2		4	1		2	1	1	2	1	2	2	2	2	7	3					9	1	2	2	1	1	2	2	1	1	2	1	225	1	2	2
46	54	1	1	1	1	2	2	2	1	90	2	5	10	7	4	0	4	3	0	2	2	2	2	2	2	2	2	1	10	5					6	1	2	2	2	2	2	2	2	2	2	1	125	1	2	2
47	65	1	1	2	2	1	2	1	2	253	2	5	9	8	8	3	4	3	1	2	1	2	1	2	2	2	2	2	9	9	10	10	10	10	7	2	2	2	2	2	2	2	2	2	3	2		2	2	2
48	55	2	1	1	1	2	2	1	1	180	2	2	13	4	2	1	4	2	1	1	1	2	2	2	2	1	1	2	10	9	10	9	9	9	5	2	2	2	2	2	2	2	2	2	3	1	220	1	2	2
49	29	2	1	2	2	1	2	2	1	188	2	2	5	11	11	7	2	4	3	2	2	2	2	2	2	1	2	1	8	3					7	1	2	2	2	1	2	2	1	2	2	2		2	2	2
50	30	1	1	2	2	2	2	1	1	140	1	5	18	11	9	5	4	4	3	2	2	2	1	2	2	2	2	2	5	1	6	0	0	0	4	2	2	1	2	1	2	2	1	2	1	1	185	1	1	2

No.	Age	Sex	Weakness	Sensory	Hemianopia	Dysarthria	Ataxia	Aphasia	FD	onset to CT	Wake up	Subtype	NIHSS Presentation	NIHSS 24 hr	NIHSS Discharge	NIHSS 90 d	MRS Presentation	MRS Discharge	MRS 90 d	DM	HTN	CAD	Smoking	Prior stroke	TIA	VHD	AF	Side	NCCT	CTASI	CBV	CBF	MTT	TTP	FU	CT/ DwI	Dense ICA	Dense MCA	MCA dot	Thrombus on CTA	Prox ICA	Dist ICA	Prox MCA	Dist MCA	Collateral Score	Thrombolysis	Time from onset	IV	IA	Bridging
51	44	2	1	1	1	1	2	2	1	132	2	5	14	8	5		4	3		1	2	2	2	2	2	2	2	1	5	5					4	1	2	1	1	1	2	2	1	2	1	1	160	2	2	1
52	63	1	1	1	1	1	2	1	1	181	2	1	19	5	4	1	4	1	1	2	1	2	2	2	2	2	2	2	6	0					8	1	2	2	2	1	1	1	2	2	1	1	210	1	2	2
53	62	1	1	2	1	1	2	2	1	61	2	2	14	12	7	7	4	3	3	2	1	2	1	1	2	2	1	1	2	1					1	1	2	1	2	1	2	2	1	2	1	1	100	2	2	1
54	60	1	1	2	2	1	2	2	2	255	2	5	0	0	0	0	0	0	0	2	1	2	1	1	1	2	2	1	9	8					8	1	2	2	2	1	2	2	1	2	3	2		2	2	2
55	72	2	1	2	1	2	2	1	1	284	2	2	18	18	16	16	4	4	4	2	2	1	2	2	2	2	1	2	1	0					1	1	1	1	2	1	1	1	1	2	1	2		2	2	2
56	56	1	1	2	1	2	2	1	1	413	1	1	18	18	12	11	4	4	3	1	2	1	1	2	2	2	2	2	4	0					1	1	2	1	1	1	2	2	1	2	1	2		2	2	2
57	49	2	1	1	1	1	2	1	1	285	2	2	10	2	1	0	4	2	0	2	2	2	2	2	2	1	2	1	8	7	10	8	8	8	8	2	2	2	2	1	2	2	1	2	3	2		2	2	2
58	56	1	1	1	2	1	2	2	2	193	1	3	7	3	3	0	4	2	0	1	2	2	2	2	2	2	2	1	8	8	10	10	7	7	8	1	2	2	2	2	2	2	2	2	3	2		2	2	2
59	43	1		2	2	2	2	2	2	82	2	2					5	6		1	2	2	2	2	1	1	1	1	1	0					0	1	1	1	2	1	1	1	1	2	1	2		2	2	2
60	43	0		2	2	2	2	2	2	82	2									2	2	2	2	2	2	2	2	2	4	1					0	2	1	1	2	1	1	1	1	2	1	2		2	2	2
61	53	1	1	2	1	2	2	1	1	192	2	5	19	14	2	1	5	2	1	2	1	2	2	2	2	2	2	2	4	1					3	1	2	2	2	1	2	2	1	2	1	2		2	2	2
62	73	1	1	2	2	2	2	1	2	147	2	1	8	2	1	0	4	1	0	2	2	2	2	2	1	2	2	2	10	7	10	10	10	10	10	2	2	2	2	2	2	2	2	2	3	2		2	2	2
63	76	1	1	2	1	2	2	1	1	203	2	2	18	20	16	16	4	4	4	2	1	2	2	2	2	2	2	2	3	1	3	1	1	1	2	1	2	1	1	1	1	2	2	1	1	2	2		2	2	2
64	69	1	1	2	1	1	2	1	1	210	2	1	20	20			5	6		1	1	1	2	1	2	2	2	1	5	0					0	1	1	1	2	1	1	1	1	2	0	1	230	1	2	2
65	68	1	1	2	1	2	2	1	1	152	2	2	20	14	7	4	5	3	3	1	1	1	2	2	2	2	1	2	6	6					6	1	2	2	2	2	2	2	2	2	3	2		2	2	2
66	73	2	1	2	1	1	2	1	1	67	2	2	21	14	8	8	5	4	4	1	2	2	2	1	1	2	1	2	7	4					6	1	2	2	2	1	1	1	1	2	3	1	135	2	2	1
67	80	2	1	2	1	1	2	2	1	119	2	2	16	5	2	3	5	4	2	2	1	1	2	1	2	2	1	1	7	2					7	1	2	2	2	1	2	2	2	1	1	2		2	2	2
68	62	2	1	2	2	2	1	2	1	23	2	5	14	3	0	1	4	2	0	1	1	1	2	2	2	2	2	2	8	8					8	2	2	2	2	1	2	2	2	1	3	1	45	1	2	2
69	65	2	1	1	1	2	2	2	1	62	2	1	15	9	8		5	4		2	2	2	2	2	2	2	2	1	8	1					7	1	2	2	2	1	1	1	2	2	1	1	127	1	2	2
70	80	1	1	2	1	1	2	2	1	175	1	2	17	14	13		4	4		2	1	2	1	2	2	2	2	1	2	2					2	1	2	1	2	1	2	2	1	2	1	1	200	1	2	2
71	77	1	1	2	2	1	2	1	1	66	2	2	5	1	1		4	1		2	1	2	2	2	2	2	1	2	7	6					6	1	2	2	2	2	2	2	2	2	2	1	135	1	2	2
72	61	1	1	2	1	2	2	1	1	165	1	1	11	13	12	11	4	4	3	2	2	2	1	2	2	2	2	2	7	3	6	4	4	4	5	1	2	2	2	1	1	1	1	2	2	1	220	2	2	1
73	52	1	1	1	2	1	2	2	1	173	2	5	8	4	2		4	2		1	2	2	1	2	2	2	2	1	8	8					8	1	2	1	2	1	2	2	1	2	3	1	210	1	2	2
74	61	2	1	1	2	1	2	1	1	175	2	5	7	1	0	0	4	0	0	2	1	1	2	2	2	2	2	2	10	10					10	2	2	2	2	2	2	2	2	2	3	1	215	1	2	2
75	55	2	1	2	1	1	2	2	1	67	2	2	8	6	5		4	4		2	2	2	2	2	2	2	2	1	10	10					10	1	2	2	2	2	2	2	2	2	3	1	100	1	2	2

No.	Age	Sex	Weakness	Sensory	Hemianopia	Dysarthria	Ataxia	Aphasia	FD	onset to CT	Wake up	Subtype	NIHSS Presentation	NIHSS 24 hr	NIHSS Discharge	NIHSS 90 d	MRS Presentation	MRS Discharge	MRS 90 d	DM	HTN	CAD	Smoking	Prior stroke	TIA	VHD	AF	Side	NCCT	CTASI	CBV	CBF	MTT	TTP	FU	CT/ DwI	Dense ICA	Dense MCA	MCA dot	Thrombus on CTA	Prox ICA	Dist ICA	Prox MCA	Dist MCA	Collateral Score	Thrombolysis	Time from onset	IV	IA	Bridging
76	55	2	1	2	2	2	2	1	1	129	2	2	15	15	5		5	3		2	2	2	2	2	2	2	2	2	9	8					8	1	2	2	2	2	2	2	2	2	3	2		2	2	2
77	19	2	1	2	1	1	2	2	1	191	2	2	7	3	1	1	4	1	0	2	2	2	2	2	1	1	2	1	7	7					7	1	2	2	2	1	2	2	1	2	3	1	240	1	2	2
78	55	1	1	1	1	1	2	2	1	183	2	3	7	4	0	0	4	0	0	1	2	1	1	2	2	2	2	1	10	10					10	1	2	2	2	2	2	2	2	2	3	1	225	1	2	2
79	81	1	1	1	1	1	2	2	1	117	2	2	16	14	11		4	3		1	1	1	2	2	2	2	2	1	7	7					6	1	2	2	2	1	2	2	2	1	2	1	210	1	2	2
80	64	2	1	2	1	2	2	2	1	132	2	1	8	3	2	0	4	1	0	2	1	2	2	1	2	2	2	1	9	9					9	1	2	2	2	2	2	2	2	2	3	1	160	1	2	2
81	83	1	1	2	1	2	2	1	1	85	2	2	26	10	7	7	4	4	4	1	1	1	1	2	2	2	2	1	2	1					0	1	2	1	2	1	2	2	1	1	1	1	115	1	2	2
82	57	1	1	1	1	1	2	2	1	161	2	1	9	20	20	9	4	4	3	1	1	2	2	1	2	2	2	2	9	0					6	1	2	2	2	1	1	1	2	2	1	1	200	1	2	2
83	51	2	1	2	2	1	1	2	1	91	2	3	8	6	5	0	4	3	0	1	1	2	2	1	2	2	2	1	10	10					9	2	2	2	2	2	2	2	2	2	3	1	140	1	2	2
84	55	2	1	2	2	1	1	2	1	52	2	3	8	6	6	0	4	2	2	1	1	2	2	2	2	2	2	2	10	8					8	2	2	2	2	2	2	2	2	2	3	1	85	1	2	2
85	60	2	1	2	2	1	1	2	1	126	2	1	7	9	7	7	4	4	4	1	1	2	2	2	2	2	2	1	3	0					3	1	2	2	2	1	2	2	1	2	1	1	170	1	2	2
86	82	2	1	2	1	2	2	1	1	137	2	2	21	7	7	5	4	4	4	2	1	2	2	2	2	2	2	2	6	4					4	1	2	2	2	1	1	1	2	2	3	1	185	1	2	2
87	67	1	1	2	1	1	2	2	1	95	2	1	7	5	2	0	4	2	0	1	1	1	1	2	2	2	2	1	7	4					6	1	2	2	1	2	2	2	2	2	2	1	135	1	2	2
88	42	2	1	2	2	1	2	2	1	213	2	5	8	5	5	1	4	3	2	2	2	2	2	2	2	2	2	1	8	8					7	1	2	2	2	2	2	2	2	2	3	1	220	1	2	2
89	58	1	1	1	2	2	2	2	2	127	2	3	6	4	3	0	4	3	2	1	2	2	2	2	2	2	2	2	9	9					7	1	2	2	2	2	2	2	2	2	3	1	145	1	2	2
90	55	1	1	2	1	1	2	2	1	235	1	1	10	11	10		4	4		2	1	2	1	2	2	1	2	1	7	1	7	1	1	1	5	1	2	2	2	1	1	1	2	2	1	2		2	2	2
91	41	1	1	2	1	1	2	2	1	355	2	1	15	15	14		5	4		2	1	2	1	2	2	2	2	1	5	3					2	1	2	1	1	1	1	1	1	1	1	2		2	2	2
92	49	1		1	2	1	2	2	1	170	1	3	5	3	3		4	3		2	2	2	2	2	2	2	2	2	8	8					9	2	2	2	2	2	2	2	2	2	3	2		2	2	2
93	37	1	1	2	2	2	2	1	1	230	2	1	18	19	14		4	4		1	2	2	1	2	2	2	2	2	5	0					3	1	1	1	2	1	1	1	1	1	2	2		2	2	2
94	20	1	1	2	2	1	2	2	1	240	1	5	11	11	5		4	4		2	2	2	2	2	2	2	2	1	8	7	8	3	3	3	8	1	2	2	2	2	2	2	2	2	3	2		2	2	2
95	84	2	1	2	2	2	2	1	1	213	2	5	11	10	5	8	4	5	4	2	1	2	2	2	2	2	2	1	7	4					2	1	2	1	2	1	2	2	1	2	2	2		2	2	2
96	52	2	1	2	2	2	2	1	1	139	2	1	19				4	6		2	2	2	2	2	2	2	2	2	1	1					1	1	1	1	2	1	1	1	1	2	1	2		2	2	2
97	69	1	1	2	2	2	2	1	1	279	2	2	21	16	18	14	5	4	4	1	1	1	2	1	2	2	2	2	6	6	6	6	6	6	5	1	2	2	2	2	2	2	2	2	2	2		2	2	2
98	60	1	1	2	2	2	2	1	1	180	2	2	10	10	4	0	4	2	1	1	1	2	2	1	2	1	2	2	9	8	9	7	7	7	9	1	2	2	2	2	2	2	2	2	3	1	225	1	2	2
99	51	1	1	2	2	1	2	2	1	97	2	2	14	6	0	0	5	0	0	1	2	1	2	2	2	1	1	1	6	4					2	1	2	1	2	1	2	2	1	2	1	1	140	2	2	1
100	68	1	1	2	1	2	2	1	1	162	1	1	12	11	11	7	4	3	1	1	1	2	1	1	2	2	2	2	7	6	7	2	1	1	7	1	2	2	2	1	1	2	2	2	3	2		2	2	2

No.	101	102	103	104	105
Age	60	67	45	58	78
Sex	1	2	1	1	2
Weakness	1	1	1	1	1
Sensory	1	`	1	1	2
Hemianopia	2	1	1	1	2
Dysarthria	1	2	2	1	1
Ataxia	2	2	2	2	2
Aphasia	1	1	1	2	2
FD	1	1	1	1	2
onset to CT	222	163	190	342	201
Wake up	1	2	2	2	2
Subtype	1	5	5	5	3
NIHSS Presentation	9	12	21	14	13
NIHSS 24 hr	9	9	19		4
NIHSS Discharge	9	7	18		1
NIHSS 90 d	7	5	14		0
MRS Presentation	4	3	5	5	4
MRS Discharge	4	3	4	6	1
MRS 90 d	3	2	4		0
DM	1	1	2	1	1
HTN	1	2	1	1	2
CAD	1	2	1	1	2
Smoking	2	2	2	2	2
Prior stroke	2	2	2	2	2
TIA	2	1	2	2	2
VHD	2	2	2	2	2
AF	2	2	2	2	2
Side	1	2	2	1	2
NCCT	7	7	3	3	10
CTASI	6	6	2	3	10
CBV				3	10
CBF				3	10
MTT				3	10
TTP				3	10
FU	7	6	3	0	10
CT/DwI	1	1	1	1	2
Dense ICA	2	2	1	2	2
Dense MCA	2	2	1	2	2
MCA dot	1	2	2	2	2
Thrombus on CTA	1	2	1	1	2
Prox ICA	1	2	1	2	2
Dist ICA	1	2	1	2	2
Prox MCA	2	2	1	1	2
Dist MCA	1	2	2	2	2
Collateral Score	2	3	1	2	3
Thrombolysis	2	2	1	2	2
Time from onset			220		
IV	2	2	1	2	2
IA	2	2	2	2	2
Bridging	2	2	2	2	2

KEY TO MASTER CHART

- Sex- 1= Male, 2= Female
- Clinical symptoms (Weakness to FD)- 1= Yes, 2= No
- Stroke Subtype- 1= Large vessel, 2= Cardioembolic, 3= Lacunar, 4= Specific cause, 5= Undetermined.
- Wake up stroke- 1= Yes, 2= No
- Risk Factors (DM to AF)- 1= Yes, 2= No
- CT/ DWI- 1= CT, 2= DWI
- Vessel Occlusion (all cells)- 1= Yes, 2= No
- Thrombolysis (Y/N, IV, IA, Bridging)- 1= Yes, 2= No
- Time of CT and thrombolysis presented in minutes.

ABBREVIATIONS USED IN MASTER CHART

- FD- Facial Deviation
- NIHSS- National Institute of Health Stroke Scale
- MRS- Modified Rankin Scale
- DM- Diabetes Mellitus
- HTN- Hypertension
- CAD- Coronary artery disease
- TIA- Transient ischemic attack
- VHD- Valvular heart disease
- AF- Atrial fibrillation
- NCCT- Non contrast computed tomography
- CTASI- CT angiogram source image
- FU- Follow up
- CBV- Cerebral blood volume
- CBF- Cerebral blood flow
- MTT- Mean transit time
- TTP- Time to peak
- DWI- Diffusion weighted imaging
- MCA- Middle cerebral artery
- ICA- Internal carotid artery
- IV- Intravenous
- IA- Intraarterial

ANNEXURE V
ABBREVIATIONS

- FD- Facial Deviation
- NIHSS- National Institute of Health Stroke Scale
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- MTT- Mean transit time
- TTP- Time to peak
- DWI- Diffusion weighted imaging
- MCA- Middle cerebral artery
- ICA- Internal carotid artery
- IV- Intravenous
- IA- Intraarterial
- ASPECTS- Alberta stroke program early CT score
- ECASS- European Cooperative Acute Stroke Study
- CTP- CT perfusion
- ICH- Intracranial hemorrhage
- rtPA - Recombinant tissue plasminogen activator
- EIC- Early ischemic change
- AIS- Acute ischemic stroke
- BA- Basilar artery
- IC- Inernal capsule
- I- Insula
- C- caudate
- L- Lentiform
- CSF- Cerebrospinal fluid
- NINDS- National Institute of Neurological Disorders and Stroke
- PROACT- Prourokinase Acute Cerebral Infarct Trial
- ACA- Anterior Cerebral artery
- PCA- Posterior cerebral artery
- MDCT- Multidetector CT
- FLAIR- Fluid attenuation inversion recovery
- SWI- Susceptibility weighted imaging
- MRA- Magnetic resonance angiogram
- TOF- Time of flight
- GRE- Gradient refocused echo
- CEMRA- Contrast enhanced magnetic resonance angiogram
- TICI score- Thrombolysis in cerebral infarction score