A

ASSESSMENT OF COLLATERAL STATUS USING MULTIPHASIC CT ANGIOGRAPHY IN THE ACUTE ANTERIOR CIRCULATION ISCHEMIC STROKE: ITS CORRELATION WITH CLINICAL AND RADIOLOGIC OUTCOMES

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled "Assessment of collateral status using multiphasic CT angiography in the acute anterior circulation ischemic stroke: its correlation with clinical and radiologic outcomes" for the degree for DM "NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY" has been carried out by Dr. Adhithyan R under our supervision and guidance. 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 "Assessment of collateral status using multiphasic CT angiography in the acute anterior circulation ischemic stroke: its correlation with clinical and radiologic outcomes" has been prepared by me under the supervision and guidance of Dr.Kesavadas (Professor), Dr.Sylaja (Professor), Dr.Bejoy Thomas (Professor), Dr.Jaydevan (Add. Professor), Dr.Santhosh K (Associate Professor), Sree Chitra Institute for Medical Sciences and Technology, Trivandrum.

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CONTENTS

Introduction

INTRODUCTION:

Computed tomography Angiography (CT) remains the initial imaging modality of choice in hyper-acute stroke. Non-contrast CT (NCCT) excludes intracranial hemorrhage and tumor and detects early signs of infarction. CT angiography (CTA) can rapidly provide useful information that may influence management and may indicate the extent of vessel occlusion, all of which can influence clinical outcome and recanalization.

Recently, leptomeningeal collaterals in acute stroke have been shown to have a significant impact upon the clinical and radiological outcome of the patients. Collaterals can be studied by various imaging modalities including CT, MRI, catheter angiography and transcranial Doppler. However, in the majority of the stroke centers throughout the world, plain CT followed by CT angiography is the initial and in many cases sole imaging modality to assess the acute stroke patients for major vessel occlusion as well as triage for intravenous thrombolysis or mechanical thrombectomy. Infarct has shown to evolve from a few hours to days and it varies depending upon the intracranial collaterals of the patient. In almost the majority of the studies, collateral status was evaluated by single-phase CT angiography.

Recently, the concept of multiphase CT angiography is evolving and few centers have adopted this as an initial imaging modality for acute stroke patients. The benefits of multiphase CT angiography over single-phase CT angiography has to be validated for large-scale implementation.

We hypothesized that multiphase CT angiography collaterals due to its dynamicity would predict the clinical as well as radiologic outcomes of the patients better than the static single-phase CT angiography. It would also a good prognostic marker for the risk of major hemorrhagic transformation.

So we designed this study as a comparison of multiphase CTA collateral scores with the single-phase collateral scoring system in acute stroke patients and its correlation with early clinical outcome (NIHSS at discharge), late clinical outcome (mRS 90 days), radiologic outcomes (ASPECTS 24 hours, hemorrhagic transformation).

Aims & Objectives

AIMS AND OBJECTIVES

“Comparison of the multiphasic computed tomographic (CT) angiography collateral scoring system with already available single-phase CT scoring system, in assessing intracranial vascular collateral status, in patients with acute anterior circulation ischemic stroke and its ability in determining clinical as well as radiological-outcomes”

Review of Literature

REVIEW OF LITERATURE

1.INTRODUCTION:

Acute stroke is the second most common cause of death worldwide after coronary artery disease. Globally approximately 6.3 million deaths (1) were reported due to acute stroke in 2015. Acute stroke may be ischemic or hemorrhagic. Atherosclerosis and embolism are major causes of acute ischemic stroke. In the acute ischemic stroke, arterial recanalization by either intravenous thrombolysis or mechanical thrombectomy remains the principal treatment. Cerebral neuronal damage is not uniform in the initial few hours after stroke onset. Depending upon intra cranial collaterals, infarct may not be complete for hours or even days (2). In some patients infarct gets completely developed in a few hours and other the ischemic tissue remains viable for few days, depending upon the degree of leptomeningeal collaterals which have a significant protective role. (3)

2.ANATOMY OF COLLATERAL CIRCULATION: (4)

Collateral types	**Vessels**
Large-artery communications between the extracranial and intracranial circulations	Ophthalmic artery, maxillary artery, superficial temporal artery, occipital artery. Mainly in chronic occlusion.
Circle of Willis	Anterior and posterior communicating artery. 50% - complete.
Leptomeningeal collaterals	Important routes in acute occlusion. Small arteriolar communications allowing retrograde perfusion. Between ACA and MCA. Between MCA and PCA.

3.FACTORS AFFECTING COLLATERALS DEVELOPMENT:

History of hypertension is associated with poor intracranial collaterals (5). Use of statins prior to stroke was linked to better collaterals (6). Potential of collaterals developing decreases with age. Hyperglycemia, dehydration, hyperthermia, cardiac failure, pulmonary compromise, renal failure, electrolyte disturbance, diffuse atherosclerosis were also shown to reduce the development of collaterals.

Incomplete circle of Willis also leads to reduced collateral blood flow. Rapidness of occlusion also has an impact on collaterals. Gradual onset major vessel occlusion like moya-moya disease have good collaterals development than acute occlusion.

4.IMAGING OF COLLATERALS:

Conventional digital subtraction angiography (DSA), CT angiography, MR angiography, Trans cranial Doppler (TCD) are the imaging methods available to evaluate intracranial collaterals

4.1DSA:

The gold standard method allowing assessment of all three major type of collaterals.

A. Kucinski et al method (7):

Good if >= three MCA branches up to M2 segment, retrograde filling. Poor < three MCA branches retrograde filling.

B. American Society of Interventional and Therapeutic Neuroradiology and the Society of Interventional Radiology (ASTIN/SIR) (8): 5-point scale.

0	No collaterals visible to the ischemic site
1	Slow collateral to the periphery Persistence of the defect
2	Rapid filling of collaterals to the periphery Persistence of the defect
3	Slow collaterals to the periphery Complete angiographic blood flow
4	Rapid filling of collaterals to the periphery Complete angiographic blood flow

4.2 CT ANGIOGRAPHY EVALUATION OF COLLATERALS:

Advantages of CT angiography for collateral assessment:

- Widely available.
- Rapid assessment.
- Good spatial resolution for assessment of leptomeningeal collaterals.
- CT perfusion, multiphasic angiograms, cervical vessel imaging can be done simultaneously.

Single-phase CT angiography collateral scoring methods for anterior circulation ischemic stroke:

A.Tan scale(8):

0- absent collateral supply in the occluded MCA territory.

1- Collateral supply filling <= 50% but >0% of the occluded MCA territory.

2 - Collateral supply filling > 50% but < 100% of the occluded MCA territory.

3 - 100% collateral supply of the occluded MCA territory.

Patients with high TAN collateral score had lower pretreatment perfusion defects, smaller final infarct and also final functional outcome, as well as recanalization rates.

B.Modified Tan Scale:

Simplest and rapid system, with less interobserver variation.

Good- >= 50% of the MCA territory.

Poor - <50% of the MCA territory.

C.Miteff System :

3-point score grading of middle cerebral artery collateral branches with respect to the Sylvain fissure. One study showed miteff is more reliable predictor of good outcome than other single-phase scoring systems(11). Patients with good collaterals have lower NIHSS score (3), small infarct size and better prognosis.

3 - vessels reconstituted distal to the occlusion.

2-vessels seen at the Sylvian fissure.

1-vessels seen only in the distal superficial branches.

D.Maas System (9):

5-point score comparing collaterals on the affected hemisphere against those on the unaffected side.

5 -exuberant.

4-more than the contralateral side.

3-equal to the contralateral side.

2-less than the contralateral side.

1-no vessel seen.

E.Alberta Stroke Program Early CT Score (ASPECTS) 20 Point Grading Scale(10):

Collaterals are scored in each of the 10 regions corresponding to the ASPECTS system, to form a score from 0 to 20

0- artery not seen.

1- less prominent.

2- equal or more prominent

4.3 MRI EVALUATION OF COLLATERALS:

A.T2 FLAIR:

In patients with MCA occlusion, prominent distal T2 FLAIR hyperintense signals (12,13) is associated with smaller initial ischemic infarct, larger diffusion-perfusion mismatch, better NIHSS score and smaller subacute ischemic lesion volume. Although definitely not proved, distal T2 FLAIR hyperintense signal may be said to be related to good collateral flow distal to the occlusion site (14) (15).

B.Arterial spin labelling (ASL):

Territorial ASL gave information regarding intracranial collaterals, comparable to DSA in steno occlusive patients. (16)

3D pseudo-continuous ASL with multiple post label delays had been used to estimate antegrade and collateral flow in unilateral MCA stenosis. (17)

ASL collaterals detected in acute stroke were showed to correlate with neurological outcome of mRS at discharge. (18,19)

C.Susceptibility weighted imaging (SWI)

-SWI was shown to accurately predict intracranial collateral circulation in acute infarcts and can be used for prognostication and curative evaluation.(20)

-SWI-diffusion mismatch was also proved to identify patients who benefit from reperfusion therapy (21).

4.4TRANS CRANIAL DOPPLER:

High velocity, low resistance flow pattern (22,23) in ipsilateral ACA or PCA in patients with MCA occlusion was associated with leptomeningeal collaterals and is termed flow diversion(FD). 30% difference of flow velocity between right and left ACA is associated with leptomeningeal collaterals. FD is more commonly seen with ACA than PCA. FD was shown associated with CT angiography collaterals, admission infarct volume, and 24-hour infarct volume. FD can be used as bedside prognostic tool in anterior circulation stroke.

4.5 LATEST IMAGING-MULTIPHASIC CT COLLATERAL SCORING (24):

Multiphase CT angiography is the latest modification of the CT angiography protocol for better evaluation of intra cranial collaterals. This imaging modality is still not widely used. This was first used in the ESCAPE trial (25). In this type of angiography, time-resolved angiograms from the skull base to the vertex would be taken in three phases at peak arterial, peak venous and late venous phases. Radiation dose and acquisition time is lower than CT perfusion. Unlike CT perfusion, post-processing and additional contrast are not required.

Multiphasic CT is using a six-point scale (ALBERTA stroke program) for assessing pial collaterals (later discussed in materials and methods), by comparing with the normal hemisphere in analyzing the number of phases delay as well as the extent, prominence or absence of vessels in the ischemic territory. Multiphasic CT Collateral scales are finally graded as, 0 and 1-poor, 2 and 3- intermediate, 4 and 5- good.

5. COLLATERALS AND STROKE CLINICAL, RADIOLOGICAL OUTCOMES:

- CT collaterals (26) were shown to correlate well with CT perfusion imaging data. In patients of IMS III trial (27), better collaterals were proved to have **small infarct core and larger mismatch**. Some stroke trials used CT perfusion and Ct angiography collaterals as an imaging tool for inclusion criteria of patients for endovascular management.

  In stroke trials like Extend IA (28), SWIFT prime (29) CT perfusion was used. While CT collaterals were used in the ESCAPE trial. Ct perfusion has various disadvantages like post-processing time, variations in CTP acquisition and post-processing software.
- Good base line collaterals at sylvian fissure were associated with **good functional recovery (30) and reduced mRS at 90 days.** This was mediated through reduced final infarct volume.
- Poor intracranial collaterals were associated with a high incidence of **hemorrhagic transformation** (31,32). In one study (31), the rate of significant hemorrhage (> 25ml) after intra arterial therapy, was seen in 25% of patients with poor collateral, while it was only 2.7% in patients with poor collaterals. Hence, intra arterial therapy was cautioned in patients with very poor collaterals.
- Good collaterals in angiography were associated with **successful recanalization (33,35)** in Solitaire FR With the Intention for Thrombectomy (SWIFT) study (34).

- ASA revised guidelines 2018 (36) for acute stroke management, mentioned that “it may be reasonable to include collateral status into **clinical decision making in some patients to include for mechanical thrombectomy**” with a level of evidence C (limited data) and class 2b class of recommendation.
- In patients with good collaterals, there would be a **better dissolution of thrombus with IV-tPA** (Tissue plasminogen activator) by transporting fibrinolytic to either side of the thrombus. In systematic review and meta - analysis (37,38) of the impact of collateral status in functional outcomes after thrombolysis showed good collateral were associated with better recanalization and reperfusion rate as well as good long term functional outcome.

6. **POSTERIOR CIRCULATION COLLATERALS ASSESSMENT:**

-One study (39) used a collateral staging method 0 to 2. 0=no pcom, 1=1 pcom and 2 both pcom present. Presence of pretreatment bilateral pcom is associated with favorable outcome after endovascular therapy.

-Another CT angiography collateral scoring method (10 point scoring) was provided by Erik et al(40). In this method, each PICA, AICA, SCA if visible, is given a score of 1. Each Pcom is given a score if diameter less than PCA and 2 if more than PCA. Score 6 to 10 is good.

-Qureshi at al (41) gave a posterior circulation angiographic collateral scoring method-Grades I and II - retrograde filling of the basilar artery through PCA with or without filling of the superior cerebellar artery, respectively. Grades III and IV - bilateral or unilateral anastomoses of cerebellar arteries or PCAs, respectively.

7. COLLATERALS THERAPEUTICS FOR ACUTE ISCHEMIC STROKE:

Experimental collateral therapeutics like inhaled nitric oxide(42), high dose albumin(43), sphenopalatine ganglion stimulation (44), transient aortic occlusion(45) had been showed to improve collaterals in animal models. However, before the implementation of these methods, further studies regarding collaterals pathophysiology and its implications have to be evaluated in large-scale studies.

Materials & Methods

MATERIALS AND METHODS

Institutional Ethics Committee (IEC) approval was obtained vide letter No. **SCT/IEC/987/OCT-2016** (Annexures). This was a prospective study conducted in department of IS&IR, SCTIMST, between October 2016 and May 2018. Consecutive patients who were evaluated for inclusion into the study.

Informed written consent was obtained from each and every patient/guardian after explanation of all aspects of the study as per consent form and details were noted as per proforma.(Annexures)

All patients with acute stroke who underwent both plain CT followed by multiphase CT angiography evaluation were included in the study. No pregnant woman, prisoner, staff, student or healthy volunteer was inducted into this study.

INCLUSION CRITERIA:

1. Patient presenting to the SCTIMST stroke or emergency department with symptoms consistent with the acute ischemic stroke.
2. Age > 18 yrs.
3. Pre-treatment multi-phase CTA done within 8 hours of stroke symptom onset.
4. Pre-treatment NIHSS score >=5
5. Patients consenting for their inclusion in the study.

EXCLUSION CRITERIA:

1. Intracranial haemorrhage (ICH) identified on baseline CT.
2. Previous moderate to large stroke in the ipsilesional hemisphere.
3. Unable to have CT-angiography performed due to contrast allergy, known chronic/acute kidney failure history, pregnancy or other reasons.
4. Patients aged less than or equal to eighteen years.

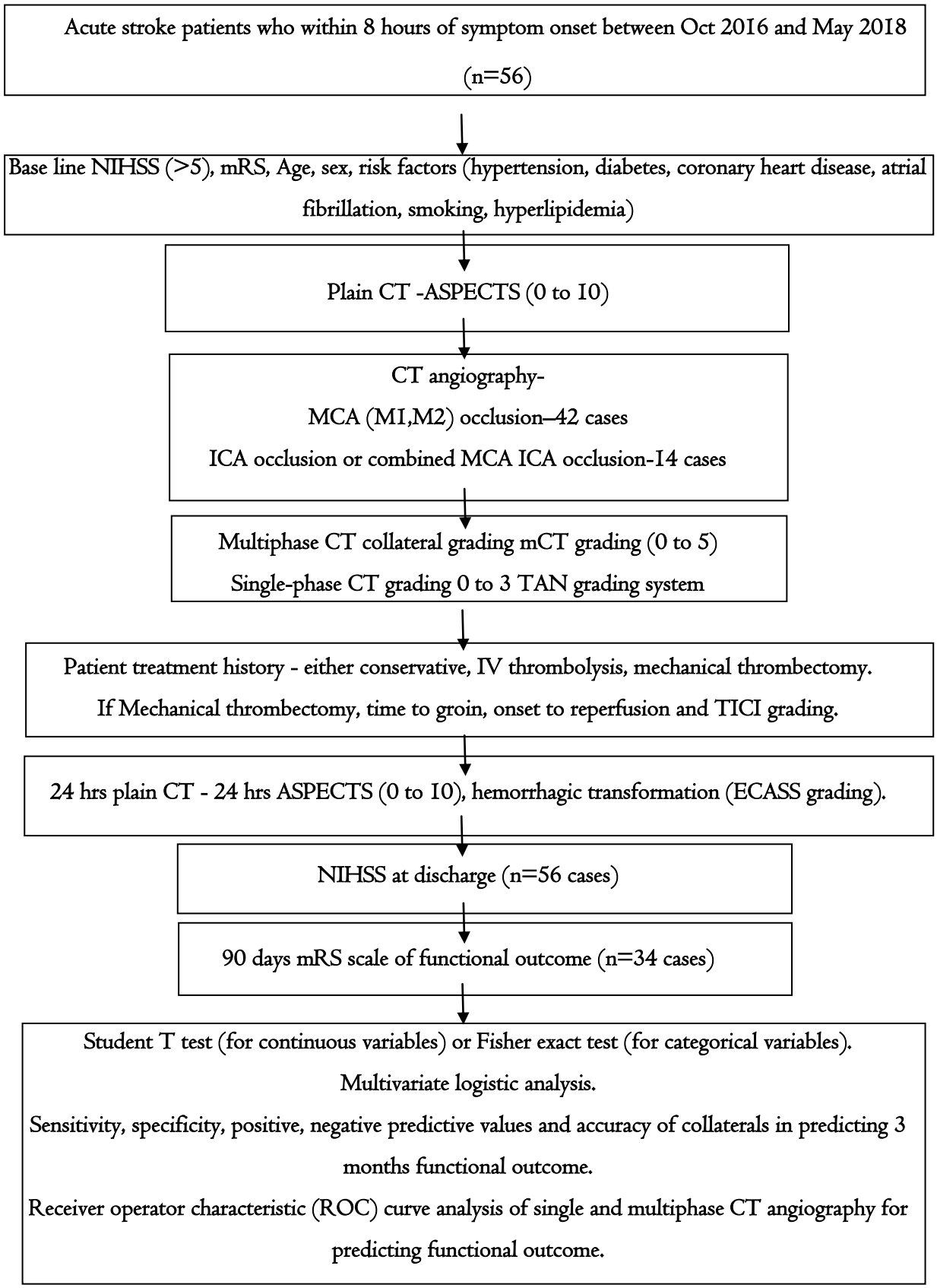
STUDY DESIGN

1. IEC approval was obtained vide letter SCT/IEC/987/OCT-2016
2. Written informed consent of all eligible patients was obtained.
3. Patients' history and other clinical details were documented as per Performa.
4. Patients underwent plain CT followed by multiphase CT angiography, as per existing hospital protocol. In Plain CT, ASPECTS (0 to 10) details were noted.
5. In multiphase CT angiography, major vessel occlusion was noted. Only MCA (M1, M2) or ICA occlusion or combined MCA ICA occlusion cases who presented within 8 hours of symptom onset were included.
6. Then multiphase CT collateral grading was assessed (0 to 5). Then single phase CT grading 0 to 3 as per most widely used TAN grading system was assessed.
7. Base line NIHSS, mRS of the patient were assessed and recorded by certified neurologist. Age, sex, risk factors (hypertension, diabetes, coronary heart disease, atrial fibrillation, smoking,

hyperlipidemia) of the patients were recorded.

8. Patients treatment history details- either conservative, iv thrombolysis, mechanical thrombectomy were included in the study.
9. In patients who had undergone mechanical thrombectomy, time to groin, onset to reperfusion and mTICI grading were also included in the study.
10. All patients underwent 24 hrs plain CT as per our institutional protocol and details of CT ASPECTS (0 to 10), hemorrhagic transformation (ECASS grading) were assessed.
11. All patients were examined for NIHSS at discharge. Those patients who were alive at discharge were followed after 90 days to assess mRS scale of functional outcome. Good and poor functional outcomes were defined by mRS scores of 0–2 and 3–6, respectively.
12. Categorical and continuous variables were tabled. Statistical differences of these variables in single and multiphase CT collateral groups were assessed by student T test (for continuous variables) or Fisher exact test (for categorical variables). Multivariate logistic was done for variables with significant difference. Statistical analysis of the data was performed and sensitivity, specificity, positive, negative predictive values and accuracy of both the single and multiphase CT angiography collaterals in predicting 3 months functional outcome (mRS) was assessed. Receiver operator characteristic (ROC) curve analysis of single and multiphase CT angiography for predicting functional outcome along with area under curve (AUC), Youden’s J, test efficiency individually for both collateral grading as assessed.

FLOWCHART OF STUDY DESIGN:



STUDY PROTOCOLS:

HEAD PLAIN CT:

Examinations ware performed in the 256 slice CT scanner (Philips). All patients who fulfilled the inclusion criteria, undergone standard unenhanced CT with 0.625-mm section thickness. It was reformed into 3mm thick images to see for ASPECTS at admission.

MULTIPHASE CT ANGIOGRAPHY:

Scanning was triggered by using bolus tracking, with the region of interest placed in the posterior aortic arch with the trigger threshold set at 150 HU. Three phases of cerebral angiograms of brain vasculature ware acquired.

The first phase covers the aortic arch to vertex region during peak arterial phase. Subsequent two phases cover the skull base to the vertex in peak venous and late venous phase respectively. Images were acquired at an interval of 8 seconds apart.

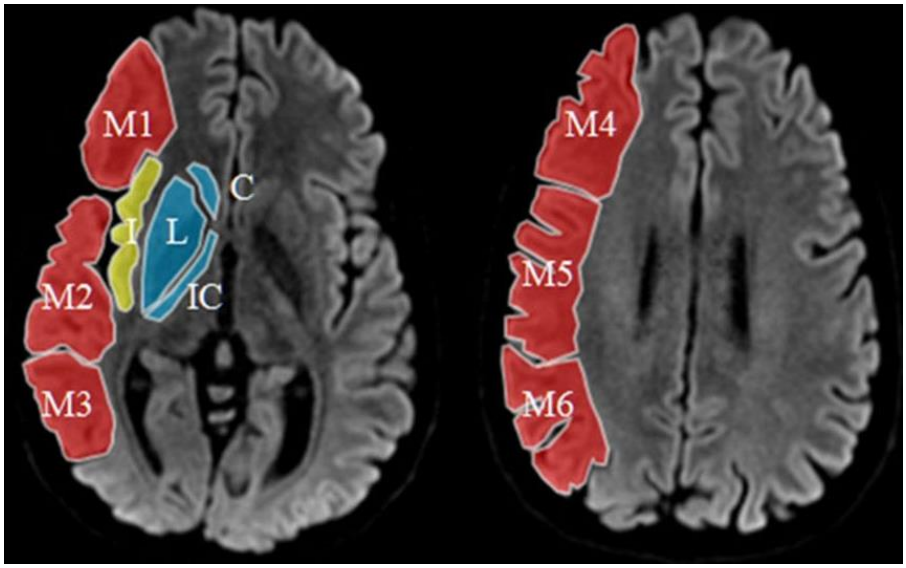
A total of 50 mL of contrast material (Iohexol, Omnipaque/ Iodixanal, Visipaque) was be injected at a rate of 5 mL/sec and followed by 30 ml normal saline chase.

Source images were reformatted into 3-mm-thick axial, coronal, and sagittal projections.

DEFINITIONS OF PARAMETERS:

Plain CT ASPECTS:

Alberta stroke programme early CT score (ASPECTS) (46,47) is a 10-point scale to assess early ischemic changes in acute middle cerebral artery stroke in plain CT. Two levels of the brain are read, one at the level of basal ganglia and another at the level of ventricles just above basal ganglia. One point is deducted from the initial score of 10 if any of the regions involved. Caudate, internal capsule, lentiform nucleus, insula, M1 to M3 (at the level of basal ganglia), M4 to M6 (at the level of ventricles). Plain CT ASPECTS was calculated in our study at the time of admission as well as in 24 hours follow up CT, to assess the extent of stroke.



NIHSS:

NIHSS (48,49) is a 42-point quantitative measure to evaluate the neurological deficit in stroke patients. It can be performed quickly and has good interrater agreement. 11 items (level of consciousness, horizontal eye movement, visual field, facial palsy, motor arm, motor leg, limb ataxia, sensory, language, speech, extinction and inattention) were evaluated in NIHSS, and each item has scores 0 to 4 depending upon patient ability. Maximum score is 42 and minimum score is 0.

Patients with scores less than 5 were considered minor stroke and excluded in our study. Patients with MCA M1/ ICA occlusion with NIHSS 5 to 25 were taken for mechanical thrombectomy.

mRS:

mRS is a 6 point clinical outcome score (50, 51). It is the widely used disability/ dependency assessment scale of daily activities of people after acute stroke. Its scale ranges from 0 to 6, with 0 being no symptoms and 6 being dead. In our study, mRS of the patients at the time of admission, at discharge and 90 days follow up were calculated. mRS at 90 days follow up with scores <=2 were considered good functional outcome, while scores>2 were considered bad outcome.

Modified Rankin Scale (mRS)

Score	Description
0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities
2	Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance
3	Moderate disability; requiring some help, but able to walk without assistance
4	Moderately severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance
5	Severe disability; bedridden, incontinent and requiring constant nursing care and attention
6	Dead
	TOTAL (0–6): ____

SINGLE PHASE CT COLLATERAL GRADING:

In our study we used the most widely used single-phase intracranial collateral scoring method –TAN system. TAN system scoring is a 3-point scoring system done in traditionally followed single-phase CT angiography. We have applied this system in the first phase of the multiphase CT angiography. Scores 0 and 1 were considered poor collaterals. 2 and 3 scores were considered good collaterals.

TAN COLLATERAL SCORE	FINDINGS IN THE FIRST PHASE OF CT ANGIOGRAPHY
0	No collateral supply in the occluded MCA territory.
1	<=50% collateral supply in occluded MCA territory
2	>50 to <100% collateral supply in occluded MCA territory
3	>=100% collateral supply in occluded MCA territory.

MULTIPHASE CT COLLATERAL GRADING :

We used the multiphase CT angiography scoring developed by ALBERTA stroke program (25). It is based upon scoring intracranial collaterals in the affected MCA ischemic territory, in three individual subsequent phases of multiphase intracranial CT angiography. Scores 0 to 3 were considered poor collaterals. Scores 4 and 5 were considered good collaterals.

MULTIPHASE CT ANGIOGRAPHY COLLATERAL SCORE	FINDINGS IN CT ANGIOGRAPHY
0	Compared to asymptomatic contralateral hemisphere there are no vessels in any phase within the occluded vascular territory
1	Compared to asymptomatic contralateral hemisphere there are just a few vessels visible in any phase within the occluded vascular territory
2	Compared to asymptomatic contralateral hemisphere there is a delay of two phases in filling in of peripheral vessels and decreased prominence and extent or a one-phase delay and some regions with no vessels in some part of the territory occluded
3	Compared to asymptomatic contralateral hemisphere there is a delay of two phases in filling in of peripheral vessels but prominence and extent is the same or there is a one phase delay and decreased prominence /reduced number of vessels in some part of the territory occluded
4	Compared to asymptomatic contralateral hemisphere there is a delay of one phase in filling in of peripheral vessels, but prominence and extent is the same
5	Compared to asymptomatic contralateral hemisphere, there is no delay and normal/increased prominence of peripheral vessels/normal extent within the occluded arteries territory within the symptomatic hemisphere

ECASS II HEMORRHAGIC TRANSFORMATION SCALE:

We used the European Cooperative Acute Stroke Study (ECASS II) hemorrhagic transformation scale to look for any hemorrhagic transformation in the follow up 24 hours CT. ECASS II PH2 was considered poor radiological outcome in the follow up CT (52,53).

ECASS II HEMORRHAGIC TRANSFORMATION SCALE	BLEED STATUS IN 24 HRS FOLLOW UP CT
Haemorrhagic infarction type 1 (HI1)	Petechial haemorrhages at infarct margins
Haemorrhagic infarction type 2 (HI2)	Petechial haemorrhages throughout the infarct no mass-effect due to bleed
Parenchymal hematoma type 1 (PH1)	≤30% of the infarcted area Minor mass effect due to bleed
Parenchymal hematoma type 2 (PH2)	>30% of infarct zone, substantial mass effect attributable to the haematoma

MODIFIED TREATMENT IN CEREBRAL ISCHEMIA (mTICI) SCALE.(54)

mTICI Grades	**Definitions**
Grade 0	No perfusion
Grade 1	Antegrade reperfusion past the initial occlusion, but limited distal branch filling with little or slow distal reperfusion
Grade 2a	Antegrade reperfusion of less than half of the occluded target artery previously ischemic territory
Grade 2b	Antegrade reperfusion of more than half of the previously occluded target artery ischemic territory
Grade 3	Complete antegrade reperfusion of the previously occluded target artery ischemic territory

STATISTICS

The patient demographic data, risk factors, base line plain CT, CT angiography collateral status, treatment history, follow up radiological and clinical outcomes were tabulated in Microsoft Excel format.

Categorical and continuous variables were tabled.

1. Statistical differences of these variables in single and multiphase CT collateral groups were assessed by **student T test (for continuous variables) or Fisher exact test (for categorical variables)**.
2. **Multivariate logistic regression and linear regression analysis** were done for variables with significant difference in student T/ Fisher exact test, to assess the odds ratio, p value and linear regression coefficient value of the variables.
3. **Sensitivity, specificity, positive, negative predictive values, likelihood ratios and accuracy** of both the single and multiphase CT angiography collaterals in predicting 3 months functional outcome (mRS) was assessed.
4. **Receiver operator characteristic (ROC) curve analysis** of single and multiphase CT angiography for predicting functional outcome along with area under curve (AUC), youden's J, test efficiency were calculated individually for both collateral grading were assessed.
5. **Spearman coefficient** was done to assess the correlation of single and multiphase CT angiography with variables.

Results

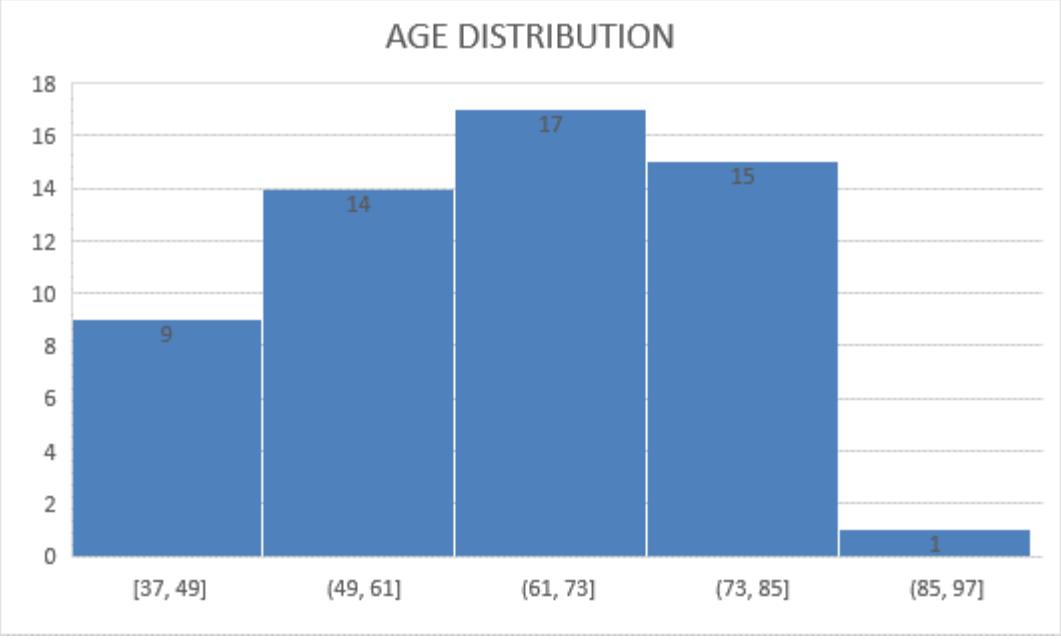
RESULTS

DEMOGRAPHIC DETAILS

A total of 56 consecutive patients with anterior circulation acute stroke with major vessel (M1, M2 or ICA or combined), who presented to the institute between October 2016 and 30 June 2018 were included in this prospective study.

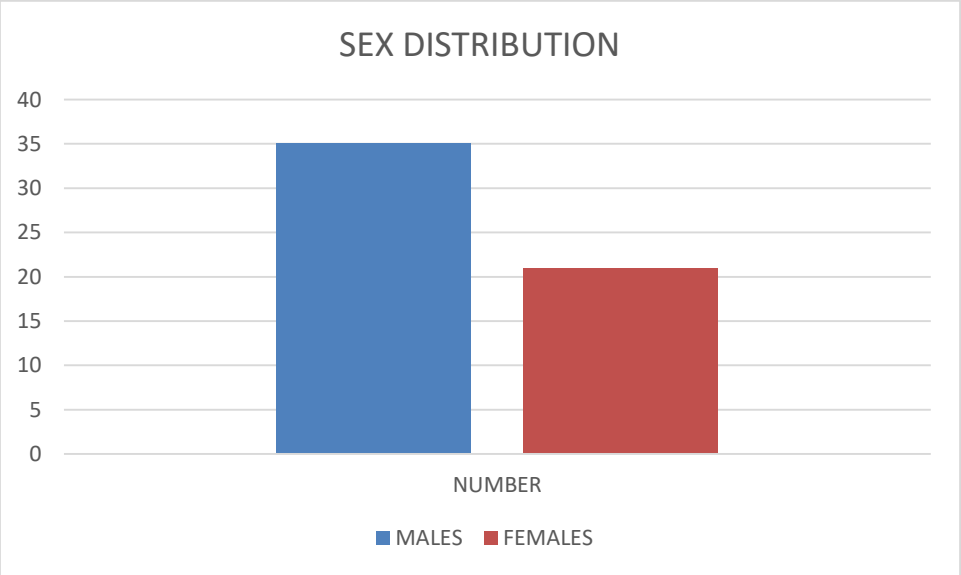
The age of patients in the study ranged from 37 to 86 years, with the mean age of 63 years.

FIGURE 1: AGE IN YEARS



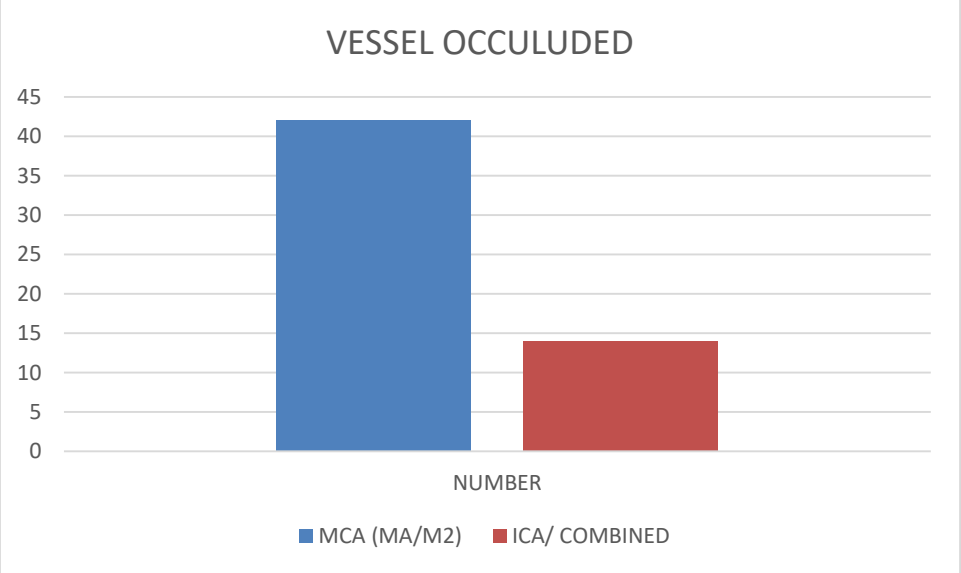
There were 35 males and 21 females in the study group. The male to female sex ratio within the cohort was 5:3.

FIGURE 2: SEX DISTRIBUTION



There were 42 MCA occlusion and 14 cases of ICA/ combined ICA-MCA occlusion cases in this study.

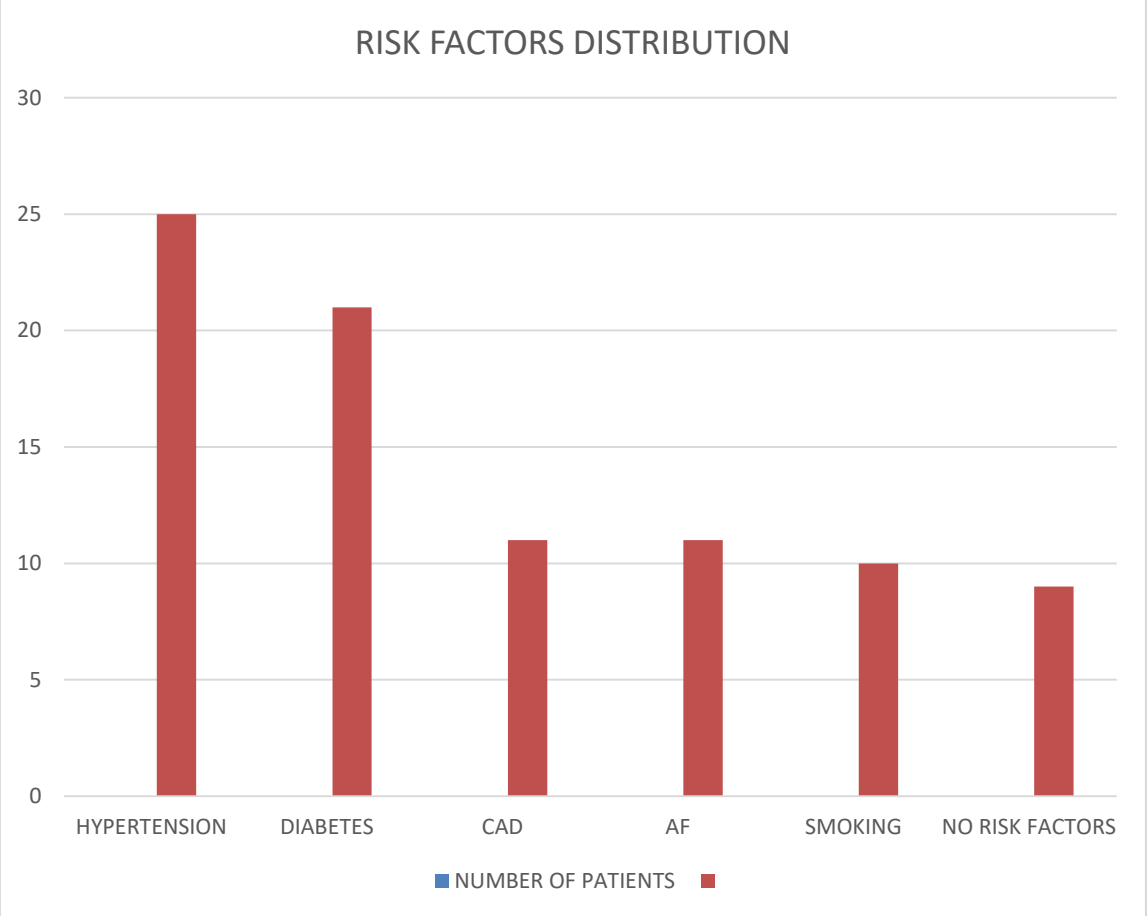
FIGURE 3: VESSEL OCCLUDED



RISK FACTORS:

The commonest risk factor of our patients was hypertension (n=25), diabetes (n=21) followed by CAD (11 cases), AF (11 cases) and smoking (10 cases). 9 patients had no risk factors.

FIGURE 4: RISK FACTORS DISTRIBUTION



Inter-observor reliability calculated after evaluating by two independent observors of 20 random cases (n=20) , showed a excellant inter rater reliability, with kappa vaule of 0.9 in both single phase and multiphase CT collaterals evaluation.

VARIABLES	TOTAL	CC STATUS ON SINGLE PHASE POOR (0 TO 1)	GOOD (2 TO 3)	P=	CC STATUS ON MULTIPHASE POOR (0 to 3)	GOOD(4,5)	P=
PATIENTS, N(%)	56	39(69%)	17(30%)		32(57%)	24(42%)	
AGE (MEAN+/-SD) YEARS	63 (+/-12)	65(+/-14)	63(+/-11)	0.632	65.3(+/-11)	61.41(+/-13)	0.260
MALE	34(60%)	27(69%)	7(41%)	0.0001	21(65%)	13(54%)	0.003
SMOKING	10(18%)	6(15%)	4(23%)	0.206	5(16%)	5(20%)	0.581
DIABETES	22(39%)	18(46%)	4(23%)	0.001	13(40%)	9(37%)	0.774
HYPERLIPIDEMIA	10(18%)	6(15%)	4(23%)	0.203	6(18%)	4(16%)	0.850
HYPERTENSION	25(45%)	21(54%)	4(23%)	0.0001	16(50%)	9(37%)	0.086
ATRIAL FIBRILLATION	10(18%)	5(13%)	5(29%)	0.008	6(18%)	4(16%)	0.850
CAD	10(18%)	9(23%)	1(5%)	0.0004	8(25%)	2(8%)	0.002
NIHSS AT ADMISSION (MEAN+/-SD)	16(+/-6.4)	17.6+/-5.7	12.3(+/-6.3)	0.002	17.7+/-6	13+/-6	0.010
mRS AT ADMISSION	4.1(+/-0.4)	4.2+/-0.4	4.0+/-0.5	0.192	4.3+/-0.4	4 +/-0.4	0.007
ASPECTS AT ADMISSION	5.5(+/-2.3)	5.1+/-2.4	6.7+/-1.7	0.019	4.7+/-2.3	6.6+/-1.8	0.002
OCCULSION SITE % MCA ICA/ICA+MCA	 75% 25%	 79.5% 20.5%	 65% 35%	 0.026 0.026	 75% 25%	 75% 25%	 1 1
MECHANICAL THROMBECTOMY	29(51.7%)	19(48.70%)	10(58.82%)	0.160	14(43.75%)	15(62.5%)	0.010
IVTPA ONLY	4(7%)	3(17%)	1(5%)		3(9%)	1(4%)	
TIME TO GROIN	51(+/-22)	53+/-23	49+/-18	0.671	54+/-24	49+/-20	0.571

FIGURE 5: BASELINE CLINICAL CHARACTERISTICS ACCORDING TO COLLATERAL CIRCULATION STATUS IN BOTH THE SCTA AND MCTA GROUPS (SIGNIFICANCE BASED UPON FISHER EXACT T TEST, STUDENT T TEST) (RED COLOR-SIGNIFICANT BASED UPON BY P VALUE)

Mean NIHSS score of the 56 patients was 16 (+/-6). Mean ASPECTS at admission was 6 (+/2). Mean time from symptom onset to CT was 3 hours 20 minutes. 29 patients (52%) undergone mechanical thrombectomy and stent retrievers were used in all cases.

Mechanical thrombectomy was done as per universally followed guidelines (ASPECTS>=6, NIHSS 5 to 25, M1/ T occlusion). Mean door to groin puncture was 51 (+/-22) minutes. 9 patients received both intravenous thrombolysis and mechanical thrombectomy, while 4 cases (7%) received only intravenous thrombolysis. TICI 2B or 3 recanalization was attained in 76% (22 out of 29) patients. Mean time from stroke onset to recanalization was 263 +/-80 minutes. 24 hours follow up mean CT ASPECTS score was 4. Of the 56 patients, 6 patients had PH2 ECASS2 type of haemorrhagic transformation and 3 patients had PH1 bleed. 7 patients had died in hospital while on treatment. Mean NIHSS at discharge of the 49 alive patients was 8. 34 patients came for follow up after 90 days and 48% (17) patients attained good functional outcome of mRS <=2.

Patients with good collaterals (in both sCT and mCT) had a younger age (65 vs 61 years), but not statistically significant. Males had statistically poor collaterals compared to females. Among the risk factors only patients with coronary heart disease had statistically significant poor multiphasic CT collaterals (25% vs 8%p=0.002). Patients with hypertension, atrial fibrillation, diabetes, hyperlipidaemia had poor multiphasic collaterals, but not statistically significant. While in single phase CT collaterals assessment, patients with coronary heart disease, diabetes and hypertension had poor collaterals. Among patients with good collaterals in mCT, 62% undergone thrombectomy and while among patient with poor collaterals in mCT, 43% undergone thrombectomy (p-0.01). There is no

difference in time to groin between patients with good or bad collaterals in both sCT and mCT.

VARIABLE	ODD RATIO	P VALUE	C.I
Female sex	1.68	0.47	0.40 to 6.96
Coronary heart disease	0.69	0.67	0.13 to 3.72
NIHSS at admission	0.86	0.017	0.76 to 0.97
mRS at admission	0.21	0.063	0.04 to 1.08
ASPECTS at admission	1.49	0.019	1.06 to 2.09
Mechanical thrombectomy	3.42	0.089	0.82 to 14.20
Single phase CT collateral scoring	**2.27**	0.276	0.518 to 9.98
Multiphase CT collateral scoring	**15.16**	0.001	2.80 to 81.09
24 hrs CT ASPECTS	1.65	0.005	1.16 to 2.35

FIGURE 6: MULTIVARIATE ANALYSIS OF PREDICTORS OF GOOD FUNCTIONAL OUTCOME (RED COLOR-SIGNIFICANT VARIABLES)

In multivariate logistic regression model (Table 6) adjusted for sex, coronary heart disease, NIHSS at admission, mRS at admission, CT ASPECTS at admission, mechanical thrombectomy, Single phase collateral score, multiphase collateral score and 24 hours followup CT ASPECTS, only NIHSS at admission, ASPECTS at admission, mRS at admission, mechanical thrombectomy, multiphase collateral score and 24 hrs admission were found to have independent predictors of favourable outcomes. Odd's ratio of multiphase collateral score is 15.1(p=0.001), and is only 2.2 for single phase collateral score (p=0.2). Mechanical thrombectomy showed odd's ratio of 3.4 and next most important variable is 24 hours CT volume (ASPECTS).

Variables	Linear regression coefficient
CC mCT (0 to 5)	0.43
MT (attempt or not attempted)	0.25
mRS admission (0 to 6)	-0.20
CC sCT (0 to 3)	0.09
Sex (M/F)	0.15
NIHSS admission (0 to 42)	-0.02
CAD (presence or absence)	0.03
ASPECTS at admission (0 to 10)	0.006
24 hrs ASPECTS (0 to 10)	0.02
Intercept	-0.45

FIGURE 7 MULTIPLE LINEARREGRESSION ANALYSIS OFPREDICTORS OF FUNCTIONAL OUTCOME

Y (GOOD FUNCTIONAL OUTCOME)
= 0.15(FEMALE) + 0.03(NO CAD)-0.02(NIHSS SCORE)-0.20 (mRS SCORE) +0.006 (ASPECTS SCORE)+0.25 (MECHANICAL THROMBECTOMY)+0.43(GOOD MULTIPHASE CT SCORE)+0.02(ASPECTS)-0.45

R2=0.51. RSS=4.1.

Similarly, linear regression analysis of variables (figure 7) was done and regression coefficient of variables was attained. Regression coefficient of multiphase collateral score is 0.43.

	Single phase			Multiphasic		
	Good	Poor	p	Good(4,5)	Poor(0,1,2,3)	p
mRS 90 days <=2	7/13 54%	11/23 47%	0.172	(14/17) 82%	(4/18) 22%	0.001
PH 2 bleed	12% (2/17)	10% (4/39)	0.87	0%	18% (6/32)	<0.001
Time to recanalization (minutes)	309(+/-54)	244(+/-82)	0.159	282(+/-93)	240(+/-53)	0.220
TICI (2b,3)	70%	79%	0.194	86 %	75%	0.07
NIHSS at discharge	6.8 (+/-8.3)	9.4(+/-6.4)	0.341	5.5 (+/-7.3)	11.6(+/-5.9)	0.003
ASPECTS 24 hours	4.5(+/-3.1)	3.7(+/-2.3)	0.398	5.2 (+/-2.6)	3.0(+/-2.2)	0.002

FIGURE 8: CLINICAL, FUNCTIONAL AND RADIOLOGICAL OUTCOMES ACCORDING TO COLLATERAL CIRCULATION STATUS IN BOTH THE sCTA AND mCTA GROUPS (RED COLOR-SIGNIFICANT BASED UPON BY P VALUE)

Patients with good collateral scoring were found to be functional independent (mRS<=2), when analyzed after 90 days. 82% of the patients with good mCT collateral score were functional independent (p=0.001). Early radiological outcome (ASPECTS 24 hrs, 5.2 vs 3.0, p=0.002) and clinical outcome (NIHSS at discharge, 11.6 vs 5.5, p=0.003) were also significantly better in patients with mCT collateral score. None of the patients with good mCT collateral score patients had significant haemorrhagic transformation (PH2, p<0.001). There is no difference in time to recanalization and TICI scoring between patients with good and poor mCT collaterals.

Patients with good single-phase collateral score were found to have good mRS at 90days, NIHSS at discharge and ASPECTS at 24 hours, but none reach statistical significance.

	Grading	mRS (<=2)	mRS (>2)	Sensitivity Specificity of good outcome	Predictive values(CI) of good outcome	Likelihood ratio of good outcome	Accuracy of good outcome
mCT	Good	14/17 82%	3/17 17%	**Sens=78%** (68 to 85%) **Spec=81%** (72 to 88%)	**PPV 0.82** (0.75 to 0.82) **NPV 0.76** (0.69 to 0.82)	**PLR=4.2** (2.75 to 6.6) **NLR=0.27** (0.18 to 0.29)	**79.8%** (73 to 85%)
	Poor	4/17 23%	13/17 76%				
sCT	Good	7/13 54%	6/13 46%	**Sens=53.4%** (43to 63%) **Spec=53.5%** (43to 63%)	**PPV 0.54** (0.47 to 0.60) **NPV 0.53** (0.46 to 0.59)	**PLR=1.15** (0.87 to 1.52) **NLR=0.87** (0.66 to 1.15)	**53.5%** (46 to 60%)
	Poor	11/23 47%	12/23 53%				

FIGURE 9: SPECIFICITY, PREDICTIVE, LIKELIHOOD AND ACCURACY VALUES OF GOOD FUNCTIONAL OUTCOME BY COLLATERAL SCORES.

Patients with good mCT collateral scores have 78% sensitivity, 81 specificity and 80% accurate in predicting good functional outcome. In contrast, single phase CT had only 54% accuracy. Positive predictive value was 0.82 and negative predictive value was 0.76 for mCT scoring. mCT collateral scoring method has high positive likelihood ratio of 4.2, compared to sCT positive likelihood ratio of 1.15.

Variable	Multi phase CT (R)	Single phase CT(R)
NIHSS admission	-0.33(p=0.03)	-0.28(p=.01)
ASPECTS admission	+0.55(p=-0.05)	+0.32(p=0.01)
NIHSS discharge	-0.52(p=0.0001)	-0.22(p=0.11)
ASPECTS 24 hrs	+0.51(p=0.05)	+0.21(p=0.10)
mRS 90 days	-0.74 (p=0.0001)	-0.32(p=0.05)

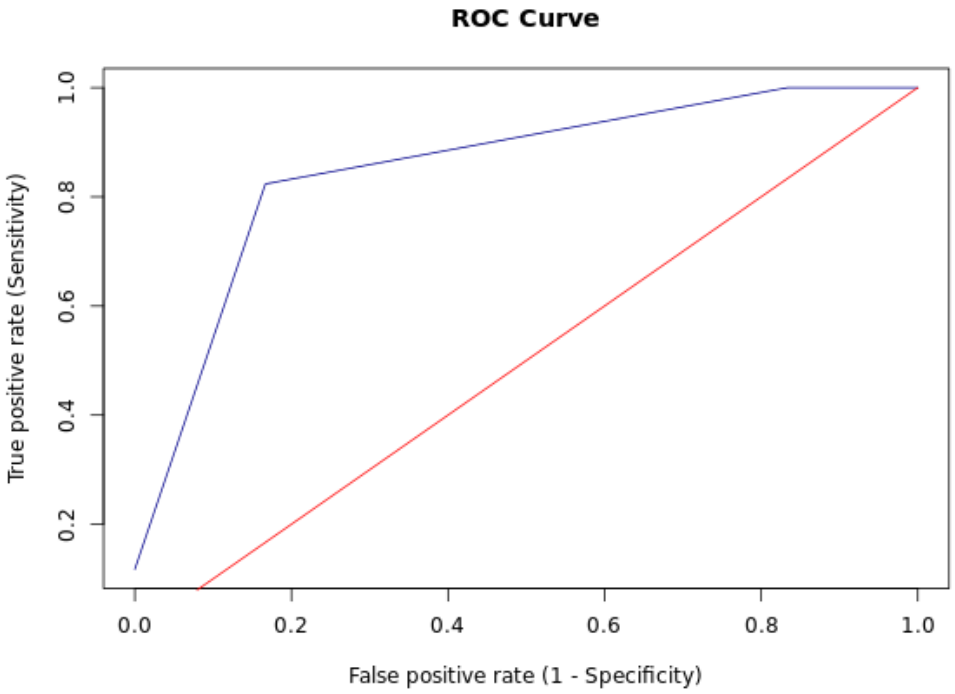
FIGURE 10: SPEARMAN RANK CORRELATION OF SINGLE PHASE AND MULTIPHASE COLLATERAL SCORING

Multiphase CT scoring was found to have statistically better spearman rank correlation ($p<0.05$) "R" value than single phase collateral scoring system, with NIHSS at admission, ASPECTS at admission, NIHSS at discharge, ASPECTS at discharge and mRS at 90 days.

mCT	Total no	% taken for thrombectomy/ Iv TPA	% taken for thrombectomy
0	1	3%	3%
1	4	0%	0%
2	8	12.5%	0%
3	19	59%	54%
4	22	63%	57%
5	2	100%	100%

FIGURE 11: RATE OF THROMBECTOMY BY MULTIPHASE COLLATERAL SCORE

Patients taken for mechanical thrombectomy (figure 12) were more prone to have collateral scoring of 3 to 5 in multiphase CT angiography. Only 3% patients with mCT collateral score of 0 to 2 were taken for mechanical thrombectomy. This analysis implies an alternative approach of multiphase CT scoring as imaging tool for identifying patients for mechanical thrombectomy.



Area under ROC curve

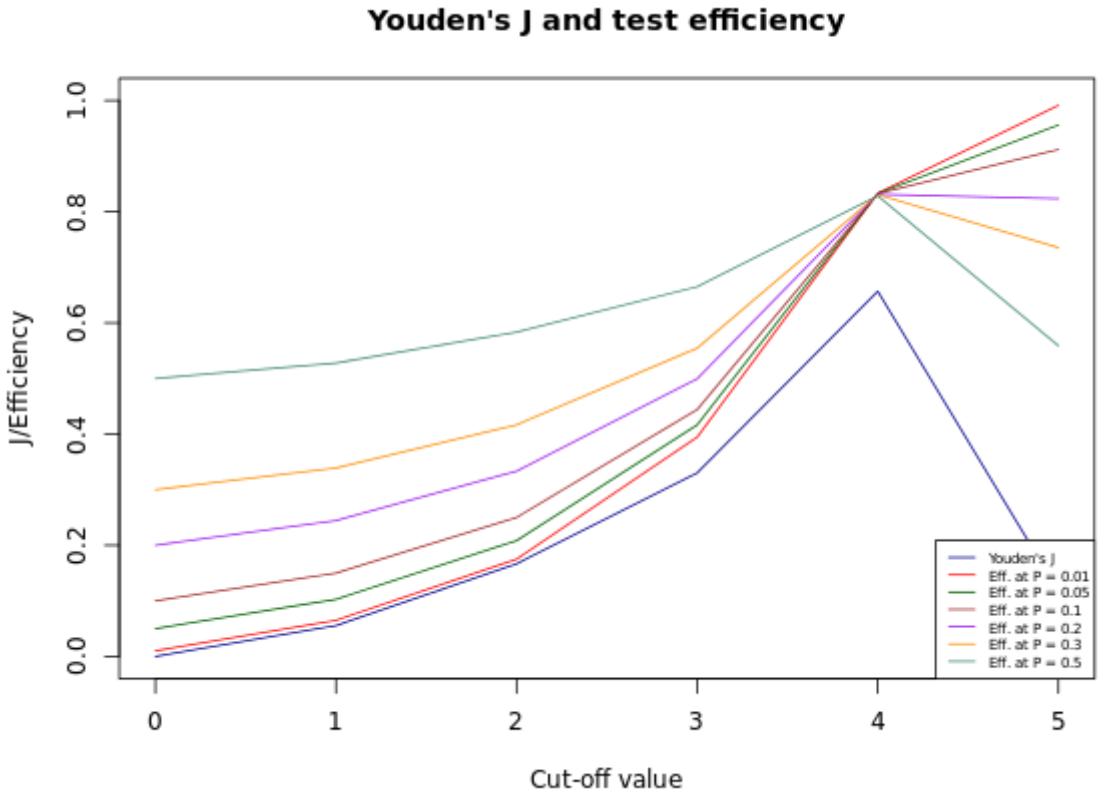
Area under curve (AUC)	0.853
95% CI for AUC	0.732-0.974

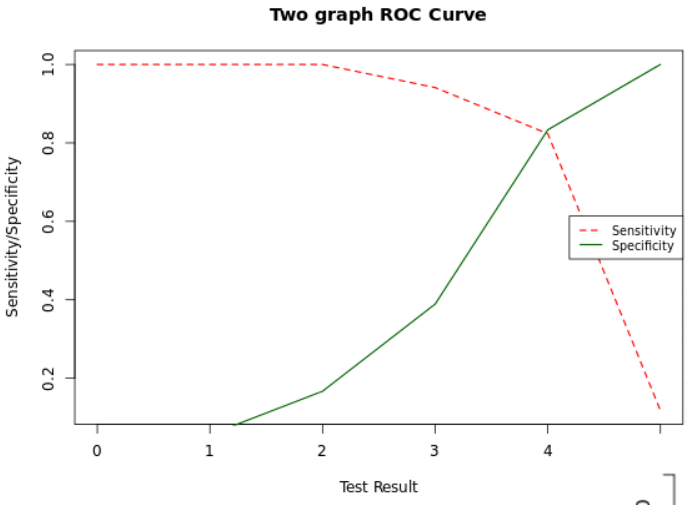
	Cut-point	Sensitivity	Specificity
Youden's J	4	0.824	0.833

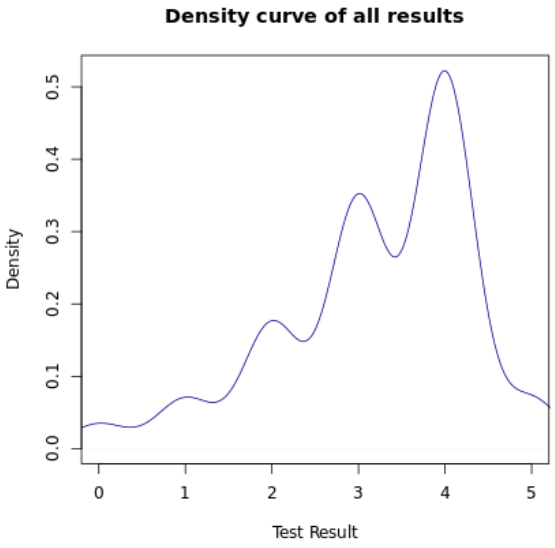
FIGURE 12: ROC CURVE ANALYSIS OF MULTIPHASE CT COLLATERAL SCORE IN PREDICTING GOOD OUTCOME. AUC (AREA UNDER CURVE) AND YOUDEN'J CUT POINT ATTACHED.

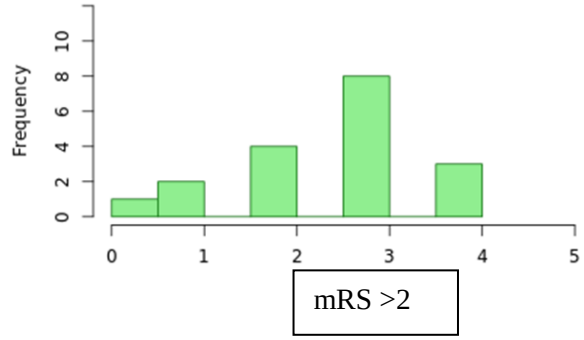
Finally, ROC curve analaysis was done separately for mCT and sCT collateral scoring for predicting good functional outcome. Area of curve was 0.853 (C.I=0.73 to 0.97) for mCT collateral scoring (figure 13), indicating mCT is good indicator (0.8 to 0.9) of predicting long-term functional independence. By Youden's J point, mCT collateral score of 4 is found to be optimum cut off point in predicting good functional outcome, with sensitivity of 82% and specificity of 83%.

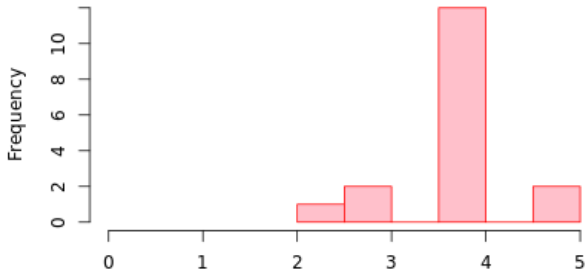
While sCT scoring (figure 14) had AUC value of 0.609 (C.I=0.43 to 0.78), indicating it as poor predictor of functional independence. Youden's J point for sCT collateral scoring shown that score of 2 is the optimum cut off point with sensitivity of 41% and specificity of 76%.



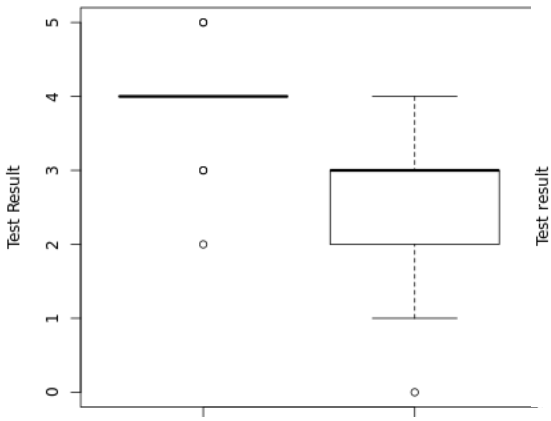




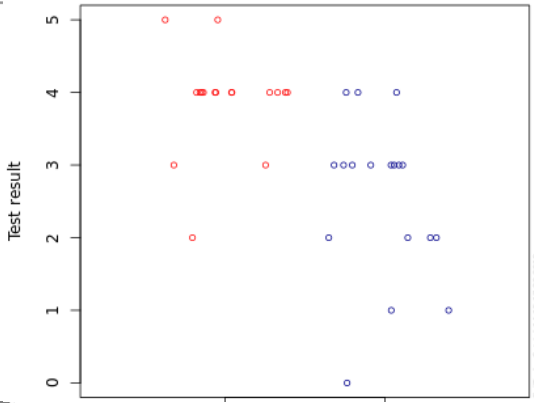




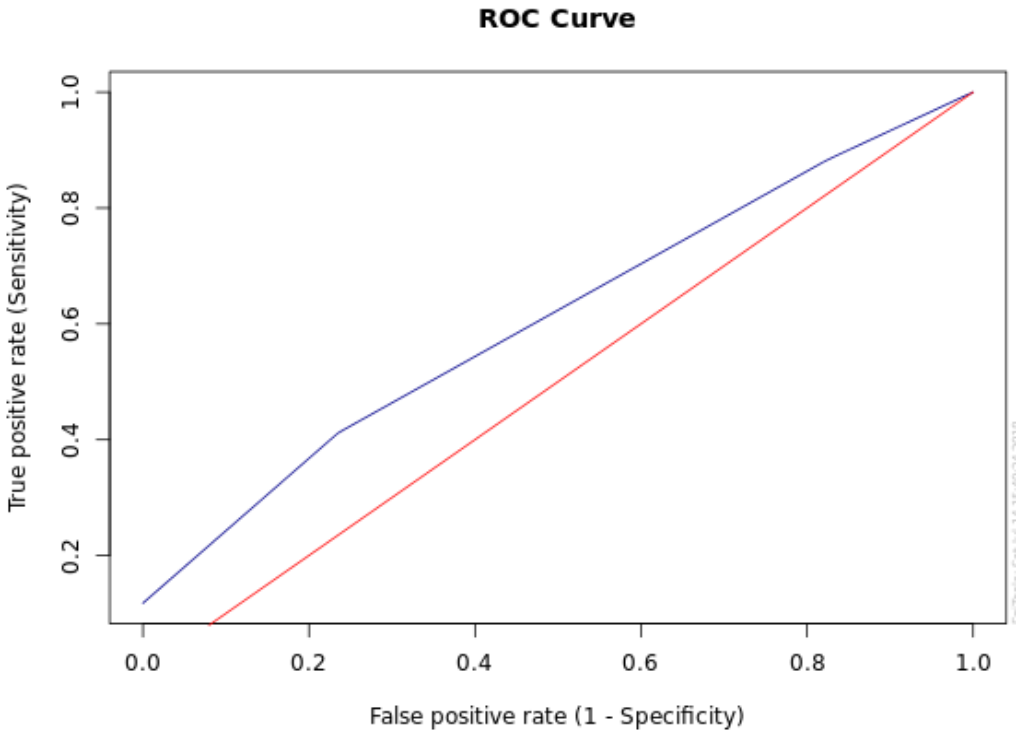
mRS<=2



Box plot results of good outcome by m CT score



Strip chart results of good outcome by m CT score

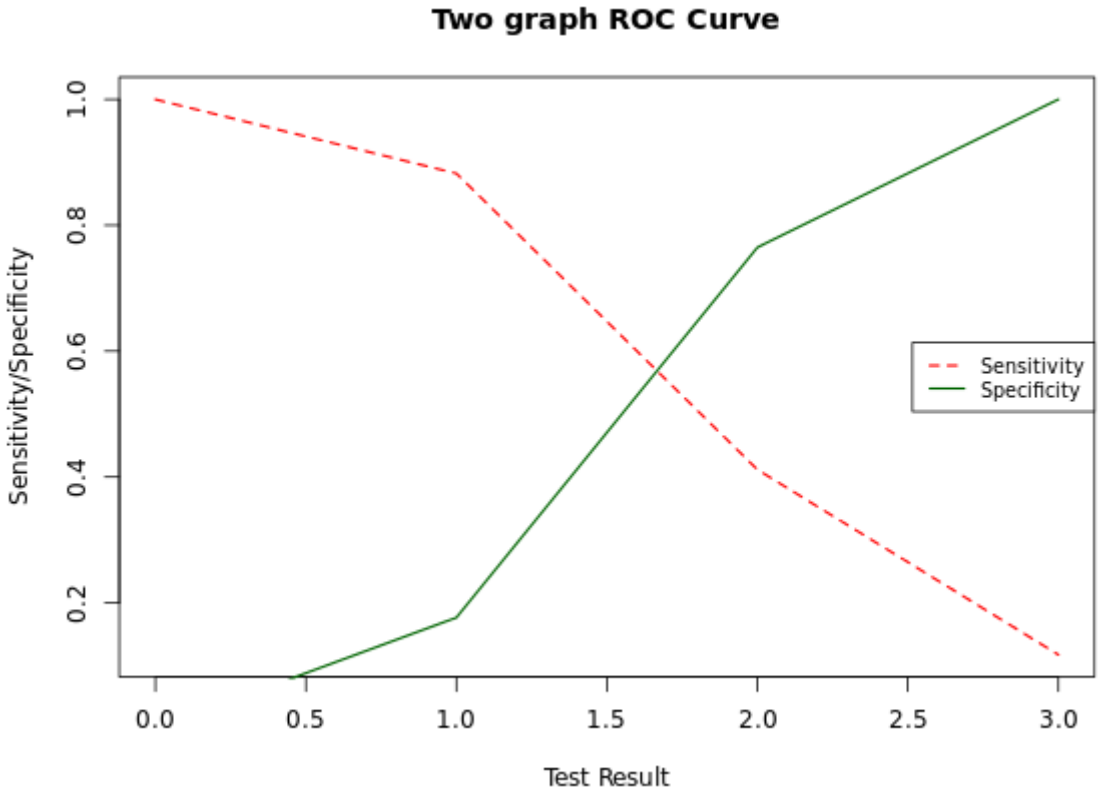


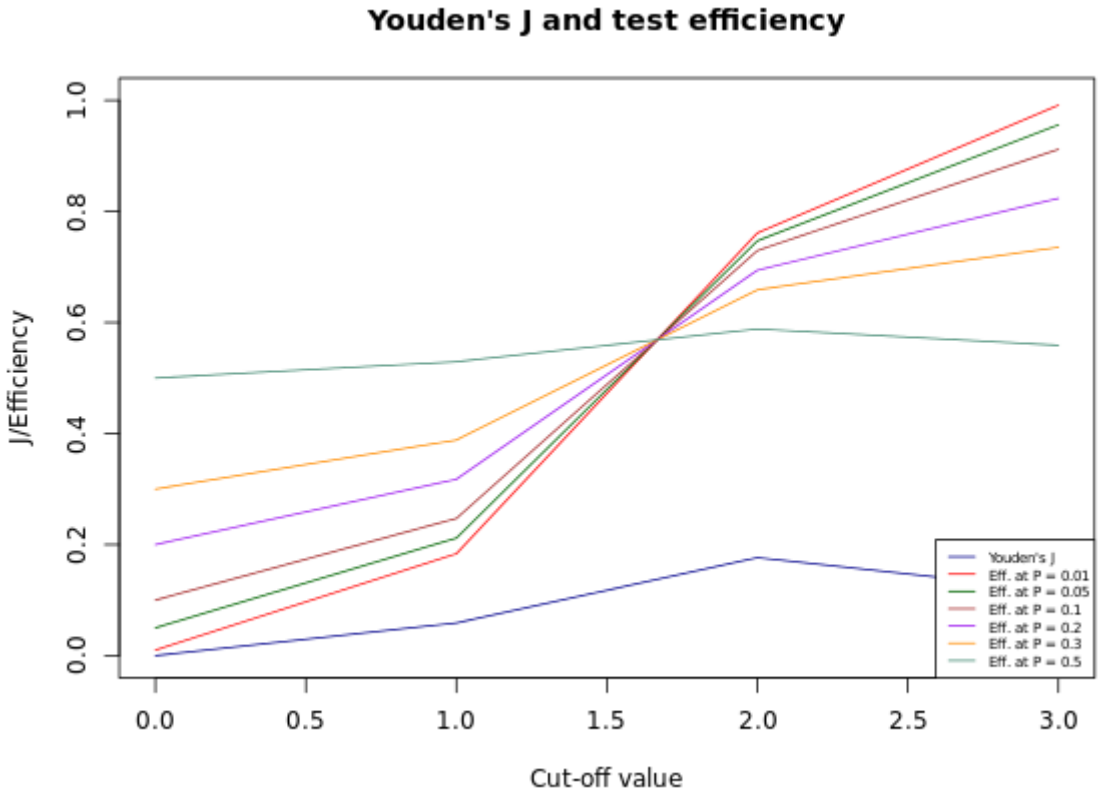
Area under ROC curve

Area under curve (AUC)	0.609
95% CI for AUC	0.433-0.785

	Cut-point	Sensitivity	Specificity
Youden's J	2	0.412	0.765

FIGURE 13: ROC CURVE ANALYSIS OF SINGLEPHASE CT COLLATERAL SCORE IN PREDICTING GOOD OUT COME. AUC (AREA UNDER CURVE) AND YOUDEN'J CUT POINT ATTACHED.


Two graph ROC Curve
Sensitivity/Specificity
1.0
0.8
0.6
0.4
0.2
Sensitivity
Specificity
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Test Result


Youden's J and test efficiency
J/Efficiency
1.0
0.8
0.6
0.4
0.2
0.0
Youden's J
Eff. at P = 0.01
Eff. at P = 0.05
Eff. at P = 0.1
Eff. at P = 0.2
Eff. at P = 0.3
Eff. at P = 0.5
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Cut-off value

Representative Cases

CASE 1:

60 years female **Risk factors:**

Diabetes

Time from symptom onset to CT: 65 min **NIHSS at admission:21**

mRS at admission:4 **ASPECTS at**

admission:6

Vessel occluded: Left M1 occlusion **No IV thrombolysis**

Mechanical thrombectomy done. **Door to puncture-40**

min

Time from onset to recanalization-230 minutes.

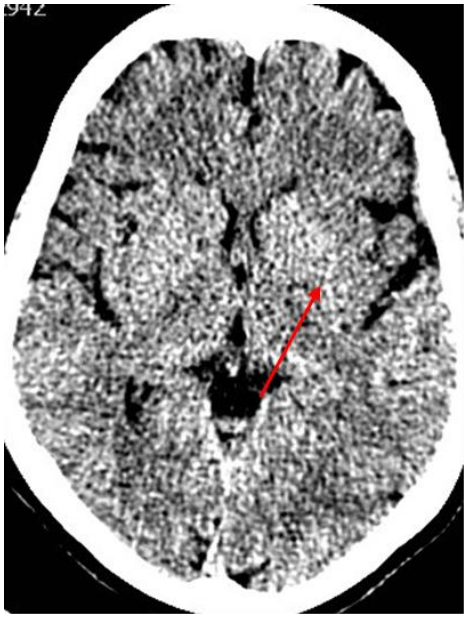
Single phase collateral: 1 (poor) **Multiphase collateral:**

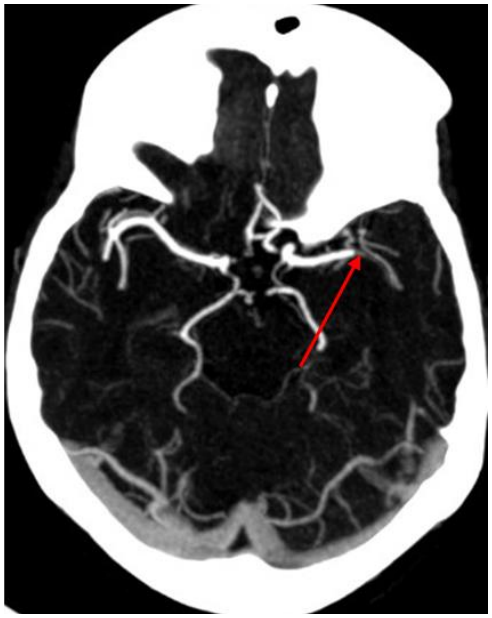
4 (good)

24 hours CT ASPECTS:5 **Hemorrhagic**

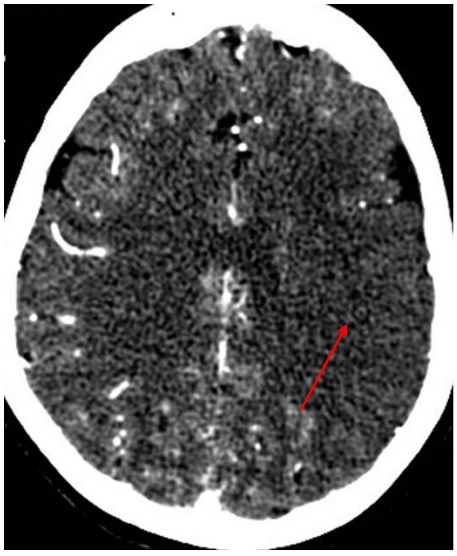
transformation: No

NIHSS discharge-5 **mRS 90 days-1**

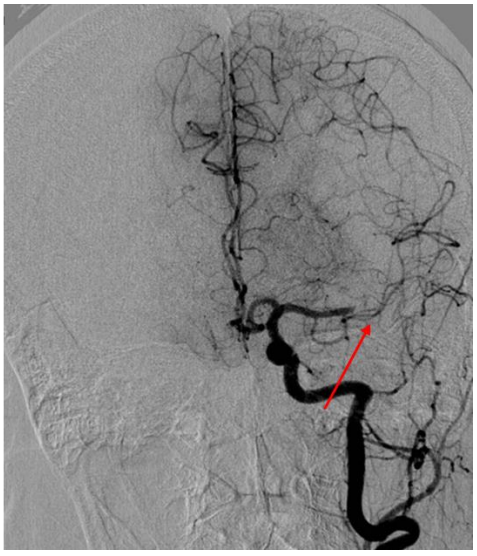




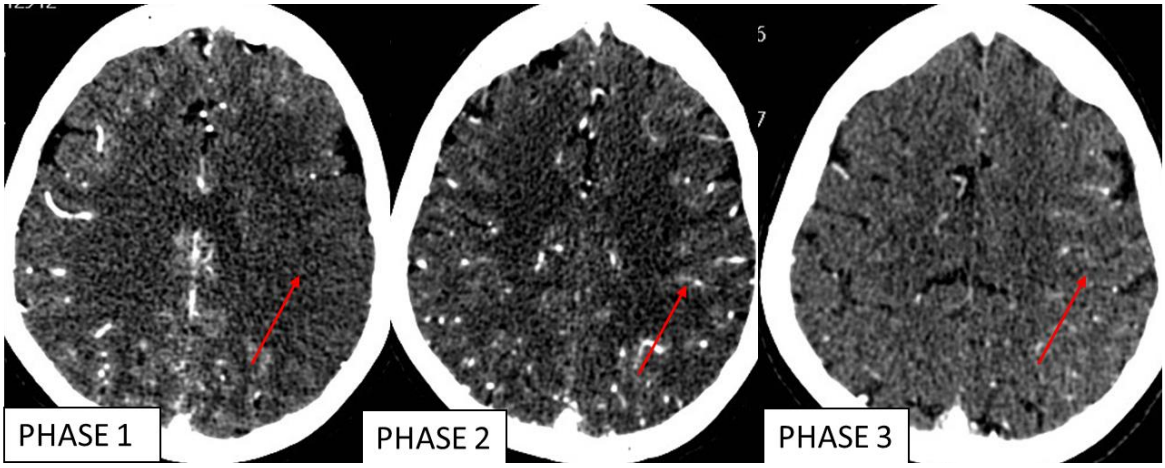
PLAIN CT AT ADMISSION: **ASPECTS 6.** **CT ANGIOGRAPHY:** **LEFT M1 OCCULSION**



SINGLE PHASE CT ANGIOGRAPHY (TAN): **GRADE 1 (POOR)**



DSA: **LEFT M1 OCCLUSION.**



MULTIPHASE CT ANGIOGRAPHY: GRADE 4(GOOD)

24 HOURS CT: ASPECTS 5

CASE 2:

51 years male **Risk factors:**

Hypertension

Time from symptom onset to CT: 4 hours 15min. NIHSS at admission:24

mRS at admission:4 **ASPECTS at admission:7**

Vessel occluded: Left M1 occlusion **No IV thrombolysis**

Mechanical thrombectomy done. **Door to puncture-35 min**

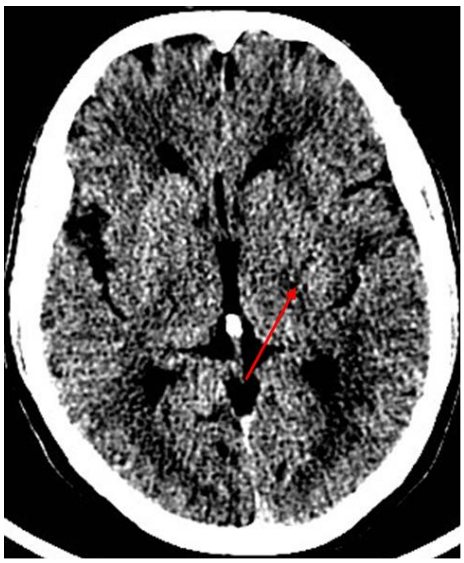
Time from onset to recanalization-310 minutes.

Single phase collateral: 1 (poor) **Multiphase collateral: 4 (good)**

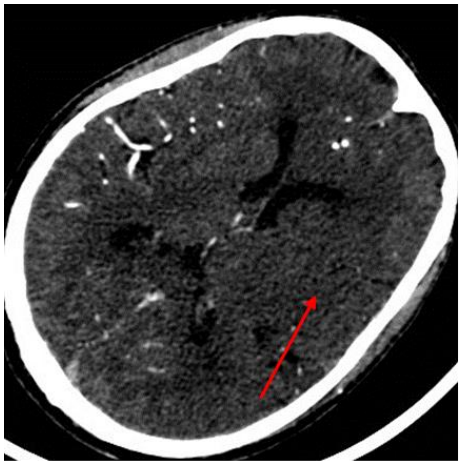
24 hours CT ASPECTS:6 **Hemorrhagic transformation: No**

NIHSS discharge-0 **mRS 90 days-1**

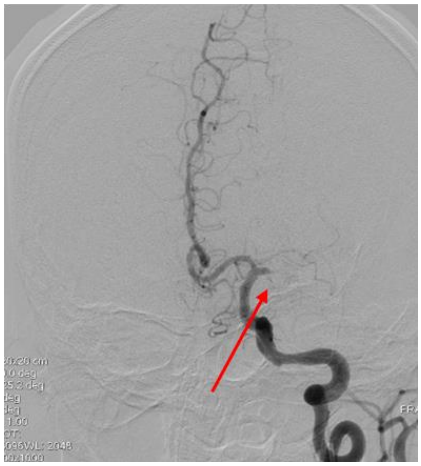
PLAIN CT AT ADMISSION: ASPECTS 7



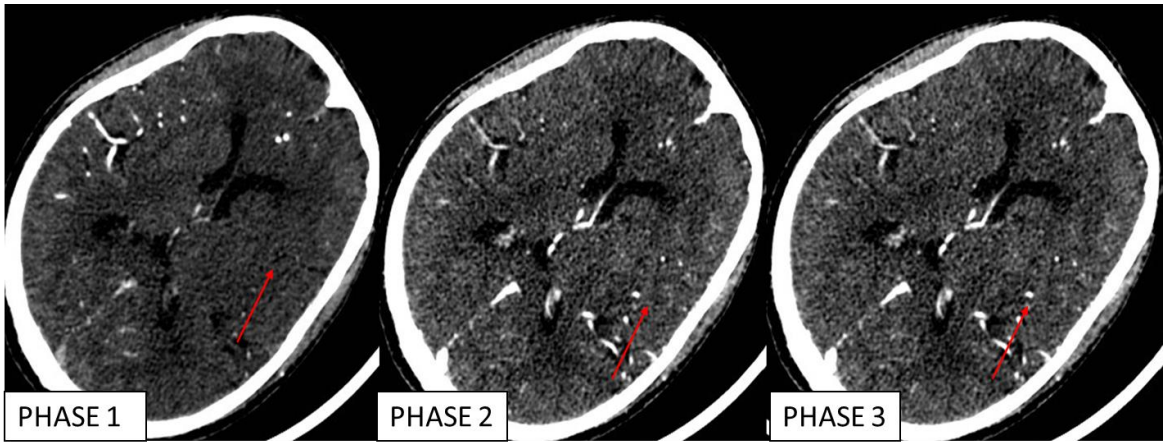
CT ANGIOGRAPHY: LEFT M1 OCCULSION



SINGLE PHASE CT ANGIOGRAPHY (TAN): GRADE 1. (POOR)



DSA: LEFT M1 OCCULSION



MULTIPHASE CT ANGIOGRAPHY: GRADE 4(GOOD)

24 HOURS CT: NO HEMORRHAGE TRANSFORMATION AND ASPECTS 6

CASE 3:

69 years female **Risk factors: Atrial fibrillation**

Time from symptom onset to CT: 8 hours **NIHSS at admission:25**

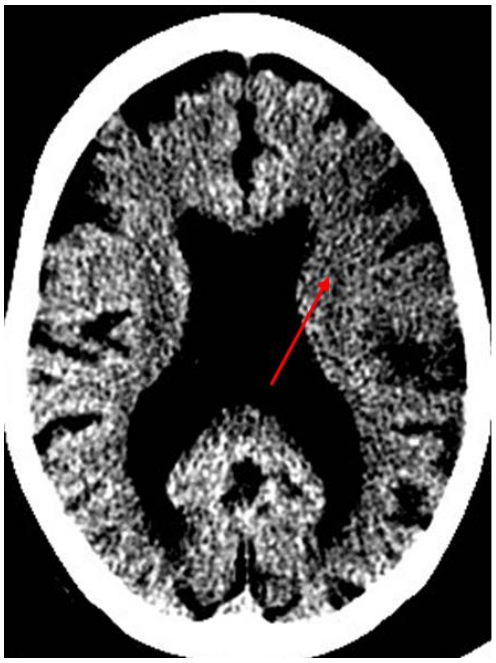
mRS at admission:5 **ASPECTS at admission:4**

Vessel occluded: Left M1 occlusion **No intravenous or intra-arterial therapy**

Single phase collateral: 2 (good) **Multiphase collateral: 3 (poor)**

24 hours CT ASPECTS:3 **Hemorrhagic transformation: PH2**

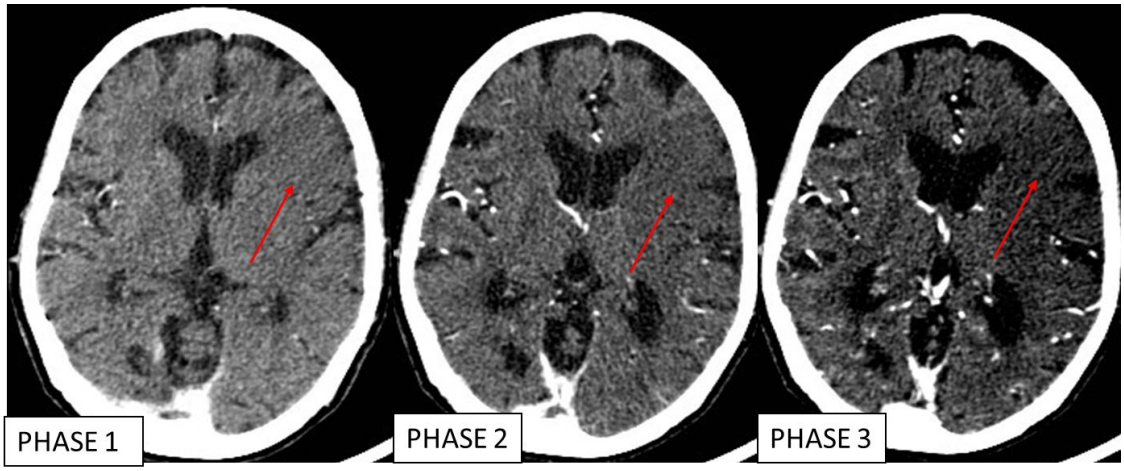
On discharge: died/mRS 6



PLAIN CT AT ADMISSION: ASPECTS 4

CT ANGIOGRAPHY: LEFT M1 OCCULSION

SINGLE PHASE CT ANGIOGRAPHY (TAN): GRADE 2 (GOOD)



MULTIPHASE CT ANGIOGRAPHY: GRADE 2 (POOR)

24 HOURS CT: PH2 HEMORRHAGE TRANSFORMATION/ ASPECTS 3

CASE 4:

40 years female **Risk factors: Atrial fibrillation**

Time from symptom onset to CT: 2 hours 50 min **NIHSS at admission:8**

mRS at admission:4 **ASPECTS at admission:7**

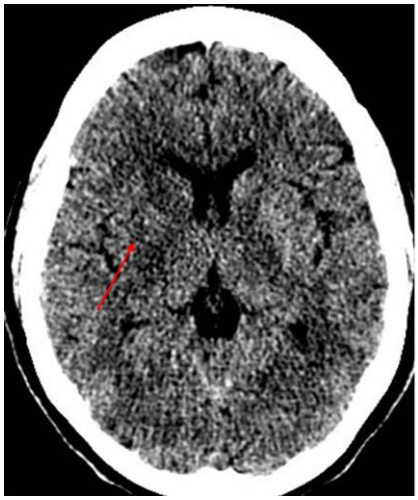
Vessel occluded: Right M1 occlusion **No intravenous thrombolysis**

Mechanical thrombectomy –attempted but failed. Door to puncture -35 min.

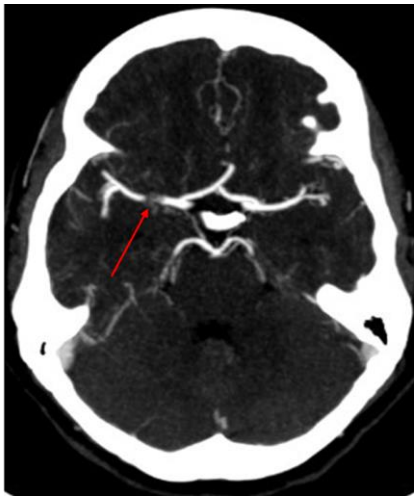
Single phase collateral: 3 (good) **Multiphase collateral: 5 (good)**

24 hours CT ASPECTS:7 **Hemorrhagic transformation: No**

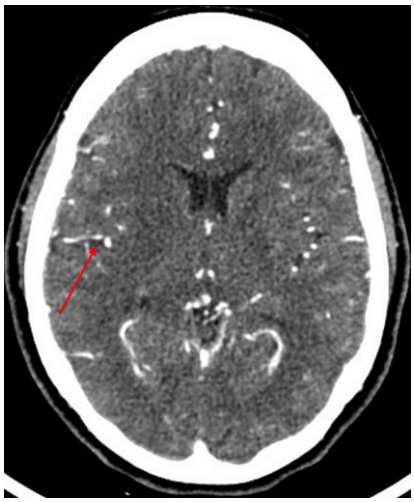
NIHSS at discharge: 0 **mRS 90 days:0**



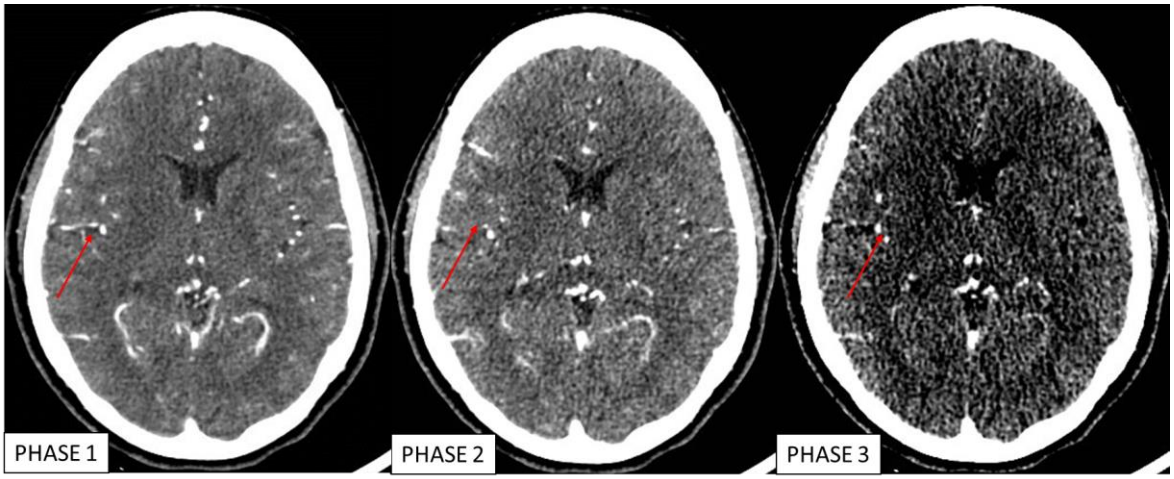
PLAIN CT AT ADMISSION:
ASPECTS 7



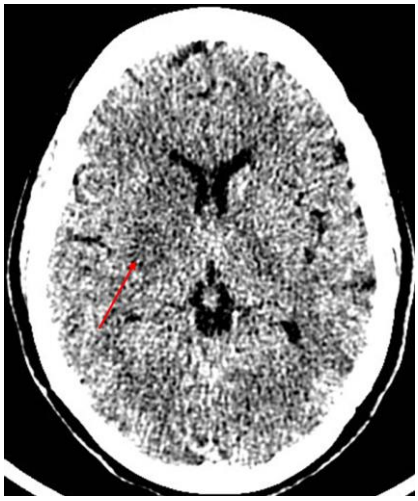
CT ANGIOGRAPHY:
RIGHT M1 OCCULSION



SINGLE PHASE CT ANGIOGRAPHY (TAN): **GRADE 3 (GOOD)**



MULTIPHASE CT ANGIOGRAPHY: GRADE 5 (GOOD)



24 HOURS CT: NO HEMORRHAGE TRANSFORMATION AND CT ASPECTS 7

CASE5:

60 years male **Risk factors:**

Diabetes, hyperlipidemia

Time from symptom onset to CT: 5 hours 30 min NIHSS at admission:8

mRS at admission:4 **ASPECTS at admission:8**

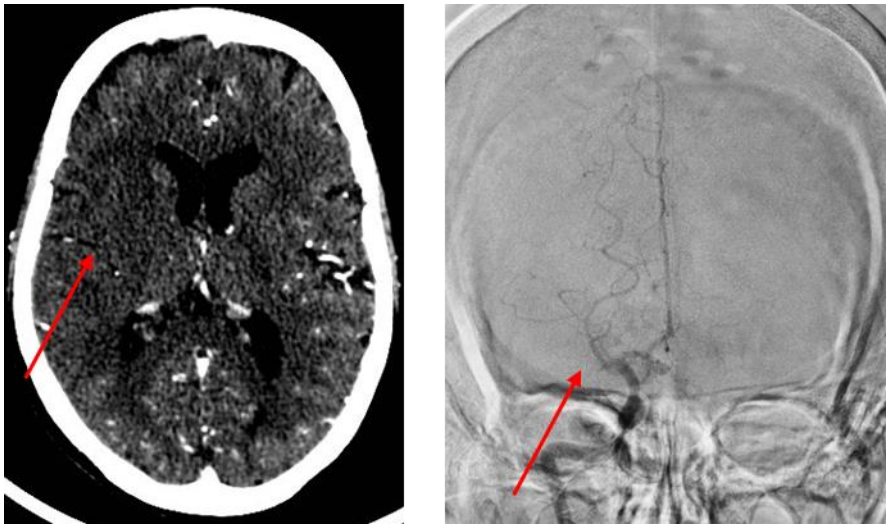
Vessel occluded: Right M1 occlusion **No intravenous therapy**

Single-phase collateral: 1 (poor) **Multiphase collateral: 4 (good)**

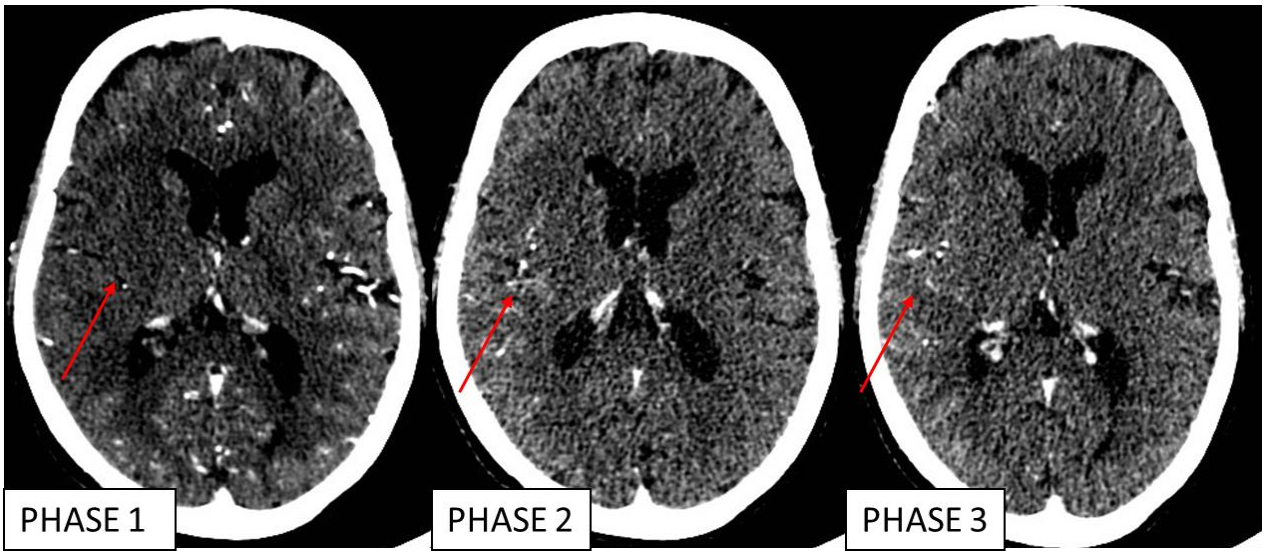
24 hours CT ASPECTS: 8 **Hemorrhagic transformation: No**

NIHSS at discharge: 2 **mRS at 90 days:2**

PLAIN CT AT ADMISSION: ASPECTS 8 **CT ANGIOGRAPHY: RIGHT M1 OCCULSION**



SINGLE PHASE CT ANGIOGRAPHY. DSA: RIGHT M1 OCCULSION (TAN): GRADE 1 (POOR)



MULTIPHASE CT ANGIOGRAPHY: GRADE 4 (GOOD)

24 HOURS CT: NO HEMORRHAGE TRANSFORMATION/ ASPECTS 8

Discussion

Risk factors and collaterals:

Among risk factors, we have shown only coronary heart disease (CHD) as statistically significant variable prone to have poor multiphase CT collaterals. This may be due to reduced ejection fraction in patients with CHD, secondarily leading to poor intra cranial blood flow and collateral formation.

Patients with hypertension and hyperglycemia were shown to have poor mCT collaterals, but not statistically significant. Prior studies with angiography also showed patients with hyperglycemia had poor collaterals, but did not achieve independent predictor status in multivariate analysis (55). There is no significant relationship of atrial fibrillation and smoking to intracranial collaterals in both single and multiphase angiography in our study as in Multicenter Randomized Clinical Trial of Endovascular Treatment of Acute Ischemic Stroke in the Netherlands (MRCLEAN) (56). Among sex, males were shown to have less collateral formation compared to females.

Collaterals and intracranial hemorrhages:

Previously, few studies have shown patients with good collaterals have been less prone to have symptomatic intra cerebral hemorrhagic transformation (31,32,56). In our study, none of the patients with good mCT collateral score had ECASS2 PH2 type of hemorrhagic transformation, while 6 patients (18%) of patients with poor collaterals had PH2 type of bleeding. By this, multiphase CT is 100% specific in predicting patients who are prone to significant hemorrhagic transformation. This is a new prognostic indicator found by our study.

Collaterals and mechanical thrombectomy:

Patients who had undergone mechanical thrombectomy were shown to have better mCT collaterals, although there is no difference in single-phase CT collaterals. However there is no significant difference in time to groin, time to recanalization and TICI scoring between patients with good and poor single as well as multiphase CT collaterals.

Among patients who were taken for mechanical thrombectomy, most of them (97%) had mCT collaterals of 3 to 5. Since mechanical thrombectomy was done in our cases based upon the universally accepted guidelines and not based upon mCT collateral scoring, we can now retrospectively assume mCT collateral scoring would be one of the best imaging tools to predict patients who may benefit from mechanical thrombectomy.

In our study, we have achieved good recanalization (TICI 2B OR 3) in 76 % patients, on par to stroke trials. Mean time to recanalization was 263 minutes.

Collaterals and clinical-radiological scores at admission:

Both patients with good single phase and mCT collateral scoring have good initial NIHSS score (13 vs 17 for multiphase, 17 vs 12 in single phase). This was in agreement with prior studies involving single-phase collateral systems. Radiologically also, patients with good collaterals have good initial CT ASPECTS (6.6 vs 4.7 in multiphase). This is because of the sustained perfusion of the penumbra by the good leptomeningeal collaterals.

Collaterals and radiological outcomes:

Multiphase CT scoring was shown to better correlate with 24 hrs CT infarct volume, while sCT scoring shows no statistically significant correlation. In patients with good mCT collaterals (mean ASPECTS 5 vs 3 in better vs poor collaterals), 24 hrs ASPECTS was shown to be significantly better than patients with good sCT collaterals (mean ASPECTS 4.5 vs 3.7 in better vs poor collaterals).

Collaterals and early clinical outcomes:

Unlike single-phase collaterals, multiphase collaterals were shown to better and statistically significant correlate and predict the early clinical outcome i.e NIHSS at discharge. Patients with good mCT collaterals had lower mean NIHSS at discharge. Mean NIHSS was 5 in patients with good mCT collaterals, while mean NIHSS was 11 in patients with poor mCT collaterals.

Collaterals and long-term clinical outcome:

Patients with good mCT were shown to have better clinical outcome than sCT collaterals scoring method. 86 % of the patients with good mCT collaterals are functionally independent, compared to 54% in sCT collaterals system. Only 22% of the patients with poor mCT collaterals, had good mRS<=2. Also mCT was shown to have very high spearman correlation of -0.74 with 90 days mRS.

Cut off value of collateral scoring by ROC:

There were no studies, which predicted the cutoff of collateral scoring methods to predict good functional outcome. In this study, we analyzed scoring methods with ROC and Youden for mRS 90 days. Cutoff scoring value of 4 and above in mCT scoring, was shown to predict good functional independency with good sensitivity and specificity. For sCT scoring method of 0 to 3, Youden's cut off of 2 and above was shown to better predict good clinical outcome, even though sensitivity and specificity was less than < 50%.

Multivariate analysis of variables:

Since multiple variables may predict the functional outcome, we did multivariate logistic regression analysis, to look into the odd ratio of independent variables. mCT collateral scoring method have the highest odds ratio of around 15, when compared to next important variable of mechanical thrombectomy of 3.4.

Single-phase CT collaterals had an odds ratio of 2.2 but not in significant level. Other variables like NIHSS at admission, ASPECTS at admission and discharge were also shown to have significant p value on logistic regression analysis in addition to multiphase CT collaterals and mechanical thrombectomy.

Studies involving multiphase CT collateral scoring:

1. Multiphase CT collateral scoring was first introduced by **BK Menon et al** (24) and is published as **a new tool for imaging triage of acute stroke patients**. In this study, they used information of the PRoveIT (Precise and Rapid assessment of collaterals using multi-phase CTA in the triage of patients with acute ischemic stroke for IA Therapy) study of 147 patients.

   These study inclusion criteria used acute stroke within 12 hours, unlike our study, which included only patients within 8 hours which may be more informative to assess the response to interventional procedures.

   Of the 147 patients, 3 are PCA occlusion, 24 are distal vessel occlusion and 33 are no occlusion. These distal occlusion and no occlusion cases may not informative. So in our study we included only major vessel anterior circulation occlusions.

   Totally 31 patients had undergone intra-arterial therapy in this study which is almost similar (29 patients) to our study. In this study, ROC curve analysis was done which showed a C statistic value of 0.6 for mCT collateral score in predicting mRS at 90 days and is better than single phase CT collateral scoring. In our study, C statistic for mCT collateral scoring was much higher at 0.85 and is significantly better than single phase CT collateral scoring. Radiation dose of multiphase CT angiography was less than the CT perfusion in their institute.

2. **Alan flores at al, (32)** showed **Poor collateral circulation in multiphase Ct angiography predicts malignant MCA infarction progression**. Totally 82 patients of proximal MCA or terminal ICA occlusion were included. Mean NIHSS at admission (16 NIHSS) and age (63years) are similar to our study. 15 patients had malignant infarct transformation.

   In univariate analysis, patients with malignant stroke were associated with lower multiphasic collateral scores (2.2 vs 3.7). On multivariate analysis, mCT collateral was an only independent predictor of malignant stroke. This is in concordance with our results of multiphase CT collateral better correlating with 24 hours infarct volume in terms of CT ASPECTS (ASPECTS of 5 in good mCT collateral vs 3 ASPECTS in poor mCT collaterals, p=0.002 and good spearman correlation of +0.52).

3. Recently a study by **Alvaro et al (33) including BK Menon,** evaluated **multiphase CT angiography in acute stroke patients treated with endovascular reperfusion therapies**.

   In this study, logistic regression analysis of age, NIHSS, ASPECTS, mCT angiography collateral, single-phase CT angiography collaterals and recanalization, only age and mCT angiography were shown to be independent predictor of functional outcome.

In our study of multivariate logistic regression analysis including sex, coronary heart disease, NIHSS at admission, mRS at admission, ASPECTS at admission, use of mechanical thrombectomy, single phase collateral, multiphase collaterals and 24 hours ASPECTS, only multiphase CT collaterals, use of mechanical thrombectomy, NIHSS at admission, mRS at admission, ASPECTS at admission and at 24 hours were found to be significant independent predictors of 90 days mRS.

This result of the collateral score was similar to our study, but in our study additionally told ASPECTS, NIHSS score also shown as independent predictors of functional outcome.

Multiphase CT collateral scoring attained highest ODD ratio in their study similar to our results but value is much higher in our study (Odd ratio of 15 in our study vs odd ratio of 5 in their study). Odd ratio of NIHSS, ASPECTS was almost similar (0.86 our study vs 1.06 alvaro study for NIHSS, 1.49 our study vs 1.13 in Álvaro study for ASPECTS for admission).

In this study even though the symptomatic hemorrhagic transformation is less in patients with good mCT collaterals, it did not attain a statistical significant level. However, in our study none of the patients with good mCT collaterals developed PH2 type of bleeding, while 18% of the patients with poor collaterals developed PH2 bleeding. So future studies must come to prove our hypothesis of accuracy of mCT collateral score in predicting hemorrhagic transformation.

4. **Santos et al** studied the **use of multiphase CT angiography for thrombus perviousness assessment by thrombus attenuation increase** (TAI) in arterial, venous, delayed and time invariant CT angiography. They found an association of TAI with arterial phase CT angiography was optimal and multiphase CT angiography gives no added advantage in thrombus perviousness assessment.

5. **Ondrej et al** studied the **single-phase vs multiphase CT angiography in MCA clot detection and its benefits for less experienced radiologists and neurologists**. In this study 10 radiologist and10 neurologists (3 experienced and 7 less experienced) assessed 20 single phase and multiphase CT angiography cases of M2 occlusion. This study showed that multiphase CT angiography improves detection of M2 occlusion in less experienced physicians.

6. **ESCAPE trial of Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke (25)**, it was mentioned multiphasic CT angiography was used in majority of patients. In this study large infarct core or poor collaterals on multiphasic Ct angiography were excluded. However they used moderate-to-good collaterals as filling of 50% or more of the MCA pial arterial circulation on multiphase CTA, which is different from the currently used multiphasic CT angiography collateral scoring.

LIMITATIONS:

Even though this was a prospective study with inclusion of consecutive cases of acute anterior circulation ischemic stroke presenting to our institute there were a few limitations in this study.

1. The number of patients included in the study was 56, which was limited in number, even though this was one of the largest prospective studies, which assessed intracranial collaterals.
2. Only anterior circulation ischemic stroke was included. Posterior circulation strokes collaterals studies have to be studied in future studies.
3. The inclusion of patients with conservative as well as mechanical thrombectomy did cases. However to overcome this bias multivariate logistic regression analysis was done.
4. The number of mechanical thrombectomy cases were limited (n=29).

Conclusion

CONCLUSION:

This study with prospective evaluation of 56 patients represents the one of the largest available prospective studies of intracranial collaterals of patients with anterior circulation major vessel occlusion in literature.

1. ***Multiphasic CT collateral grading system was significantly much better than the traditional single-phase collateral grading system in predicting early radiological and functional outcome as well as long-term functional outcome.***
2. ***Good multiphase CT collateral scoring was the strongest predictor of long-term functional independence, irrespective of endovascular management in our study.***
3. ***Patients with good mCT collaterals would have better initial clinical and radiological findings.***
4. ***mCT collaterals system more accurately predict the hemorrhagic transformation.***
5. ***Good and intermediate mCT collaterals (3 to 5) can be used as an alternate cut off value limit as a triage for mechanical thrombectomy.***
6. ***Cut off value of mCT collateral scoring of 4 and 5 better predicts a good functional outcome.***

Hence, multiphasic CT angiography has to be added to the existing acute stroke imaging protocols.

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*A*nnexures

APPENDIX A

TITLE OF THE STUDY: ASSESSMENT OF COLLATERAL STATUS USING MULTIPHASIC CT ANGIOGRAPHY IN THE ACUTE ANTERIOR CIRCULATION ISCHEMIC STROKE: ITS CORRELATION WITH CLINICAL AND RADIOLOGIC OUTCOMES

Study number: SCT/IEC/987/OCT-2016

There is a clinical suspicion that you have acute stroke, and it has to be evaluated with CT angiography, for assessing your brain & neck vessel status and choosing the best modality of management in your case. The CT angiography investigation as a part of clinical evaluation helps to diagnose the acute stroke and plan the treatment.

The CT angiography is a type of CT study done routinely in most acute stroke patients, to assess the blood vessels of the brain and neck. It is helpful for the diagnosis of the acute stroke, blood vessels affected and in choosing the best modality of treatment to be undertaken in the patients.

This study is designed to evaluate the role of CT angiography findings to assess the prognosis of acute stroke. This study has the advantage of likely providing more accurate prognostic indices and therefore directing the better mode of treatment.

You are being requested to participate in this study which is likely better in assessing the prognosis of the acute stroke and therefore in better individual patient management. Also, there is no additional risk anticipated as the investigation involves the existing institute protocol.

What is CT ANGIOGRAPHY and does it have any harmful effects?

CT ANGIOGRAPHY is an advanced imaging technique which uses X ray radiation and iodine based contrast to image body part. Some patients may rarely develop allergic reactions to the contrast agent. This investigation is not to be done for with kidney failure, pregnancy patients. This CT angiography is being done as a part of clinical evaluation of your disease; however certain data from this study will be used for research purpose as part of this study.

If you take part what will you have to do?

This study will only analyze the results of the routinely ordered imaging investigations you will undergo for your illness. You will not be required to undergo any other additional investigation modality for this study.

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.

What will happen if you develop any study related injury?

This study only analyzes the results of the CT angiography investigation which you will be undergoing as part of your disease evaluation. Thus we do not expect any injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at this institute by the experienced team of medical professionals.

‘

Will you have to pay for the study?

The study will only analyze the results of the investigations which you will undergo in natural process of the management of your disease process at this institute. No extra cost will be borne by you for this particular study.

What happens after the study is over?

If the study is found useful, the study will help better assess the prognosis of the acute stroke patients and better assess the mode of treatment to be chosen for the patients. The study may or may not be helpful to you directly.

Will your personal details be kept confidential?

The results of this study may 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.

CONSENT FORM

Participant's name: Date of Birth / Age (in years): I_____ _____, son/daughter of _____ (Please tick boxes)

1. I Declare that I have read the above information provide to me regarding the study the collaterals score in acute stroke, have clarified any doubts that I had. [ ]
2. 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 [ ]
3. 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 [ ]
4. I understand that my identity will not be revealed in any information released to third parties or published [ ]
5. I voluntarily agree to take part in this study [ ]
6. 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

APPENDIX B:

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES & TECHNOLOGY

PROFORMA

General Instructions

Please fill in all the questions

Write Yes / No/NA wherever applicable

If the response is not known please write UK If additional info is available please elaborate

1. **PROFORMA SERIAL NUMBER**:
2. **AGE (YEARS)** :
3. **SEX (M/F)** :

4. CLINICAL PRESENTATION:

TIME TO CT < 8 HRS : YES/ NO

5. EXAMINATION FINDINGS AT ADMISSION

NIHSS SCORE AD ADMISSION (0 TO 42) :

mRS (0 TO 6) :

6. CLINICAL RISK FACTORS:

- HYPERTENSION
- DIABETES MELLITUS
- DYSLIPIDAEMIA
- ATRIAL FIBRILLATION
- SMOKING
- CORONARY ARTERY DISEASE

7. CT FINDINGS AT ADMISSION:

a. CT PLAIN (ASPECTS SCORE) :

b. CT ANGIOGRAPHY :

BI) VESSEL TERRITORY (MCA M1/M2 OR MCA M1/M2+ICA OR ICA OCCULSION):

BII}MULTIPHASE CT COLLATERAL SCORE (0 TO 5) :

BIII)TAN SCORING SYSTEM(0 TO 3) :

8. **TREATMENT DETAILS**:
CONSERVATIVE/IV THROMBOLYSIS/MECHANICAL THROMBECTOMY.
IF MECHANICAL THROMBECTOMY
-DOOR TO GROIN (IN MINUTES) :
-ONSET TO REPERFUSION (IN MINUTES) :

9. POST TREATMENT IMAGING FINDINGS (24 HRS CT)
ASPECTS SCORE (0 TO 10) :
HEMORRHAGE HI TYPE 1/ HI TYPE 2/PH TYPE 1/PH TYPE 2:

10. **NIHSS AT DISCHARGE (0 TO 42)** :

11. 90 DAYS mRS FUNCTIONAL OUTCOME(0 TO 6) :

PRINCIPAL INVESTIGATOR MASTER KEY PROFORMA

PROFORMA SERIAL NUMBER:

1.1 Name

1.2 Hospital No

1.3 Address

1.4 Phone number

1.5 Mobile

1.6 Email id

1.7 Date of admission

1.8 Date of discharge/death

APPENDIX C:

ABBREVIATIONS:

ASPECTS-Alberta Stroke Program Early CT Score

CT-computed tomography

CTA- Computed Tomography Angiography

MRI- Magnetic Resonance Imaging

DWI- Diffusion Weighted Imaging ADC- Apparent Diffusion Coefficient

HI- hemorrhagic infarction

ICA- Internal Carotid Artery

ICA-internal cerebral artery

ICH- Intra Cerebral Haemorrhage

IVTPA-intravenous thrombolysis

MCA- middle cerebral artery

mCT- multiphase CT

MRA- Magnetic Resonance Angiography

DSA- Digital Subtraction Angiography

SWI- Susceptibility Weighed Imaging

ASL- Arterial Spin labelling

MRI-magnetic resonance imaging

mRS- modified Rankin Scale

MT-mechanical thrombectomy

NCCT- Non Contrast Computed Tomography

NIHSS-National Institutes of Health Stroke Scale

PH-parenchymatous hematoma

sCT- single phase CT

SCTIMST- Sree Chitra Tirunal Institute for Medical Sciences and Technology

MDCT- Multi Detector Computed Tomography

TOF- Time of Flight

APPENDIX D:

EXCEL SHEET:

S/ NO	Age	Sex	Risk factors	Time to CT	NIHSS at admisssion (0 to 42)	mRS at admission (0 to 6)	ASPECTS plain CT (0 to 10)	Vessel ooculded	IV TPA (N/ Yes)	Door to puncture (in min)	Groin to recanalization time (min)	TICI score	Single phase CT (0 to 3)	Multiphase score CT(o to 5)	Hemorhagic grading	24 hrs CT ASPECTS(0 to 10)	NIHSS discharge(0 to 10)	mRS at 90 days(0 to 6)
1	63	M	Sm	1 hr 35 min	16	4	6	R M1+ICA	N	29	174	2A	1	3	No	6	8	4
2	58	M	H/D	4hr 20 min	16	4	ONE	R M1+ICA	N	N		N	1	3	HI2	1	11	4
3	69	F	AF	8 hr	25	5	4	L M1	N	N		N	2	3	PH2	3	Died	6
4	81	M	H/C	2 hrs 15 min	33	5	0	L ICA+M1	N	N		N	0	0	HI1	0	Died	6
5	38	M	N	1 hr	21	4	7	L ICA+LM2	N	65	185	0	1	3	No	6	6	3
6	58	M	D/H/CAD/AF/L	3 hrs 10 min	15	4	5	R M1.	N	45	270	3	1	3	HI1	5	11	4
7	65	F	H/D/L	3 hrs 20 min	24	5	5	L M1.	N	30	Failed	0	2	3	No	0	Died	6
8	85	F	AF	3 hrs 58 min	19	5	5	L ICA+M1	N	47	Failed	0	2	3	No	1	21	NF
9	42	F	N	2 hrs 40 minutes	23	4	2	L M1.	N	N			1	1	HI1	0	22	NF
10	48	F	N	2 hr 20 min	26	5	8	RM1.	yes	73	246	2B	1	3	HI1	2	died	6
11	61	M	D/H/L/CAD	2 hr 40 min	21	4	5	LM1.	yes	25	229	2A	0	1	PH2	3	died	6
12	74	M	D/H/CAD.	6 hrs	16	4	5	RM1.	N	35		2B	1	3	PH2	5	died	6
13	65	M	D/CAD/L	2 hr	9	4	6	RM2	yes	N			0	2	HI1	6	14	NF
14	74	M	CAD.	3 hrs	14	4	6	RM1.	N	80	318	2B	1	3	PH2	6	2	NF
15	62	F	D/H/L/AF	7 hrs	23	4	2	LM2.	N	N			1	2	No	1	16	NF
16	54	M	H/CAD	1 hr 35 min	21	4	9	LICA+M1	yes	60	180	2B	0	3	No	5	10	2
17	65	F	N	2 hrs 15min	24	5	3	RM1.	N	N			0	1	HI2	2	13	4
18	56	F	N	5 hr 30 min	10	4	2	R ICA+RM1	N	N			1	2	No	1	12	NF
19	65	M	N	1 hr 35min	16	5	3	RM1.	N	N			1	2	No	2	14	4
20	60	F	D/H/L	2 hr 10min	15	4	2	RICA+M1	N	N			1	2	HI1	0	died	6
21	76	M	H/CAD	6 hr	10	4	5	RM1.	N	N			1	2	HI1	4	7	NF
22	80	M	H/D/CAD	3 hr 30min	19	5	1	RM1.	N	N			1	2	HI1	1	20	5
23	85	M	H/Sm	2 hr20min	23	5	8	LM2.	yes	N			1	3	PH1	3	20	NF
24	78	M	D/H/Af	2hr45min	16	5	8	RM1.	N	40	253	3	1	3	HI1	6	7	NF
25	74	M	CAD.	3hrs.	14	4	6	RM1.	N	90	328	2b	1	3	PH2	6	2	2
26	76	M	H/AF	2 hrs 45min	6	4	10	RM2.	N	N			2	3	PH2	7	4	2
27	54	M	L/Sm	7 hrs 15min	18	4	5	LM1	N	N			1	3	No	3	16	NF
28	64	F	D/H	2 hrs 15min	22	4	4	LM1.	N	105	283	3	1	3	No	5	7	NF
29	68	M	H/sm	4 hr 5 min	7	4	4	RM1.	N	N			0	2	No	0	2	2
30	59	M	H	1hr 50 min	16	4	5	RM1.	yes	40	180	3	1	3	No	5	16	NF
31	54	M	D/H/Sm/	5hr 30min	15	4	4	RM2	N	N			0	1	HI2	3	14	NF
32	81	M	H/D	3 hr 45min	18	5	7	RM1.	Yes	N			1	3	PH1	1	16	NF
33	49	F	AF	4 hrs 45 min	6	3	8	T occulsion	N	N	N	N	2	4	No	0	2	3
34	65	M	D/H/C	1 hrs 10 min	23	4	7	L ICA+LM2	N(sugar)	30	Failed	0	1	4	HI1	4	20	NF
35	52	F	AF	3 hrs 10 min	6	4	8	RM1.	Yes	N			2	4	No	8	0	NF
36	40	F	N	2 hrs 50 min	8	4	7	R M1	Yes	35	Failed	0	3	5	No	7	0	0
37	67	F	N	3 hrs 40 min	17	4	7	R ICA+RM1	N	65	345	2B	3	5	HI1	7	1	0
38	48	M	Sm	2 hours 30 minutes	8	4	5	RM2	N	N			1	4	No	5	2	2
39	42	M	Sm	4 hrs 45 min	6	3	6	LM1	N	25	370	2B	2	4	HI1	6	1	0
40	60	F	D	1 hr 5 min	21	4	5	L M1	N(INR)	40	105	3	1	4	PH1	5	5	1
41	51	M	H	4 hr 15min	24	4	7	LM1.	N	35	310	2B	1	4	No	6	0	1
42	63	M	D/H/L/CAD.	2hr 45min	9	4	10	RICA.	N	N			2	4	No	10	1	1
43	84	M	H/Sm	3hr 15min	14	4	5	LICA.	N	N			2	4	No	0	23	NF
44	75	F	D	2 hr 40 min	23	4	6	LM1.	yes	90	290	2B	1	4	No	6	2	NF
45	60	M	D/L	5 h 30 min	10	4	8	RM1.	no	60	410	3	1	4	No	8	0	2
46	67	M	D/L/Sm	3hr 30 min	8	4	9	RM1.	yes	60	330	2b	2	4	No	6	5	0
47	65	F	D	2 hr 35min	14	4	6	RM1.	yes	35	205	3	2	4	PH1	5	13	4
48	86	M	H/AF	2 hrs 35 min	12	4	7	RM1.	N	50	250	2B	2	4	No	6	4	NF
49	68	F	H/L/CAD	4hr20min	17	4	6	RM1.	N	55	335	3	1	4	HI2	6	4	NF
50	46	F	AF	3hr20min	10	4	6	RM1.	N(INR)	90	328	3	2	4	No	6	1	2
51	67	M	D/H/AF	25min	16	4	10	RM1.	yes	30	85	3	1	4	No	8	0	0
52	75	M	H/AF	4 hr	13	4	9	LM2	N(INR)	N			1	4	No	7	8	4
53	72	F	D	2 hr 50min	21	5	4	LM2	N	N			1	4	H12	3	15	NF
54	37	F	N	2hr.	8	4	2	RM1.	N	N			1	4	HI1	1	4	0
55	51	M	H	4 hrs 15min	24	5	7	LM1	N	35	310	2b	1	4	No	6	0	1
56	84	M	H/sm	3hrs 15min	14	4	5	LICA.	N	N			2	4	No	0	23	NF

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ASSESSMENT OF COLLATERAL STATUS USING MULTIPHASE CT ANGIOGRAPHY IN THE ACUTE ANTERIOR CIRCULATION ISCHEMIC STROKE: ITS CORRELATION WITH CLINICAL AND RADIOLOGIC OUTCOMES THESIS SUBMITTED IN PARTIAL FULFILLMENT FOR DEGREE OF OF THE SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM, INDIA SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM This is to certify that the work incorporated in this thesis titled "Assessment of collateral status using multiphase CT angiography in the acute anterior circulation ischemic stroke: its correlation with clinical and radiologic outcomes" for the degree for DM "NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY" has been carried out by Dr. The work done in connection with this thesis has been carried out by the candidate himself and is genuine. Department of Imaging Sciences and Interventional Radiology, Dr Sylaja PN Dr Bejoy Thomas Dr Jayadevan E R Dr Santhosh K I hereby declare that this thesis titled "Assessment of collateral status using multiphase CT angiography in the acute anterior circulation ischemic stroke: its correlation with clinical and radiologic outcomes" has been prepared by me under the supervision and guidance of Dr.Kesavadas (Professor), Dr.Sylaja (Professor), Dr.Bejoy Thomas (Professor), Dr.Jaydevan (Add. Professor), Dr.Santhosh K (Associate Professor), Sree Chitra Institute for Medical Sciences and Technology, Trivandrum. I am deeply indebted to my

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3-point score grading of middle cerebral artery collateral branches with respect to the Sylvain fissure. One study showed miteff is more reliable predictor of good outcome than other single-phase scoring systems(11). Patients with good collaterals have lower NIHSS score (3), small infarct size and better prognosis. 3 - vessels reconstituted distal to the occlusion. 1-vessels seen only in the distal superficial branches. 5-point score comparing collaterals on the affected hemisphere against those on the unaffected side. E.Alberta Stroke Program Early CT Score (ASPECTS) 20 Point Grading Scale(10): Collaterals are scored in each of the 10 regions corresponding to the ASPECTS system, to form a score from 0 to 20 In patients with MCA occlusion, prominent distal T2 FLAIR hyperintense signals (12,13) is associated with smaller initial ischemic infarct, larger diffusion-perfusion mismatch, better NIHSS score and smaller subacute ischemic lesion volume. Although definitely not proved, distal T2 FLAIR hyperintense signal may be said to be related to good collateral flow distal to the occlusion site (14) (15). Territorial ASL gave information regarding intracranial collaterals, comparable to DSA in steno 3D pseudo-continuous ASL with multiple post label delays had been used to estimate antegrade and collateral flow in unilateral MCA stenosis. (17) ASL collaterals detected in acute stroke were showed to correlate with neurological outcome of mRS at discharge. (18,19) -SWI was shown to accurately predict intracranial collateral circulation in acute infarcts and can be used for prognostication and curative evaluation (20) -SWI-diffusion mismatch was also proved to identify patients who benefit from reperfusion therapy

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6. Then multiphase CT collateral grading was assessed (0 to 5). Then single phase CT grading 0 to 3 as per most widely used TAN grading system was assessed. 7. Base line NIHSS, mRS of the patient were assessed and recorded by certified neurologist. Age, sex, risk factors (hypertension, diabetes, coronary heart disease, atrial fibrillation, smoking, hyperlipidemia) of the patients were recorded. 8. Patients treatment history details- either conservative, iv thrombolysis, mechanical thrombectomy were included in the study. 9. In patients who had undergone mechanical thrombectomy, time to groin, onset to reperfusion and TICI grading were also included in the study. 10. All patients underwent 24 hrs plain CT as per our institutional protocol and details of 24 hrs ASPECTS (0 to 10), hemorrhagic transformation (ECASS grading) were assessed. 11. All patients were examined for NIHSS at discharge. Those patients who were alive at discharge were followed after 90 days to assess mRS scale of functional outcome. Good and poor functional outcomes were defined by mRS scores of 0–2 and 3–6, respectively. Statistical differences of these variables in single and multiphase CT collateral groups were assessed by student T test (for continuous variables) or Fisher exact test (for categorical variables). Multivariate logistic was done for variables with significant difference. Statistical analysis of the data was performed and sensitivity, specificity, positive, negative predictive values and accuracy of both the single and multiphase CT angiography collaterals in predicting 3 months Receiver operator characteristic (ROC) curve analysis of single and

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4. Receiver operator characteristic (ROC) curve analysis of single and multiphase CT angiography for predicting functional outcome along with area under curve (AUC), youden's J, test efficiency were calculated individually 5. Spearman coefficient was done to assess the correlation of single and multiphase CT angiography with variables. A total of 56 consecutive patients with anterior circulation acute stroke with major vessel (M1, M2 or ICA or combined), who presented to the institute between October 2016 and 30 June 2018 were included in this prospective study. The age of patients in the study ranged from 37 to 86 years, with the mean age of 63 years. There were 35 males and 21 females in the study group. The male to female sex ratio within the cohort was 5:3. There were 42 MCA occlusion and 14 cases of ICA/ combined ICA-MCA occlusion cases in this study. The commonest risk factor of our patients was hypertension (n=25), diabetes (n=21) followed by CAD (11 cases), AF (11 cases) and smoking (10 cases). Mean NIHSS score of the 56 patients was 16 (+/-6). Mean time from symptom onset to CT was 3 hours 20 minutes. 29 patients (52%) undergone mechanical thrombectomy and stent retrievers were used in all cases. Mechanical thrombectomy was done as per universally followed guidelines (ASPECTS>=6, NIHSS 5 to 25, M1/ T occlusion). Mean door to groin puncture was 51 (+/-22) minutes. 9 patients received both intravenous thrombolysis and mechanical thrombectomy, while 4 cases (7%) received only intravenous thrombolysis. TICI 2B or 3 recanalization was attained in 76% (22 out of 29) patients. Mean time from stroke onset to recanalization was 263 +/-80 minutes. 24 hours

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श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013)

SCT/IEC/987/OCTOBER-2016

07.12.2016

Dr. Adhithyan R
Senior Resident
Department of IS & IR
SCTIMST, Thiruvananthapuram

Dear Dr. Adhithyan,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "ASSESSMENT OF COLLATERAL STATUS USING MUTIPHASIC CT ANGIOGRAPHY IN THE ACUTE ANTERIOR CIRCULATION ISCHEMIC STROKE: ITS CORRELATION WITH CLINICAL AND RADIOLOGIC OUTCOMES" (IEC/987) on 14th October, 2016.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the Chairman, IEC, SCTIMST, dated 21.09.2016 with check list*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Patient Information Sheet and Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co- Investigators*

Revised submission

1. *Covering letter addressed to the Chairman, IEC, SCTIMST, dated 20.11.2016*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *IEC Recommendation Letter dated 07.11.2016*
5. *Project Proposal*
6. *Proforma*
7. *Patient Information Sheet and Consent Form in English and Malayalam*
8. *CV of Principal Investigator and Co- Principal Investigators*