

**“DECOMPRESSIVE HEMICRANIECTOMY: PREDICTORS OF
FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC
STROKE AFTER SURGERY-A RETROSPECTIVE STUDY IN
SINGLE INSTITUTE”**



THESIS

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SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL

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TRIVANDRUM, INDIA

DR. NITHIN RAJ S D

DEPARTMENT OF NEUROSURGERY

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND

TECHNOLOGY

TRIVANDRUM, INDIA

*SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND
TECHNOLOGY*

TRIVANDRUM, INDIA



CERTIFICATE

This is to certify that the work incorporated in this thesis titled

**“DECOMPRESSIVE HEMICRANIECTOMY: PREDICTORS OF
FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC
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SINGLE INSTITUTE”**

for the degree of

M.Ch NEUROSURGERY

has been carried out by DR. NITHIN RAJ S D

*under my supervision and guidance. The work done in connection with this thesis has
been carried out by the candidate himself and is genuine.*

Dr. Mathew Abraham
Professor & Head
Principal Guide
Department of Neurosurgery,
SCTIMST, Trivandrum.

Dr. Jayanand Sudhir
Assistant Professor
Co - Guide
Department of Neurosurgery,
SCTIMST, Trivandrum.

DECLARATION

I hereby declare that this thesis titled **“DECOMPRESSIVE HEMICRANIECTOMY: PREDICTORS OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AFTER SURGERY-A RETROSPECTIVE STUDY IN SINGLE INSTITUTE”**

is a consolidated report based on a bonafide study during the period 1st January 2012 to 30th June 2017 has been prepared by me under the supervision and guidance of Prof. Mathew Abraham, Prof. and Head, Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

The thesis is submitted to SCTIMST in a partial fulfilment of rules and regulations of M.Ch Neurosurgery examination.

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Dr.Nithin Raj S D

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INTRODUCTION

INTRODUCTION

Large hemispheric infarctions because of middle cerebral artery (MCA) or internal carotid artery (ICA) occlusion constitute a major cause of severe morbidity and mortality. Neurological deterioration occurs as a consequence of space-occupying cerebral edema in approximately 10% of all hemispheric strokes. Mortality ranges between 41 and 79% with conservative

treatment in the intensive care unit(1). The incidence of hemispheric infarcts ranges between 10 and 20 per 100 000 per year(1)(2) Large hemispheric infarctions occur as a consequence of a thrombotic or embolic occlusion of the distal ICA or the proximal MCA trunk without sufficient collateral flow. Most patients have risk factors for vascular disease such as hypertension, diabetes, hypercholesterolemia, tobacco abuse, history of transient ischemic attacks or ischemic strokes, congestive heart failure, and coronary artery disease. Atrial fibrillation is more frequent in patients with MCA and ICA territory strokes compared to the remaining stroke population(3)(4)(5). The patients present with hemiparesis, hemiplegia, hemisensory loss, homonymous hemianopia contralateral to the site of infarction, partial and fixed gaze palsy (6) towards the non affected hemisphere, and depressed level of awareness. Non-dominant hemispheric infarctions are associated with visual, motor, and sensory neglect. Language disturbance such as fluent, non-fluent, and mostly global aphasia are typical for infarctions localized to the dominant hemisphere. Neurological decline starts mostly within the first 48h (2), in 36% within 24 h, and 68% within 48 h(7). Death occurs within 5 days(8) as a result of brain death in the majority of patients. Hemispheric brain swelling leads to brain tissue shifts with subsequent brain stem distortion, bi hemispheric dysfunction through mechanical displacement, vascular compression, uncal and transtentorial herniation.

However, the era of decompressive craniectomy resulted in a dramatic decrease of mortality and severe disability. Decompressive hemicraniectomy is a life saving palliative surgery to relieve brain compression in which the skull is opened and a bone flap is removed to allow the edematous brain to swell outward, thereby preventing intracranial tissue shifts and life-threatening herniation. Most of existing data on decompressive hemicraniectomy are from the following RCTS: Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY Trial, Germany)(9), Sequential-Design, Multicenter, Randomized, Controlled Trial of Early Decompressive Craniectomy in Malignant Middle Cerebral Artery Infarction (DECIMAL Trial, France)(5) and Hemicraniectomy after middle cerebral artery infarction with life-threatening Edema trial (HAMLET Trial, UK)(5). While decompressive hemicraniectomy in malignant stroke has been shown to significantly reduce mortality, approximately 40% of survivors become severely disabled with mRS of 4 or more.(10). The prospective trials and pooled analyses published to date do not provide conclusive results on quality of life and depression in patients who survived malignant MCA infarction after surgery and those aspects deserve further investigation. Furthermore the timing of surgery has not been sufficiently addressed in any of the 3 above mentioned European RCTs. Early decompression within 48 hours has been the norm. On the other hand, post stroke edema often peaks later than 48 hours after symptom onset and there might be a role for a wider time window within which decompressive surgery can be done. The HAMLET study(5) allowed delayed surgery up to 96 hours after stroke onset, and secondary outcome analyses showed that surgery within 48 hours significantly reduced the probability of severe disability or death (mRS 5 or 6), whereas delayed hemicraniectomy did not influence outcome. Another debate whether was to perform decompressive craniectomy in patients with malignant MCA

infarction on the speech dominant hemisphere is based on the assumption that in the presence of aphasia, functional outcome and quality of life may be worse as compared with patients with non-dominant infarction. This assumption, however, is currently not supported by data available in the literature, because mortality, functional outcome, and quality of life do not seem to depend on whether the dominant hemisphere is involved. On the contrary, neuropsychological deficits seen in patients with infarcts on the non-dominant hemisphere, as attention deficits or depression, may be as disabling as aphasia. Another factor has been proven to be beneficial in not only reducing mortality, but also improving morbidity in some trials, was that younger subjects <60 years were recruited(11). The mortality rate and functional outcome, were significantly worse in patients > 60 years(9)of age following decompressive craniectomy for malignant infarction. Thus age is an important factor to consider in patient selection for surgery. All the well recognised RCTs in the area, DECIMAL , DESTINY and HAMLET study, are from data from developed country scenario. The post surgery long term rehabilitation in Indian scenario is mostly restricted to the support by family member with lack of comprehensive rehabilitation care system. We need to see that for the existing level of rehabilitation that the patient's family can offer him/her, whether the outcome in our scenario is satisfactory or not. The result of this study shall help us to tell the patient's relatives of the ground reality of outcome of the procedure in our scenario eg: If most patients end up at mRS> 4 then bystanders need to be aware of the huge amount of time and energy they have to spend on the taking care of patient for the rest of his/her life/whether they will ever have a possibility of being functional indenpendency.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Stroke is the fourth leading cause of death, accounting for 5.2% of all deaths(11)About four-fifths of strokes are due to blockage of an artery in the brain. When the artery is blocked, part of the brain is damaged, this is called a cerebral infarct. If a large artery is blocked the area of brain damage can be large. Intravenous thrombolysis within 3 to 4.5 hours of onset of stroke improves outcomes in acute ischemic stroke, however, space-occupying, large hemispheric infarction, usually resulting from acute occlusion of the internal carotid artery (ICA) or the middle cerebral artery (MCA), represents a devastating sub-group of severe ischemic stroke(12). Life-threatening, space-occupying brain oedema occurs in 1–10% of patients with a supratentorial infarct and usually manifests itself between the second and fifth day after stroke onset(13). Poor outcome is mostly explained by the volume of cerebral tissue that is damaged. Early deterioration and death is often the result of oedema in the infarcted tissue. Oedema causes mass-effect with distortion, tissue shift and increased intracranial pressure. Patients with a large cerebral infarction generally have a poor prognosis. Approximately 40% of patients with total anterior cerebral infarction (TACI) syndrome deteriorate during the first week, and half of them die during the first month(14).

Etiology:

Stroke etiology is mainly based on the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification(15)(16):

- (1) large-artery atherosclerosis
- (2) Small vessel occlusion (Lacunar)
- (3) Cardio-embolism

(4) Stroke of other determined etiology

(5) Stroke of undetermined etiology.

Table 1: Stroke of other determined etiology:

Vasculitis
Arterial dissection
Polycythemia, thrombocythemia, TTP
Systemic lupus erythematosus
Sickle cell disease
Vascular spasm
Meningitis and fungal vasculitis
Hypercoagulability (Factor V Leiden, Prothrombin 20210A mutation, antiphospholipid antibody syndrome)
Inherited metabolic disorders (Fabry disease, homocystinuria, mitochondrial disorders)
Fibromuscular dysplasia and other angiopathies

Stroke of undetermined etiology :

Include 3 heterogeneous groups:

- (a) Two or more causes
- (b) Negative evaluation
- (c) Incomplete evaluation.

Negative evaluation was defined as no likely etiology despite extensive evaluation.

Fig 1: Pathophysiology of Ischemic stroke:(17)

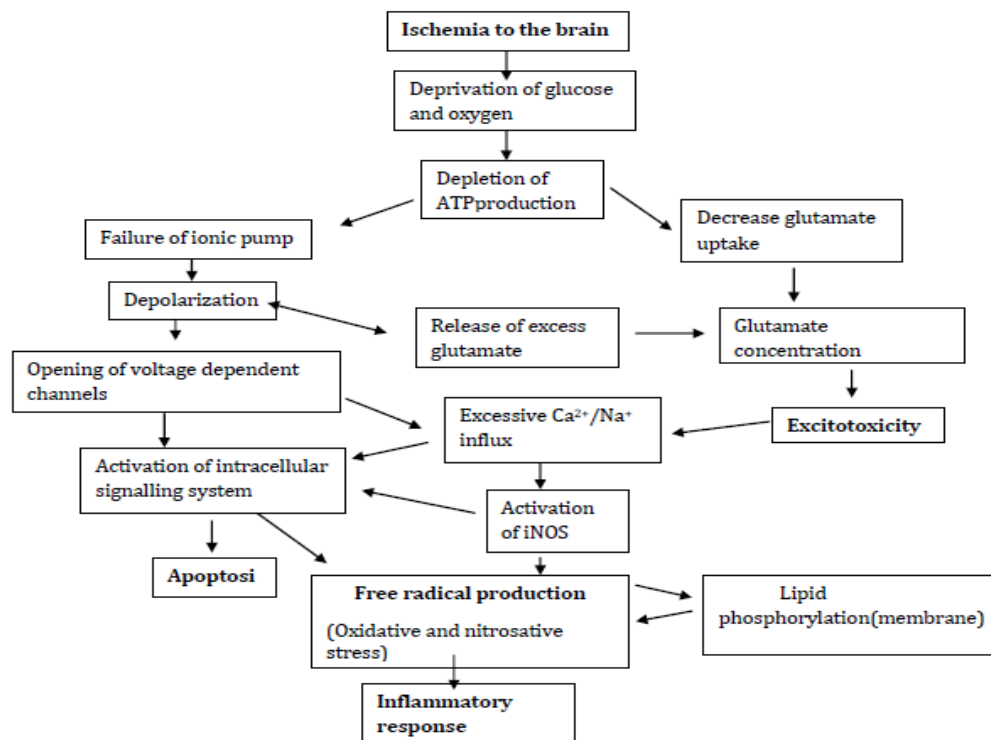


Table 2: Risk factors for ischemic stroke:(17)

Fixed risk factors	
• Age • Gender (male > female except at extremes of age) • Race (Afro-Caribbean > Asian > European) • Previous vascular event - Myocardial infarction - Stroke - Peripheral vascular disease • Heredity • High fibrinogen	
Modifiable risk factors	
• Blood pressure • Cigarette smoking • Hyperlipidaemia • Heart disease - Atrial fibrillation - Congestive cardiac failure - Infective endocarditis	• Diabetes mellitus • Excessive alcohol intake • Oestrogen-containing drugs - Oral contraceptive pill - Hormone replacement therapy • Polycythaemia

Clinical presentation:

The patients present with hemiparesis, hemiplegia, hemisensory loss, homonymous hemianopia contralateral to the site of infarction, partial and fixed gaze palsy towards the non-affected hemisphere, and depressed level of awareness. Non-dominant hemispheric infarctions are associated with visual, motor, and sensory neglect. Language disturbance such as fluent, non-fluent, and mostly global aphasia are typical for infarctions localized to the dominant hemisphere(7). Clinical signs for development of cerebral edema include nausea and emesis, decreasing level of consciousness to coma, increasing pupillary size ipsilateral to the infarct, hemiparesis ipsilateral to the infarct, unilateral or bilateral flexor or extensor posturing, altered breathing pattern, respiratory failure, bradycardia, and hypertension (Cushing response). The first sign is drowsiness followed by pupillary asymmetry, periodic breathing, and extensor plantar response ipsilateral to the site of infarction. Death occurs within 5 days as a result of brain death in the majority of patients.

Radiological diagnosis of ischemic stroke:**1) Computer tomography-**

NCCT is faster, more widely available, and less expensive method of diagnosing acute stroke. However, changes due to hyperacute ischemic stroke may not be visible on early NCCT scans. Advanced methods are used to detect early changes of ischemia like CT angiography (CTA) and perfusion CT (PCT).

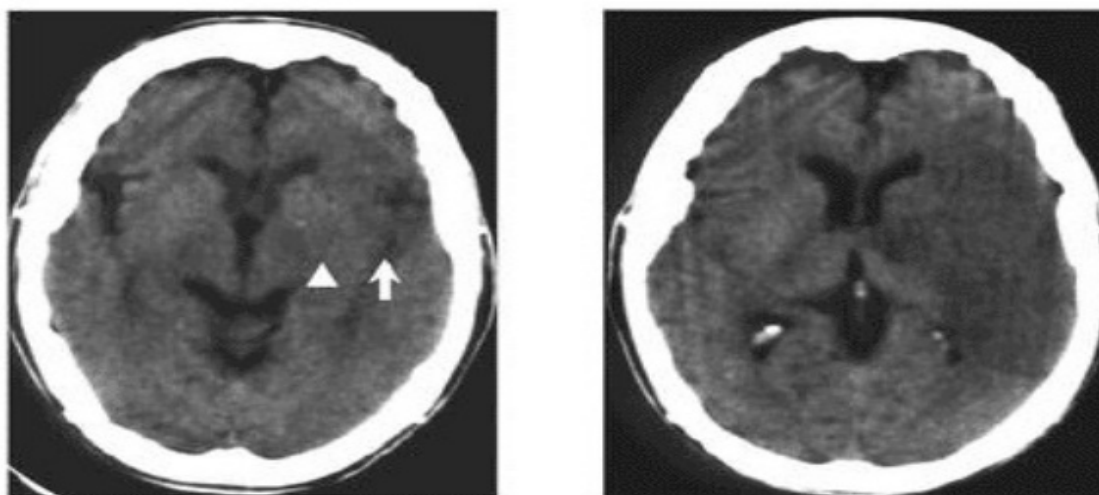


Fig 2: CT 12 hrs and 36 hours after onset of left MCA territory infarct

Hemorrhage classification	Radiographic appearance
Hemorrhage infarction type 1 (HI1)	Small hyperdense petechiae
Hemorrhage infarction type 2 (HI2)	More confluent hyperdensity throughout the infarct zone; without mass effect
Parenchymal hematoma type 1 (PH1)	Homogeneous hyperdensity occupying <30% of the infarct zone; some mass effect
Parenchymal hematoma type 2 (PH2)	Homogeneous hyperdensity occupying >30% of the infarct zone; significant mass effect. Or, any homogenous hyperdensity located beyond the borders of the infarct zone

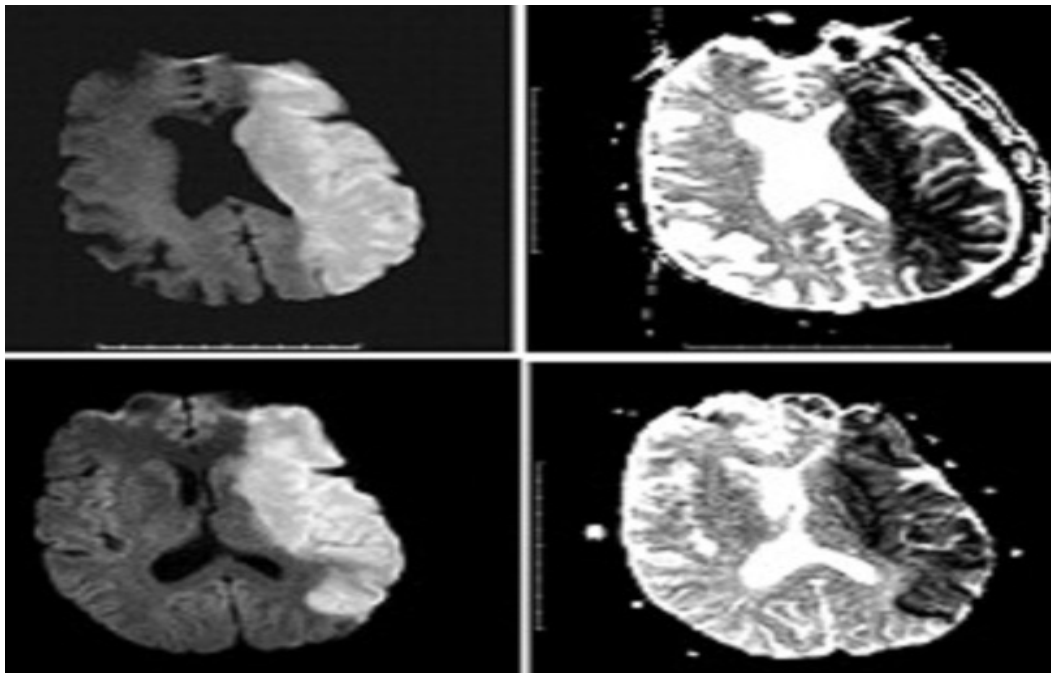
Table 3: Hemorrhagic conversion grading on plain CT scan(18)

2) MRI-

MRI is a better method of early evaluation for treatment of patients with stroke. Overall, MRI has a sensitivity of 83% and CT has a sensitivity of 26% for the diagnosis of any acute stroke (19). The techniques used for evaluation include diffusion-weighted imaging, perfusion weighted MRI, and magnetic resonance angiography (MRA). MRI diffusion-weighted imaging volume of 82 cm³ when performed 6 hours has a high specificity

(98%) but low sensitivity (52%).(19). A MRI diffusion-weighted imaging volume of 145 cm³ obtained before 14 hours was associated with 100% sensitivity and 94% specificity in detecting infarcts(20)

Fig 3: MRI diffusion restriction if left MCA territory and corresponding low ADC levels.



3) Doppler Ultrasound

Transcranial Doppler (TCD) imaging is a non invasive screening technique that measures blood flow velocity and direction in segments of large intracranial arteries to assess intracranial artery disease. Carotid duplex ultrasonography (CUS), which is a union of Doppler analysis and real-time ultrasound, is a useful tool for screening for cervical carotid artery disease. Conditions such as intimal thickening, atherosclerotic plaque, and proximal dissections can be identified by CUS.

4) Catheter Angiography

In some cases, etiologic diagnoses cannot be made by use of non invasive imaging techniques so invasive methods like DSA used. The measurement of luminal diameter narrowing by angiography (catheter, CTA) is the most reliable method for identification of candidates for surgical carotid endarterectomy (CEA). Catheter angiography is widely used in patients who will undergo stent placement in the intracranial circulation or mechanical thrombectomy for acute ischemic stroke.

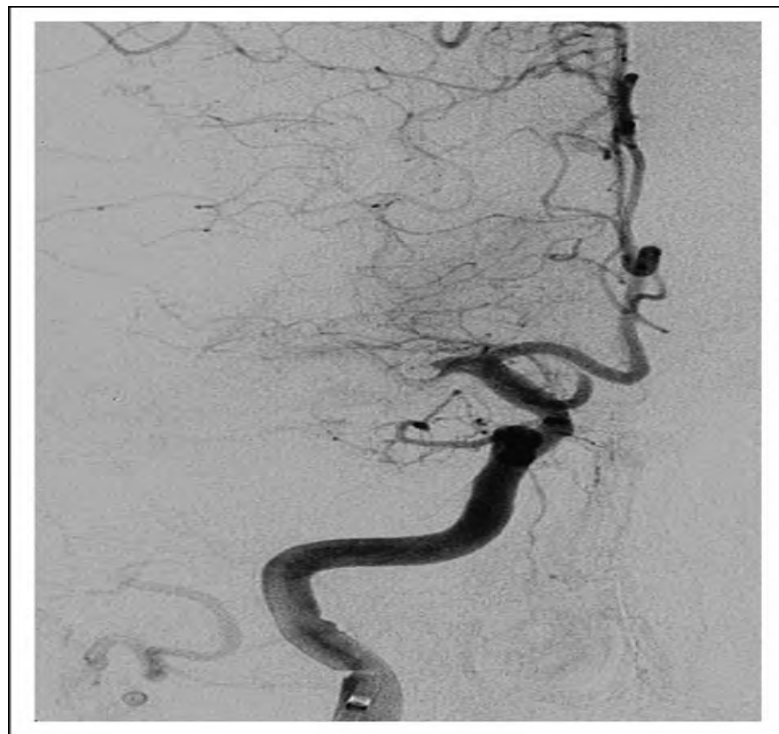


Fig 4: Occlusion of M1 right MCA in right ICA injection in DSA

Management Of Acute Ischemic Infarct:

Successful re-canalization of the hypo-perfused or occluded MCA or ICA within a narrow time window of 3–4 hr can be lifesaving and decrease the size of infarction, thereby preventing the development of malignant brain edema. (21). Intravenous recombinant tissue plasminogen activator (rtPA) administered within 3h of onset of the

first stroke symptom is the approved acute stroke treatment. Intra-arterially administered recombinant pro-urokinase within 6h of stroke onset provided re-canalization by 66%(22). But risk of intra-cerebral hemorrhagic conversion is high if patient is not in acute stroke or out of this window period of 3-5 hours.

Mechanical re-canalization can be done by Mechanical Embolus Removal in Cerebral Ischemia (MERCI) (21) or a cork screw shaped device to pull the thrombus out the Penumbra stroke or a clot aspirator. But none of these devices have been evaluated in randomized controlled trial regarding their effect on long-term outcome.

Intensive care management:

ICU treatment aims at reducing oedema and intracranial pressure in stroke patients using hyperventilation, mannitol, diuretics, corticosteroids or barbiturates. No medical treatment has been proven effective. However, once brain swelling produces clinical signs and imaging features of mass effect with tissue shift, case-fatality becomes higher, despite intensive medical treatment(3)

Surgical decompression:

Surgical decompression seeks to create space to accommodate the increased volume created by the swollen brain. This can be accomplished by opening the cranial vault and dura or by removing non-viable or non-essential brain tissue. These strategies are described as 'external' or 'internal' decompression respectively(23). External decompression involves hemi-craniectomy with or without duroplasty. Internal decompression involves the removal of brain tissue, either the infarcted region or non-eloquent regions of the brain. These techniques are sometimes combined. The rationale of this treatment modality consists of opening of the skull and removal of a bone flap to

allow the edematous brain to swell outward, thereby preventing intracranial tissue shifts and life-threatening downward herniation.

History of Decompressive craniectomy:

The idea of opening the skull to relieve pressure is an old concept. It was exemplified in the Greek myth of Athena, goddess of wisdom, according to Hesiod in the poem *Theogony* (circa 700 BC). Zeus, the supreme god of Olympus, after swallowing his first wife Metis, had a severe and progressively worsening headache attributed to the growth of his daughter Athena inside his skull. Hephaestus, the god of fire and metalwork, struck Zeus' head with an axe splitting his cranium in order to alleviate his pain, and Athena was born through this primitive craniotomy (23). The ancient Egyptians performed trephinations with local anesthesia, prepared by mixing ground marble with vinegar. The success of these procedures is evidenced by the discovery of healed wounds in skulls unearthed from tombs dating back 6000 years. On the tomb of Bany Hassan, there are paintings that depict a surgeon performing cranial surgery with the patient seated (23). The modern concept of decompressive surgery was born with the statement of Kocher, in 1901: *"If there's no CSF pressure, but brain pressure exists, then pressure relief must be achieved by opening the skull."* This author introduced the concept of elevated intracranial pressure as a global phenomenon requiring a large skull opening to be treated. Harvey Cushing designed a standard sub-temporal decompressive surgery for treatment of elevated intracranial pressure in the beginning of the 20th century (24). The landmark work of Guerra and colleagues (1999) described their results using decompressive craniectomy for traumatic brain swelling.

Surgical technique of standard decompressive craniectomy:(25)

Skin incision: A large reverse question mark skin incision is made. The incision begins 2 to 3 cm lateral to midline behind the hairline, extends at least 12-15 cm posteriorly, and then curves around and down to the posterior root of zygoma. The skin and temporalis muscle are reflected anteriorly as a myo-cutaneous flap.

Bone removal: The limits of bone removal are 2-3 cm from midline, avoiding frontal sinus and superior sagittal sinus, till middle cranial fossa base. The antero-posterior extent is at-least 12-15cms.

Dural opening: The dura is opened in a stellate fashion to maximize cerebral decompression. The bulging brain covered with pericranium spread over the brain instead of a watertight duraplasty.

The bone flap was placed in a subcutaneous pocket overlying the abdomen until subsequent cranioplasty.

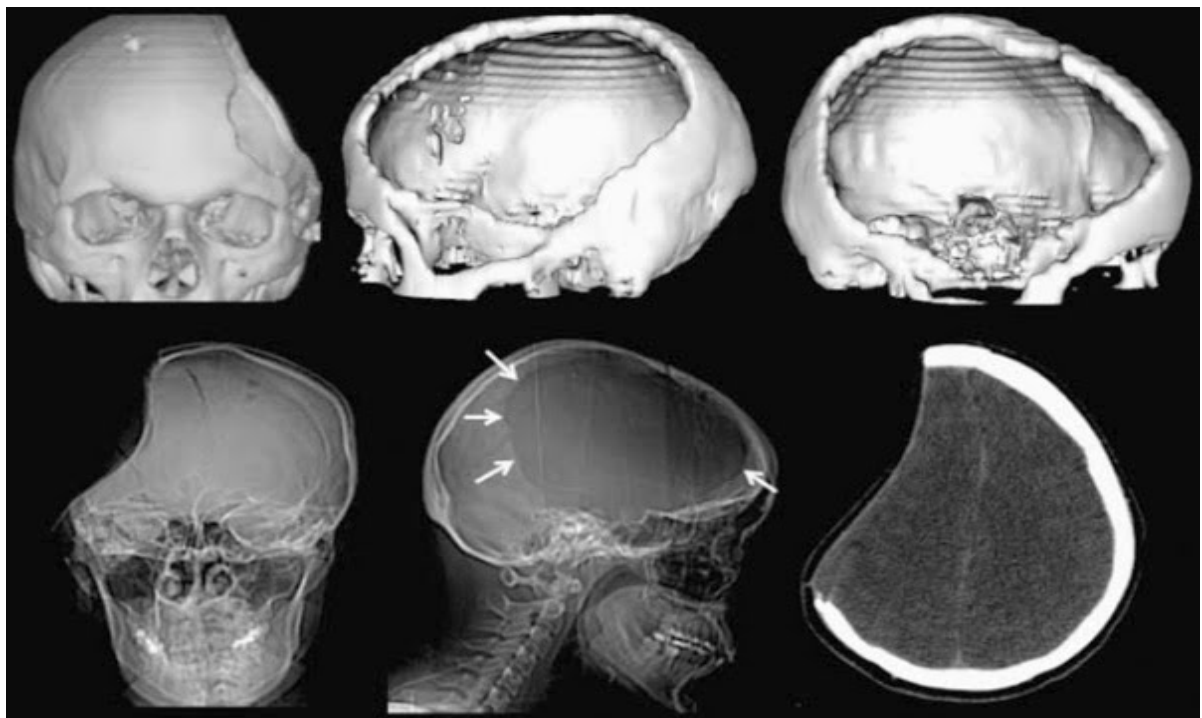


Fig 5: Re-constructed NCCT image showing post decompressive hemi-craniectomy status

Risks and complications of Decompressive hemicraniectomy:

Immediate complications include Secondary cerebral haemorrhage, insufficient decompression, surgical site infections, contra-lateral subdural effusions, brain herniation through the craniectomy defect.(23) Problems with flap storage and sterilization and metabolic changes associated with lack of bony covering.

Delayed complications include the sinking flap syndrome, extra-axial fluid collections, hydrocephalus, and development of subdural hematomas. The rates of infections at the time of DHC or re-placement of the bone flap range from 5% to 10%(20). Infection rates at the time of cranioplasty may be related to the type of bone flap used. Synthetic materials used as flaps may lead to a foreign body reaction, whereas autologous bone flaps may be associated with higher rates of infection(26). The sinking flap syndrome is felt to occur as a result of the pressure gradient between the atmospheric pressure and intracranial vault. This leads to severe headaches, changes in mentation, and seizures. Placing patients supine often relieves the clinical symptoms with replacement of the bone flap being curative.



Fig 6: Sinking flap syndrome.(23)(27)

The development of communicating hydrocephalus as a result of DC may be a common occurrence which is treated by CSF diversion procedures. In-hospital medical complications due to patient immobility and survival from the DHC can impact the clinical outcomes of the patient. A National Inpatient Sample database over a 6-year period in the United States found the rates of pneumonia to be 11.1%, gastrointestinal bleeding 2.4%, and sepsis 4.76% in 252 patients studied. Each of these complications was associated with an increased rate of mortality and were significantly higher compared with patients with a similar co-morbidity index(28)

Rationale of Decompressive hemicraniectomy for hemispheric infarcts:

Malignant infarction treated only by conservative approaches results in a mortality rate of 80% within the 1st week of the stroke.(13)(29)(30) Edema that does not respond to medical treatment necessitates DH as a life-saving procedure.

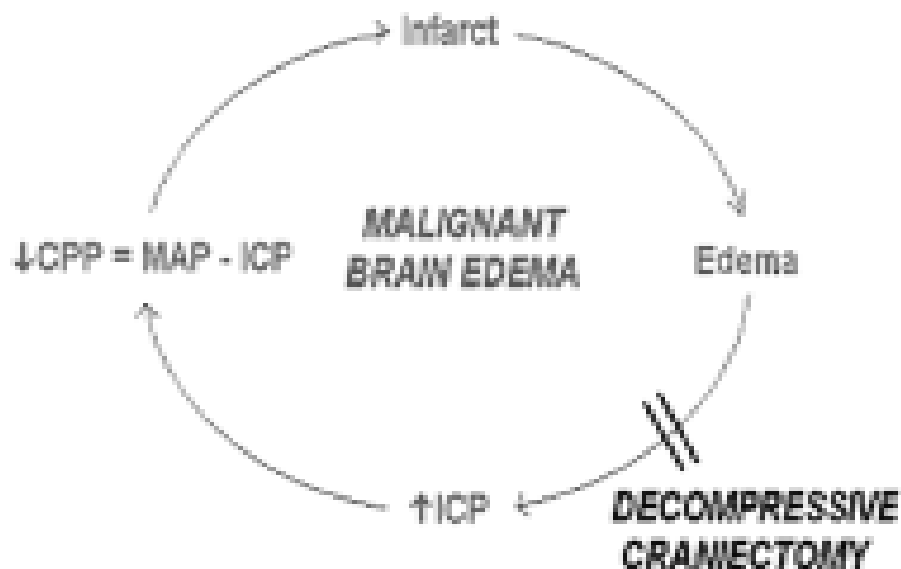


Fig: 7 Schematic demonstrating the possible mechanism of decompressive craniectomy in breaking the cycle of malignant infarction. CPP = cerebral perfusion pressure; MAP = mean arterial pressure(1)

Studies have demonstrated that DH surgery can result in a reduction of mortality rate to 30% and, if decompression is performed within 24 hours of stroke onset, to 10%.(13)withthe long-term prognosis appears to be favorable if patients survive the acute phase of the stroke(20). The eligibility of patients with ischemicstroke to undergo DH might be further informed by functional outcome, mortality, and quality of life data. Patient selection for DH relies onneurological examination, baseline patient characteristics,stroke presentation, imaging evaluation, and time from onset of symptoms to surgery. Recent observational studies have strongly suggested that age is a main predictor of poor functional outcome after decompressive surgery(31).The time point for decompressive surgery is another clinical factor that is associated with the efficacy of decompressive surgery on patients with malignant MCA infarction(32).In addition, recent studies indicated DC for malignant MCAinfarction thus resulted in a significant reduction in mortality, butnearly all survivors suffer moderately severe or severe disability (defined as mRS4 or 5). Although, higher age is an important predictor of unfavorable outcome in patients underwent decompressive surgery, early DC didincrease the probability of survival and reduce poor functional outcome in patients 60 years of age.

Functional Outcome and Quality of Life(33)

Early hemi-craniectomy significantly reduces mortality aftermalignant MCA infarction and also increases theprobability of survival with moderately severe disability (mRS of >4)(34)(35)(36). Looking at motor function,the benefit of surviving malignant MCA infarction after hemi-craniectomy seems to be largely outweighed by the high incidence of moderately severe or severe disability in survivors(31). From thepatients perspective, neuropsychological deficits, aphasia, ordepression may have an equally strong impact on

quality of life as compared with motor function. NIHSS (National Institute of Health Stroke Scale)(37) was developed in 1989 is a reliable, valid and responsive tool for measuring stroke severity; it is useful both in clinical practice and research. It can be used in people with language and cognitive deficits along with motor deficits. Importantly, the NIHSS is quick to administer (less than 10 minutes).(37))

Other factors such as psychosocial environment, caregiver burden, familial support, and financial support should be additionally considered in patients undergoing surgical intervention for stroke.

Table 4: NIHSS scoring system

National Institutes of Health Stroke Scale	
Score = 0	No stroke
Score = 1-4	Minor stroke
Score = 5-15	Moderate stroke
Score = 15-20	Moderate to severe stroke
Score = 21-42	Severe stroke

National Institutes of Health Stroke Scale score	
1a. Level of consciousness	0 = Alert; keenly responsive 1 = Not alert, but arousable by minor stimulation 2 = Not alert; requires repeated stimulation 3 = Unresponsive or responds only with reflex
1b. Level of consciousness questions: What is the month? What is your age?	0 = Answers two questions correctly 1 = Answers one question correctly 2 = Answers neither question correctly
1c. Level of consciousness commands: Open and close your eyes. Grip and release your hand.	0 = Performs both tasks correctly 1 = Performs one task correctly 2 = Performs neither task correctly
2. Best gaze	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation
3. Visual	0 = No visual loss 1 = Partial hemianopia 2 = Complete hemianopia 3 = Bilateral hemianopia
4. Facial palsy	0 = Normal symmetric movements 1 = Minor paralysis 2 = Partial paralysis 3 = Complete paralysis of one or both sides
5. Motor arm 5a. Left arm 5b. Right arm	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity; limb falls 4 = No movement
6. Motor leg 6a. Left leg 6b. Right leg	0 = No drift 1 = Drift 2 = Some effort against gravity 3 = No effort against gravity 4 = No movement
7. Limb ataxia	0 = Absent 1 = Present in one limb 2 = Present in two limbs
8. Sensory	0 = Normal; no sensory loss 1 = Mild-to-moderate sensory loss 2 = Severe to total sensory loss
9. Best language	0 = No aphasia; normal 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute, global aphasia
10. Dysarthria	0 = Normal 1 = Mild to moderate dysarthria 2 = Severe dysarthria
11. Extinction and inattention	0 = No abnormality 1 = Visual, tactile, auditory, spatial, or personal inattention 2 = Profound hemi-inattention or extinction
Total score = 0-42.	

Timing of Surgery

From the patho-physiological point of view, earlier decompression should prevent brain tissue damage by avoiding or reducing exposition to increased intracranial pressure in the course of development of ischemic brain edema(38). On the other hand, post stroke edema often peaks later than 48 hours after symptom onset(39)(40). Therefore, there might be a wider time window within which decompressive surgery may be beneficial for such patients.

Age Limit for Surgery

None of the European RCTs investigating hemi-craniectomy in malignant infarction included patients 60 years(41). Because a considerable proportion of the patients experiencing this type of stroke belong to this age cohort, it still remains unclear if those patients would benefit from surgical treatment. Data from observational studies indicate that hemi-craniectomy may lead to improved survival, however, at the cost of poor outcome and functional dependency in patients 60 years of age(42).

Treatment of Dominant Hemisphere Infarction

The debate whether to perform decompressive craniectomy in patients with malignant MCA infarction on the speech dominant hemisphere is based on the assumption that in the presence of aphasia, functional outcome and quality of life may be worse as compared with patients with non-dominant infarction(43). This assumption, however, is currently not supported by data available in the literature, because mortality, functional outcome, and quality of life do not seem to depend on whether the dominant hemisphere is involved(44)(45)(32). On the contrary, neuropsychological deficits seen in patients with infarcts on the non-dominant hemisphere, as attention deficits or depression, may be

as disabling as aphasia(46)So surgery should be offered irrespective of hemisphere involved if indicated.

AIMS AND OBJECTIVE

AIMS AND OBJECTIVE

-The purpose of this study is to identify predictors of functional outcome for decompressive hemi-craniectomy (DH) in ischemic stroke

-To better define the selection criteria for surgery in patients with ischemic stroke

MATERIALS AND METHODS

MATERIALS AND METHODS

All patients with supra-tentorial unilateral hemispheric ischemic stroke treated surgically from the period of 1st January 2012 to 30th June 2017 were included in the study. The patients will be selected from medical records. Demographic profile, clinical presentation, etiological work up determined according to TOAST criteria, affected hemisphere dominancy, pre-measurement of the midline shift at the septum pellucidum level, uncal herniation in CT head or MRI DWI and cardiac reports will be extracted from the case file. Pre-operative mRS, NIHSS and GCS and time from onset of ictus to decision for surgery noted will also be noted. In hospital complications-including ventilator support, hospital stay, hospital acquired infections, cardiac complications, need for tracheostomy, ionotropic support, will be noted. The decision to perform decompressive craniectomy was based on the presence of a space-occupying large hemispheric infarction on computed tomography (CT) scan and neurological deterioration despite maximum medical treatment, including intravenous mannitol, diuretics, steroids.

Surgical technique

Skin incision: A large reverse question mark skin incision is made. The incision begins 2 to 3 cm lateral to midline behind the hairline, extends at least 12-15cms posteriorly, and then curves around and down to the posterior root of zygoma. The skin and temporalis muscle are reflected anteriorly as a myo-cutaneous flap.

Bone removal: The limits of bone removal are 2-3 cm from midline, avoiding frontal sinus and superior sagittal sinus, till middle cranial fossa base. The antero-posterior extent is atleast 12-15cms.

Dural opening: The dura is opened in a stellate fashion to maximize cerebral decompression. The bulging brain covered with pericranium spread over the brain instead of a watertight duraplasty.

The bone flap was placed in a subcutaneous pocket overlying the abdomen until subsequent cranioplasty.

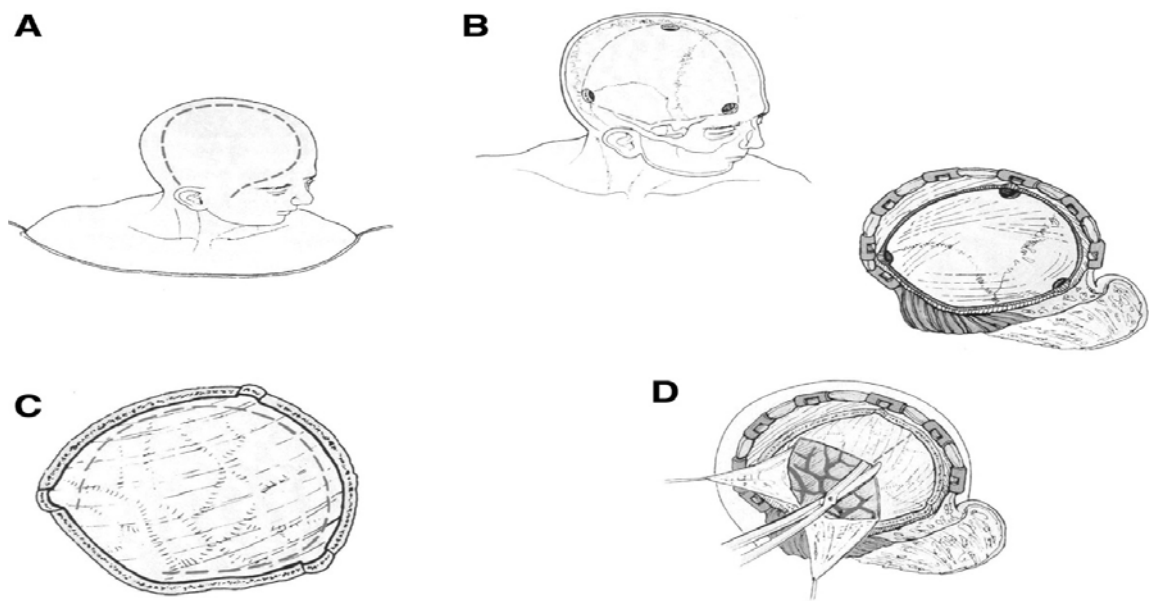


Fig 8: A, Incision. B, Simplified diagram to delineate craniotomy burr hole positioning and boundaries. C, circumferential durotomy. D, cruciate durotomy

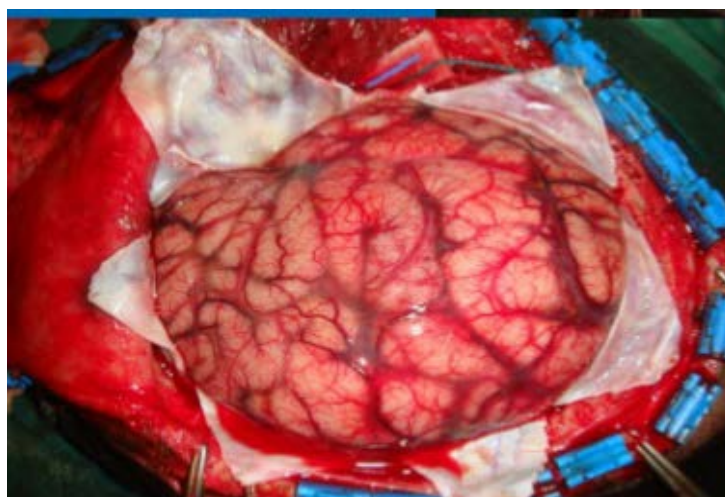


Fig 9: Showing Intra-operative image of edematous brain parenchyma after cruciate manner durotomy

Follow-up

Discharge MRS and NIHSS will be collected from the medical records as per proforma appended. At 3 month and 12 months after surgery, the patients clinical outcome was assessed with the modified Rankin Score (mRS) to rate physical disabilities. The patients with a score of 0 to 4 were included in the good outcome group, and patients with a score of 5 to 6 were included in the poor outcome group. NIHSS < 16 at discharge is considered as favourable outcome

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

Table 5: Modified Rankin Score (mRS)

Statistical analysis

Quantitative Variables were expressed as mean $\pm$ SD, qualitative variables were expressed as proportion. Between groups differences of the quantitative variables were evaluated by independent sample t test. Association of the qualitative variables were analysed by chi-square test. Multivariate analysis of binary logistic regression were

performed to identify the independent risk factors of bad outcome. P-value of <0.05 was considered as the level of statistical significant. Data analysis was performed using SPSS version 17.0.

Inclusion criteria

-Patients with supra-tentorial unilateral hemispheric infarct involving at least 2/3rd of hemisphere with or without hemorrhagic conversions.

-Ischaemic changes on CT scan or MRI that affect two-thirds or more of the supra-tentorial cerebral hemisphere and formation of space-occupying oedema.

Exclusion criteria

-Bi-hemispheric strokes

-Infra-tentorial infarcts

-Post endovascular thrombolysis or mechanical thrombectomy for acute stroke

-Those who underwent decompressive procedures for previous strokes, terminally ill, bleeding tendency.

-Pre-stroke mRS score <2

-Pre-stroke Glasgow Coma Scale <6

-Both pupils fixed and dilated

RESULTS

RESULTS

Demographic data:

A total of 51 patients were included in the study who underwent Decompressive Hemi-craniectomy for unilateral supra-tentorial hemispheric infarcts. There were 30 male and 21 female patients in the study. There were 37 patients who were below 60 years of age and 14 patients above 60 years of age with mean age at presentation was 51 ± 12.4 years, minimum being 23 years and maximum being 71 years in this study. 32 ± 15.87 years for adults. Our's being a tertiary referral centre, most of the patients reached hospital within 17.8 ± 18.5 hours from onset of symptoms with minimum of 1.5 hours and maximum of 72 hours from the onset.

Table 6: Showing characteristics of 51 patients

	Mean	sd	Min	Max
Age	51.1	12.4	23	71
NIHSS at admission	16.6	3.9	10	23
MRS at admission	4.3	0.7	2	5
GCS	10.1	2.3	7	15
SBP	142.5	25.3	100	230
DBP	86.4	15.8	60	160
Sugar at admission	167	67	83	353
Onset to admission time hours	17.8	18.5	1.5	72
Hours from onset to decision for surgery	39.3	21.2	10	90
Mid line shift	7	4.5	0	17
Duration of inotropic support (hrs)	22.8	27.7	0	120

No of ventilator days	11.1	11.2	1	28
Duration of hospital stay	21.9	9.7	3	50
Discharge NIHSS	13.6	4.3	7	26
Discharge mRS	4.5	0.8	3	6
3 month NIHSS	12.1	4.4	4	23
3month mRS	4	0.5	2	5
12 months mRS	3.6	0.7	2	6

Pre-operative functional status:

The preoperative mean MRS was 4.3 ± 0.7 with 2 being the minimum and 5 being the maximum and mean NIHSS of 16.6 ± 3.9 with 10 being minimum and 23 being maximum. The Mean GCS score was 10 ± 3 with 7 being minimum and 15 being maximum at the time of admission. Mean sugar values at admission was 167 ± 67 and mean SBP and DBP being 142.5 ± 25.3 and 86.4 ± 15.8

Table 7: Charecteristics of 51 patients.

		Frequency	Percent
Age in years	<60	37	72.5
	>60	14	27.5
Gender	Male	30	58.8
	Female	21	41.2
Hours from onset to decision for surgery	<48 hour	34	66.7
	>48 hour	17	33.3
Hemisphere affected	Left	25	49
	Right	26	51

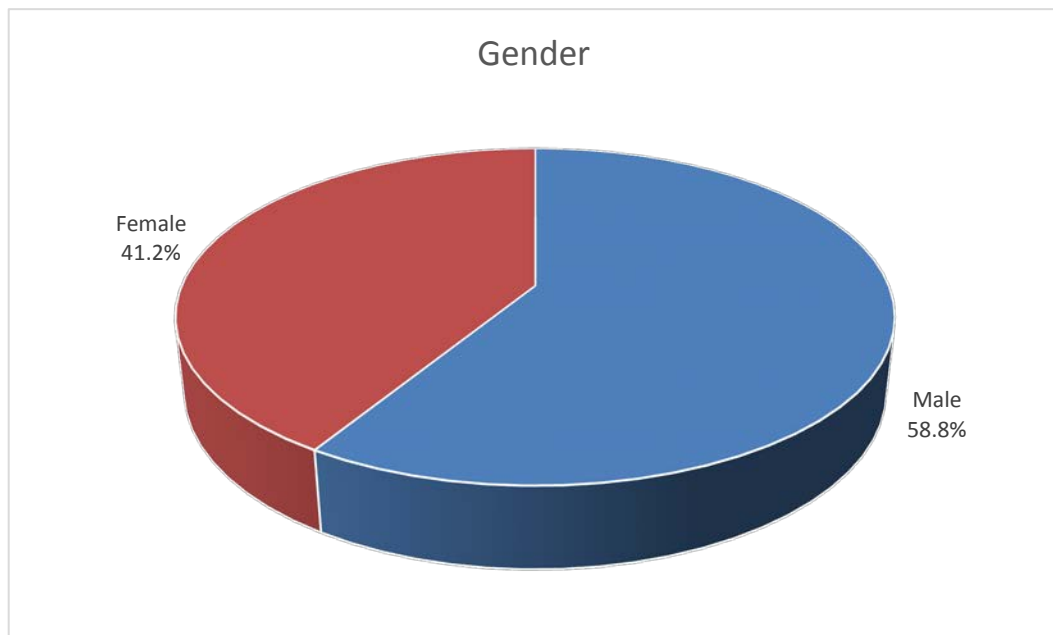


Fig 10: Gender distribution

Hours from onset to decision for surgery:

The decision to operate the patients was taken collectively by neurosurgeons and neurologists based on patients clinical condition and imaging findings once patient is admitted and evaluated. The mean timing was 39.3 ± 21.2 hours from the onset with minimum timing being 10 hours and maximum being 90 hours. So 34(66.7%) patients underwent surgery within 48 hours of onset of symptoms and remaining 17(33.3%) underwent surgery beyond 48 hours of onset of symptoms.

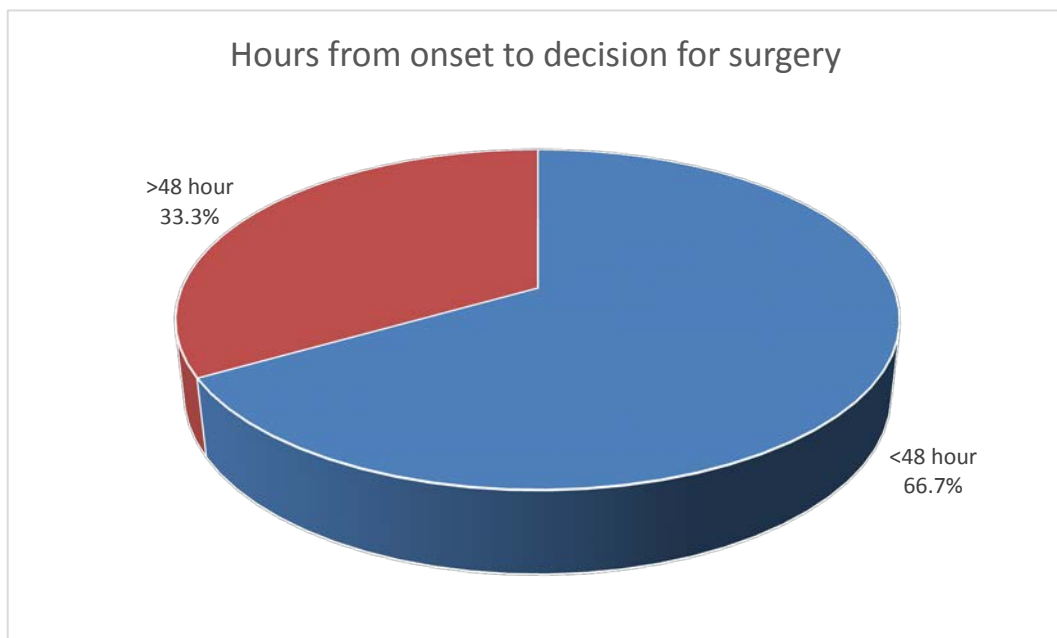


Fig 11: Hours from the onset to surgery

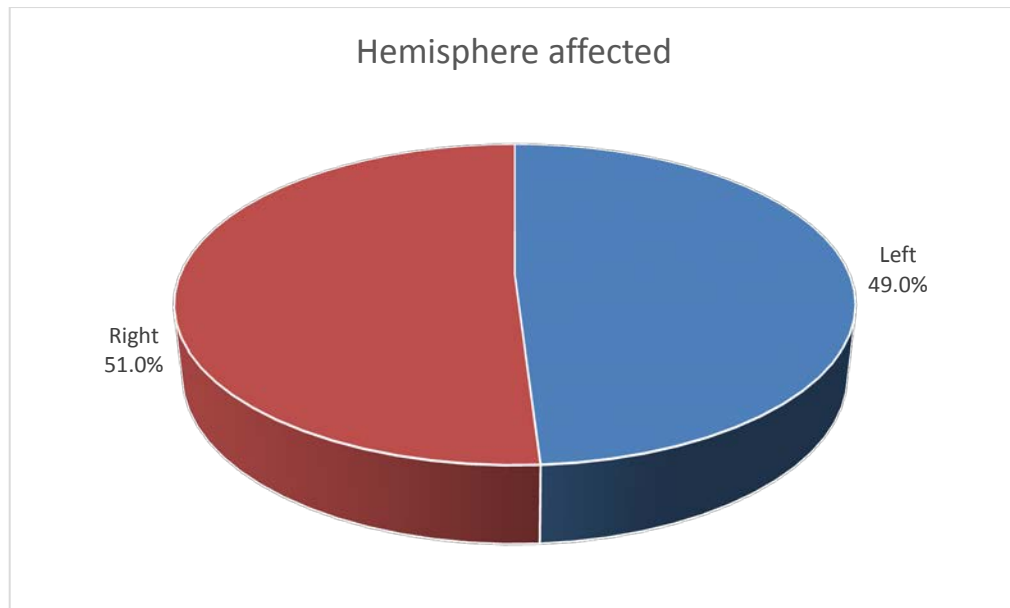


Fig 12: percentage of hemisphere effected.

Presentation and Co-morbididties:

25(49%) patients presented with dominant Hemispheric infarcts with aphasia and right sided hemiparesis to complete hemiplegia and 26(51%) with non-dominant hemispheric infarcts with left sided hemiparesis to complete hemiplegia and cognitive impairments.

Seizures present in 6(11.8%) patients. Most common Co-morbidity was Hypertension in 30(58.8%) patients followed by Diabetes mellitus in 18(35.3%) followed by cardiac arrhythmias in 17(33.3%) patients and ischemic heart disease in 14(27.5%) patients and dyslipidemia in 13(25.5%) of patients.

Table 8: Distribution of Co-morbidities among the patients

		Frequency	Percent
Co morbidities	Diabetes	18	35.3
	Hypertension	30	58.8
	dyslipidemia	13	25.5
	cardiac arrhythmias	17	33.3
	Ischemic heart diseases	14	27.5

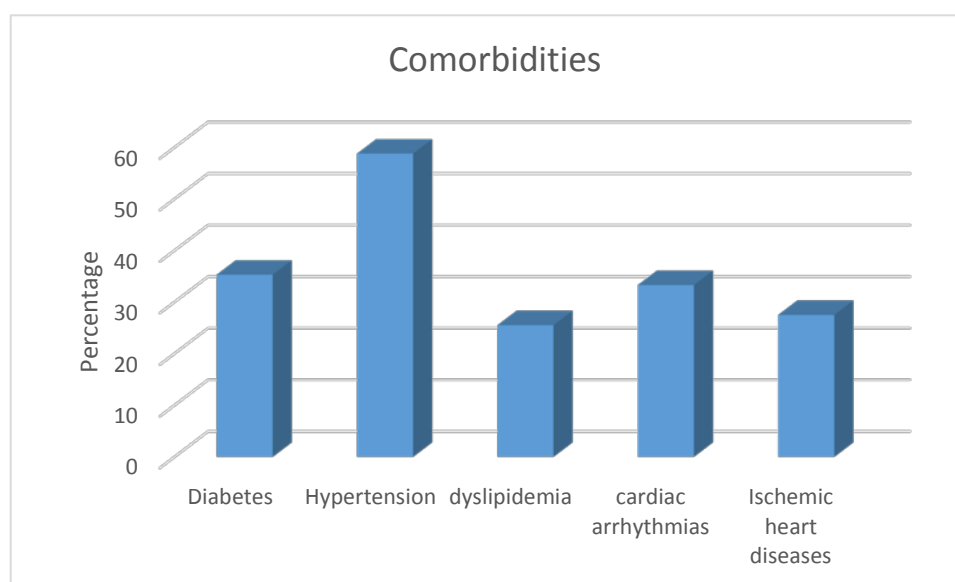


Fig 13: : Distribution of Co-morbidities among the patients

Etiology:

Etiology was based on TOAST classification of stroke, and the most common etiology for stroke in this study was Cardio-embolic phenomenon in 24(47.1%) of patients, followed by undetermined etiology, whose etiology is either unknown or needed awaiting further investigations to confirm etiology in 15(29.4%) patients, followed by large vessel atherosclerosis in 8(15.7%) of patients, other etiology like vasculitis in 4(7.8%) patients with no patients having etiology of lacunar infarcts.

Table 9: Etiology and symptoms of the patients

		Frequency	Percent
Symptoms	Aphasia	25	49
	Seizures	6	11.8
Etiology	Large vessel	8	15.7
	Cardio embolic	24	47.1
	Other etiology	4	7.8
	Indeterminate	15	29.4
	Lacunar	0	0

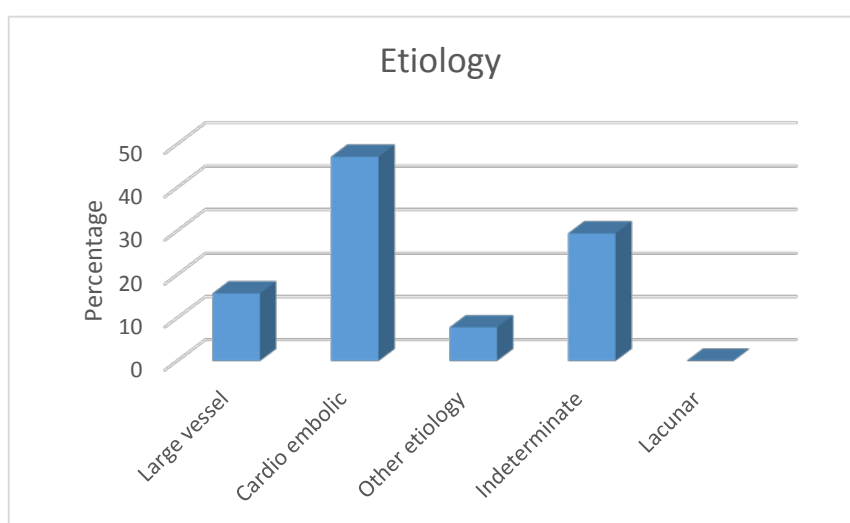


Fig 14: Etiology of the patients.

Pre-operative Imaging data:

Either CT Scan of brain or MRI done based on patients clinical condition and acuteness of symptoms. 42(82.4%) of patients had MCA territory infarcts and 9(17.6%) of patients had MCA+ACA territory infarcts. 34(66.7%) of patients had no hemorrhagic conversion of infarcts at the time of surgery with 6(11.8%) patients had <30% of infarcted area being converted to hemorrhage at the time of surgery and 11(21.6%) patients had >30% of infarcted area being converted to hemorrhage at the time of surgery. No Midline shift at the time of surgery was seen in 13(25.5%) of patients with 27(52.9%) of patients having MLS of <10mm and 11(21.6%) patients had MLS >10mm with uncal herniation being present in 16(31.4%) of patients at the time of surgery.

Table 10: Radiological feature of the patients

		Frequency	Percent
hemorrhagic conversion grade	No	34	66.7
	<30%	6	11.8
	>30%	11	21.6
midline shift	No MLS	13	25.5
	1-10 mm MLS	27	52.9
	>10 mm MLS	11	21.6
Herniation		16	31.4
arterial territory infarction	MCA Territory infarct	42	82.4
	MCA + ACA territory infarct	9	17.6
Intubation prior to surgery		14	27.5
Peri and post op hypotension requiring inotropes		24	47.1

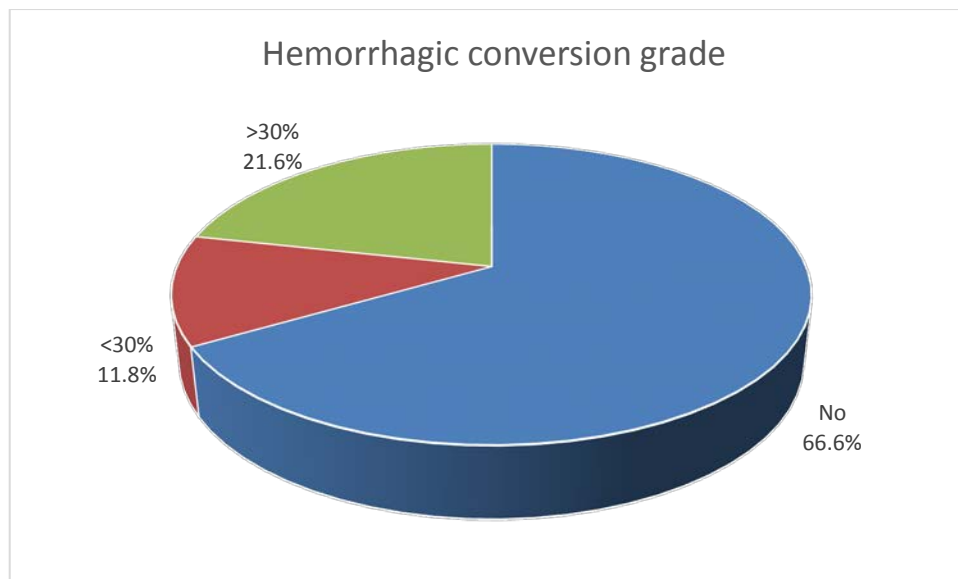


Fig 15: Hemorrhagic conversion grades

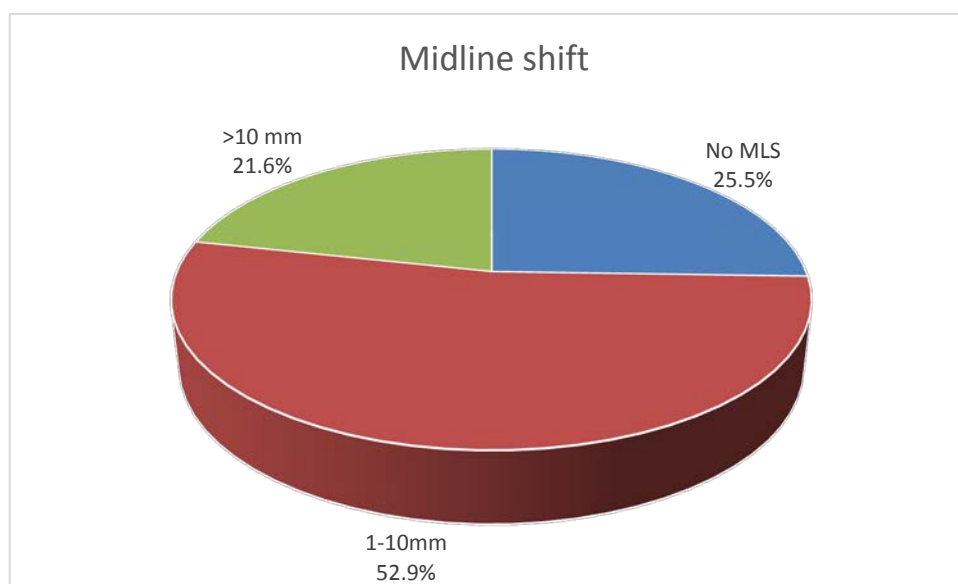


Fig: 16: Midline shift in milimeters

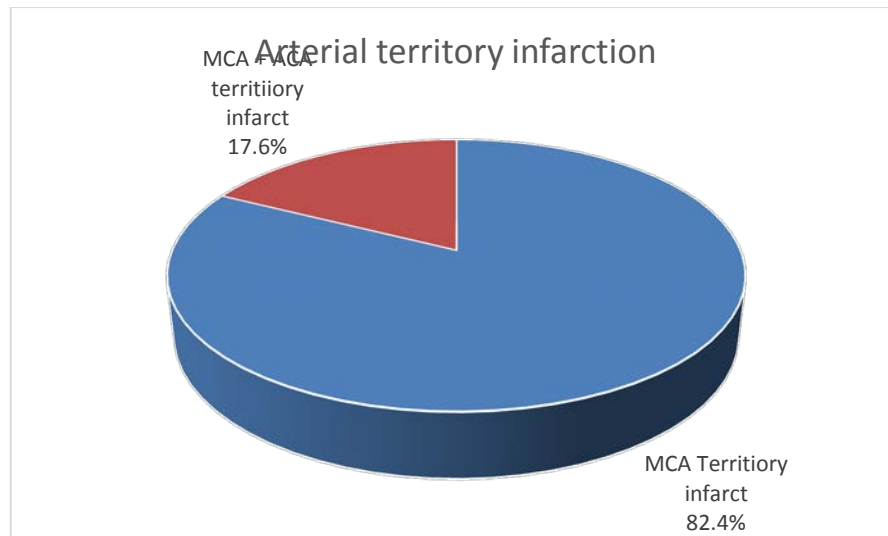


Fig 17: Arterial territory involved.

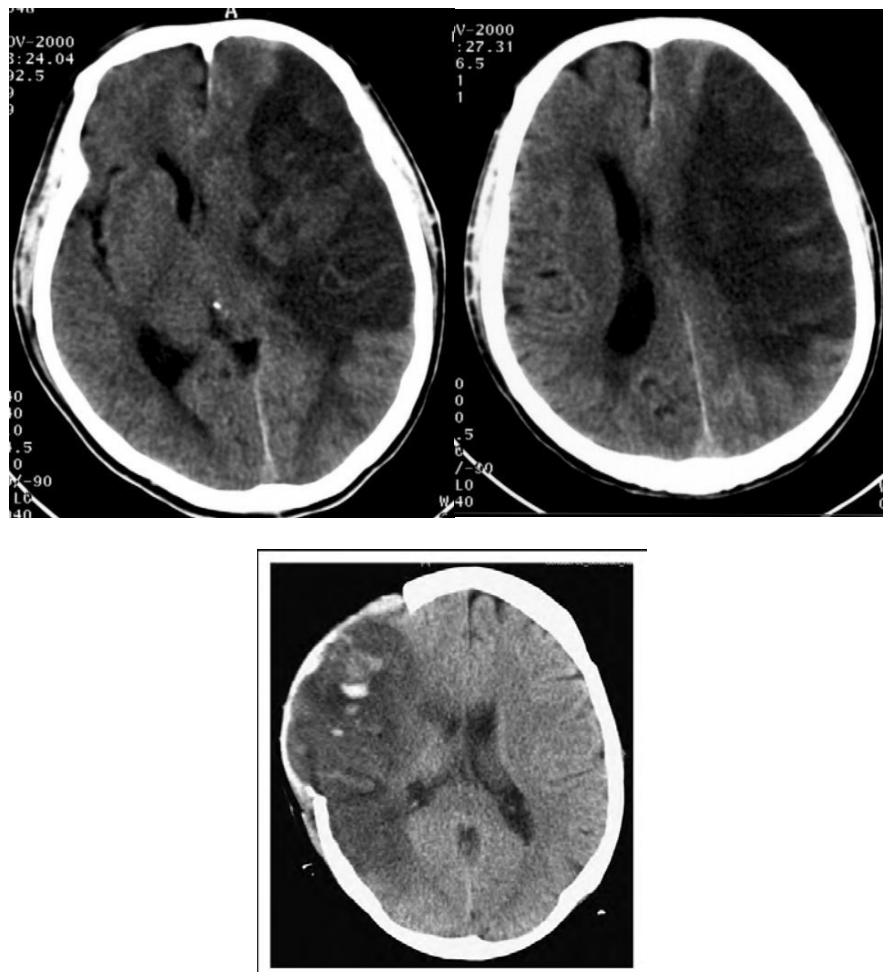


Fig 18: Plain CT scan showing evolving infarcts on left MCA territory with hemorrhagic transformation in the right MCA territory.

Pre-op and intra-operative events:

14(27.5%) of patients required pre-op intubation in view of decreasing sensorium and hemodynamic instability for airway protection. All the patients underwent standard decompressive hemi-craniectomy with lax duroplasty and bone flap placement in abdomen after written informed consent. Among the patients with hemorrhagic conversion at the time of surgery, all the patients with >30% conversion underwent hematoma evacuation along with standard decompressive hemicraniectomy with lax duroplasty. 24(47.1%) of patients required intra-op inotropic support in view of hemodynamic instability which was also continued post operatively with mean hours of 22.8 ± 27.7 with maximum being 120 hours post operatively.

Mean duration ventilator support post-operatively was 11.1 ± 11.7 days, with minimum being 1 day to maximum being 28 days postoperatively. 6 patients underwent tracheostomy in view of long term ventilatory support and was slowly weaned off from ventilator, out of which 3 patients had tracheostomy de-cannulated at discharge and 3 was on metal tracheostomy at the time of discharge. Mean duration of hospital stay was 29.9 ± 9.7 days with minimum of 3 days and maximum of 50 days duration.

Functional outcome on follow up:

NIHSS score of <16 was considered favourable outcome in our study. 76% of patients had <16 NIHSS at discharge and 81% had < 16 NIHSS at 3 months follow up with mortality being 17.6% at the end of 3 months. MRS score of <4 was considered favourable outcome in our study. 66.7 % of patients had <4 MRS at discharge and 92.9% had < 4 MRS at 3 months follow up with mortality being 17.6% at the end of 3 months. At 12 months follow up 90.2% patients had <4 MRS with mortality being 19.6%.

Table 11: NIHSS scores on admission, discharge and at 3 months of follow up

NIHSS score	Admission Group		Discharge		3 months	
	n	%	n	%	n	%
<16	26	51.0	32	76.2	34	81.0
>16	25	49.0	10	23.8	8	19.0
Total	51	100.0	42	100.0	42	100.0

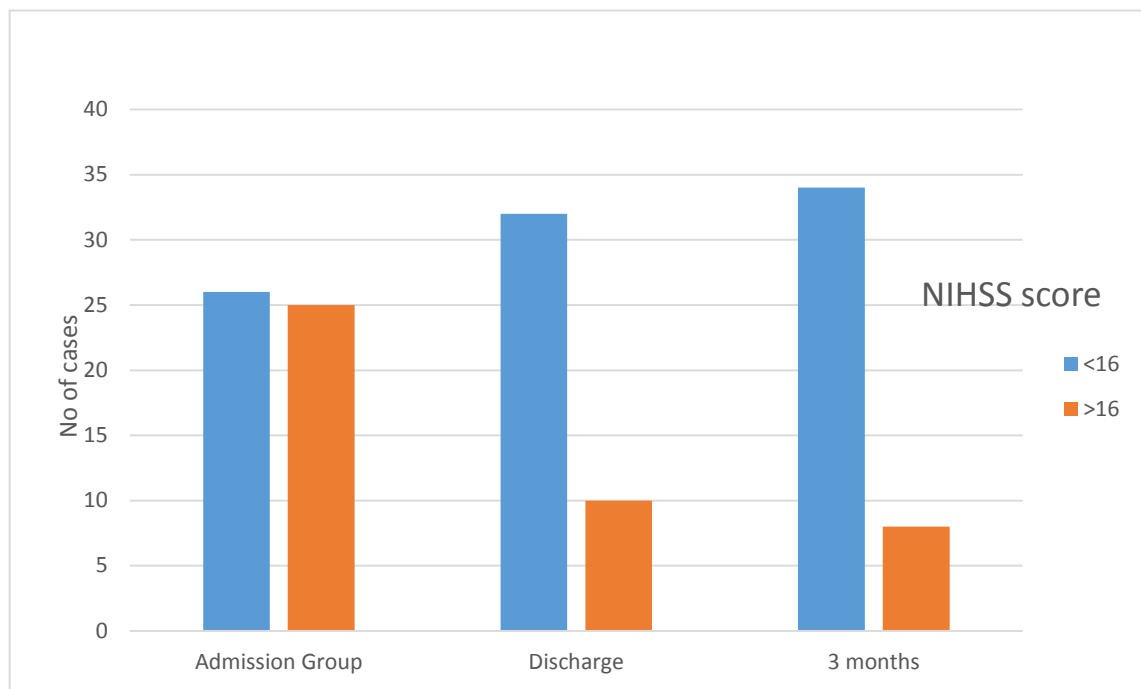
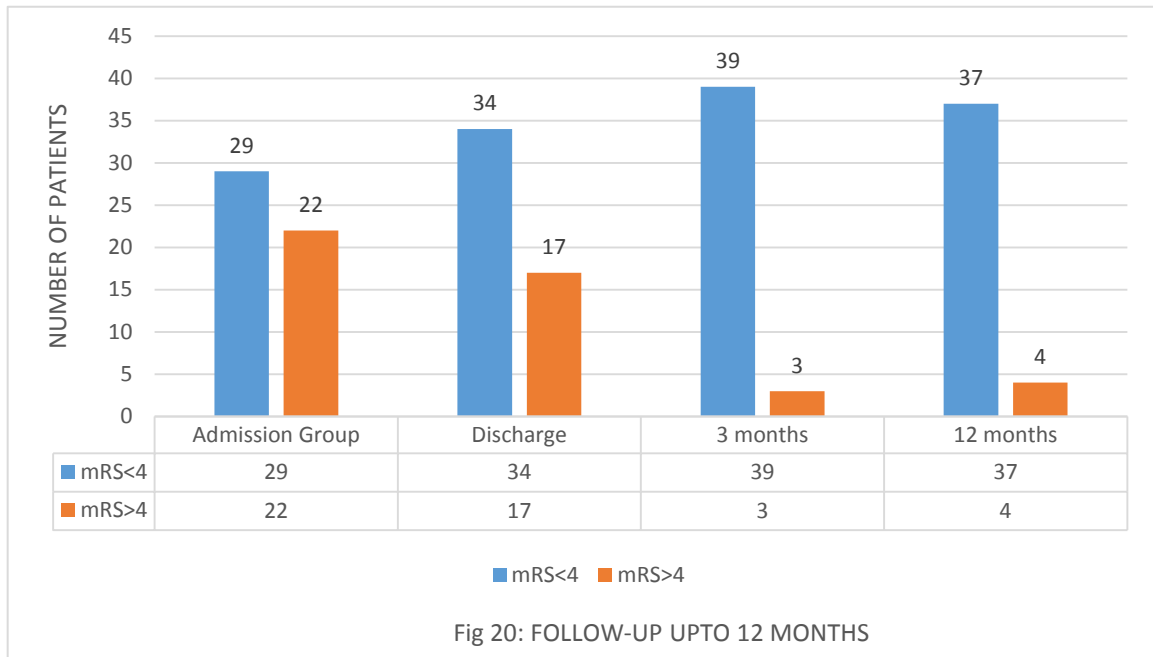


Fig 19: NIHSS scores on admission, discharge and at 3 months of follow up

Table 12: MRS at admission, discharge, 3 months and 12 months of follow up

MRS Score	Admission Group		Discharge		3 months		12 months	
	n	%	n	%	n	%	n	%
<4	29	56.9	34	66.7	39	92.9	37	90.2
>4	22	43.1	17	33.3	3	7.1	4	9.8
Total	51	100.0	51	100.0	42	100.0	41	100.0



Mortality at Discharge:

9(17.6%) patients died at the time of discharge. 3 patients died at 3rd post operative day due to respiratory infection, ventilator associated pneumonia and septicemia. Remaining 2 patients developed deep venous thrombosis and pulmonary embolism on post operative day 5 and 7 respectively and succumbed. 3 patients developed acute myocardial ischemia on post operative day 3 and 4 respectively. The cause of death of 1 patient was not known with suspicion of being flaring up multiple age related co-morbidities. None of the patients died due to direct cause of surgery per-say.

Mortality at follow up:

At 1 year follow up, among 42(82.5%) patients alive, one more patient was dead, with probable cause being acute myocardial event as patient not being compliant on anti-platelets therapy with known case of Ischemic heart disease. So at the last follow up available, 41(84.4%) patients being alive and mortality being 19.6% in our study

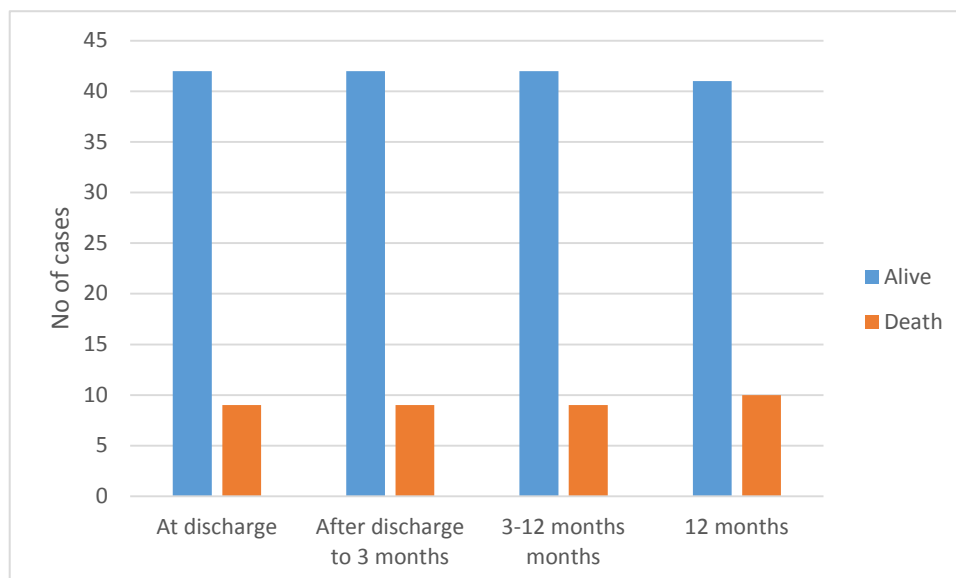


Fig 21: Mortality rates

Table 13: Mortality rates

Death	Before discharge		After discharge and before 3 months		3-12 months		12 months	
	n	%	n	%	n	%	n	%
Absent	42	82.4	42	82.4	42	82.4	41	80.4
Present	9	17.6	9	17.6	9	17.6	10	19.6
Total	51	100.0	51	100.0	51	100.0	51	100

Hospital acquired infection was present in 21(43%) of patients who underwent surgery and among the 3 patients succumbed to severe septicemia due ventilator acquired infections and remaining patient were managed aggressively with IV antibiotics based on culture and sensitivity from blood and throat, along with inotropic support with gradual improvement in patients at the time of discharge.69.4% of patients underwent surgery at or before 48 hrs from the onset of symptoms.Among the survived patients, 89.7% had undergone Bone flap replacement at the end of last follow up, with last 3 patients undergoing Titanium mesh cranioplasty as that is the recent protocol followed at our institute after discarding the bone flap in the abdomen even though there was no bone flap related complications. Remaining all the patients underwent native bone flap replacement with screws and plate fixation.

Table 14: Infection rates, and bone flap replacement rates

	Frequency	Percent
Hospital acquired infections	21	43.8
Surgery at 48 hr or less from onset	34	69.4
Bone flap replaced	35	89.7
On anticoagulant at discharge	32	88.9

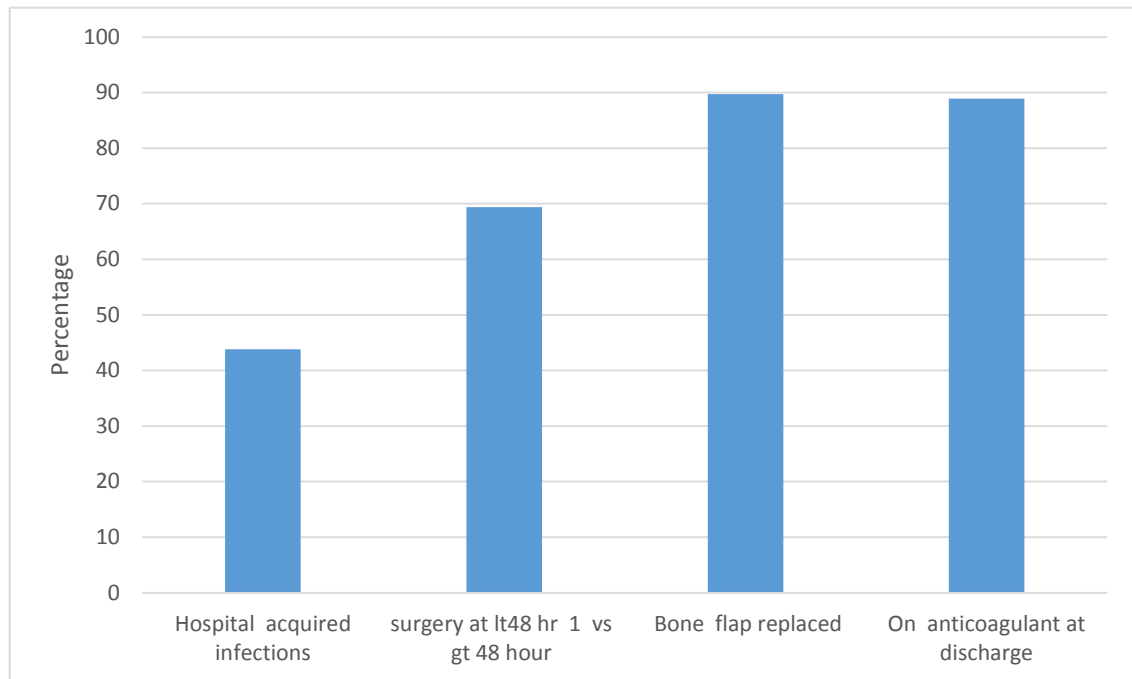


Fig 22: Infection rate, and bone flap replacement rates

Predictors for outcome at Discharge:

42(82.4%) patients survived at the time of discharge. With MRS <4 considered as favourable outcome in this study, we considered multiple variables pre-operatively to know the association of them with the outcome. Variable studied are Age, gender, onset of symptoms to decision of surgery, co-morbidities, etiology of stroke, pre-operative clinical signs and symptoms based on MRS, NIHSS, GCS, Hemisphere involved based on dominance, Imaging data like arterial territory involved, MLS, uncal herniation, Hemorrhagic conversion, peri and intra operative events like ventilator support, hospital acquired infections, inotropic support. Among these variables, uni-variate analysis showed, age >60 years, decision for surgery >48 hours from the onset of symptoms, MLS of >10mm with uncal herniation on pre-operative CT scan, pre-operative MRS>4 and NIHSS>16 showed significant association($p < 0.05$) with poor outcome at the time of discharge.

Table 15: Predictors for outcome at Discharge

		MRS at discharge				Total		p
		<4		>4				
		N	%	N	%	N	%	
Age	<60	28	82.4	9	52.9	37	72.5	0.027
	>60	6	17.6	8	47.1	14	27.5	
Gender	Male	22	64.7	8	47.1	30	58.8	0.227
	Female	12	35.3	9	52.9	21	41.2	
Hours from onset to decision for surgery	<48 hour	26	76.5	8	47.1	34	66.7	0.036
	>48 hour	8	23.5	9	52.9	17	33.3	
Diabetes	Absent	21	61.8	12	70.6	33	64.7	0.534
	Present	13	38.2	5	29.4	18	35.3	
Hypertension	Absent	12	35.3	9	52.9	21	41.2	0.227
	Present	22	64.7	8	47.1	30	58.8	
Dyslipidemia	Absent	23	67.6	15	88.2	38	74.5	0.112
	Present	11	32.4	2	11.8	13	25.5	

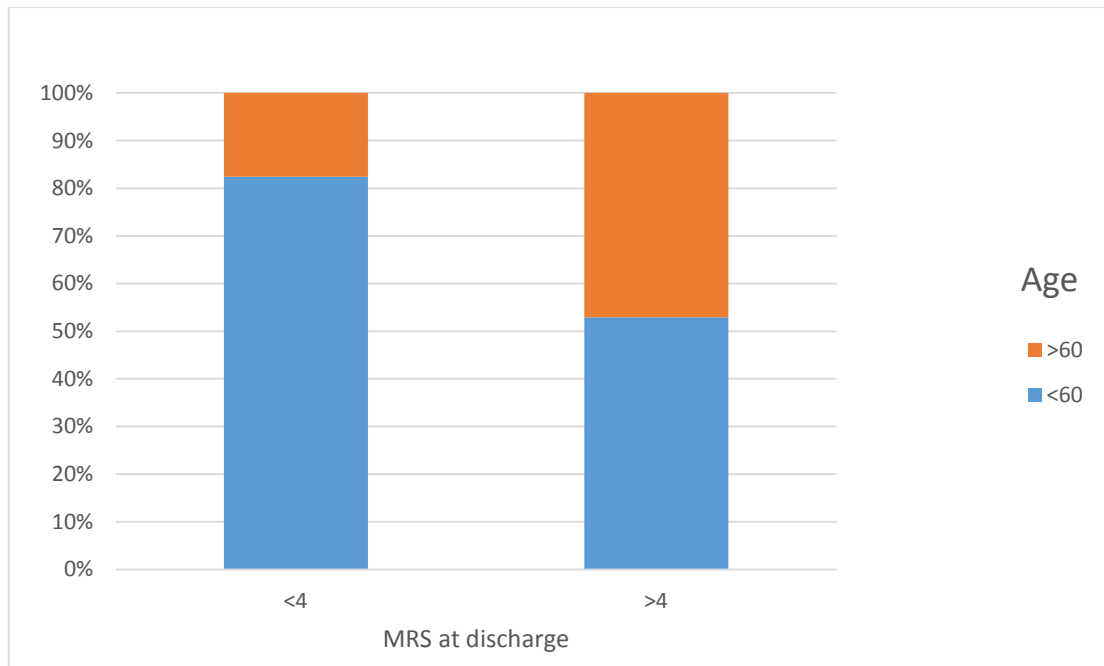


Fig 23: Age > 60 years association with poor outcome at discharge

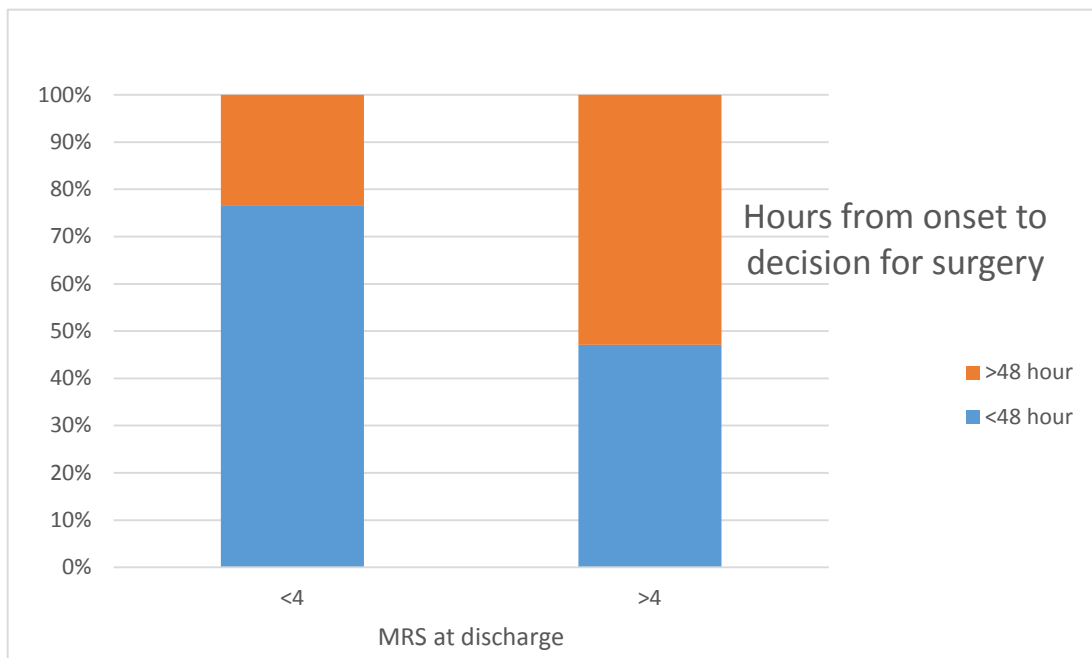


Fig 24: Onset of surgery > 48 hours associated with poor outcome at discharge

Table 16: Predictors for outcome at Discharge

		MRS at discharge				Total		p
		<4		>4				
		N	%	N	%	N	%	
Hemisphere affected	Left	16	47.1	9	52.9	25	49	0.692
	Right	18	52.9	8	47.1	26	51	
Aphasia	Absent	18	52.9	8	47.1	26	51	0.692
	Present	16	47.1	9	52.9	25	49	
cardiac arrhythmias	Absent	24	70.6	10	58.8	34	66.7	0.401
	Present	10	29.4	7	41.2	17	33.3	
Ischemic diseases heart	Absent	24	70.6	13	76.5	37	72.5	0.657
	Present	10	29.4	4	23.5	14	27.5	
Seizures	Absent	29	85.3	16	94.1	45	88.2	0.357
	Present	5	14.7	1	5.9	6	11.8	

Table 17: Etiological Predictors for outcome at Discharge

Etiology	MRS at discharge				Total	p
	<4		>4			
Large vessel	5	14.7	3	17.6	8	15.7
Cardio embolic	14	41.2	10	58.8	24	47.1
Other etiology	2	5.9	2	11.8	4	7.8
Indeterminate	13	38.2	2	11.8	15	29.4
Lacunar	0	0	0	0	0	0
						0.260

Table 18: Imaging Predictors for outcome at Discharge

		MRS at discharge				Total	p	
		<4		>4				
Hemorrhagic Conversion Grade	No	23	67.6	11	64.7	34	66.7	
	<30	6	17.6	0	0	6	11.8	
	>30	5	14.7	6	35.3	11	21.6	0.073
Midline Shift	No MLS	9	26.5	4	23.5	13	25.5	
	1-10mm MLS	21	61.8	6	35.3	27	52.9	
	>10mm MLS	4	11.8	7	41.2	11	21.6	0.048
Herniation	Absent	24	70.6	7	41.2	31	60.8	
	Present	10	29.4	10	58.8	20	39.2	0.043
Arterial Territory Infarction	MCA territory infarct	29	85.3	13	76.5	42	82.4	
	MCA + ACA territory infarct	5	14.7	4	23.5	9	17.6	0.436

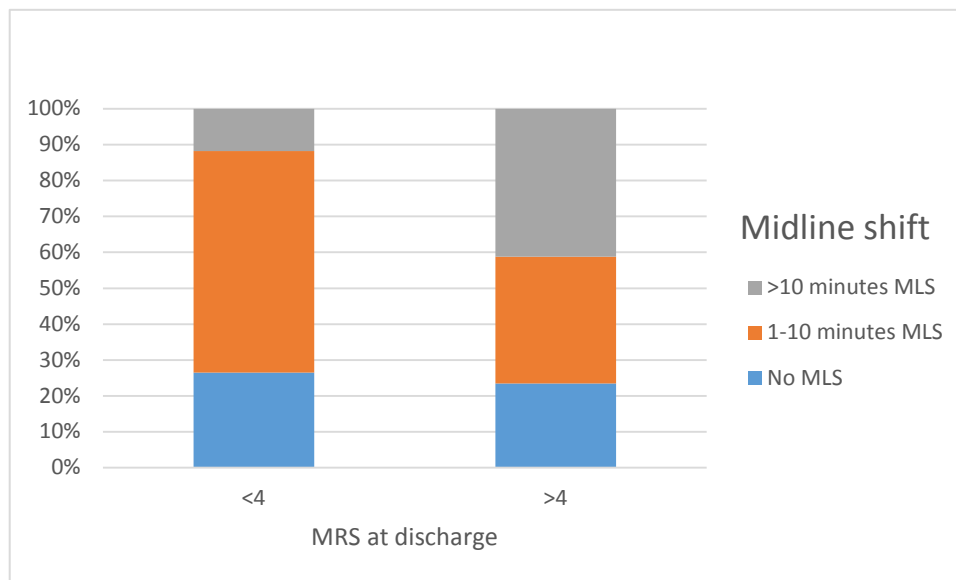


Fig 25: Midline shift > 10mm shows poor outcome at discharge

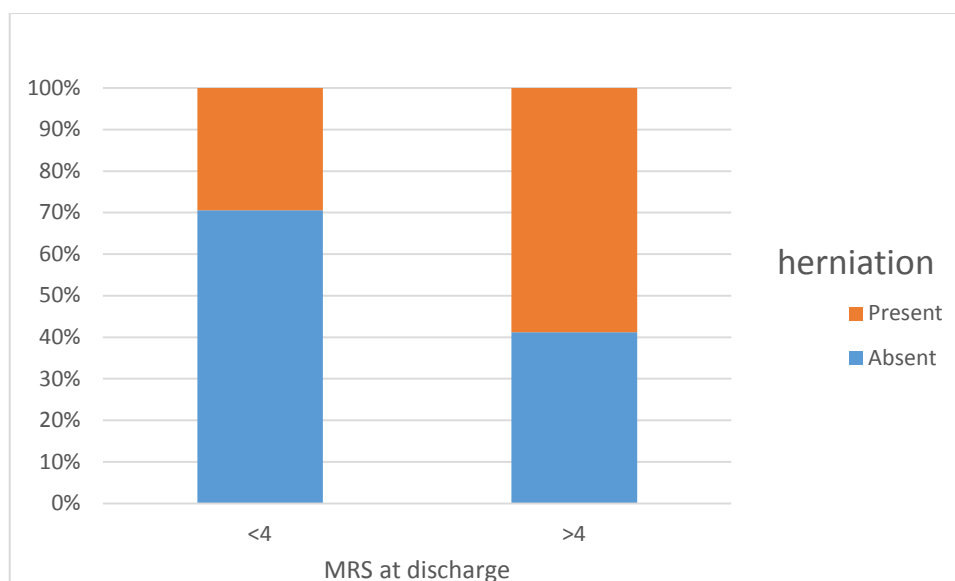


Fig 26: Presence of uncal herniation associated with poor outcome at discharge

Table 19: Predictors for outcome at Discharge

		MRS at discharge				Total	p	
		<4		>4				
Intubation prior to surgery	Absent	27	79.4	10	58.8	37	72.5	0.120
	Present	7	20.6	7	41.2	14	27.5	
Peri and post op hypotension requiring inotropes	Absent	21	61.8	6	35.3	27	52.9	0.074
	Present	13	38.2	11	64.7	24	47.1	
GCS	<8	3	8.8	1	5.9	4	7.8	0.713
	≥8	31	91.2	16	94.1	47	92.2	
NIHSS score on admission	<16	22	64.7	4	23.5	26	51	0.006
	>16	12	35.3	13	76.5	25	49	
MRS admission Group	<4	23	67.6	6	35.3	29	56.9	0.028
	>4	11	32.4	11	64.7	22	43.1	
Died before discharge	Absent	34	100	8	47.1	42	82.4	<0.001
	Present	0	0	9	52.9	9	17.6	

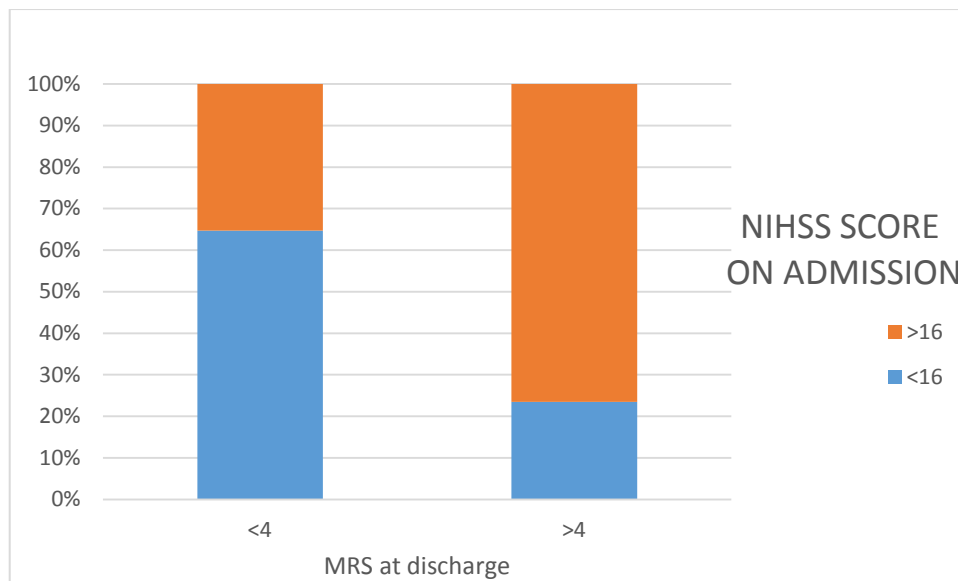


Fig 27: NIHSS >16 at admission shows poor outcome at discharge

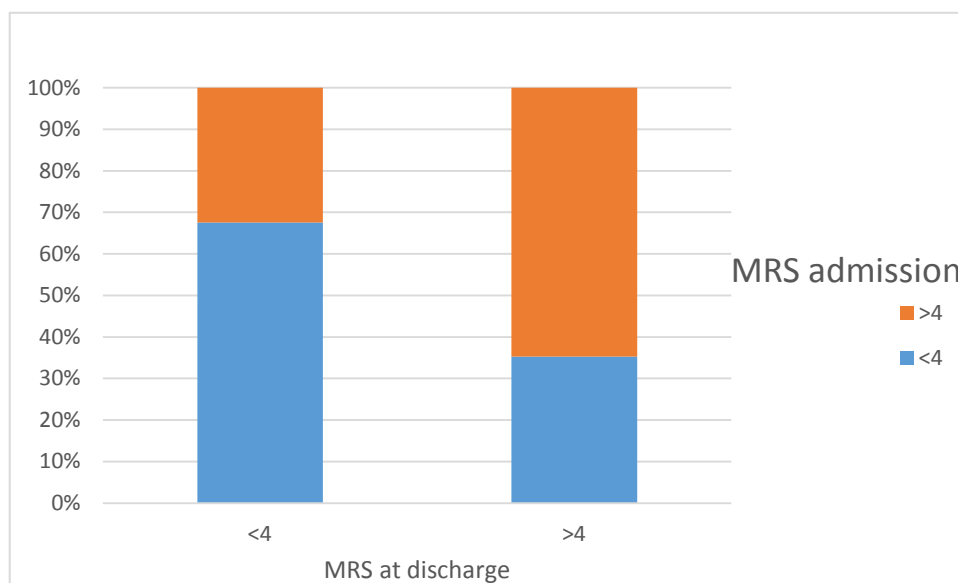


Fig 28: MRS >4 at admission shows poor outcome at discharge

Predictors for outcome at 3 months follow up:

42 patients were available for follow up at 3 months with 17.6% mortality. All the variables mentioned at the time of discharge were again studied to look for association with outcome. No significant association ($p > 0.05$) noted with outcome at 3 months follow up with most of the patients had MRS > 4 at the follow up.

Table 20: Predictors for outcome at 3 months follow up:

		MRS at 3 month				Total		p
		<4		>4				
		N	%	N	%	N	%	
Age	<60	29	74.4	3	100	32	76.2	0.315
	>60	10	25.6	0	0	10	23.8	
MRS admission	<4	26	66.7	1	33.3	27	64.3	0.246
	>4	13	33.3	2	66.7	15	35.7	
NIHSS score on admission	<16	24	61.5	1	33.3	25	59.5	0.338
	>16	15	38.5	2	66.7	17	40.5	
Hours from onset to decision for surgery	<48 hour	28	71.8	1	33.3	29	69	0.165
	>48 hour	11	28.2	2	66.7	13	31	

Table 21: Predictors for outcome at 3 months follow up:

			MRS at 3 month				Total		P
			<4		>4				
			N	%	N	%	N	%	
Hemorrhagic conversion	No		26	66.7	3	100	29	69	0.485
	<30		6	15.4	0	0	6	14.3	
	>30		7	17.9	0	0	7	16.7	
Midline shift	No MLS		10	25.6	0	0	10	23.8	0.513
	1-10 mm MLS		23	59	2	66.7	25	59.5	
	>10 mm MLS		6	15.4	1	33.3	7	16.7	
Herniation	Absent		25	64.1	2	66.7	27	64.3	0.929
	Present		14	35.9	1	33.3	15	35.7	
Arterial infarction territory	MCA Territory infarct		34	87.2	1	33.3	35	83.3	0.016
	MCA + ACA territory infarct		5	12.8	2	66.7	7	16.7	
GCS	<8		4	10.3	0	0	4	9.5	0.56
	>8		35	89.7	3	100	38	90.5	
Seizures	Absent		34	87.2	2	66.7	36	85.7	0.328
	Present		5	12.8	1	33.3	6	14.3	
Hemisphere affected	Left		19	48.7	0	0	19	45.2	0.102
	Right		20	51.3	3	100	23	54.8	

Predictors for outcome at 12 months follow up:

41 patients were available for follow up with mortality being 19.6% at the end of 12 months. Again there was no significant association ($p>0.05$) with any of the variables on the long term outcome of patients as most of the patients had MRS <4 . So the variables which had significant association at the time of discharge in outcome and mortality were not associated significantly in long term outcome.

Table 22: Predictors for outcome at 12 months follow up

		MRS at 12 month				Total		P
		<4		>4				
		N	%	N	%	N	%	
Age	<60	27	73	4	100	31	75.6	0.232
	>60	10	27	0	0	10	24.4	
MRS admission Group	<4	24	64.9	3	75	27	65.9	0.685
	>4	13	35.1	1	25	14	34.1	
NIHSS score on admission	<16	23	62.2	2	50	25	61	0.636
	>16	14	37.8	2	50	16	39	
Hours from onset to decision for surgery	<48 hour	25	67.6	3	75	28	68.3	0.762
	>48 hour	12	32.4	1	25	13	31.7	

Table 23: Predictors for outcome at 12 months follow up

			MRS at 12 month				Total	P
			<4		>4			
			N	%	N	%	N %	
Hemorrhagic conversion grade	No		26	70.3	2	50	28 68.3	
	<30		4	10.8	2	50	6 14.6	
	>30		7	18.9	0	0	7 17.1	0.092
Midline shift	No MLS		9	24.3	1	25	10 24.4	
	1-10 mm MLS		22	59.5	2	50	24 58.5	
	>10 mm MLS		6	16.2	1	25	7 17.1	0.896
Herniation	Absent		24	64.9	2	50	26 63.4	
	Present		13	35.1	2	50	15 36.6	0.558
Arterial territory infarction	MCA Territory infarct		32	86.5	3	75	35 85.4	
	MCA + ACA territory infarct		5	13.5	1	25	6 14.6	0.537
GCS	<8		4	10.8	0	0	4 9.8	
	>8		33	89.2	4	100	37 90.2	0.489
Seizures	Absent		32	86.5	3	75	35 85.4	
	Present		5	13.5	1	25	6 14.6	0.537
Hemisphere affected	Left		18	48.6	1	25	19 46.3	
	Right		19	51.4	3	75	22 53.7	0.368

Binary logistic regression model for bad out come (MRS <4 at discharge):

On univariate analysis, Age >60 years, decision for surgery >48 hours from the onset of symptoms, MLS of >10mm with uncal herniation on pre-operative CT scan, pre-operative MRS>4 and NIHSS>16 showed significant association ($p<0.05$) with patients outcome at the time of discharge. On multivariate binary logistic regression only Midline shift of >10mm with uncal herniation and NIHSS score on admission >16 were the independent risk factors of bad outcome.

Table 24: Out come (MRS <4 at discharge)

	B	S.E.	Wald	df	Sig.	OR	95% C.I. for OR	
							Lower	Upper
Age >60	1.283	0.915	1.969	1	0.161	3.609	0.601	21.67
Hours from onset to decision for surgery >48 hours	0.124	0.993	0.015	1	0.901	1.132	0.162	7.925
Herniation	1.785	0.874	4.169	1	0.041	5.962	1.074	33.09
NIHSS SCORE ON ADMISSION >16	1.741	0.846	4.239	1	0.04	5.702	1.087	29.91
MRS admission Group >4	0.869	0.997	0.759	1	0.384	2.385	0.338	16.85
Constant	-7.4	2.157	11.76	1	0.001	0.001		

DISCUSSION

DISCUSSION

Baseline demographic:

A total of 51 patients were included in our study who underwent Decompressive Hemicraniectomy for unilateral supra-tentorial hemispheric infarcts. There were 30 male (58.8%) and 21 female patients in the study. There were 37 patients who were below 60 years of age and 14(27.7%) patients above 60 years of age with mean age at presentation was 51 ± 12.4 years, minimum being 23 years and maximum being 71 years in this study. 32 ± 15.87 years for adults. Kilincer et al(2) The group consisted of 18 men and 14 women whose mean age was 58 years (range, 27–77yrs). Pillai et al(1), study consisted of 26 patients (22 men and 4 women), The mean patient age was 48.4 ± 11.2 years (range 28–66 years) with 84.5% being male patients. DESTINY trial(9) included 17 patients in their surgical group and all patients were below 60 years age (range, 30-60 years) with mean of 42.7 years with 47% of male population. DECIMAL trial(3) included 20 patients with mean age of 43.5 years, (range 22-55 years), with 45% of patients being male. HAMLET trial(5) included patients 32 patients, less than 60 years of age group with mean of 50.5 years and 63% of patients being male. Bhatia et al(46) study included a total of 36 patients. Mean age was 49.6 (range: 20-91) years and 15 patients (25%) were above 60 years of age. There were 72% male patients. Our study has 27.7% of patients above 60 years of age. Many of the RCT's done in European countries excluded the patients above 60 years of age, with their sample size being below 40 patients. There was more of male sex predominance in Indian studies compared to western population even though not statistically significant. Our's being a tertiary

referral centre, most of the patients reached hospital within 17.8 ± 18.5 hours from onset of symptoms with minimum of 1.5 hours and maximum of 72 hours from the onset.

Hemispheric predilection:

In our study 25(49%) patients presented with dominant Hemispheric infarcts with aphasia and right sided hemiparesis to complete hemiplegia and 26(51%) with non-dominant hemispheric infarcts with left sided hemiparesis to complete hemiplegia with cognitive impairments. Kilincer et al(2) had 49.5% patients in dominant hemisphere among the 36 patients with no significant predilection of either of hemisphere. Pillai et al(2) also had 47% of patients involving dominant hemisphere. DESTINY trial showed slight predilection of dominant hemisphere with 53% of patients. Bhatia et al(46) showed 55% left sided infarct with more predilection to dominant hemisphere. Badhi et al(47) had 29 patients involving the dominant hemisphere (30.5%) and 66 patients had a lesion in the non-dominant hemisphere (69.5%). There was no significant predilection of either of hemisphere in most studies as do our study.

Comorbidities:

Most common Co-morbidity in our study was Hypertension in 30(58.8%) patients followed by diabetes mellitus in 18(35.3%) followed by cardiac arrhythmias in 17(33.3%) patients and ischemic heart disease in 14(27.5%) patients and dyslipidemia in 13(25.5%) of patients. Badhi et al (47) also had 81% with hypertension followed by dyslipidemia in 48% of patients. Bhatia et al(46) had 47.7% patients with hypertension at the time of treatment and dyslipidemia being next most common co-morbidities. HAMLET trial had 38% of hypertensive patients with most of them being smokers. DECIMAL trial also had 31% of patients with hypertension, with other co-morbidities accounts less in number. Pillai et al(1) had equal number of patients with hypertension

and diabetes mellitus (38.5%). Hypertension appears to be most commonly associated with stroke, even though other co-morbidities are equally important.

Etiology:

The most common etiology for stroke in this study was Cardio-embolic phenomenon in 24(47.1%) of patients, followed by indetermined etiology, whose etiology is either unknown or needed awaiting further investigations to confirm etiology in 15(29.4%) patients, followed by large vessel atherosclerosis in 8(15.7%) of patients, other etiology like vasculitis in 4(7.8%) patients, with no patients having etiology of small vessel lacunar infarcts. Bhatia et al(46) had 58.3% patients under indetermined etiology who need further evaluation of stroke and 27.7% being cardio-embolic stroke which being the next most common cause of stroke. HAMLET study had 48% of patients un-indetermined etiology who need further evaluation of stroke and 19% being cardio-embolic stroke with only 3% being large vessel atherosclerosis. DECIMAL trial, 55% patients had no cause found i.e, etiology undetermined and cardiac embolism and carotid dissection being the next common cause of stroke. Pillai et al(1) had 38.5% patients whose etiology was not determined and another 38.5% had cardio-embolic phenomenon as the cause of stroke. Kilincer et al(2) also had cardiac-emboli as the main cause of stroke followed by large vessel atherosclerosis Based on study by Jong-wong chung et al(15) for different etiology of stroke at different vascular territory, they found that MCA territory infarcts are caused by cardiac emboli in 28.6% of patients and ACA territory infarcts in only 10% patients , with undetermined etiology leading to MCA infarcts in 35.5% of patients.

Hours from onset to decision for surgery:

Our study has compared the outcome of patients in whom surgery delayed till 48 hours or more after the stroke onset as we consider the onset of brain oedema after full blown

stroke is more severe after 48-50 hours and patient will be more beneficial if operated at or before this time. 34(66.7%) patients underwent surgery within 48 hours of onset of symptoms and remaining 17(33.3%) underwent surgery beyond 48 hours of onset of symptoms. The mean timing was 39.3 ± 21.2 hours from the onset with minimum timing being 10 hours and maximum being 90 hours. Bhatia et al(46) had mean delay to surgery from time of onset of symptoms was 56 h (9-148 hrs) from the symptom onset. HAMLET trial patients who were treated within 48 hours, the mean interval from onset to surgery was 31 hours. DECIMAL trial, even though study didn't had timing cut off for the onset of procedure, the mean timing of surgery was 20.5 ± 8.3 hours, (range 7–43 hours). Hence all the patients underwent surgery within 48 hours of onset in this study. DESTINY trial, mean timing of onset of surgery was 24 hours (range- 13.9- 36.6 hours). Hence all the patients underwent surgery within 48 hours of onset in this study. Pillai et al(1), median time from ictus to surgery was 54 hours (range 13–288 hours) Kilincer et al(2) the cut-off point of 72 hours was taken for surgery and 72% of patients underwent surgery before this. Schwab et al(13) The mean time between onset of symptoms and surgery was 39 hours (range, 6 to 112 hours). HeaADDFIRST trial(45) even allowed patient after 96 hours of onset of stroke to undergo surgery.

Pre-operative functional status:

This study had preoperative mean MRS was 4.3 ± 0.7 with 2 being the minimum and 5 being the maximum and mean NIHSS of 16.6 ± 3.9 with 10 being minimum and 23 being maximum. The Mean GCS score was 10 ± 3 with 7 being minimum and 15 being maximum at the time of admission respectively. HAMLET trial(3) had NIHSS Score of ≥ 16 for right-sided lesions or ≥ 21 for left-sided lesions which were the cut off for the study randomisation, with gradual decrease in GCS. DECIMAL trial had mean NIHSS

of 22.5 ± 5.4 , (range 16–35) at the time of randomisation. Pillai et al had mean GCS score of 9 ± 3.2 , and the mean NIHSS score was 17.7 ± 4.1 at the time of surgery. Badhi et al had mean NIHSS score of 16 ± 5 with range of 1-32 at the time of admission. Ines C Kiphuth et al(48) had mean NIHSS score of 22 (range 19-28). DESTINY trial had mean NIHSS of 21 (range- 19-26). Most of the studies included preoperative NIHSS score for predicting the functional outcome in the patients with many studies included NIHSS above 20 on admissions.

Pre-operative Imaging data:

In this study 6(11.8%) patients had <30% of infarcted area being converted to hemorrhage at the time of surgery and 11(21.6%) patients had >30% of infarcted area being converted to hemorrhage at the time of surgery. Several studies like DESTINY, DECIMAL, HAMLET, Bhidu et al have included hemorrhagic transformation among the exclusion criteria. In the present study, we did not observe any difference in outcome in this subgroup of patients to their outcome. Pillai et al(1) also had included hemorrhagic conversion of infarcts with no significant outcome value on patients as compared to non hemorrhagic infarcts.

Mortality at Discharge:

9(17.6%) patients died at the time of discharge. None of the patients died due to direct cause of surgery per-say. HeaADFIRST trial(45) mortality was 25%, HAMLET trial had 16%, DECIMAL trial had 25%, DESTINY trial had 18% mortality at the discharge or during 1st month of follow up. Most of the above mentioned RCT's had significant high mortality in medically managed group. Bhatia et al had 62% patients died during the hospital stay in medical management group as compared to 13% deaths in the hemi-craniectomy group. Most of European studies excluded patients age above 60 years but

over study included patients above 60 years. Zhao et al(49) have reported that the benefit of the procedure can be extended to patients 80 years of age. Among the 9 patients who died during discharge in this study 5 patients were below 60 yrs of age and 4 were above 60 years. As most of the deaths in our study is related to medical co-morbidities and co-morbidities increases as age increase so these are to be taken into consideration along with increasing age. None of the patients died due to direct cause of surgery per-say hence surgery may not be attributed directly the cause of death.

Functional outcome on follow up:

NIHSS score of <16 was considered favourable outcome in our study. 76% of patients had <16 NIHSS at discharge and 81% had < 16 NIHSS at 3 months. MRS score of <4 was considered favourable outcome in our study. 66.7% of patients had <4 MRS at discharge and 92.9% had < 4 MRS at 3 months followup. At 12 months follow up 90.2% patients had <4 MRS. Bhatia et al had 58.5% with MRS <4 at the discharge as well as 3 months of follow up and at 12 months it was 66.2%, HAMLET trial, DECIMAL trial and DESTINY trial had around 75% patient with MRS below 4 at the end of 12 months follow up. Badih et al had almost 66% of patients with mrs<4 at 90 days of follow up. Pillai et al has 68% of NIHSS <16 at 6 months and 92% at 1 yr follow up. Ines C Kiphuth et al(48) had 60% of patients with MRS <4 at 6 months and 65% at 1 year follow up. Schwab et al and Rieke et al(50) emphasized that DH procedure not only reduces mortality, but also improves outcome as the follow up increases. However Holtkamp et al(42) stressed that most patients require extensive rehabilitative therapy and lifelong assistance. We should admit that, the differences between discharge, 3 months and 1 year outcomes are highly dependent on the quality of the long-term care and rehabilitation. Most of our patients in our setting receive home-based care through

family members and local physicians with no standardized post-hospital care units are available. This lack of standardized care can be the main limitation in the assessment of long-term functional outcome.

Predictors for outcome at Discharge and long term follow up:

Among the multiple variables, univariate analysis showed, age >60 years, decision for surgery >48 hours from the onset of symptoms, MLS of >10mm with uncal herniation on pre-operative CT scan, pre-operative MRS>4 and NIHSS>16 showed significant association ($p < 0.05$) with poor outcome at the time of discharge. At 1 year of follow up there was no significant association ($p > 0.05$) with any of the variables on the long term outcome of patients as most of the patients had MRS <4. So the variables which had significant association at the time of discharge in outcome and mortality were not associated significantly in long term outcome. Many studies like HAMLET, DECIMAL, DESTINY trials had considered age >60 years as bad outcome predictors at short term follow up and did not include patients above 60 years in their study. Ahmet arc et al(51) studied all the patients above 60 years of age and found that only 8% of patients above 60 years had good outcome in comparison with 58% good outcome in younger patients. Other studies like Zhao et al(49) have reported that the benefit of the procedure can be extended to patients 80 years of age. DESTINY II(52) trial reported that hemi-craniectomy significantly improves survival without being associated with severe disability in patients 61 years of age and older (38%) compared with 18% in the control group with a lower mortality rate in the surgery group. Surgery within 48 hours is considered arbitrary as there are many studies which showed benefits even after 72 hours of onset(13). But pre-operative poor GCS with MRS > 4 and NIHSS >16, with mid line shift and uncal herniation sets in from 2-4 days(53) of stroke onset, so early

decompression within 48 hours is more beneficial for immediate outcome of the patients. Schwab et al suggests that surgery within 24 hours before mass effects sets in is more beneficial. But ours being a tertiary referral centre, most of the patients reached hospital by 17.8 ± 18.5 hours from onset of symptoms so decision on surgery may be delayed as most of the population opts for initial conservative management. Rieke et al(50)supports the notion that outcome is worse when surgery is performed during the stages of herniation and mid line shift. There was no significant difference in the outcome of patients with hemisphere involved in our study. Many studies (54)(3)(2), also support that mortality, functional outcome, and quality of life are not significantly altered by the involved hemisphere. Therefore, patients should be offered surgical decompression irrespective of side of infarction. Pre-operative low sensorium, with NIHSS >16 and MRS >4 is associated with poor outcome in immediate course which is supported by many studies in literature(5)(11). This is directly related to severe brain oedema, mass effect and severe irreversible neuronal damage which effects the outcome of patients adversely. Long term patients outcome in our study setup mainly depends on house-hold care by family members and local physician so while discussing decompressive craniectomy, patients and families should be approached with extreme honesty regarding long term functional dependency and long term care for the patients, while every effort is made not to influence their decision.

CONCLUSION

CONCLUSION

- Decompressive craniectomy for malignant supra-tentorial unilateral hemispheric infarction increases the probability of survival that can yield acceptable functional outcomes in many of the patients. Careful individualized patient selection and early surgery may improve the functional outcome for these patients.
- From our Univariate analysis, age >60 years, clinical signs of herniation and those operated outside 48 h of stroke had poor outcome neurologically at the time of discharge and multivariate analysis showing Preoperative NIHSS>16 and clinical signs of herniation significant association with poor outcome. However in long term none of these predictors were associated significantly on functional outcome.
- Furthermore, the possibility of long term cognitive and physical dependance needs to be discussed with the patients and their families before deciding upon decompressive hemicraniectomy as most of the patients receive home-based care through family members and local physicians in their long term follow up.

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ANNEXURE

Annexure-1 Proforma:

- I.Demographics

Ia	Age	
Ib	Gender	
Ic	Onset to admission time	
Id	Hospital stay duration	
II.Clinical features		
Ila	hemisphere affected	Dominant/Non dominant
Ilb	Aphasia	y/n
	GCS at admission	
Ilc	NIHSS at admission	
Ild	MRS at admission	
Ile	BP at admission	
Ile	Anti platelet consumption	
IIf	B sugar at admission	
Ilg	Cardiac arrhythmias	Atrial/Ventricular/none
Ilh	Ischemic heart disease	NO/old MI/fresh ACS
Ili	Seizures	Y/N
Ilj	ETIOLOGY	LAA/Cardio/Cryptogenic/Dissection
III IMAGING		
IIIa	CT/MR at admission	Infarct >2/3
IIIb	Hemorrhagic conversion	y/n
IIIc	Midline shift	
IIId	Herniation	Transtentorial/uncal/both/none
IIIi	Arterial territory	MCA/ACA
IV SURGERY		
Iva	Hours from onset of ictus to onset of surgery	
IVi	Peri/postop ACS/cardiac failure/arrhythmias	
IVj	Post op CT Infarct expansion	

VI.IN STAY	HOSPITAL		
Vic		Hospital acquired infections VAP UTI DVT/PE Wound infection-scalp Pseudomeningocele Wound infection- abdominal Meningitis Acute renal failure Hepatic dysfunction septicemia	
VII OUTCOME	DISCHARGE		
VIIa		Discharge NIHSS	
VIIb		Discharge MRS	

- VIII FOLLOWUP 3 MONTHS

VIIIa	Follow up available Y/N	
VIIIb	3 month NIHSS	
VIIIc	3 month MRS	
VIIId	If expired-cause of death Neurological worsening Infections Cardiac others	
VIIIf	Flap replaced Y/N	

- IX FOLLOWUP 12 MONTHS

IXa	Follow up available Y/N	
IXb	12 month MRS	
IXc	If expired-cause of death Neurological worsening Infections Cardiac others	

Annexure 2. -Abbreviations

ACA = anterior cerebral artery

DC= Decompressive craniectomy

DH= Decompressive hemicraniectomy

NCCT= Non contrast computer tomography

TAIC= Total anterior circulation infarction

CUS= Carotid duplex ultrasonography

GCS= Glosgow coma scale

DSA= Distal subtraction angiogram

ICU= Intensive care unit

TTP= Thrombocytopenic purpura

RCT's= Randomised control trails

CBF = cerebral blood flow

CBV = cerebral blood volume.

EEG = electroencephalography

ICA = internal carotid artery

MCA = middle cerebral artery

MCA/MC = middle cerebral artery

mRS = modified Rankin Scale

NIHSS=National Institute Health Stroke Scale

PCA = posterior cerebral artery

SBP= Systolic blood pressure

DBP= Diastolic blood pressure.



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया

SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
Thiruvananthapuram - 695 011, Kerala, India
(An Institute of National Importance under Govt. of India)

Grams : Chitramet, Phone : +91-471-2443152, Fax : +91-471-2550728 / 2446433, E-mail : sct@sctimst.ac.in, Website : www.sctimst.ac.in

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

SCT/IEC/1067/AUGUST-2017

21.08.2017

Dr. Nithin Raj SD
Senior Resident
Department of Neurosurgery
SCTIMST, Thiruvananthapuram

Dear Dr. Nithin Raj,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "DECOMPRESSIVE HEMICRANIECTOMY: PREDICTORS OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AFTER SURGERY-A RETROSPECTIVE STUDY IN SINGLE INSTITUTE (IEC/1067)" on 19th August, 2017.

The following documents were reviewed:

1. Covering letter addressed to the Chairman, IEC, SCTIMST dated 14.07.2017 with check list
2. TAC Approval Letter
3. IEC Application Form
4. Project Proposal
5. Copy of IEC Recommendation Letter dated 06.07.2017
6. Copy of forwarding letter from HOD, dated 30.05.2017
7. Proforma
8. CV of Principal Investigator and Co-Principal Investigators

Page 1 of 2

The following members of the Ethics Committee were present at the meeting held on 19th August, 2017 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Lekha Pandit	MD.DM Neurology, PhD (Bioscience)	Female	Clinician	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
5.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
6.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
7.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
8.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
9.	Dr. P. Manickam	BSMS, MSc (Epid)., PhD	Male	Health Science Expert/ Social Scientist	No
10.	Dr. Christina George	MD Psychiatry	Female	Clinician	No
11.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
12.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
13.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
14.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
15.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

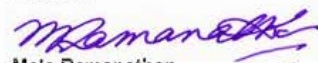
The IEC approved the conduct of the study in the present form.

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).

Sincerely,



Mala Ramanathan
Member Secretary, IEC



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INTRODUCTION Large hemispheric infarctions because of middle cerebral artery (MCA) or internal carotid artery (ICA) occlusion constitute a major cause of severe morbidity and mortality. Neurological deterioration occurs as a consequence of space-occupying cerebral edema in approximately 10% of all hemispheric strokes. Mortality ranges between 41 and 79% with conservative treatment in the intensive care unit(1) .

The incidence of hemispheric infarcts ranges between 10 and 20 per 100 000 per year(1)(2) Large hemispheric infarctions occur as a consequence of a thrombotic or embolic occlusion of the distal ICA or the proximal MCA trunk without sufficient collateral flow. Most patients have risk factors for vascular disease such as hypertension, diabetes, hypercholesteremia, tobacco abuse, history of transient ischemic attacks or ischemic strokes, congestive heart failure, and coronary artery disease.

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KEY TO MASTER CHART

Sex- 1= male

2= female

Hours from onset to surgery- 1= <48 hours

2= >48 hours

Mid line shift- 0= 0mm shift

1= 1-10mm shift

2= >10 mm shift

MRS- 1= <4

2= >4

NIHSS-1= <16

2= >16

Hemisphere invovled- 1= non dominant

2= dominant

Aphasia- 1= present

0 =absent

Vascular territory involved- 0=MCA territory

1= MCA+ACA territory

Pre-op intubation- 1= present

0=absent

Pre-op inotropes- 1= present

0=absent

Co-morbidities-1= present

0=absent

Etiology- 1=large vessel atherosclerosis

2=cardio-embolic

3=lacunar

4=other known etiology

5=undetermined etiology

Seizure, aphasia- 1= present

0= absent

Hemorrhagic conversion grade- 0= no hemorrhagic conversion

1= <30% conversion

2= >30% conversion

Herniation- 0= absent

1= present

Death- 0= absent

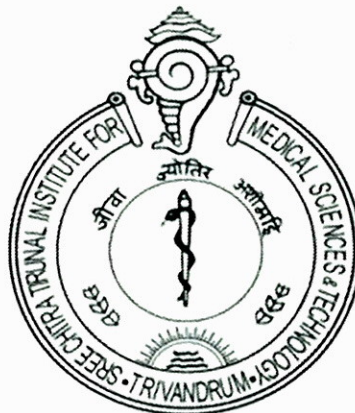
1= present

Bone flap replacement and anticoagulant use- 0= no

1= yes

[illegible]

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TRIVANDRUM, INDIA



CERTIFICATE

This is to certify that the work incorporated in this thesis titled

**“DECOMPRESSIVE HEMICRANIECTOMY: PREDICTORS OF
FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC
STROKE AFTER SURGERY-A RETROSPECTIVE STUDY IN
SINGLE INSTITUTE”**

for the degree of

M.Ch NEUROSURGERY

has been carried out by DR. NITHIN RAJ S D

*under my supervision and guidance. The work done in connection with this thesis has
been carried out by the candidate himself and is genuine.*


Dr. Mathew Abraham
Professor & Head
Principal Guide
Department of Neurosurgery,
SCTIMST, Trivandrum.

Dr. MATHEW ABRAHAM M.S., M.Ch., F.R.C.S (Edin)
Professor and Head
Department of Neurosurgery
Sree Chitra Tirunal Institute for
Medical Sciences and Technology
Thiruvananthapuram - 695 011


Dr. Jayanand Sudhir
Assistant Professor
Co - Guide
Department of Neurosurgery,
SCTIMST, Trivandrum.



DECLARATION

I hereby declare that this thesis titled **“DECOMPRESSIVE HEMICRANIECTOMY: PREDICTORS OF FUNCTIONAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE AFTER SURGERY-A RETROSPECTIVE STUDY IN SINGLE INSTITUTE”**

is a consolidated report based on a bonafide study during the period 1st January 2012 to 30th June 2017 has been prepared by me under the supervision and guidance of Prof. Mathew Abraham, Prof. and Head, Department of Neurosurgery, Sree Chitra Tirunal Institute for Medical Sciences and Technology, Thiruvananthapuram.

The thesis is submitted to SCTIMST in a partial fulfilment of rules and regulations of M.Ch Neurosurgery examination.

Date: 30.7.2018



Dr. Nithin Raj S D

Place: Thiruvananthapuram