CORRELATION OF HEMODYNAMIC CHANGES BY TRANSCRANIAL DOPPLER WITH FUNCTIONAL OUTCOME IN ACUTE PRIMARY ISCHEMIC STROKE PATIENTS

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NEUROLOGY

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DECLARATION

I hereby declare that the thesis titled "**CORRELATION OF HEMODYNAMIC CHANGES BY TRANSCRANIAL DOPPLER WITH FUNCTIONAL OUTCOME IN ACUTE PRIMARY ISCHEMIC STROKE PATIENTS**" embodies the original work carried out by the undersigned in All India Institute of Medical Sciences, Jodhpur.

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CERTIFICATE

This is to certify that the thesis titled "**CORRELATION OF HEMODYNAMIC CHANGES BY TRANSCRANIAL DOPPLER WITH FUNCTIONAL OUTCOME IN ACUTE PRIMARY ISCHEMIC STROKE PATIENTS**" is the bonafied work of Dr. Pratik K. Patel, carried out under guidance and supervision, in the department of Neurology, All India Institute of Medical Sciences, Jodhpur.

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Dr. Pratik K. Patel

CONTENTS

LIST OF TABLES

ABBREVATIONS

ADL	:	ACTIVITY OF DAILY LIVING
AIS	:	ACUTE ISCHEMIC STROKE
ASPECTS	:	ALBERTA STROKE PROGRAMME EARLY CT SCORE
BI	:	BARTHEL INDEX
CE	:	CARDIOEMBOLIC
CVD	:	CEREBROVASCULAR DISEASE
ICP	:	INTRACRANIAL PRESSURE
LMIC	:	LOWER MIDDLE-INCOME COUNTRY
LVA	:	LARGE VESSEL ATHEROSCLEROSIS
MRS	:	MODIFIED RANKIN SCORE
NIHSS	:	NATIONAL INSTITUTES OF HEALTH STROKE SCALE
SVD	:	SMALL VESSEL DISEASE
TCD	:	TRANS CRANIAL DOPPLER
TIBI	:	THROMBOLYSIS IN BRAIN ISCHEMIA
TOAST	:	TRIAL OF ORG 10172 IN ACUTE STROKE TREATMENT

SUMMARY

Background: Acute ischemic stroke (AIS) ranks among the major non communicable diseases that confer significant morbidity and mortality. Prediction of long-term outcome in the disease can impact the approach and attitude in patient's management. Serial TCD was shown to predict short term clinical severity, however its utility to predict long term disability and functional independency was uncertain. Here we studied the role of serial TCD to predict long term disability and functional independency status in AIS.

Methodology: This is a prospective, observational, descriptive study done between January 2021 to June 2022 at the Neurology Department, All India Institute of Medical Sciences, Jodhpur. A total of 34 patients were included in the study after taking written informed consent. At baseline, data on sociodemographic parameters, clinical parameters related to disease (including NIHSS), treatment related and disability related (including MRS and Barthel index (BI) were recorded. Transcranial doppler (TCD) was done in all the patients at baseline within two hour of admission and at 48 hours. TIBI flow grading was calculated on the bases of TCD in all the patients. NIHSS, MRS and BI were further recorded on 2nd day, 30 days and 90 days after ictus. Further data on changes in TIBI and changes in the NIHSS, MRS and BI were obtained over various time line. The relation across different parameters was studied. .

Result: A total of 34 patients with AIS were recruited for the study. Data obtained showed that majority of the study subjects were elderly (mean age:61.41±14.82 years) and male (76.47%). Large vessel atherosclerosis (44.11%) followed by cardioembolic (29.41%) strokes in the anterior circulation (79.41%) were the most common aetiologies. Hypertension (58%), hyperhomocystinemia (35%), tobacco addiction

(29.50%), diabetes (23.52%), dyslipidaemia (23.52%) and obesity (20.58%) were the common risk factors. Majority of the patients had mild to moderate severity of stroke i.e. NIHSS between 1-4 (32.2%) or 5-14 (50.1%), and ASPECTS of 9 (17.64%) or 10 (41.17%). Majority of the patients had severe to total dependency at admission i.e. MRS of 4 (38.4%) or 5 (32.35%) and BI between 0-20 (44.11%) or 21-60 (23.18%). Of 34 patients, sixteen patients (47.05%) were thrombolysed with r-TPA and remaining 18 (52.95%) were managed conservatively. Median door to needle time was 120 minutes (range 16-213 minutes). Eight patients had difficult insonation window. Of the remaining 26 patients, 21 patients had improvement in TIBI scoring at 48 hours compared to baseline TIBI. Out of these 26 patients, 18 patients had improvement in NIHSS scale at 48 hours when compared to baseline. Our study showed that improvement in TIBI score at 48 hours is significantly correlated with improvement in clinical severity, i.e. NIHSS at 48 hours **(P = 0.019)**, irrespective of the treatment of the ischemic stroke (medical management versus thrombolysis/mechanical thrombectomy). At 90 days follow up, of 80.76 % patients whose TIBI flow grade had improved at 48 hours, 85.71% patients had improvement in MRS. Out of these, 94.43% had improvement in first 30 days **(P = 0.09)** and 55.55 % had improvement within 48 hours of ictus. Similarly, at 90 days follow up, 100% patients had improvement in BI if TIBI flow grade had improved at 48 hours **(P= 0.03).** Out of these, 90.47% had improvement in first 30 days and 57.55 % had improvement within 48 hours of ictus. This finding suggests that improvement in TIBI grade can predict outcome of long-term disability and functional independency consistently.

Conclusion: In AIS patients, serial improvement in the TCD flow gradings are significantly correlated with improvement in clinical severity and can predict early and late disability status and functional independence irrespective of treatment given at

admission. It is relatively inexpensive, repeatable, and its portability offers increased convenience over other imaging methods, allowing for continuous bedside monitoring

INTRODUCTION

Ischemic stroke burden in India has been increased significantly over last few decades. The prevalence rate of stroke for total population inclusive of urban and rural population in India, varied from 44.54 to 150/100000. (1) For the urban population prevalence rate was 45 to 487/100000 and 55 to 388.4/100000 for rural population of India from 1960-2018.(1) The assessment of clinical severity at the time of stroke is predominantly done by National institute of Health stroke scale (NIHSS) and by Alberta stroke programme early ct score (ASPECT) score. This clinical severity score is useful to streamline the management of ischemic stroke i.e. either conservative management versus thrombolysis and/or mechanical thrombectomy. NIHSS and ASPECT scores at the time of admission are also helpful to predict short- and long-term outcome following stroke. ((2,3) Barthel Index (BI) and Modified Rankin score (MRS) scores assess the functionality at the time of admission and are also helpful to predict long-term outcome following stroke. ((4,5) Similarly dynamic changes in the hemodynamic flow of cerebral vasculature were studied by transcranial doppler (TCD) for prediction of short-term clinical outcome in thrombolysed patients in the form of changes in NIHSS score in the ischemic stroke patients. (6) However long-term outcome prediction on the basis of the cerebrovascular hemodynamic changes observed by TCD, at the time of stroke was not evaluated. Further no study evaluated similar correlation in non thrombolysed ischemic stroke group. In this observation study we evaluate the correlation between the acute cerebrovascular hemodynamic flow changes to NIHSS Score, MRS scale and the BI score at various timelines to predict short term and long-term severity, functionality and disability outcomes irrespective of treatment (either with thrombolysis /mechanical thrombectomy or conservative management) provided at the time of admission for acute ischemic stroke.

REVIEW OF LITRATURE

The term cerebrovascular disease (CVD) refers to all disorders leading to stroke which can be either ischemic or haemorrhagic. There has been a global rise in the burden of cerebrovascular disease. The estimated global cost of stroke is over US$721 billion (0.66% of the global GDP). From 1990 to 2019, the burden (in terms of the absolute number of cases) increased substantially (70.0% increase in incident strokes, 43.0% deaths from stroke, 102.0% prevalent strokes, and 143.0% DALYs), with the bulk of the global stroke burden (86.0% of deaths and 89.0% of DALYs) residing in lower-income and lower-middle-income countries (LMIC).(7) CVD/stroke continues to be second only to ischemic heart disease in contributing to the global share of deaths since 1990 to 2016.(8) LMIC account for 85.5% of total stroke deaths worldwide and the number of disability-adjusted life years in these countries was approximately seven times that in high-income countries.(7)

In a study by Khurana et al, an attempt had been made to compile and depict the burden of stroke including the prevalence, incidence and mortality rates through a systematic review and meta-analysis of the community-based studies conducted over a period of six decades in India (from 1960 to 2018). The prevalence rate of stroke inclusive of urban and rural population, varied from 44.54 to 150/100000 (45 to 487/100000 for urban and 55 to 388.4/100000for rural population.(1) In India, the risk factors for stroke like obesity, diabetes mellitus, alcoholism, hypertension, and sedentary lifestyle are mounting with economic growth and increasing the disease burden. The foremost risk factors for stroke in India, hypertension and diabetes, need to be controlled and treated like other global high-risk populations for stroke prevention. (9)

Prehospital or initial stroke severity showed the strongest independent association to the risk of death and unfavourable outcome within 90 days. Previous studies have also indicated that stroke severity is an important determinant of patient outcome in stroke (10–12). NIHSS is the most widely used scale for stroke severity at the time of admission. (2,3) The NIHSS is a systematic, quantitative assessment tool to measure stroke -related neurological deficit. In clinical practice it can be used to evaluate and document neurological status in acute stroke patients, determine appropriate treatment and assist in standardizing communication between healthcare practitioners. The NIHSS has been shown to be a predictor of both short and long term outcomes of stroke patients.(2,3)The NIHSS is a 15-item neurological examination stroke scale used to evaluate the effect of acute cerebral infarction on the levels of consciousness, language, neglect, visual-field loss, extraocular movement, motor strength, ataxia, dysarthria, and sensory loss. Stroke severity may be stratified on the basis of NIHSS scores as follows:

- Very Severe: >25
- Severe: 15 – 24
- Mild to Moderately Severe: 5 – 14
- Mild: 1 – 4

Outcomes related to NIHSS scores at admission

- Scores of <5; 80% of stroke survivors will be discharged to home.
- Score between 6 and 13 typically require acute inpatient rehabilitation.

Scores of >14 frequently require long-term skilled care.(13,14).

The BI is an ordinal scale used to measure performance in activities of daily living (ADL). Ten variables describing ADL and mobility are scored, a higher number being a reflection of greater ability to function independently following hospital discharge. Time taken and physical assistance required to perform each item are used in determining the assigned value of each item. The BI measures the degree of assistance required by an individual on 10 items of mobility and selfcare ADL.(4)

The MRS is reliable score used to assess functional disability.(5) MRS, a clinician-reported measure of global disability, is widely applied for evaluating stroke patient outcomes and as an end point in randomized clinical trials.(15) MRS has 7 scales as mention in appendix 2. Both BI and MRS scales are widely used scales to assess the functionality of the patients and the morbidity following CVA.

ASPECTS is a 10-point quantitative topographic CT scan score used for middle cerebral artery (MCA) stroke patients. It has also been adjusted for the posterior circulation (see below). The scoring system includes segmental estimation of the middle cerebral artery (MCA) vascular territory is made, and 1 point is deducted from the initial score of 10 for every region involved:

- caudate
- putamen
- internal capsule
- insular cortex
- M1: "anterior MCA cortex," corresponding to the frontal operculum
- M2: "MCA cortex lateral to insular ribbon" corresponding to the anterior temporal lobe
- M3: "posterior MCA cortex" corresponding to the posterior temporal lobe
- M4: "anterior MCA territory immediately superior to M1"

- M5: "lateral MCA territory immediately superior to M2"
- M6: "posterior MCA territory immediately superior to M3"(16)

An ASPECTS score less than or equal to 7 predicts a worse functional outcome at 3 months as well as symptomatic haemorrhage. (17)

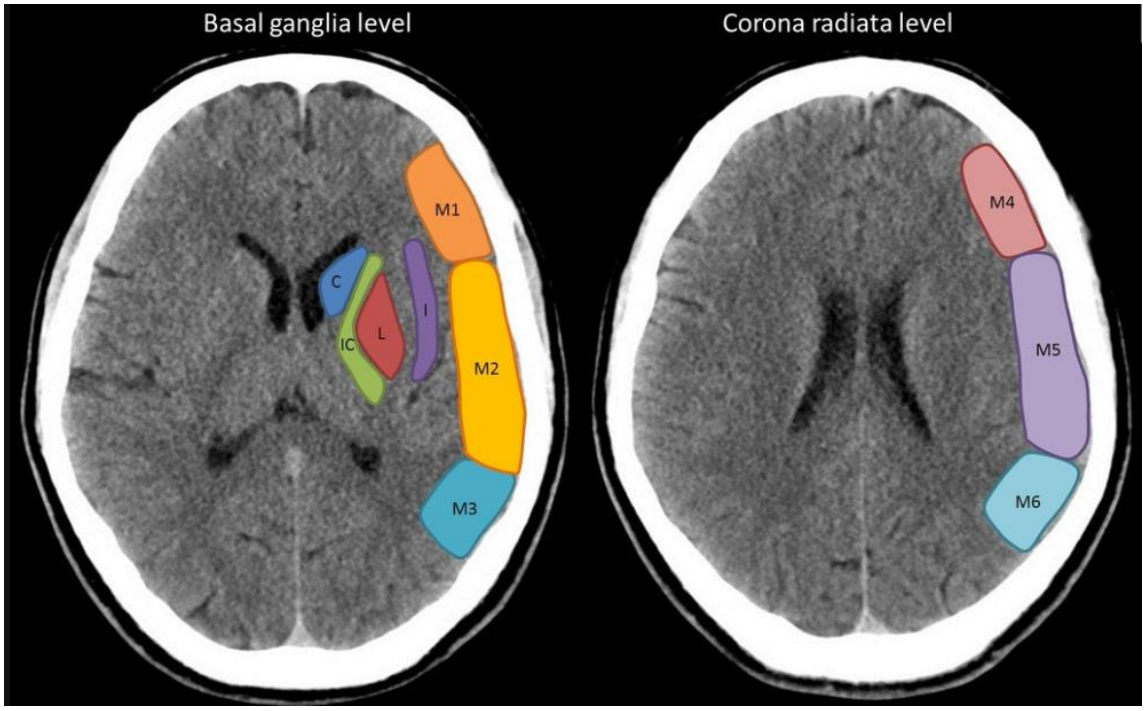


Figure 1: Annotated image for ASPECT score (18)

CT angiography source image ASPECTS (CTA-SI ASPECTS) is a semiquantitative scoring system to characterize the extent and severity of mainly middle cerebral artery ischemic stroke, although it can be adapted to other vascular territories as well. The added value of CTA-SI ASPECTS is that it directly shows the degree of collateral circulation and better delineates the infarct territory during the acute phase.(19) It has been demonstrated that a good CTA-SI ASPECTS score is a superior predictor of the final infarct size and clinical outcome to the standard ASPECTS, and most importantly it was found to be a better indicator of the possible outcome of endovascular treatment (19,20)

Neuroimaging such as perfusion studies can predict severity. CT perfusion study provides adequate sensitivity and specificity with good predictive value in the detection of acute ischemic infarct in stroke patients. This widely available and time-effective modality aids in the triage of patients for immediate endovascular intervention leading to maximal neurological benefit and improving outcomes.(21)

Role of multiphase CT angiography (mCTA) of head and neck vessels was evaluated in aprospective single-centre observational study, comprising of patients with AIS of the anterior circulation, presenting within 24 hours and undergoing neuroimaging under stroke protocol with follow-up. Non-contrast computed tomography (NCCT), mCTA, and CTP were acquired with follow-up NCCT at 24 hours and modified Rankin score (mRS) at 3 months. mCTA-SI and CTP color maps were scored by the ASPECTS method and compared amongst each other and with the outcome. The study included 55 patients. The 1st and 2nd phase of mCTA-SI correlated significantly with CBF maps ($r = 0.845$, $p < 0.01$, $r = 0.842$, $p < 0.01$ respectively). The 3rd phase of mCTA-SI correlated significantly with CBV maps ($r = 0.904$, $p < 0.01$). A favourable functional and radiological outcome was best predicted by the 1st (AUC 0.8, 95%CI 0.671–0.896) and 2nd (AUC 0.895, 95% CI 0.783–0.962$^{)}$ phase of mCTA-SI respectively.(22)

TCD is a convenient, low cost and rapidly repeatable test compared to CT and MR in ischemic stroke with more sensitivity and specificity to diagnose anterior circulation changes.(23,24) Hemodynamic changes can be assessed by performing serial TCD and can predict flow changes compared to one time MR angiography.(25)

TCD, first described in 1982, is a non-invasive ultrasound (US) study that involves the use of a low-frequency (≤2MHz) transducer probe to insonate the basal

cerebral arteries through relatively thin bone windows. TCD allows dynamic monitoring of cerebral blood flow velocity (CBF-V) and vessel pulsatility over extended time periods with a high temporal resolution.(26) It is relatively inexpensive, repeatable, and its portability offers increased convenience over other imaging methods, allowing continuous bedside monitoring of CBF-V, which is particularly useful in the intensive care setting.(27)

TCD works on the principle of Doppler effect that states that where a sound wave strikes a moving object, such as an erythrocyte, the reflected wave undergoes a change in frequency (the Doppler shift fd) directly proportional to the velocity (V) of the reflector. The following equation derived from this principle is the basis for calculating CBF-V with TCD:

$$V = \frac{(c \times fd)}{2 \times f0 \times \cos \theta}$$

where c is the speed of the incident wave, $f0$ is the incident pulse frequency, and θ is the angle of the reflector relative to the Ultrasound probe.(28) TCD relies on pulsed wave Doppler to image vessels at various depths.(27).(27) Received echoes generate an electrical impulse in the US probe and are processed to calculate fd and V, to produce a spectral waveform with peak systolic velocity (PSV) and end diastolic velocity (EDV) values. An US frequency of ≤2MHz is required to penetrate the skull and reach the intracranial vasculature. Depending on procedure duration, the US probe is fixed in a headset or manually applied.

Acoustic windows are skull regions, either foramina or thin bone, that transmit US waves to the basal cerebral circulation.(29) There are four acoustic windows, namely, the transtemporal, suboccipital (transforaminal), transorbital, and

submandibular (retromandibular). The transtemporal window, located above the zygomatic ridge between the lateral canthus of the eye and auricular pinna, is most frequently used and can insonate the middle (MCA), anterior (ACA), posterior cerebral arteries (PCA), and terminal internal carotid artery (ICA) (29,30). However, between 10% and 20% of patients have inadequate transtemporal windows.(27,29,30). The target artery is insonated by selecting an appropriate acoustic window, probe angle, and sample volume depth (29). The artery is recognized through flow direction, resistance (pulsatility), and velocity in addition to waveform changes induced by dynamic manoeuvres such as proximal carotid artery compression and tapping over bony landmarks. (29,30)

Amongst various indices mean flow velocity (MFV) is a central parameter in TCD and is equal to (PSV + (EDV × 2))/3. (29) When MFV is increased, it may indicate stenosis, vasospasm, or hyperdynamic flow. A decreased value may indicate hypotension, decreased CBF, ICP, or brain stem death.(33) Focal arterial stenosis or vasospasm is represented by an increased MFV within a 5–10mm segment, usually by >30 cm/s compared with the asymptomatic side.(34) Gosling's pulsatility index (PI) provides information on downstream cerebral vascular resistance and is equal to (PSVxEDV)/ MFV.(35) Pulsatility index (PI) is normally 0.5 to 1.19. (35) Proximal stenosis or occlusion may lower the PI below 0.5 due to downstream arteriolar vasodilation whilst distal occlusion or constriction may increase the PI above 1.19 (34). A PI less than 0.5may also indicate an arterio-venous malformation as vessel resistance in proximal vessels is reduced due to continuous distal venous flow.(36) PI positively correlates with ICP; a PI change of 2.4% is reflected by a 1mmHg change in ICP.(37)

Current applications of TCD in adults and children include vasospasm in sickle cell disease, subarachnoid haemorrhage (SAH), intra- and extracranial arterial stenosis and occlusion, brain stem death, head injury, raised intracranial pressure (ICP), intraoperative monitoring, impaired vasomotor function, and cerebral micro-embolism in right to left cardiac shunts. TCD has also been widely used to investigate cerebral pressure autoregulation. Combined with waveform morphology, indices derived from flow velocity readings such as Gosling's PI and the Lindegaard ratio (LR) allow identification of increased cerebrovascular resistance, vasospasm, and hyperdynamic flow states, which characterise the above clinical conditions.(30,38–46)

One challenge of ischemic stroke therapy is to reverse the neurological deficit by reopening intracranial vessels with thrombolytic agents. Meanwhile, the clinical course of stroke may include either spontaneous improvements or deterioration related to dynamic changes in brain perfusion. These changes are associated with spontaneous thrombolysis, reocclusion, micro embolism, thrombus propagation, and/or collateralization. It would theoretically be possible to prevent or to counteract neurological deterioration or to plan conservative treatment of patients likely to improve spontaneously if the mechanisms underlying these clinical evolutions could be monitored. Digital subtraction angiography, contrast enhanced CT angiography, and magnetic resonance angiography (MRA) are useful modalities of visualizing the cerebrovascular anatomy and evaluation of collateral circulation in acute stroke.(47,48) However, in some institutions these methods may not be readily available immediately after admission of acute stroke patients. More importantly, serial examinations with these methods are difficult for patients and impractical in view of an increasing tendency toward cost containment. Accordingly, in clinical practice it is difficult to monitor dynamic changes in cerebral hemodynamic with these methods. TCD is an

alternative non-invasive, nonionizing, and inexpensive method of assessing patterns of cerebral circulation. The bedside availability, convenience to the patient, and serial or even continuous monitoring options make TCD particularly suitable and practical for emergency evaluations. Akopov et al studied 41 patients with ischemic cerebrovascular disease in anterior and posterior circulation. In this study, serial TCD was done at admission, between 24 to 48 hours and between 4 to 8 days from the ictus. They observed the hemodynamic changes in completely occluded to non-occluded symptomatic vessels.(24)

The National Institute of Neurological Disorders and Stroke trial demonstrated the clear benefit of early intravenous recombinant tissue plasminogen activator (rtPA) administered within 3 hours of onset of thrombosis. (48,49) The most profound benefit appears to be in those patients with very early initiation of treatment. Other intravenous thrombolytic trials showed only a trend towards benefit with later treatment (3-6 hours from onset) (49,50) . The site of arterial occlusion is an important factor in determining the likelihood of recanalization. In another angiographic study, occlusions in the middle cerebral artery (MCA) branch or division were associated with a 35% to 40% recanalization rate whereas internal carotid artery occlusion was associated with only an 8% recanalization rate.(51) It has been postulated that, by identifying the site of occlusion, vascular imaging before or during thrombolysis would better identify those patients most likely to benefit from thrombolytic therapies.(52) CT-angiography, magnetic resonance angiography (MRA), or conventional angiography (DSA) offer definitive evidence as to the site of occlusion in acute stroke.(53,54) The availability of these diagnostic procedures is limited in many institutions, and valuable time is lost in patient transport and technical factors.

The current literature investigating the role of TCD in identifying arterial obstruction is limited. In one study, TCD had a sensitivity of 80% and a specificity of 90% compared to DSA within 5 hours of middle cerebral artery (MCA) stroke.(55) In a prospective study involving 30 cerebral ischemia patients evaluated with TCD, MRI, and MRA within 24 hours of symptom onset, TCD showed a sensitivity of 96% and a specificity of 33% for recognizing abnormal cerebral blood flow velocities.(56) Demchuk et al evaluated all bedside TCD studies in patients with symptoms of cerebral ischemia referred between September 1997 and November 1998 by the Stroke Treatment Team to the STAT Neurosonology Service, University of Texas-Houston. On the basis of the observations, conclusive criteria for occlusion were developed for each artery at various sites.

Primary findings of TCD criteria at each site of occlusion included presence of an abnormal waveform, which was defined as one of four types-

1. Dampened Signal: Pulsatile flow with normal flow acceleration and decreased mean flow velocity (MFV) (≥30% difference compared to control).
2. Blunted Signal: Delayed flow acceleration with stepwise maximum velocity arrival during mid to late systole, compared to contralateral side and focal decreased mean flow velocity and positive end diastolic flow (low pulsatility index (PI) ≤ 1.19).
3. Minimal Signal: Presence of a flow signal with no end diastolic flow, with PI ≥1.7.
4. Absent Signal: No detectable flow at appropriate depths of insonation for the artery in question.

The sensitivity for each individual occlusion site was: proximal ICA 94%, distal ICA 81%, MCA 93% VA 56%, BA 60%. The specificity ranged from 96% to 98%. TCD is sensitive and specific in determining the site of the arterial occlusion using detailed

diagnostic criteria, including proximal ICA and distal MCA lesions. TCD has the highest accuracy for ICA and MCA occlusions. (57)

The clinical benefit of tPA in ischemic stroke is linked to accelerated clot lysis and early recanalization.(6,58) However, previous angiographic studies with systemic tPA in stroke have revealed only a 30% to 40% recanalization rate.(51)Cardiology studies suggest that circulation to and about the thrombus appears to be the most important factor associated with thrombolytic failure. Persisting perfusion or residual flow around coronary arteries is best measured angiographically and can be graded with the thrombolysis in myocardial ischemia (TIMI) flow grades.(59) In simple terms, TIMI can grade the severity of the vascular disease. Demchuk et al sought and develop a similar grading system for residual flow with use of TCD. Their study describes and evaluates a novel TCD grading system for residual flow called Thrombolysis in Brain Ischemia (TIBI; Health Outcomes Institute, Inc) in a series of systemically treated acute stroke patients.(25) The grading system has 6 grades. From grade 0 to grade 5 on the basis of flow characteristic form normal flow to absent flow. Pre and post thrombolysis changes in TIBI were compared with NIHSS. The correlation between the hemodynamic changes across the occlusion site in serial TCD in the form of changes in TIBI and improvement in NIHSS was observed. However, they studied only thrombolysed ischemic stroke patients. In non thrombolysed patients, the correlation between changes in TIBI score in serial TCD and changes in NIHSS following other drug therapy was not performed.

AIM AND OBJECTIVES

AIM OF STUDY: To correlate the change in functional outcome in ischemic stroke patients with hemodynamic changes recorded by TCD.

OBJECTIVES OF STUDY:

1. To record hemodynamic changes by TCD in ischemic stroke patients receiving versus those not receiving thrombolysis.
2. To correlate hemodynamic changes on TCD in ischemic stroke patients with or without thrombolysis with clinical and functional outcome.

MATERIALS AND METHODS

STUDY DESIGN:

This is a prospective, observational, cohort study.

STUDY PERIOD: January 2021 – June 2022

SAMPLE SIZE: According to the literature reviewed so far (3), there is an improvement in TCD parameters in 87% after 24 hours compared to baseline. In this study, the comparison of TCD parameters were observed after 48 hours.

Considering the improvement score (p)= 87%, precision+/- 10%,

Number needed= $(1.96)^2$ (0.87) (0.13) / $(0.1)^2$

=0.4343/0.01

= 43.43

Therefore, approximately 45 minimum patients should have been included.

However due to COVID pandemic, the patient recruitment had to be done in a time bound manner. As such, we were able to include only 34 patients in the study.

INCLUSION CRITERIA

1. Patients with age of 18 years or more with or without comorbidities.
2. Patients diagnosed as a case of primary ischemic arterial stroke based on clinical and radiological evaluation.
3. Those who presented within 24 hours of onset of stroke.
4. Patients whose written informed consent was available by either patient or his/her relative.

EXCLUSION CRITERIA

1. Patients with venous infract.
2. Patients with hemorrhagic infarct.
3. Patients with intracranial hemorrhage.
4. Patients with previous stroke of any etiology

STUDY METHODOLOGY

This was a prospective, observational, and descriptive study. The study was undertaken after due ethical clearance by the Institutional Ethics committee (AIIMS/IEC/2021/ 3343). Patients satisfying the inclusion and exclusion criteria were enrolled after taking informed written consent. Due to the COVID pandemic and its related management strategies and isolation policy we were not able to recruit the desired number of patients.

Demographic details of the patients like name, age, sex, residence, education and occupational status were obtained. Detailed clinical history with general physical and neurological examination were done. The NIHSS (Appendix 1) score was performed at admission and after 48 hours for all patients for predicting severity of stroke as well as for comparing the clinical outcome at admission at 48 hours. The MRS (Appendix 2) was applied to all the patients at admission, at 48 hours, 30 days and 90 days, to compare functional outcome in stroke patients. The BI score (Appendix 3) was applied to all the patients at admission, at 48 hours, 30 days and 90 days, to compare functional outcome in stroke patients. Due to the COVID pandemic, few of the patients were telephonically consulted to calculate BI and MRS scales.

In all the patients, irrespective of treatment (either treated conservatively or with thrombolysis/mechanical thrombectomy), TCD was performed with non-duplex TCD with <2 Hz frequency probe, with various transcranial insonation windows such as a)

trans temporal b) trans orbital c) trans-foraminal and d) retromandibular. On the basis of insonation characteristics (Appendix 4) of the cerebral vasculature, the following parameters-MFV, PI, PSV and PDV, were observed at baseline within 2 hours of admission and at 48 hours.

On the basis of various parameters obtained by TCD and comparing them with normative data from Indian historical controls (Appendix 5). TIBI Grading (Appendix 6) was calculated at baseline and 48 hours later.

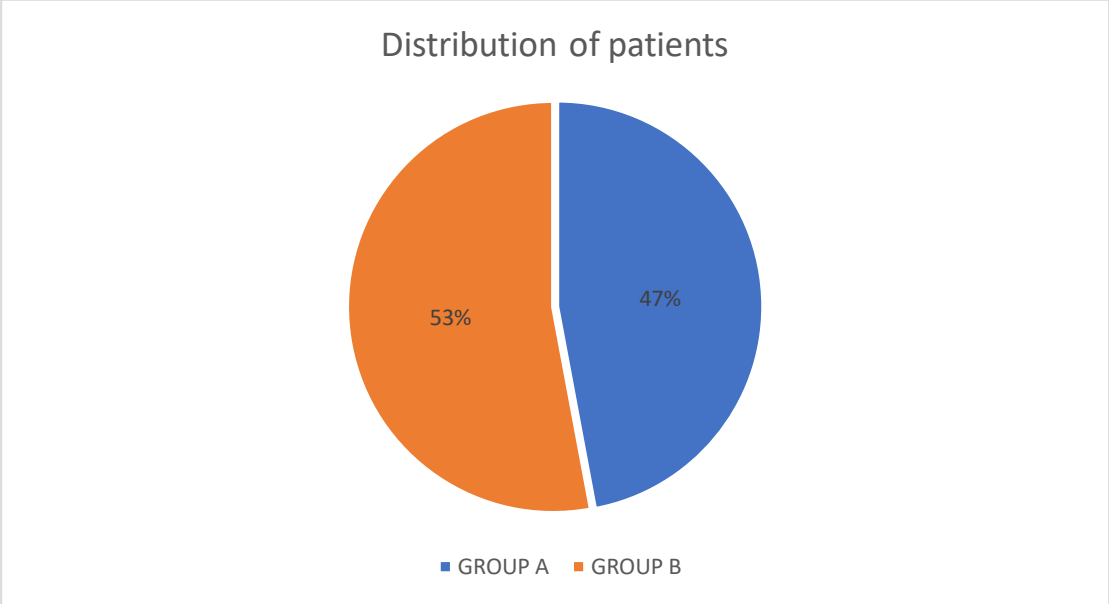
The difference between the TIBI scoring was compared with difference in NIHSS, MRS and BI score at 48 hours. Similarly, the difference between the TIBI scoring was compared with difference in MRS and BI score at 30 and 90 days to that of baseline score, respectively.

Statistical analysis done using IBM SPSS29.0. Categorical variables were analysed in proportions and compared using Fisher's exact test. Continuous variables were described. Statistical significance will be taken when $p< 0.05$.

RESULTS

A total of 34 patients were included in the study over 18 months. Of these, 16 (53%) patients underwent thrombolysis with rtPA and comprised Group A. The remaining 18 (47%) patients were managed conservatively and constituted Group B.

FIGURE 2: Distributions on the basis of treatment



Demographic results

There were a total of 8 females and 26 males in the cohort. The mean age of the patients was 61.41±14.82 years. Risk factors detected included history of coronary artery disease (CAD) in7 patients, hypertension (HTN) in 20, diabetes (DM) in 8 , obesity in 7 , dyslipidemia in 8 and hyperhomocystinemia in 12 . Eleven patients had chronic substance use (10 of tobacco and one with alcohol) and one patient had lone atrial fibrillation (AF). Two patients had history of AF with CAD. Twelve patients were on antihypertensive medications, 5 on antiplatelets, 5 on lipid lowering agents and 3 were on oral hypoglycemic agents (OHA)/ insulin.

Amongst the 16 patients of thrombolysis group (Group A), mean age was 59.31 years, 4 were female and 12 were male. Six patients (38%), had history of CAD, 9 (56%) were hypertensive, 5 (31%) were diabetic, 4 (25%) were obese, 6 (38%) had dyslipidemia and 8 (50%) had hyperhomocystinemia. Five patients had chronic substance use (4 of tobacco and one with alcohol) 2Twopatients had atrial fibrillation (AF).Six (37.5%) patients were on antihypertensive medications, 2(12.5%) on antiplatelets, 6 (31.2%) on lipid lowering agents and (18.7%) were on oral hypoglycemic agents (OHA)/ insulin.

Amongst the 18 patients of non-thrombolysis group (Group B), mean age was 63.27 years, 4 were female and 14 were male. Three patients (17%) had history of CAD, 11 (61%) were hypertensive, 3 (17%) were diabetic, 3 (11%) were obese, 2 (38%) had dyslipidemia and 4 (28%) had hyperhomocystinemia. . Six patients had chronic tobacco use. One patient had lone AF and 2 had CAD with AF. Six (33.3%) patients were on antihypertensive medications, 3 (16.6%) were on antiplatelets, one (5.55%) on lipid lowering agent and 3 (16.66%) on OHA / insulin.

TABLE 1: Sociodemographic data

RISK FACTORS	TOTAL PATIENTS (N=34)	THROMBOLYSIS GROUP A (N=16)	NON-THROMBOLYSIS GROUP B (N=18)
TOTAL	34	16	18
AGE (mean±SD)	61.41±14.82 years	59.31±5.48 years	63.27 ±12.10years
MALE	26	12	14
FEMALE	8	4	4
CAD	7	6	1
HTN	20	9	11
DM	8	5	3
OBESITY	7	4	3
DYSLIPIDEMIA	8	6	2
HYPERHOMOCYSTINEMIA	12	8	4
TOBACO	10	4	6
ALCOHOL	1	1	
Lone AF	1	2	1
AF with CAD	2	0	2
ANTI HYPERTENSIVE	12	6	6
ANTI PLATELET	5	2	3
ANTI COAGULANT	0	0	
LIPID LOWERING AGENT	6	5	1
OHA/INSULIN	6	3	3

FIGURE 3: Gender Distribution

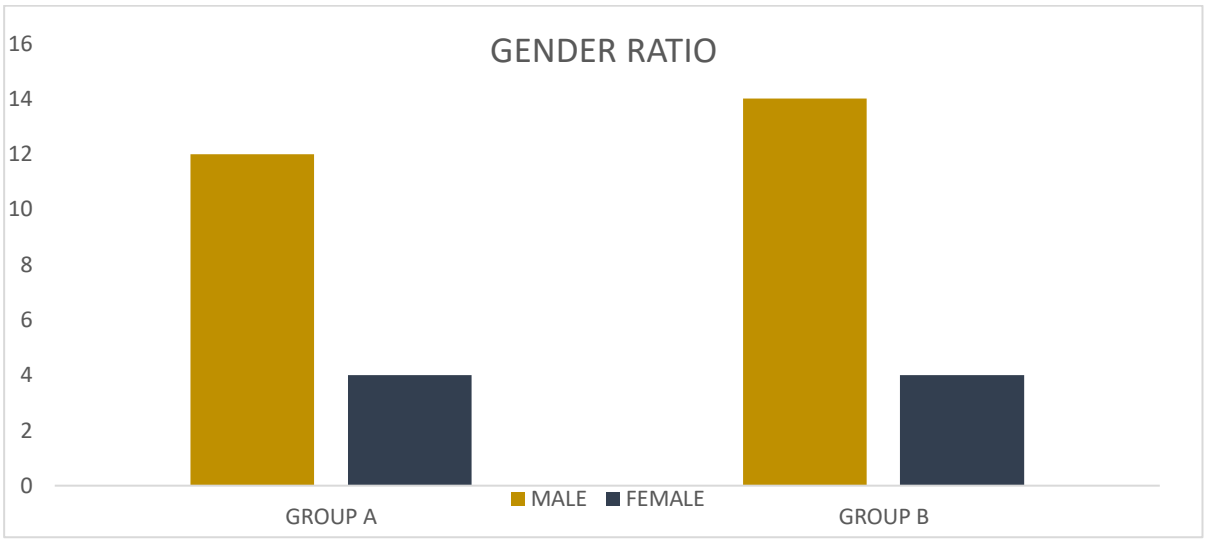


FIGURE 4: Drug history

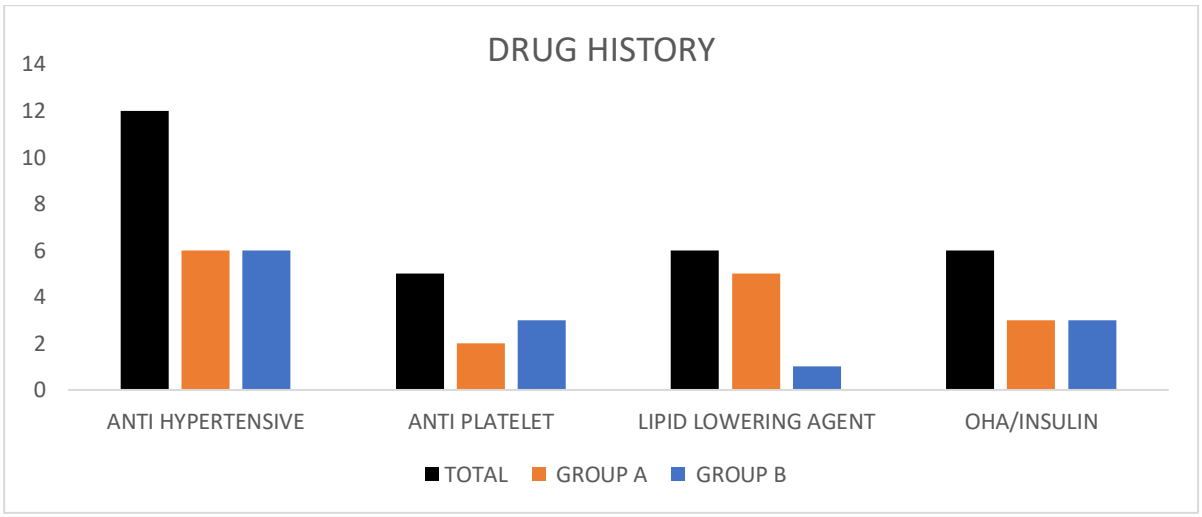
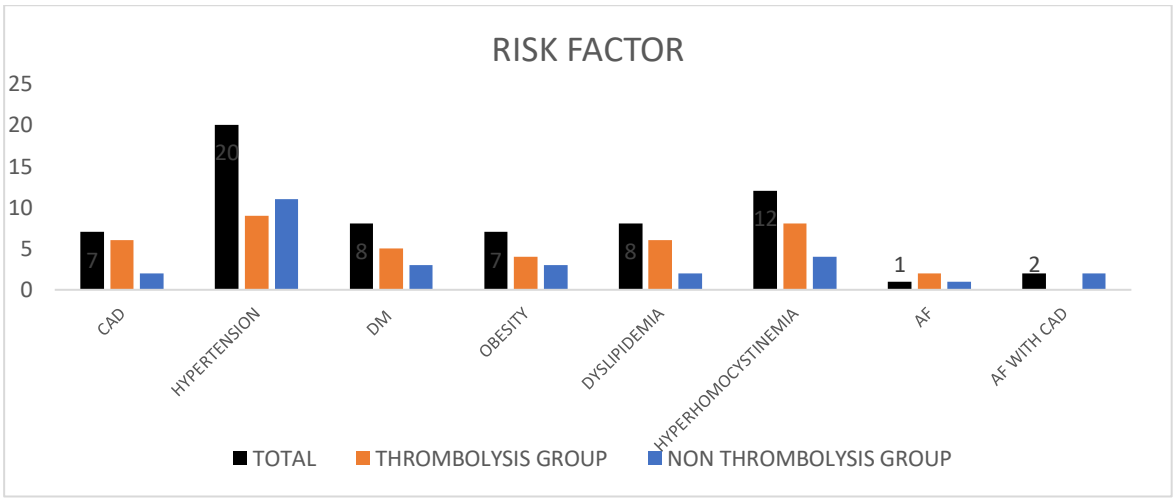


FIGURE 5: Risk factors Distribution



Clinical severity at presentation

The clinical severity of ischemic stroke was assessed by NIHSS and categorized into 34 groups as shown in (TABLE 2)- mild- 1-4, moderate- 5-14, severe- 15-24 and very severe->25.In total out of 34 patients, 11 patients had NIHSS between 1-4, 17 between 5 -14 NIHSS, and 5 were between 15-24.

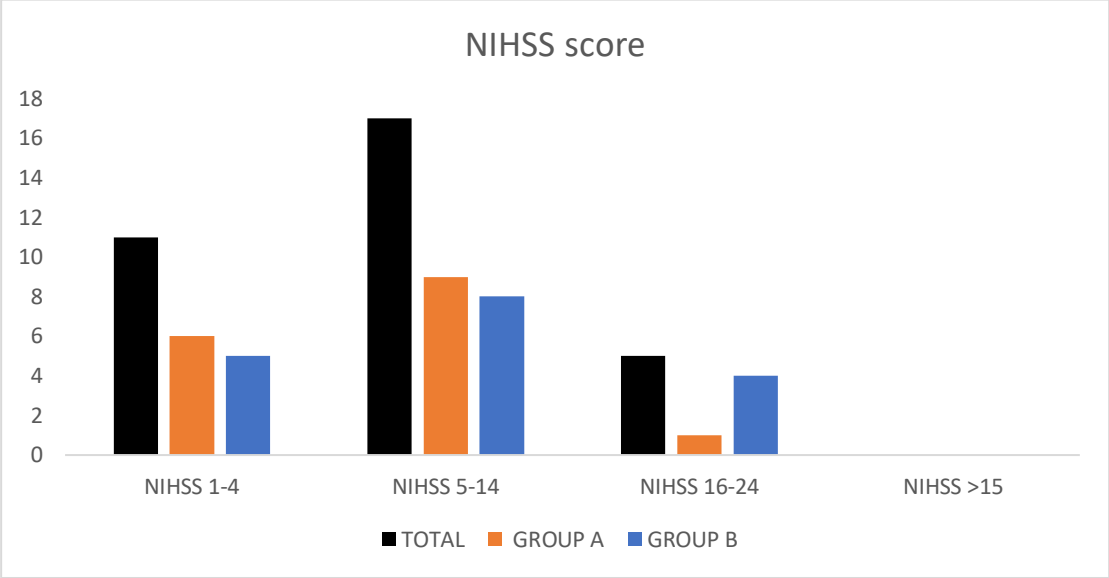
In Group A (thrombolysis group), out of 16 patients, 6 patients had NIHSS between 1-4, 9 between 5 -14 NIHSS, and only one was between 15-24.

In Group B (non-thrombolysis group), out of 18 patients, 5 patients had NIHSS between 1-4, 8 between 5 -14 NIHSS, and 4 between 15-24.

Table 2: Clinical severity at presentation using NIHSS

CLINICAL SEVERITY	TOTAL PATIENTS (N = 34)	GROUP A (N = 16)	GROUP B (N = 18)
NIHSS 1-4 (MILD)	11 (32.2%)	6 (37.7%)	5 (27.7%)
NIHSS 5-14 (MODERATE)	17 (50%)	9 (56.25%)	8 (44.4%)
NIHSS 15-24 (SEVERE)	5 (14.70%)	1 (6.25%)	4 (22.2%)
NIHSS >25 (VERY SEVERE)	0	0	0

FIGURE 6: Clinical severity distribution as NIHSS



Disability by modified Rankin score at admission

In total out of 34 patients, 3 patients had MRS of 1, 3 patients had MRS of 2, 2 patients had MRS of 3, 13 had MRS of 4 and 11 had MRS of 2. (Table 3)

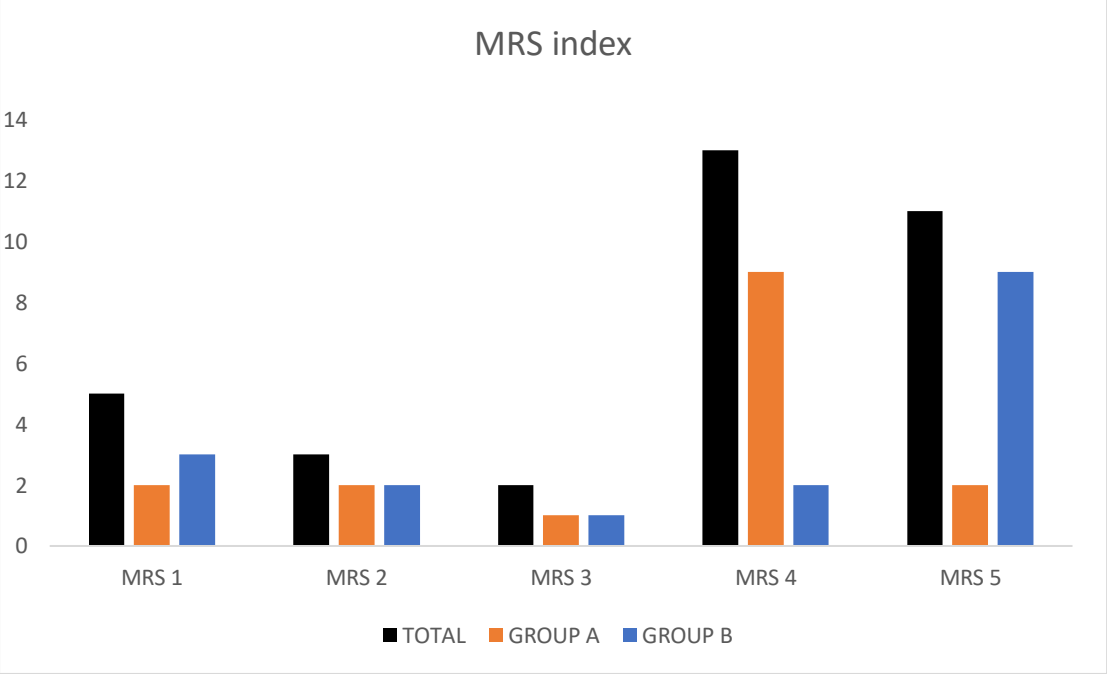
In group A out of 16 patients, 2 patients had MRS of 1, 2 patients had MRS of 2, one patient had MRS of 3, 9 had MRS of 4 and 2 had MRS of 2.

In group B out of 18 patients, 3 patients had MRS of 1, 2 patients had MRS of 2, one patient had MRS of 3, 2 had MRS of 4 and 9 had MRS of 2.

Table 3- Disability at presentation by MRS

MRS GRADE	TOTAL N=34 (%)	GROUP A N=16(%)	B GROUP B N=18(%)
MRS 1	5 (14.70%)	2 (12.5%)	3 (16.6%)
MRS 2	3 (8.82%)	2 (12.5%)	2 (11.1%)
MRS 3	2 (5.88%)	1 (6.25%)	1 (5.55)
MRS 4	13 (38.4%)	9 (56.25%)	2 (11.1%)
MRS 5	11 (32.35%)	2 (12.5%)	9 (50%)

FIGURE 7: Disability distribution as MRS



Barthel index at the time of admission

The functional independence status was assessed by BI and categorized score of 0-20 as total dependency, score of 21-60 severe dependency, score of 61-90 as moderate dependency and score between 91-100 as slight dependency.

Out of total 34 patients, 15 patients had BI between 0-20; 8 had between 21-60; 3 had between 61-90 and 4 patients had between 91-100 (Table 4).

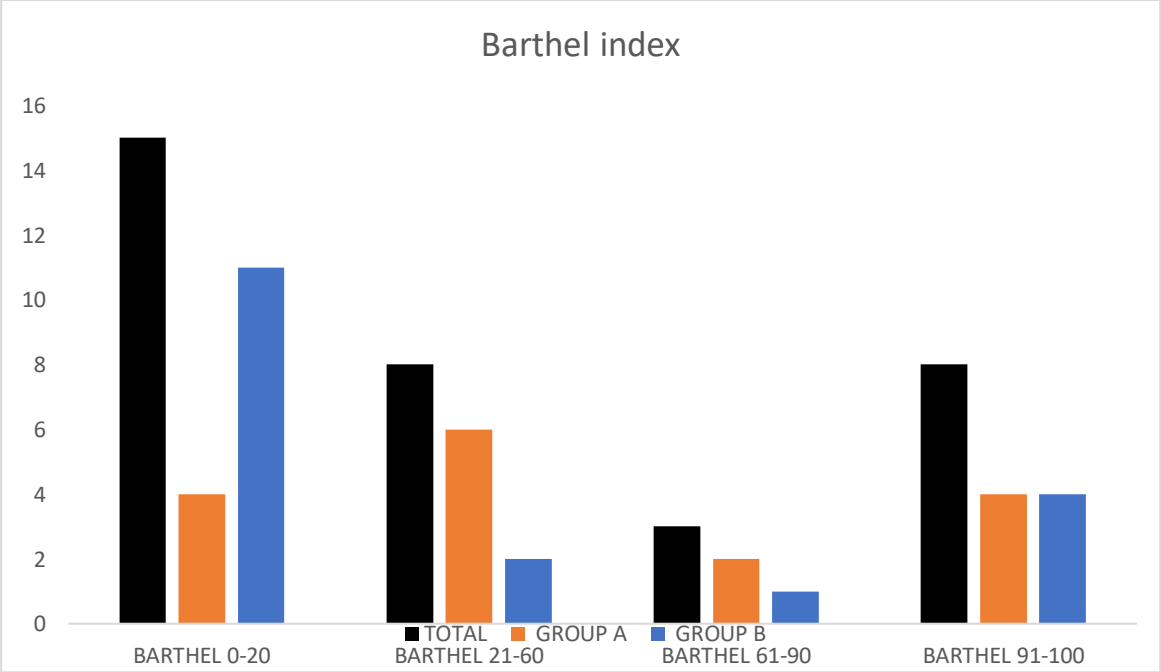
In group A out of 16 patients, 4 patients had BI between 0-20; 6 had between 21-60; 2 between 61-90 and 4 patients between 91-100.

In group B out of 18 patients, 11 patients had BI between 0-20; 2 between 61-90; one between 61-90 and 4 patients between 91-100.

Table 4: Functional independence status at presentation by BI

GRADES OF BI	TOTAL (N=34)	GROUP A (N=16)	GROUP B (N=18)
BARTHEL 0-20	15 (44.11%)	4 (25%)	11 (61.11)
BARTHEL 21-60	8 (23.18%)	6 (11.11%)	2 (11.11%)
BARTHEL 61-90	3 (8.82%)	2 (5.55%)	1 (5.55%)
BARTHEL 91-100	8 (23.18%)	4 (22.22)	4 (22.22%)

FIGURE 8: Distribution of Functional independence by using BI

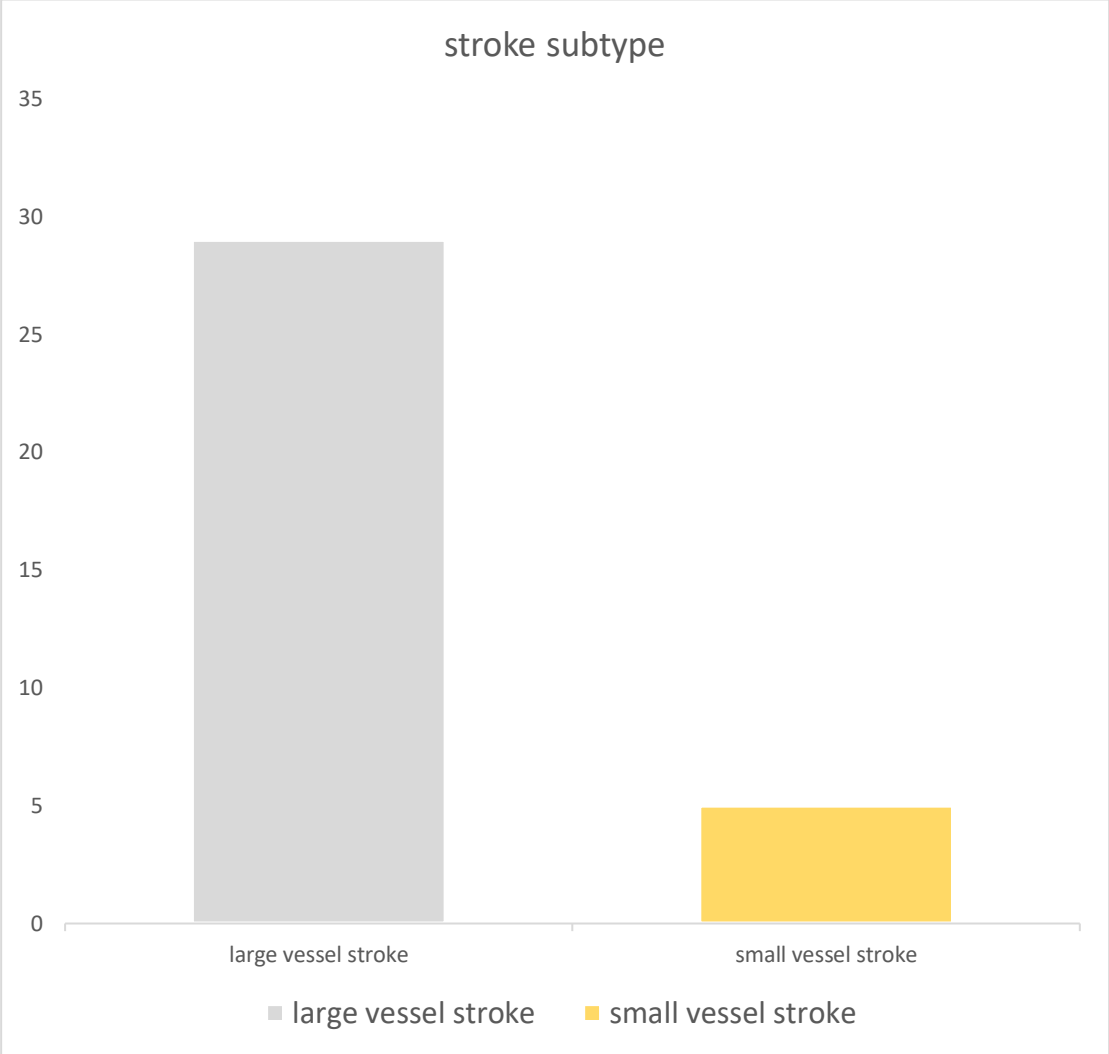


Stroke subtypes

❖ ***Large versus small vessels stroke***

Out of 34 patients, 29 patients had large vessel ischemic stroke and rest had small vessel ischemic stroke.

FIGURE 9: Distribution of large versus small vessels stroke



❖ ***Distribution of anterior vs posterior circulation stroke***

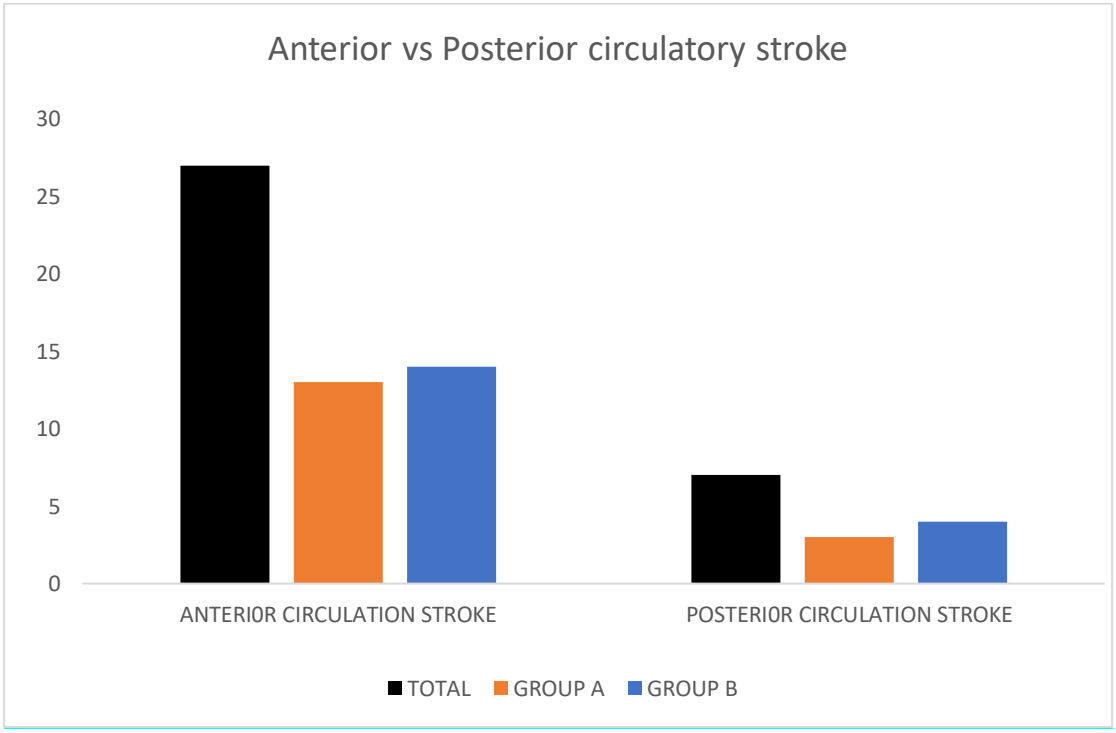
In total out of 34 patients, 27 patients had anterior circulation stroke and 7 patients had posterior circulation stroke. (Table 5)

In group A, 13 patients had anterior circulation stroke and 3 patients had posterior circulation stroke. In group B out of 18 patients, 14 patients had anterior circulation stroke and 4 patients had posterior circulation stroke.

Table 5: Distribution of anterior versus posterior circulation stroke

	TOTAL (N=34)	GROUP A (N=16)	GROUP B (N=18)
ANTERIOR CIRCULATION STROKE	27	13	14
POSTERIOR CIRCULATION STROKE	7	3	4

FIGURE 10: Distribution of anterior and posterior circulation stroke



TOAST classification of stroke

In total out of 34 patients, 15 patients had atherosclerotic large vessels disease, 10 had cardioembolic etiology, 4 had small vessel disease, 2 patients had dual etiology and in 3 patients etiology was not known. (Table 6)

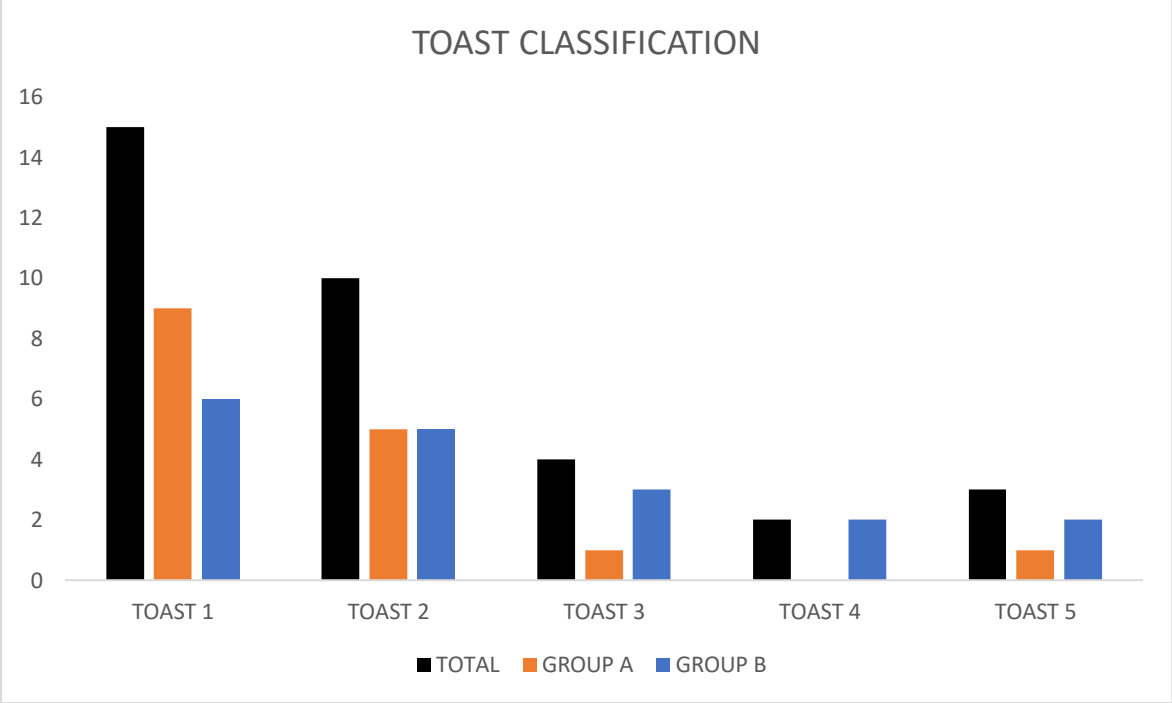
In group A, out of 16 patients: 9 patients had atherosclerotic large vessels disease, 5 had cardioembolic etiology, one had small vessel disease and in one patient etiology was not known.

In group B, out of 18 patients: 6 patients had atherosclerotic large vessels disease, 5 had cardioembolic etiology, 3 had small vessel disease 2 had mixed etiology and in 2 patients etiology was not known.

Table 6: TOAST classification

	TOTAL	GROUP A	GROUP B
TOAST 1	15 (44.11%)	9 (56.25%)	6 (33.33%)
TOAST 2	10 (29.41%)	5 (31.25%)	5 (27.77%)
TOAST 3	4 (11.76%)	1 6.25%)	3 (16.6%)
TOAST 4	2 (5.88%)	0 (0)	2 (11.1%)
TOAST 5	3(8.82%)	1 (6.25%)	2 (11.1%)

FIGURE 11: Distribution as per TOAST classification



Ictus to door time

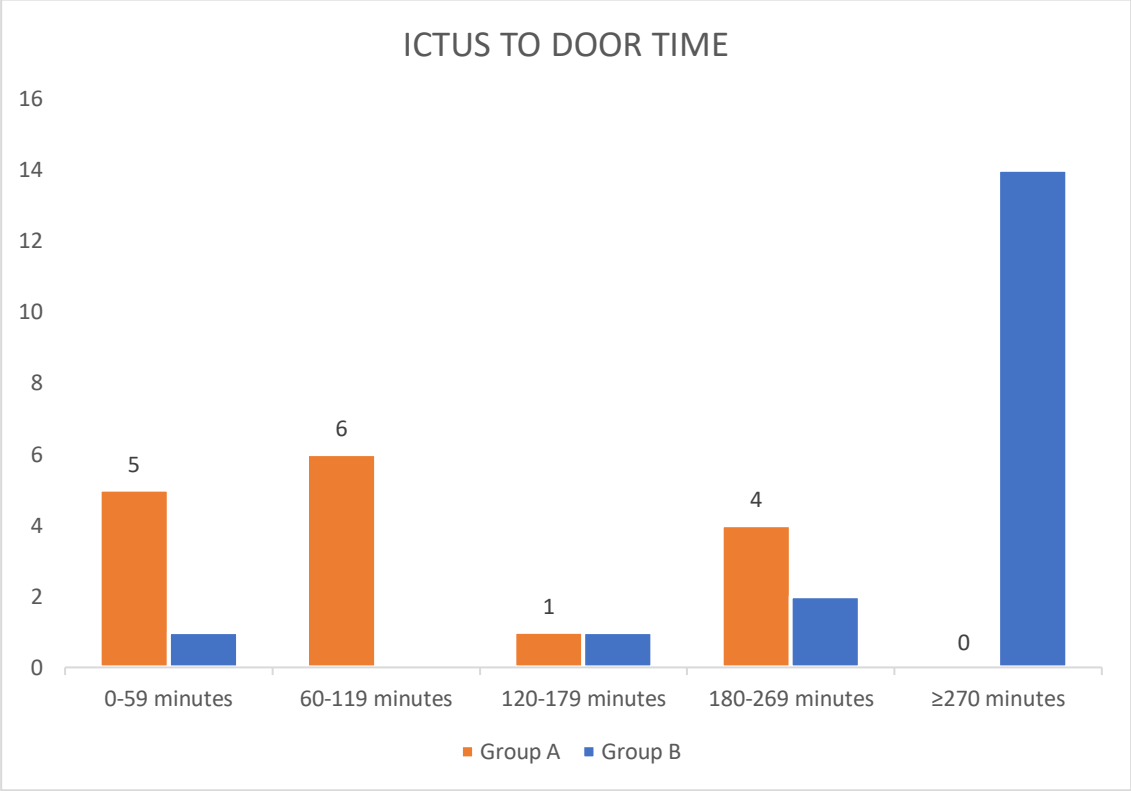
In group A out of 16 patients, five patient had ictus to door time between 0-59 minutes, 6 patients between 60-119 minutes, one patient had between 120-179 minutes and 4 patients had between 180 to 269 minutes. (Table 7).

In group B,out of 18 patients, one patient had ictus to door time between 0-59 minutes, 0 patients between 60- 119 minutes, one patient had between 120-179 minutes, 2 patients had between 180 -269 minutes and 14 patients had ≥270 minutes.

Table 7: Ictus to door time

ICTUS TO DOOR TIME	GROUP A (N=16)	GROUP B (N=18)
0-59 minutes	5	1
60-119 minutes	6	0
120- 179 minutes	1	1
180 - 269 minutes	4	2
≥270 minutes	0	14

FIGURE 12: Distribution as per ictus to door time



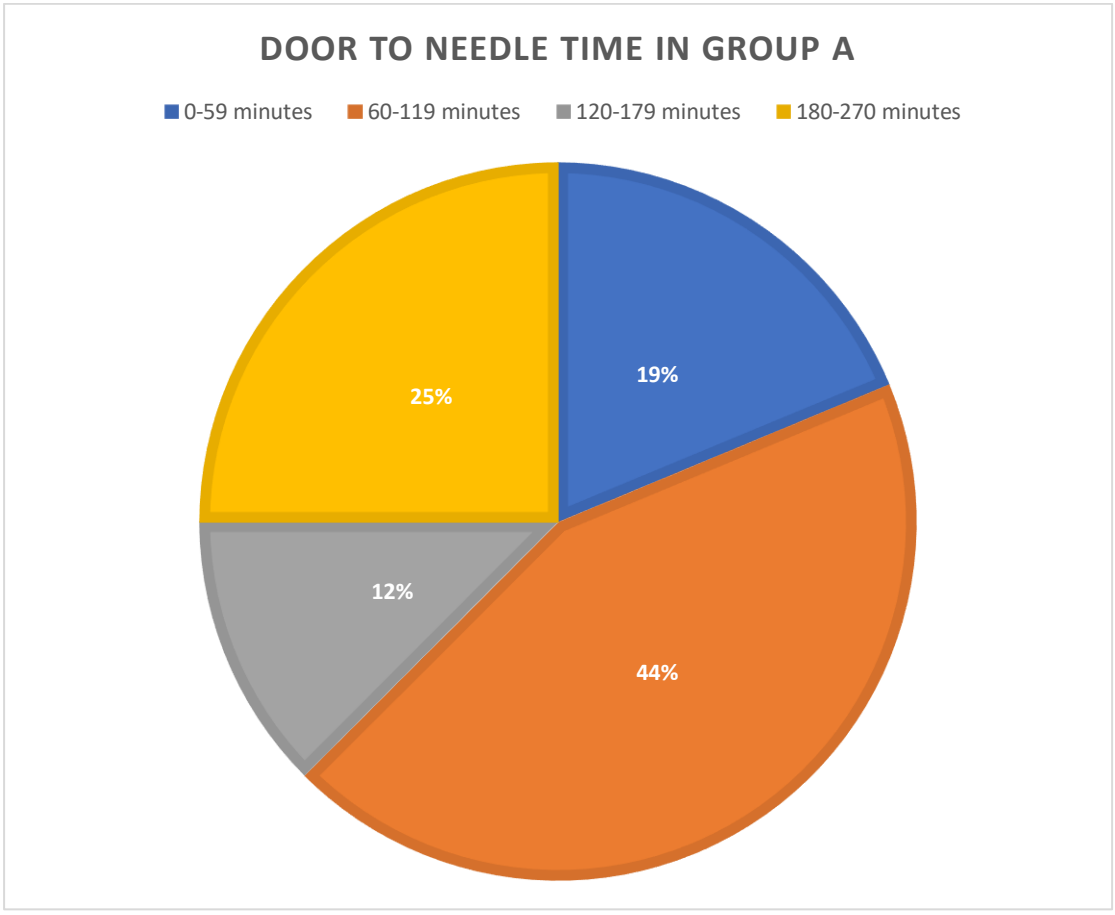
❖ ***Door to needle time***

In group A out of 16 patients, three patients had door to needle time between 0-59 minutes, 7 patients between 60- 119 minutes, 2 patients had door to needle time between 120-179 minutes and 4 had between 180-270 minutes. (Table 8)

TABLE 8: Door to needle time

Door to needle time	GROUP A (N=16)
0-59 minutes	3
60-119 minutes	7
120- 179 minutes	2
180- 270 minutes	4

FIGURE 14: Distribution as per door to needle time



Radiological characteristics

❖ ***CT severity score -ASPECTS***

In total Group, no patients had ASPECTS of 1 and 2. One patient had ASPECTS of 3, three had ASPECTS of 4, one had ASPECTS of 5, one had ASPECTS of 6 , four had ASPECTS of 7, four had ASPECTS of 8, six patients had ASPECTS of 9 and 14 patients had ASPECTS of 10.

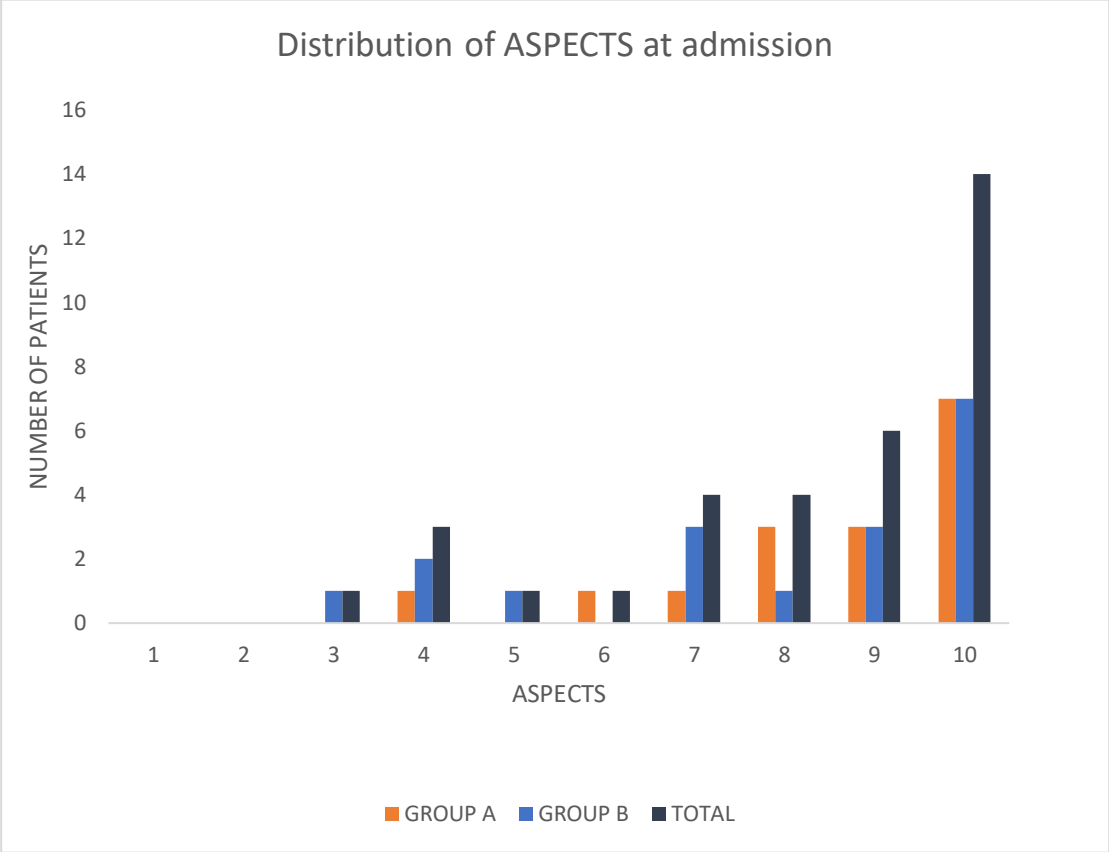
In Group A, no patients had ASPECTS of 1, 2 and 3. one had ASPECTS of 4, no patient had ASPECTS of 5, one had ASPECTS of 6 , one had ASPECTS of 7, three had ASPECTS of 8, three patients had ASPECTS of 9 and 7 patients had ASPECTS of 10.

In Group B, no patients had ASPECTS of 1 and 2. One patient had ASPECTS of 3, two had ASPECTS of 4, one had ASPECTS of 5, no patients had ASPECTS of 6 , three had ASPECTS of 7, one had ASPECTS of 8, three patients had ASPECTS of 9 and 7 patients had ASPECTS of 10.

Table 9: CT severity score – ASPECTS

ASPECTS	GROUP A (N=16)	GROUP B (N=18)	TOTAL (N=34)
1	0	0	0
2	0	0	0
3	0	1	1
4	1	2	3
5	0	1	1
6	1	0	1
7	1	3	4
8	3	1	4
9	3	3	6
10	7	7	14

FIGURE 15: Distribution as per ASPECTS



Involved artery in patients

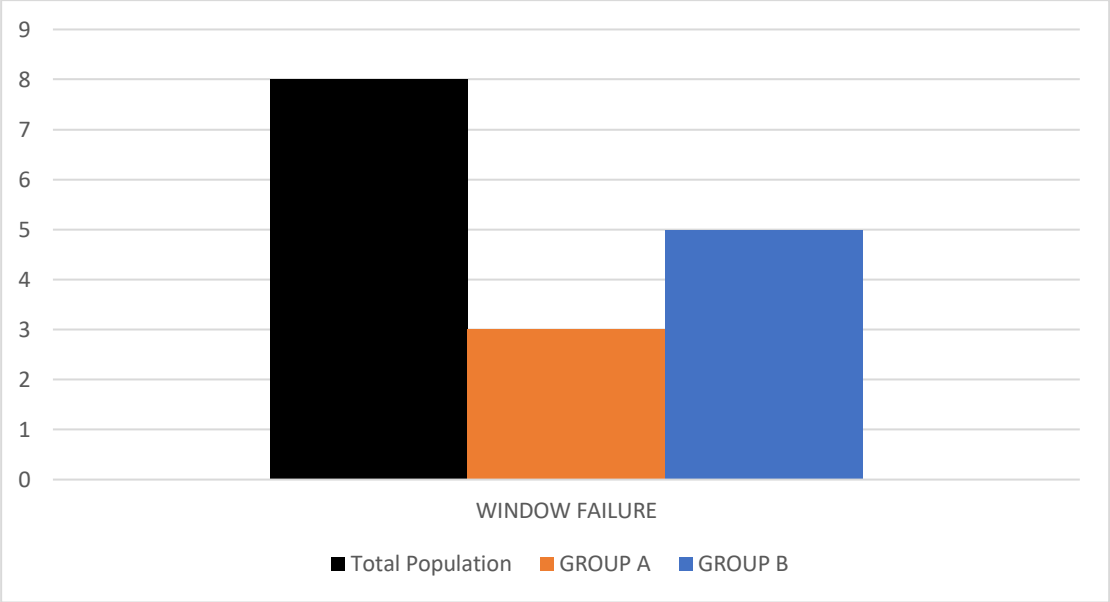
Table 10: Distribution of arterial involvement

CT ANGIOGRAPHY	Serial number of patients
LEFT VERTEBRAL	1
LEFT ICA WITH MCA	2
LEFT ICA WITH LEFT MCA	3
SMALL VESSEL DISEASE	4
SMALL VESSEL DISEASE	5
LEFT MCA	6
LEFT MCA	7
LEFT MCA	8
LEFT ICA WITH LEFT ACA	9
LEFT MCA	10
LEFT PICA	11
NON OPASIFIDED BA	12
RIGHT MCA	13
LEFT MCA	14
RIGHT ICA WITH RIGHT MCA	15
RIGHT MCA	16
RIGHT MCA	17
SMALL VESSELS DISEASE	18
LEFT MCA	19
LEFT MCA	20
LEFT MCA	21
CARDIOEMBOLIC LEFT MCA	22
LEFT SUPRACLINOID ICA ICAD	23
LEFT PCA	24
RIGHT MCA	25
SMALL VESSELS DISEASE MCA	26
LEFT MCA	27
LEFT CAROTID SOFT PLAQUE AND THROMBUS-EMBOLIC	28
MCA SMALL VESSELS	29
EMBOLIC RIGHT ACA MCA	30
LEFT ICA -MCA-ACA	31
LEFT MCA	32
ICAD ECAD WITH SVD RIGHT MCA	33
RIGHT MCA	34

Frequency of window failure in TCD

❖ Out of 34 patients, 8 (24%) patients had window failure during acquisition of flow parameters by TCD. **In Group A,** out of 16 patients, window failure was noted in 3 patients. **In group B,** out of 18 patients, window failure was noted in 5 patients.

❖ **FIGURE 16: Distribution as per Window failure**



Comparison between changes in TIBI to change in NIHSS

Change in TIBI, henceforth called Δ TIBI is the difference between the TIBI score on TCD done within 2 hours of admission to TIBI at 48 hours.

Change in NIHSS, henceforth called Δ NIHSS is the difference between the NIHSS done at admission to NIHSS done at 48 hours.

Out of 26 patients,18 patients had improvement in NIHSS scale at 48 hours when compared to baseline. Seven patients had no improvement in NIHSS and one patient had worsening of NIHSS.

Of these 26 patients, 21 patients had improvement in TIBI scoring at 48 hours compared to baseline TIBI. Four patients had static TIBI without improvement and one patient had worsening of TIBI.

Out of 21 patients with improved TIBI, 17 patients had improvement in NIHSS and 4 patients had static NIHSS.

Out of 4 patients with static (unimproved) TIBI, one patient had improvement in NIHSS and 3 had static NIHSS.

One patient with worsened TIBI had worsened NIHSS.

❖ **In Group A**, out 13 patients (3/16 had window failure), 10 patients had improvement in NIHSS scale at 48 hours when compared to baseline. Two patients had no improvement in NIHSS and one patient had worsening of NIHSS.

Of these 13 patients, 10 patients had improvement in TIBI scoring at 48 hours compared to baseline TIBI. Two patients had static TIBI without improvement and one patient had worsening of TIBI.

Out of 10 patients with improved TIBI, nine patients had improvement in NIHSS and one patient had static NIHSS.

Out of 2 patients with static TIBI, one patient had improvement in NIHSS and one had static NIHSS.

One patient with worsened TIBI had worsened NIHSS.

❖ **In group B,** out of 13 patients (3/18 had window failure), 8 patients had improvement in NIHSS scale at 48 hours when compared to baseline. Five patients had no improvement in NIHSS.

Out of these 13 patients, 11 patients had improvement in TIBI grade when compared to baseline. Two patients had static TIBI without improvement.

Out of 11 patients with improved TIBI, 8 patients had improvement in NIHSS and 3 patients had static NIHSS.

Out of 2 patients with static TIBI, 2 patients had static NIHSS.

TABLE 11: Comparison between change in TIBI to change in NIHSS at 48 hours

Comparison in total patients at 48 hours				
	Number of patients showing TIBI improvement	Number of patients with abnormal TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in NIHSS	17	1	0	18
Number of patients without improvement in NIHSS	4	3	0	7
Number of patients with worsening of NIHSS	0	0	1	1
Comparison in GROUP A at 48 hours				
Number of patients showing improvement in NIHSS	9	1	0	10
Number of patients without improvement in NIHSS	1	1	0	2
Number of patients with worsening of NIHSS	0	0	1	1
Comparison between in GROUP B at 48 hours				
Number of patients showing improvement in NIHSS		0	0	8
Number of patients without improvement in NIHSS		2	0	5
Number of patients with worsening of NIHSS		0	0	0

❖ Therefore, on assessing the correlation between improvement in TIBI and NIHSS, in total population of 21 patients with improved TIBI, 17 patients had improvement in NIHSS: (TABLE 11 A). Out of 5 patients with worsened TIBI, 4 patients had no improvement in NIHSS.

❖ Similarly, in Group A out of 10 patients with improved TIBI, 9 patients had improvement in NIHSS (TABLE 11 B). Out of 3 patients with worsened TIBI, 2 patients had no improvement in NIHSS.

❖ In Group B out of 11 patients with improved TIBI, 8 patients had improvement in NIHSS (TABLE 11 C). Out of 2 patients with worsened TIBI, 2 patients had no improvement in NIHSS.

TABLE 11 A

TOTAL POPULATION	**IMPROVEMENT IN NIHSS**	**NO IMPROVEMENT NIHSS**	**P = 0.019 (S)**
IMPROVEMENT IN TIBI	17	4	
NO IMPROVEMENT IN TIBI	1	4	

TABLE 11 B

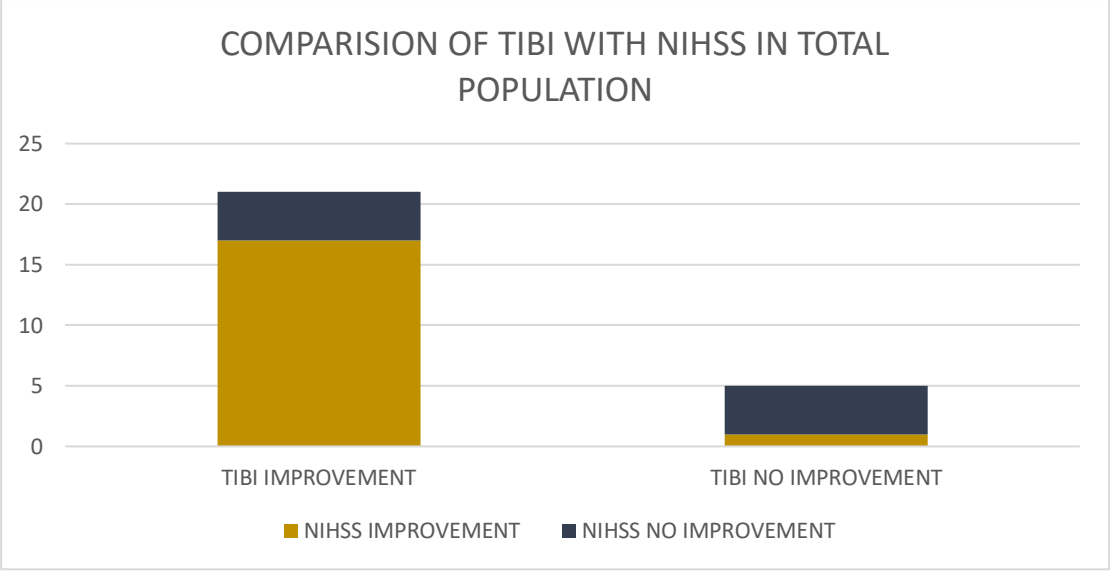
GROUP A	**IMPROVEMENT IN NIHSS**	**NO IMPROVEMENT NIHSS**	**P = 0.1048 (NS)**
IMPROVEMENT IN TIBI	9	1	
NO IMPROVEMENT IN TIBI	1	2	

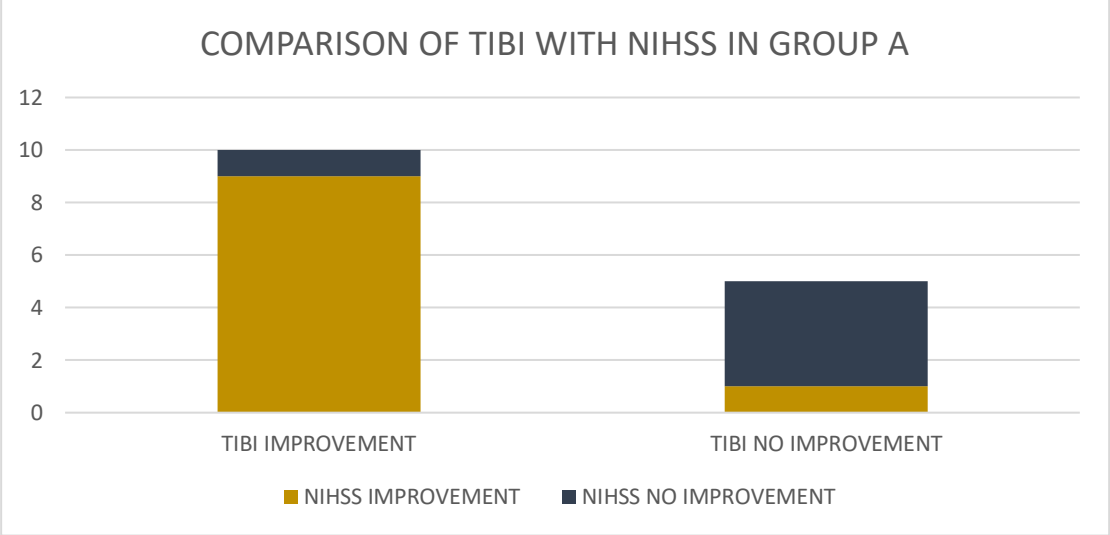
TABLE 11 C

GROUP B	**IMPROVEMENT IN NIHSS**	**NO IMPROVEMENT NIHSS**	**P = 0.1282 (NS)**
IMPROVEMENT IN TIBI	8	3	
NO IMPROVEMENT IN TIBI	0	2	

Level of significance P = < 0.05

S- significant NS- not significant





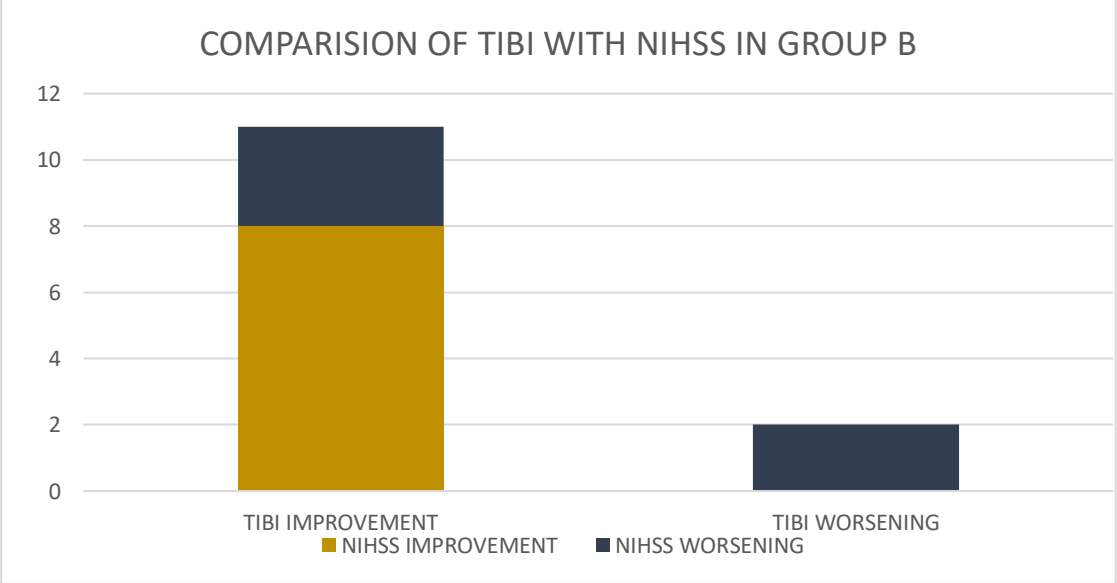


FIGURE 17: Comparison between change in TIBI to change in NIHSS at 48 hours

Comparison between changes in TIBI to changes in MRS at 48 hours

Changes in MRS denoted as Δ MRS is the difference between the MRS done at admission to MRS done at 48 hours.

❖ **In total** out of 26 patients without window failure, 11 patients had improvement in MRS at 48 hours when compared to baseline (Table 12). Fourteen patients had no improvement in MRS and one patient had worsening of MRS.

Out of 21 patients with improved TIBI, 10 patients had improvement in MRS and 11 patients had static MRS.

Out of 4 patients with static TIBI, one patient had improvement in MRS and 2 had static MRS and onepatient had worsened MRS.

One patient with worsened TIBI had static MRS.

❖ **In Group A**, out of 13 patients, 6 patients had improvement in MRS scale at 48 hours when compared to baseline. Six patients had no improvement in MRS and one patient had worsening of MRS.

Out of the 10 patients with improved TIBI, 5 patients had improvement in MRS and 5 patients had static MRS.

Out of 2 patients with static TIBI, one patient had improvement in MRS and onepatient had worsened MRS. One patient with worsened TIBI had static MRS.

❖ **In group B,** out of 13 patients, 5 patients had improvement in MRS scale at 48 hours when compared to baseline. Eight patients had no improvement in MRS.

Out of 11 patients with improved TIBI, 5 patients had improvement in MRS and 6 patients had static MRS.

Out of 2 patients with static TIBI, 2 patients had static MRS.

❖ Therefore, on assessing the correlation between improvement in TIBI and MRS at 48 hours, in the total populationout of 21 patients with improved TIBI, 10 patients had improvement in MRS (TABLE 12 A).Out of 5 patients with worsened TIBI, 4 patients had no improvement in MRS.

❖ In Group A out of 10 patients with improved TIBI, 5 patients had improvement in MRS (TABLE 12 B).Out of 3 patients with worsened TIBI, 2 patients had no improvement in MRS.

❖ In Group B out of 11 patients with improved TIBI, 5 patients had improvement in MRS (TABLE 12 C).Out of 2 patients with worsened TIBI, 2 patients had no improvement in MRS.

TABLE 12: Comparison between change in TIBI to change in MRS at 48 hours

Comparison in total patients at 48 hours				
Parameters	Number of patients showing TIBI improvement	Number of patients with TIBI static	Number of patients with TIBI worsening	Total
Number of patients showing improvement in MRS	10	1	0	11
Number of patients without improvement in MRS	11	2	1	14
Number of patients with worsening of MRS	0	1	0	1
Comparison in GROUP A at 48 hours				
Number of patients showing improvement in MRS	5	1	0	6
Number of patients without improvement in MRS	5	0	1	6
Number of patients showing with worsening of MRS	0	1	0	1
Comparison in GROUP B at 48 hours				
Number of patients showing improvement in MRS	5	0	0	5
Number of patients without improvement in MRS	6	2	0	8
Number of patients with worsening of MRS	0	0	0	0

TABLE 12 A:

Parameters in TOTAL group	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.2282 (NS)
IMPROVEMENT IN TIBI	10	11	
NO IMPROVEMENT IN TIBI	1	4	

TABLE 12 B:

Parameters in GROUP A	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.4405 (NS)
IMPROVEMENT IN TIBI	5	5	
NO IMPROVEMENT IN TIBI	1	2	

TABLE 12 C:

Parameters in GROUP B	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.3589 (NS)
IMPROVEMENT IN TIBI	5	6	
NO IMPROVEMENT IN TIBI	0	2	

Level of significance P = < 0.05

S- significant NS- not significant

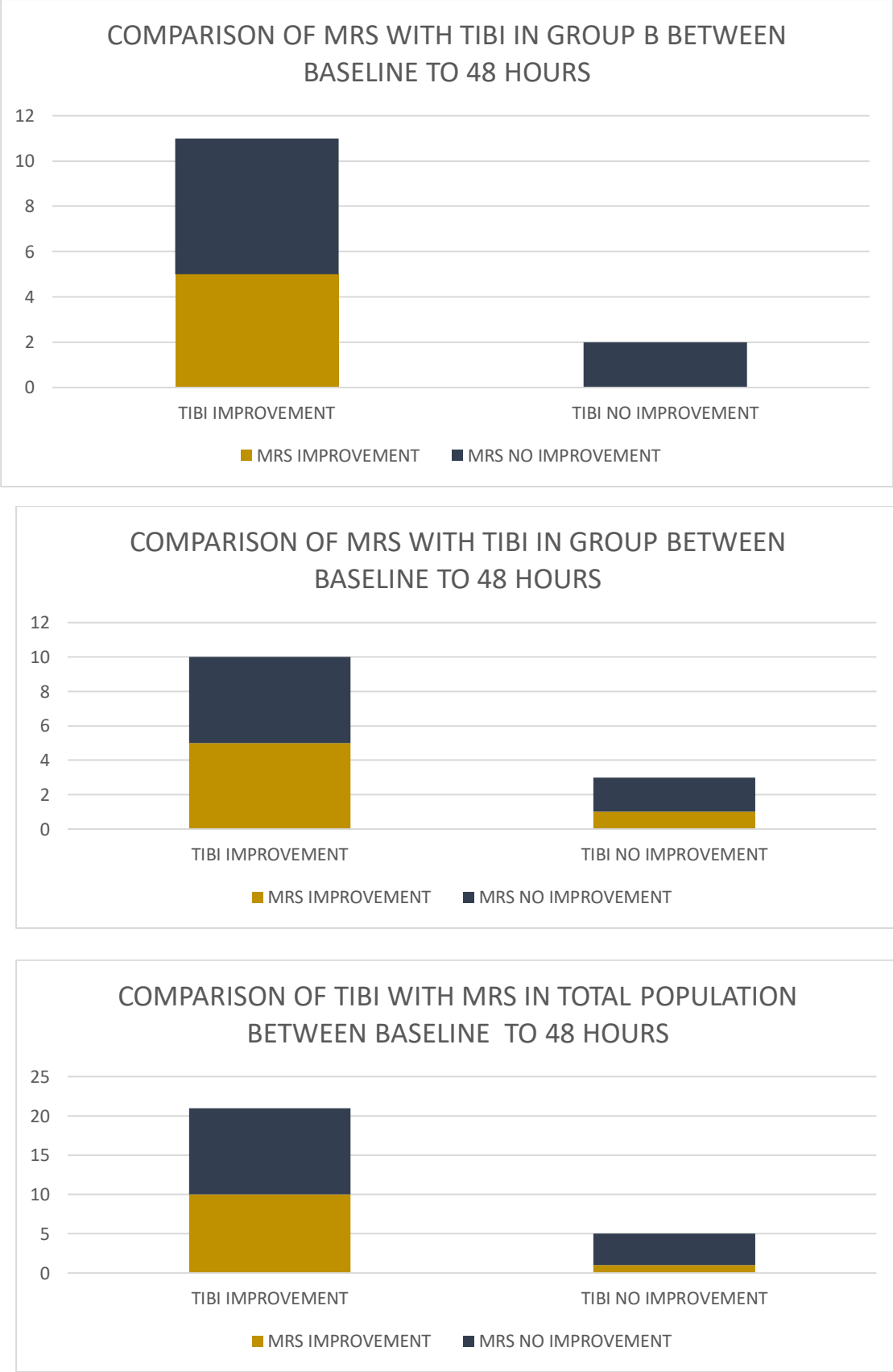


FIGURE 18: Comparison between change in TIBI to change in MRS at 48 hours

Comparison between changes in TIBI to changes in MRS at 30 days

Delta TIBI defined as -Δ TIBI = baseline TIBI between 2 hours of admission – TIBI at 48 hours)

Delta MRS defined as -Δ MRS = baseline MRS at the time of admission- MRS at 30 days)

❖ **In total** of 26 patients, 19 patients had improvement in MRS at 30 days when compared to baseline. Seven patients had no improvement in MRS and 0 patient had worsening of MRS (Table 13).

Out of the 21 patients with improved TIBI, 17 patients had improvement in MRS and 4 had static MRS. Out of 4 patients with static TIBI, 2 patients had improvement in MRS and 2 had static MRS. One patient with worsened TIBI had static MRS.

❖ **In Group A**, out of 13 patients, 10 patients had improvement in MRS scale at 30 days when compared to baseline. Three patients had no improvement in MRS and none had worsening of MRS.

Out of the 10 patients with improved TIBI, 9 patients had improvement in MRS and one patient had static MRS. Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS. One patient with worsened TIBI had static MRS.

❖ **In group B,** out of 13 patients, 9 patients had improvement in MRS scale at 30 days when compared to baseline. Four patients had no improvement in MRS.

Out of the 11 patients with improved TIBI, 8 patients had improvement in MRS and 3 patients had static MRS.Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS.

❖ Thus, in the total of 21 patients with improved TIBI, 17 patients had improvement in MRS (TABLE 13 A).Out of 5 patients with worsened TIBI, 3 patients had no improvement in MRS.

❖ **In Group A**

of 10 patients with improved TIBI, 9 patients had improvement in MRS (TABLE 13 B).Out of 3 patients with worsened TIBI, 2 patients had no improvement in MRS.

In Group B of 11 patients with improved TIBI, 8 patients had improvement in MRS (TABLE 13 C).Out of 2 patients with worsened TIBI, 2 patients had no improvement in MRS.

TABLE 13: Comparison between change in TIBI to change in MRS at baseline to 30 days

Comparison between Delta TIBI to Delta MRS in total patients (Baseline within 2 hours of admission -30 days)				
	Number of patients showing TIBI improvement	Number of patients with abnormal TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in MRS	17	2	0	19
Number of patients without improvement in MRS	4	2	1	7
Number of patients with worsening of MRS	0	0	0	0
Comparison between Delta TIBI to Delta MRS in GROUP A (Baseline within 2 hours of admission -30 days)				
Number of patients showing improvement in MRS	9	1	0	10
Number of patients without improvement in MRS	1	1	1	3
Number of patients with worsening of MRS	0	0	0	0
Comparison between Delta TIBI to Delta MRS in GROUP B (Baseline within 2 hours of admission -30 days)				
Number of patients showing improvement in MRS	8	1	0	9
Number of patients without improvement in MRS	3	1	0	4
Number of patients with worsening of MRS	0	0	0	0

TABLE 13 A:

Parameters in Total group	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	**P = 0.09** (NS)
IMPROVEMENT IN TIBI	17	4	
NO IMPROVEMENT IN TIBI	2	3	

TABLE 13 B:

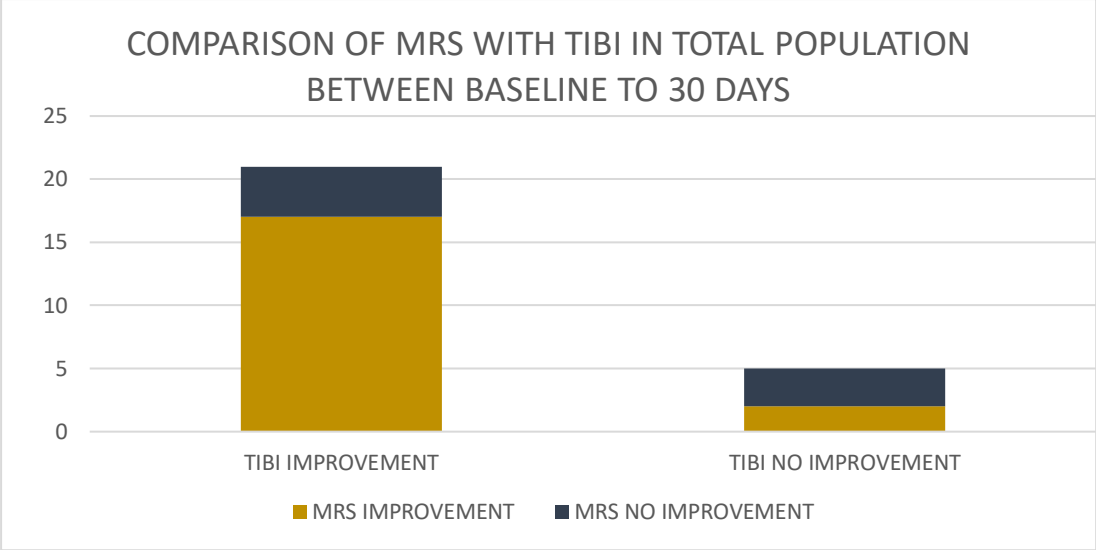
Parameters in GROUP A	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.10 (NS)
IMPROVEMENT IN TIBI	9	1	
NO IMPROVEMENT IN TIBI	1	2	

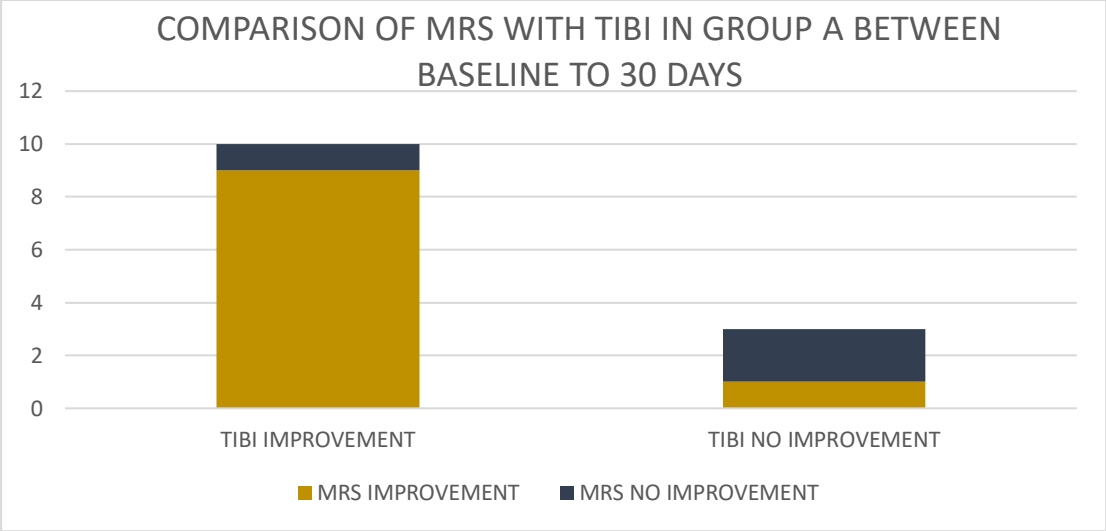
TABLE 13 C

Parameters in GROUP B	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.461 (NS)
IMPROVEMENT IN TIBI	8	3	
NO IMPROVEMENT IN TIBI	1	2	

Level of significance P = < 0.05

S- significant NS- not significant





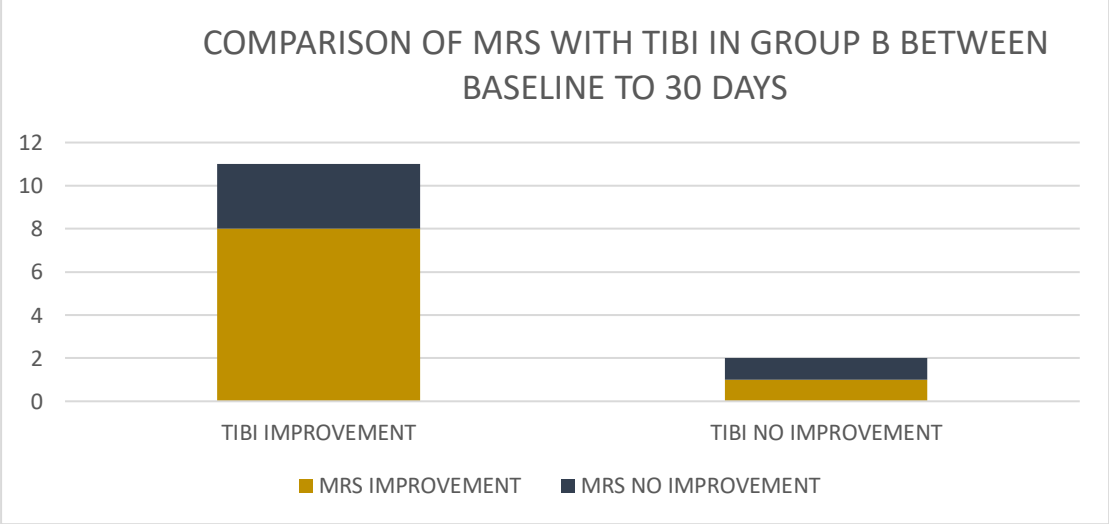


FIGURE 19: Comparison between change in TIBI to change in MRS at baseline to 30 days

Comparison between change in TIBI with change in MRS between second day to 30 days

Delta TIBI i.e., Δ TIBI = baseline TIBI between 2 hours of admission – TIBI at 48 hours

Delta MRS i.e., Δ MRS = MRS on day 2- MRS at 30 days)

❖ **In total** of 26 patients, 12 patients had improvement in MRS at 30 days when compared to MRS at 2nd day (Table 14). Fourteen patients had no improvement in MRS and none had worsening of MRS.

Out of the 21 patients with improved TIBI, 10 patients had improvement in MRS and 11 patients had static MRS. Out of the 4 patients with static TIBI, 2 patients had improvement in MRS and 2 had static MRS. One patient with worsened TIBI had static MRS.

❖ **In Group A**, of 13 patients, 7 patients had improvement in MRS scale at 30 days when compared to MRS at 2nd days. Six patients had no improvement in MRS and none had worsening of MRS.

Out of the 10 patients with improved TIBI, 6 patients had improvement in MRS and 4 patient had static MRS. Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS. One patient with worsened TIBI had static MRS

❖ **In group B,** of 13 patients, 5 patients had improvement in MRS scale at 30 days when compared to MRS at 2nd day. Eight patients had no improvement in MRS.

Out of the 11 patients with improved TIBI, 4 patients had improvement in MRS and 7 patients had static MRS. Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS.

TABLE 14: Comparison between change in TIBI to change in MRS between 2 to 30 days

Comparison between Delta TIBI to Delta MRS in total patients (48 hours -30 days)				
Parameters	Number of patients with TIBI improvement	Number of patients with abnormal TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in MRS	10	2	0	12
Number of patients without improvement in MRS	11	2	1	14
Number of patients with worsening of MRS	0	0	0	0
Comparison between Delta TIBI to Delta MRS in GROUP A (48 hours -30 days)				
Number of patients showing improvement in MRS	6	1	0	7
Number of patients without improvement in MRS	4	1	1	6
Number of patients with worsening of MRS	0	0	0	0
Comparison between Delta TIBI to Delta MRS in GROUP B (48 hours -30 days)				
Number of patients showing improvement in MRS	4	1	0	5
Number of patients without improvement in MRS	7	1	0	8
Number of patients with worsening of MRS	0	0	0	0

Comparison between change in TIBI with change in MRS between baseline to 90 days.

Delta TIBI i.e., Δ TIBI = baseline TIBI between 2 hours of admission – TIBI at 48 hours.

Delta MRS i.e., Δ MRS = baseline MRS at the admission - MRS at 90 days

❖ **In total** out of 26 patients, 21 patients had improvement in MRS at 90 Days when compared to baseline (Table 15). Three patients had no improvement in MRS and 2 patients had worsening of MRS.

Out of the 21 patients with improved TIBI, 18 patients had improvement in MRS and 3 patients had static MRS. Out of the 4 patients with static TIBI, 3 patients had improvement in MRS and one had worsened MRS. One patient with worsened TIBI had worsened MRS.

❖ **In Group A**, of 13 patients, 11 patients had improvement in MRS scale at 90 days when compared to baseline. One patient had no improvement in MRS while one had worsening of MRS.

Out of the 10 patients with improved TIBI, 9 patients had improvement in MRS and one patient had static MRS.

Of the 2 patients with static TIBI, both had improvement in MRS. One patient with worsened TIBI had worsened MRS.

❖ **In group B,** out of 13 patients, 10 patients had improvement in MRS scale at 90 days when compared to baseline. Two patients had no improvement in MRS and one had worsening of MRS.

Of the 11 patients with improved TIBI, 9 patients had improvement in MRS and 2 had static MRS.

Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS.

❖ Analysing the correlation between change in TIBI and Δ MRS (0-90 days), of the total 21 patients with improved TIBI, 18 patients had improvement in MRS (TABLE 15A). Out of 5 patients with worsened TIBI, 2 patients had no improvement in MRS.

❖ In Group A, of the 10 patients with improved TIBI, 9 patients had improvement in MRS (TABLE 15 B). Out of 3 patients with worsened TIBI, 1 patient had no improvement in MRS.

❖ In Group B, out of 11 patients with improved TIBI, 9 patients had improvement in MRS (TABLE 15 C). Of the 2 patients with worsened TIBI, one patient had no improvement in MRS.

TABLE 15: Comparison between change in TIBI to change in MRS between 0 to 90 days

Comparison between Delta TIBI to Delta MRS in total population (at admission -90 days)				
Parameters	Number of patients showing TIBI improvement	Number of patients with static TIBI	Number of patients with TIBI worsening	Total
Number of patients showing improvement in MRS	18	3	0	21
Number of patients without improvement in MRS	3	0	0	3
Number of patients with worsening of MRS	0	1	1	2
Comparison between Delta TIBI to Delta MRS in GROUP A (at admission -90 days)				
Number of patients showing improvement in MRS	9	2	0	11
Number of patients without improvement in MRS	1	0	0	1
Number of patients with worsening of MRS	0	0	1	1
Comparison between Delta TIBI to Delta MRS in GROUP B (at admission -90 days)				
Number of patients showing improvement in MRS	9	1	0	10
Number of patients without improvement in MRS	2	0	0	2
Number of patients with worsening of MRS	0	1	0	1

TABLE 15 A:

Parameters in Total group	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.2021 (NS)
IMPROVEMENT IN TIBI	18	3	
NO IMPROVEMENT IN TIBI	3	2	

TABLE 15 B:

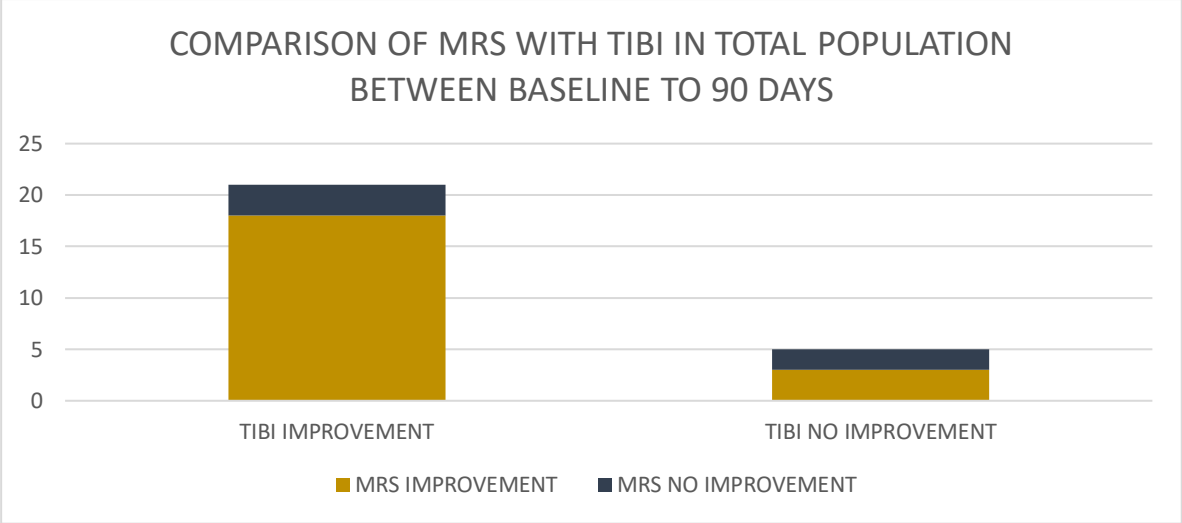
Parameters in GROUP A	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.3846 (NS)
IMPROVEMENT IN TIBI	9	1	
NO IMPROVEMENT IN TIBI	2	1	

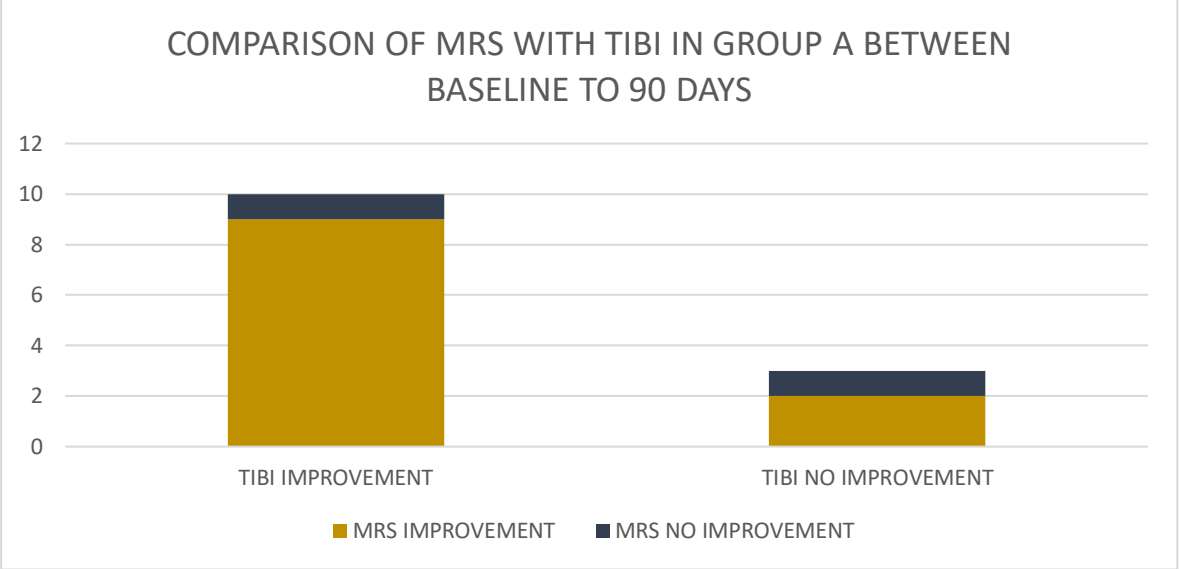
TABLE 15 C:

Parameters in GROUP B	IMPROVEMENT IN MRS	NO IMPROVEMENT MRS	P = 0.3846 (NS)
IMPROVEMENT IN TIBI	9	2	
NO IMPROVEMENT IN TIBI	1	1	

Level of significance P = < 0.05

S- significant NS- not significant





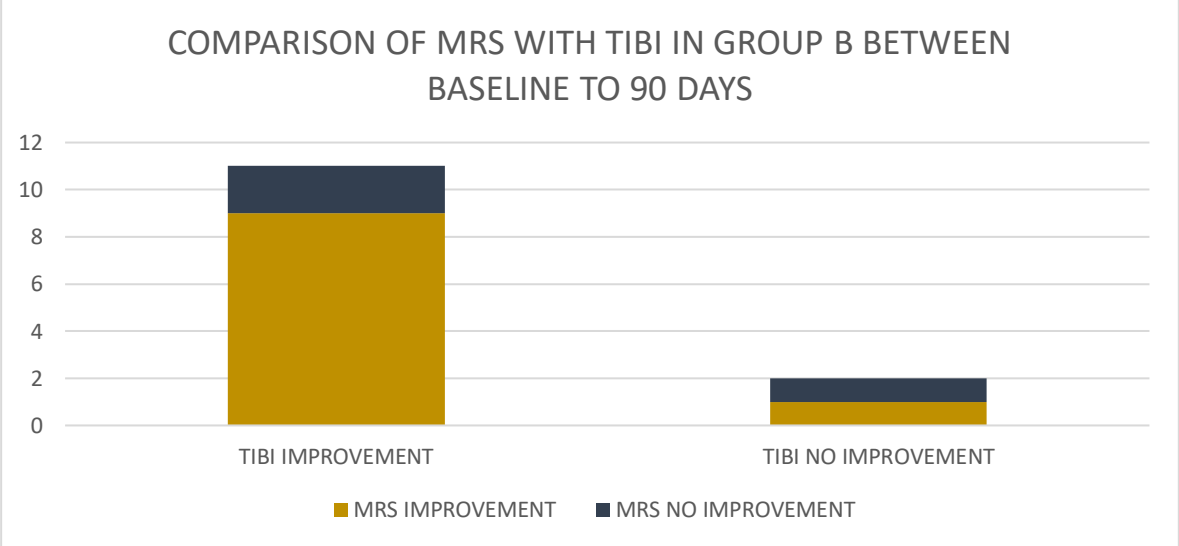


FIGURE 20: Comparison between change in TIBI to change in MRS between 2 to 30 days

Comparison between changes in TIBI with changes in MRS between 30 to 90 days

Delta TIBI i.e. Δ TIBI = baseline TIBI between 2 hours of admission – TIBI at 48 hours.

Delta MRS i.e.Δ MRS = MRS at 30 days - MRS at 90 days

- **In total** of 26 patients, 8 patients had improvement in MRS at 90 days when compared to MRS at 30 days (Table 16). Sixteen patients had no improvement in MRS and 2 patients had worsening of MRS.

  Out of the 21 patients with improved TIBI, 7 patients had improvement in MRS and 14 patients had static MRS. Of the 4 patients with static TIBI, one patient had improvement in MRS, 2 had static MRS and one had worsened MRS. One patient with worsened TIBI had static MRS.

- **In Group A**, out of 13 patients, 4 patients had improvement in MRS scale at 90 days when compared to MRS at 30 days. Eight patients had no improvement in MRS and one patient had worsening of MRS.

  Of the 10 patients with improved TIBI, 3 patients had improvement in MRS and 7 patients had static MRS. Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS. One patient with worsened TIBI had worsened MRS.

- **In group B,** of 13 patients, 4 patients had improvement in MRS scale at 90 days when compared to MRS at 30 days. Four patients had no improvement in MRS while one had worsening of MRS.

  Of the 11 patients with improved TIBI, 4 patients had improvement in MRS and 7 patients had static MRS. Out of the 2 patients with static TIBI, one patient had improvement in MRS and one had static MRS.

TABLE 16: Comparison between change in TIBI to change in MRS between 30 to 90 days

Comparison between Delta TIBI to Delta MRS in total patients (at 30 days -90 days)				
Parameters	Number of patients showing TIBI improvement	Number of patients with abnormal TIBI but without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in MRS	7	1	0	8
Number of patients without improvement in MRS	14	2	0	16
Number of patients with worsening of MRS	0	1	1	2
Comparison between Delta TIBI to Delta MRS in GROUP A (at 30 days -90 days)				
Number of patients showing improvement in MRS	3	1	0	4
Number of patients without improvement in MRS	7	1	0	8
Number of patients with worsening of MRS	0	0	1	1
Comparison between Delta TIBI to Delta MRS in GROUP B (30 -90 days)				
Number of patients showing improvement in MRS	4	0	0	4
Number of patients without improvement in MRS	7	1	0	8
Number of patients with worsening of MRS	0	1	0	1

Comparison of improvement in MRS over different time intervals in patients with TIBI improvement at 48 hours

❖ In the total 21 patients with improved TIBI, 18 (90%) patients showed MRS improvement compared to baseline (TABLE 17, 18).

❖ Ten patients showed improvement in MRS between baseline to 48 hours,

Ten patients showed improvement in MRS between 2-30 days. Of these, 7 patients had first time improvement between 2 to 30 days while 3 patients had further improvement in MRS.

Between 30 -90 days, 7 patients had improvement in MRS (one patient for first time and 6 had further improvement).

❖ In GROUP A, 9/10 patients with improved TIBI (90%) showed MRS improvement compared to baseline (TABLE 17, 18).

Five patients showed improvement in MRS between baseline to 48 hours.

Six patients showed improvement in MRS between 2-30 days. Of these, 4 patients had first time improvement between 2 to 30 days while 2 patients had further improvement in MRS.

Between 30 -90 days, 3 patients showed improvement in MRS (all three patients had further improvement in MRS which was started earlier).

❖ In GROUP B, 9/11 patients with improved TIBI (81.81%) showed MRS improvement compared to baseline (TABLE 17,18).

Five patients showed improvement in MRS between baseline to 48 hours.

Four patients showed improvement in MRS between 2-30 days. All 4 Patients had first time improvement in MRS.

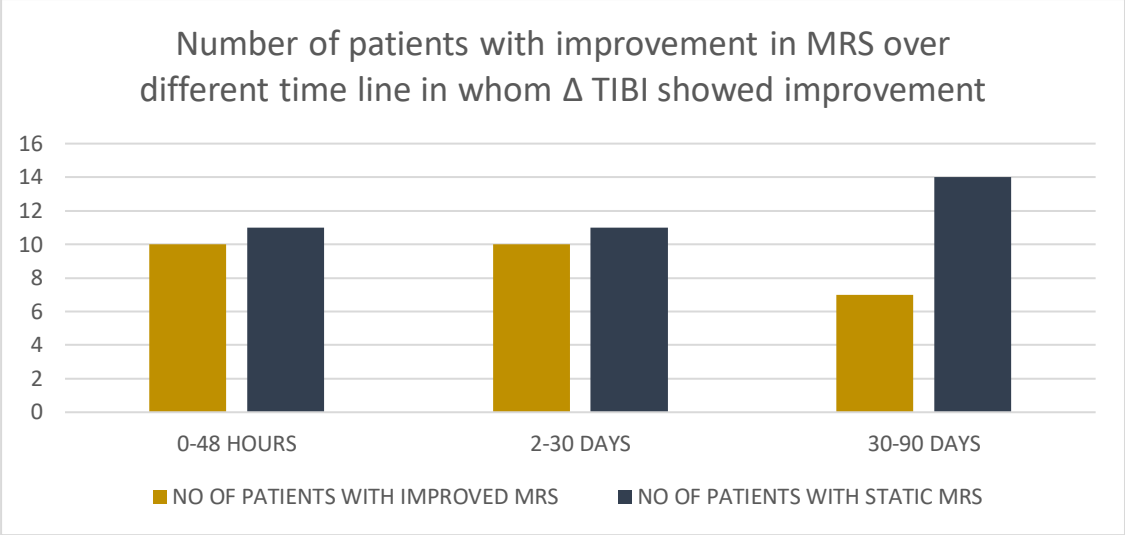
Between 30 -90 days, one patient had first time improvement in MRS and three patients had further improvement in MRS which was started earlier.

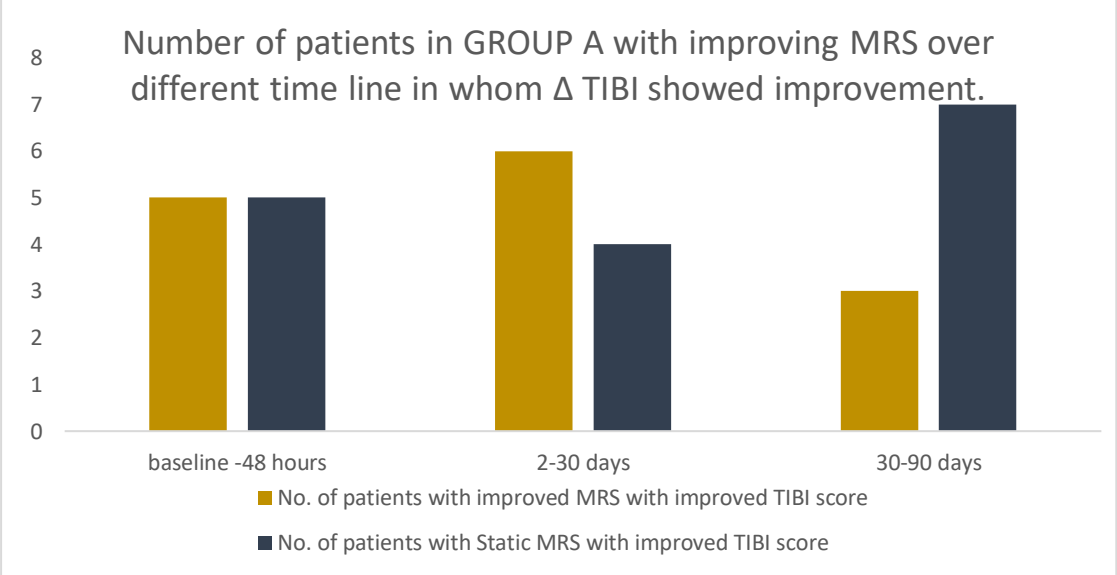
TABLE 17: Distribution of patients with improvement in MRS over different time intervals in those with TIBI improvement at 48 hours

	Number of patients showing 1st time improvement in MRS			Number of patients showing further improvement in MRS		
	TOTAL (N=21)	GROUP A (N=10)	GROUP B (N=11)	TOTAL (N=21)	GROUP A (N=10)	GROUP B (N=11)
BASELINE -48 HOURS	10	5	5	0	0	0
2-30 DAYS	7	4	3	3	2	1
30-90 DAYS	1	0	1	6	3	3

TABLE 18: Distribution of patients with cumulative improvement in MRS over different time intervals in those with TIBI improvement at 48 hours

	Number of patients showing cumulative improvement in TOTAL population	Number of patients showing cumulative improvement in MRS in GROUP A	Number of patients showing cumulative improvement in MRS in GROUP B
BASELINE -48 HOURS	10	5	5
2-30 DAYS	10	6	4
30-90 DAYS	7	3	4





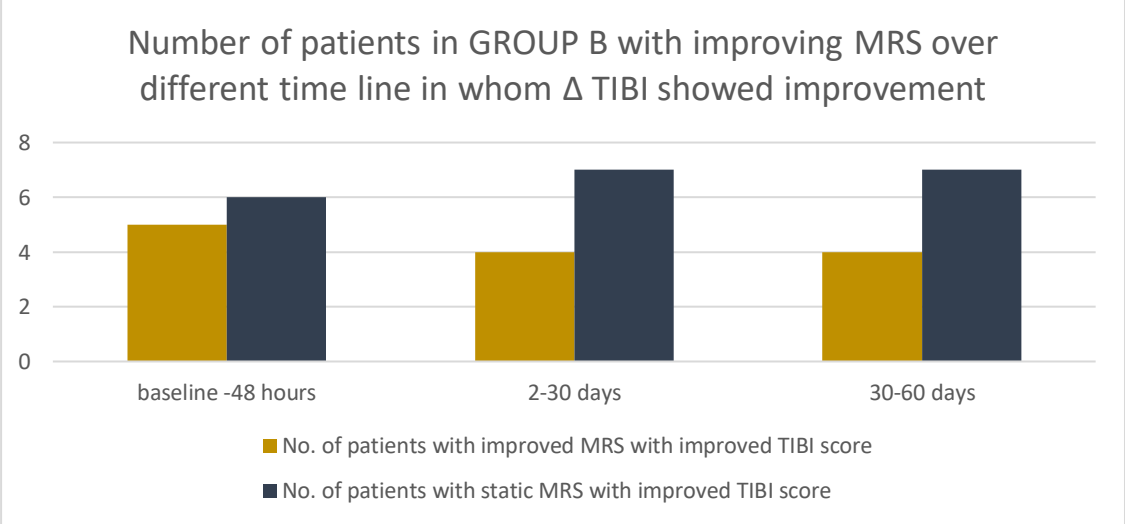


FIGURE 21: Distribution of patients with improvement in MRS over different time intervals in those with TIBI improvement at 48 hours

Comparison between change in TIBI to change in BI at 48 hours

Change in BI i.e. Δ BI = BI at admission- BI at 48 hours

Out of **total** of 26 patients, 13 patients had improvement in BI score at 48 hours when compared to baseline (Table 19). Twelve patients had no improvement and one had worsening of BI score.

Out of the 21 patients with improved TIBI, 12 patients had improvement in BI score and 9 had static BI score.

Out of the 4 patients with static TIBI, one patient had improvement in BI score, 2 had static BI and one patient had worsened score.

One patient with worsened TIBI had static BI score.

❖ **In Group A**, out 13 patients, 7 patients had improvement in BI score at 48 hours when compared to baseline. Five patients had no improvement and one had worsening of BI score.

Out of the 10 patients with improved TIBI, 6 patients had improvement in BI score and in 4 it remained static. BARTHEL score and one had worsened BI score.

One patient with worsened TIBI had static BI score.

❖ **In group B,** out of 13 patients, 6 patients had improvement in BI score at 48 hours when compared to baseline. Seven patients had no improvement in BI score.

Out of the 11 patients with improved TIBI, 6 patients had improvement in BI score and in 5 it remained static.

Out of 2 patients with static TIBI, both had static BI score.

❖ On correlating improvement in TIBI with BI in the total group,
out of 21 patients with improved TIBI, 12 patients had improvement in BI (TABLE 19 A).
Out of 5 patients with worsened TIBI, 4 patients had no improvement in BI.
❖ In Group A, of 10 patients with improved TIBI, 6 patients had improvement in BI (TABLE 19 B). Out of 3 patients with worsened TIBI, 2 patients had no improvement in BI.

❖ In Group B, out of 11 patients with improved TIBI, 6 patients had improvement in BI (TABLE 19 C). Out of 2 patients with worsened TIBI, both had no improvement in BI.

TABLE 19: Comparison between change in TIBI to change in BI at 48 hours

Comparison between Delta TIBI to Delta BI in total group at 48 hours				
Parameters	Number of patients showing TIBI improvement	Number of patients with abnormal TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in BI score	12	1	0	13
Number of patients without improvement in BI score	9	2	1	12
Number of patients with worsening of BI score	0	1	0	1
Comparison between Delta TIBI to Delta BI in GROUP A at 48 hours				
Δ	Number of patients showing TIBI improvement	Number of patients with TIBI abnormal without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in BI score	6	1	0	7
Number of patients without improvement in BI score	4	0	1	5
Number of patients with worsening of BIscore	0	1	0	1
Comparison between Delta TIBI to Delta BI in GROUP B at 48 hours				
Parameters	Number of patients showing TIBI improvement	Number of patients with TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in BI score	6	0	0	6
Number of patients without improvement in BI score	5	2	0	7
Number of patients with worsening of BI score	0	0	0	0

TABLE 19 A

Parameters in Total group	IMPROVEMENT IN BI	NO IMPROVEMENT IN BI	P = 0.1413 (NS)
IMPROVEMENT IN TIBI	12	9	
NO IMPROVEMENT IN TIBI	1	4	

TABLE 19 B

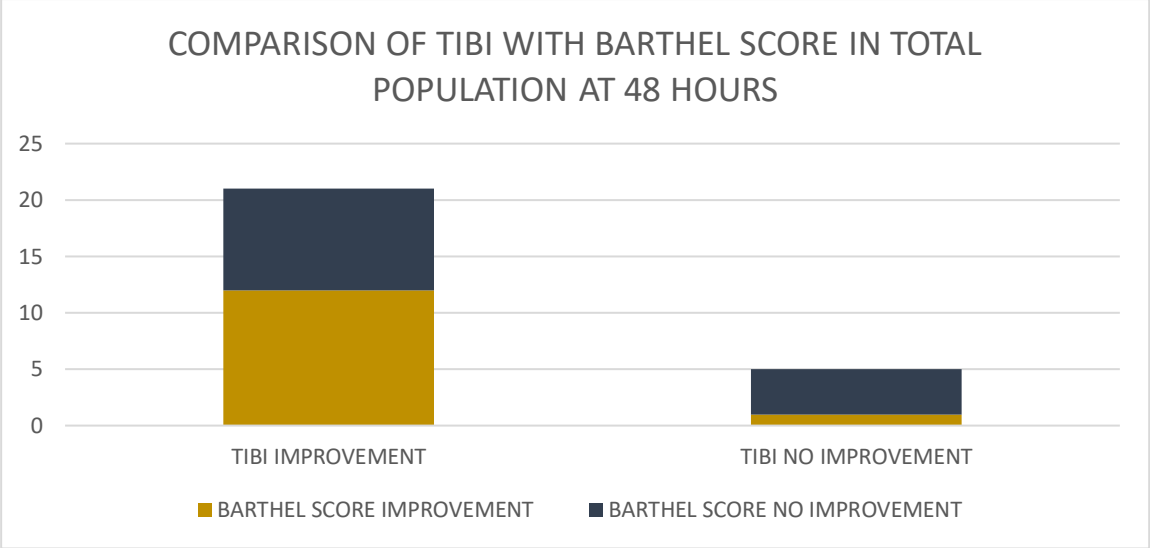
Parameters in GROUP A	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.3671 (NS)
IMPROVEMENT IN TIBI	6	4	
NO IMPROVEMENT IN TIBI	1	2	

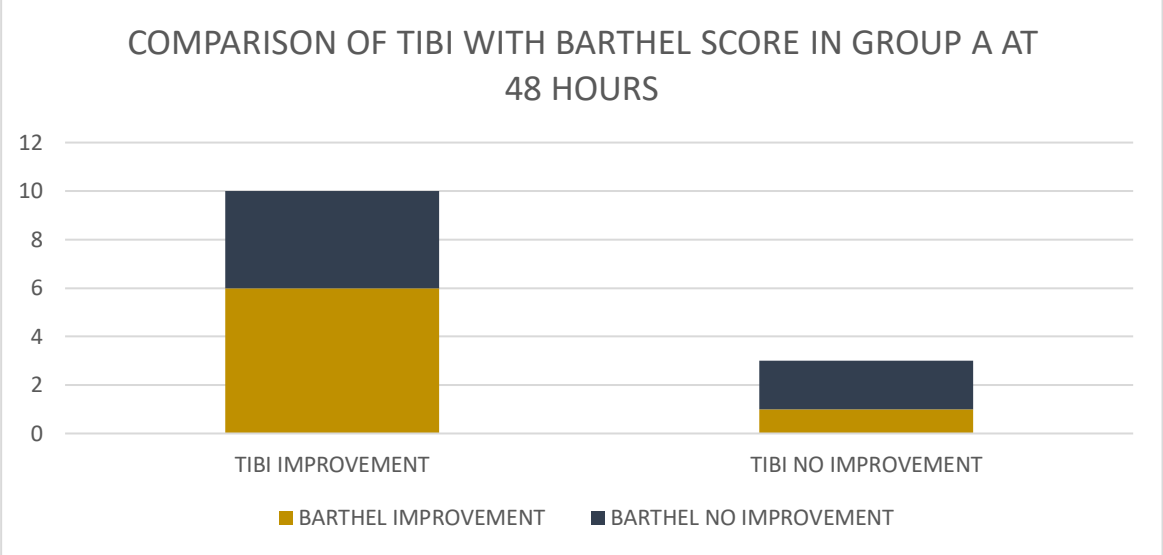
TABLE 19 C

Parameters in GROUP B	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.2692 (NS)
IMPROVEMENT IN TIBI	6	5	
NO IMPROVEMENT IN TIBI	0	2	

Level of significance P = < 0.05

S- significant NS- not significant





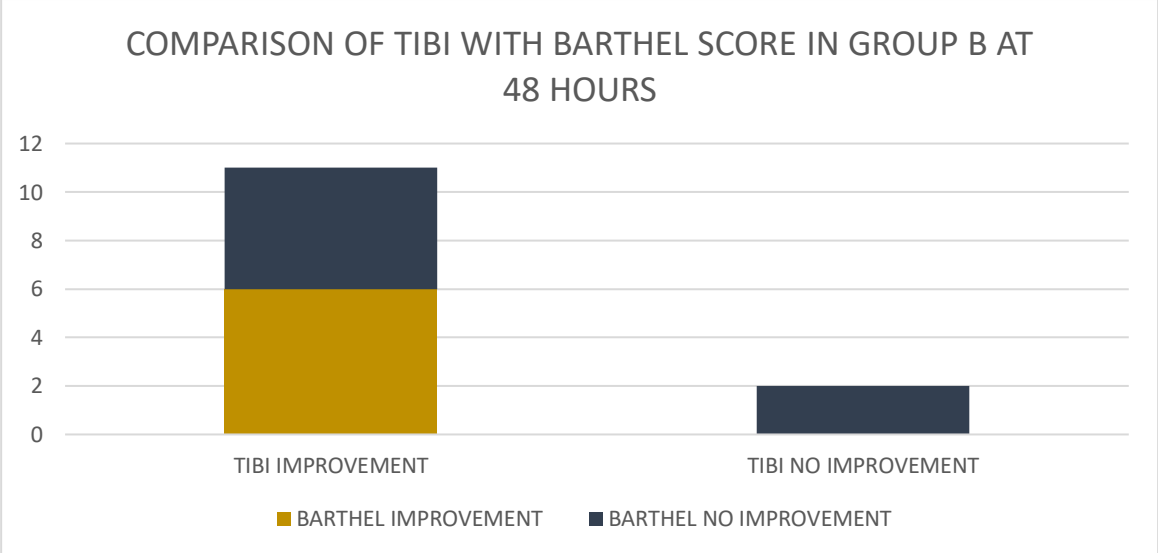


FIGURE 22: Comparison between change in TIBI to change in BI at 48 hours

Comparison between changes in TIBI to changes in BI between baseline to 30 days:

Delta BI i.e., Δ BI = BI at admission – BI at 30 days)

❖ **Out of tot**al 26 patients, 19 patients had improvement in BI (Table 20) at 30 days when compared to baseline. Two patients had no improvement in BI score and no patient had worsening of BI.

Out of 21 patients with improved TIBI, 19 patients had improvement in BI and two patients had static BI. Out of 4 patients with static TIBI, three patients had improvement in BI and one had static BI and 1 patient had worsened BI. One patient with worsened TIBI had worsened BI.

❖ **In Group** A, out of 13 patients, 11 patients had improvement in BI at 30 days (Table 20) when compared to baseline. One patient had no improvement in BI and one patient had worsening of BI.

Out of 10 patients with improved TIBI, 9 patients had improvement in BI and one patient had static BI. Out of 2 patients with static TIBI, two patients had worsened BI. One patient with worsened TIBI had worsened BI.

❖ **In group B,** Out of 13 patients, 10 patients had improvement in BI at 30 days when compared to baseline (TABLE 20). 2 patients had no improvement in BI.

Out of 11 patients with improved TIBI, 10 patients had improvement in BI and one patient had static BI. Out of 2 patients with static TIBI, one patient had static BI and one had improvement.

❖ On corelating improvement in TIBI with Improvement in BI In Total population: (TABLE 20 A) Out of 21 patients with improved TIBI, 19 patients had improvement in B. Out of 5 patients with worsened TIBI, two patients had no improvement in BI

❖ In Group A (TABLE 20 B) Out of 10 patients with improved TIBI, nine patients had improvement in BI. Out of 3 patients with worsened TIBI, one patient had no improvement in BI.

❖ In Group B (TABLE 20 C) Out of 11 patients with improved TIBI, ten patients had improvement in BI. Out of 2 patients with worsened TIBI, 1 patient had no improvement in BI.

TABLE 20: Comparison between change in TIBI to change in BI between base line-30 days

Comparison between Delta TIBI to Delta BI in total group at 30 days				
Parameters	Number of patients showing TIBI improvement	Number of patients with abnormal TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in BI score	19	3	0	22
Number of patients without improvement in BI score	2	1	0	3
Number of patients with worsening of BI score	0	0	1	1
Comparison between Delta TIBI to Delta BI in GROUP A at baseline to 30 days				
Δ	Number of patients showing TIBI improvement	Number of patients with TIBI abnormal without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in BI score	9	2	0	11
Number of patients without improvement in BI score	1	0	0	1
Number of patients with worsening of BI score	0	0	1	1
Comparison between Delta TIBI to Delta BI in GROUP B at baseline to 30 days				
Parameters	Number of patients showing TIBI improvement	Number of patients with TIBI without change	Number of patients with TIBI worsening	Total
Number of patients showing improvement in BI score	10	1	0	11
Number of patients without improvement in BI score	1	1	0	2
Number of patients with worsening of BI score	0	0	0	0

TABLE 20 A

Parameters in Total population	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.1404 (NS)
IMPROVEMENT IN TIBI	19	2	
NO IMPROVEMENT IN TIBI	3	2	

TABLE 20 B

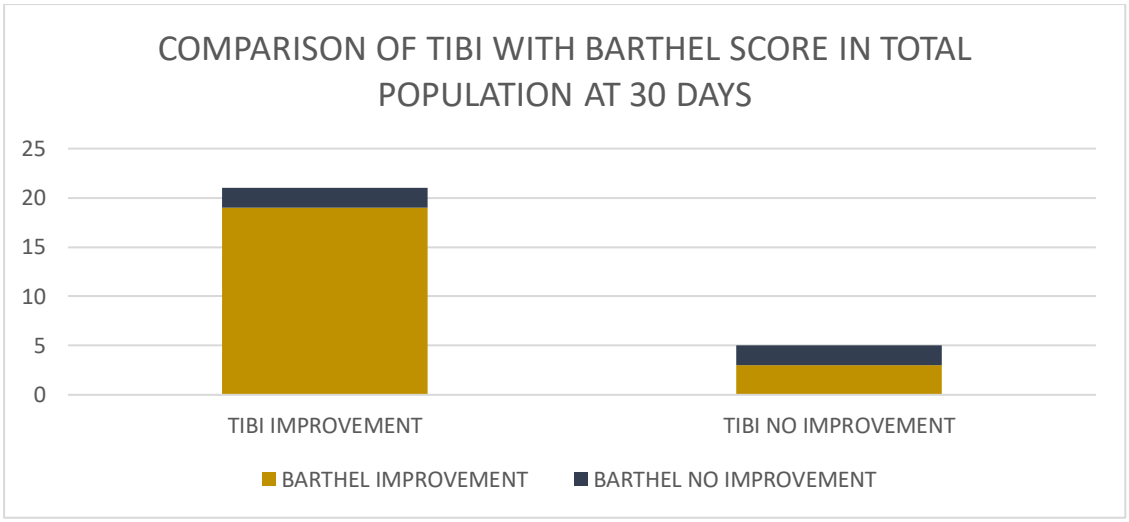
Parameters in GROUP A	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.3846 (NS)
IMPROVEMENT IN TIBI	9	1	
NO IMPROVEMENT IN TIBI	2	1	

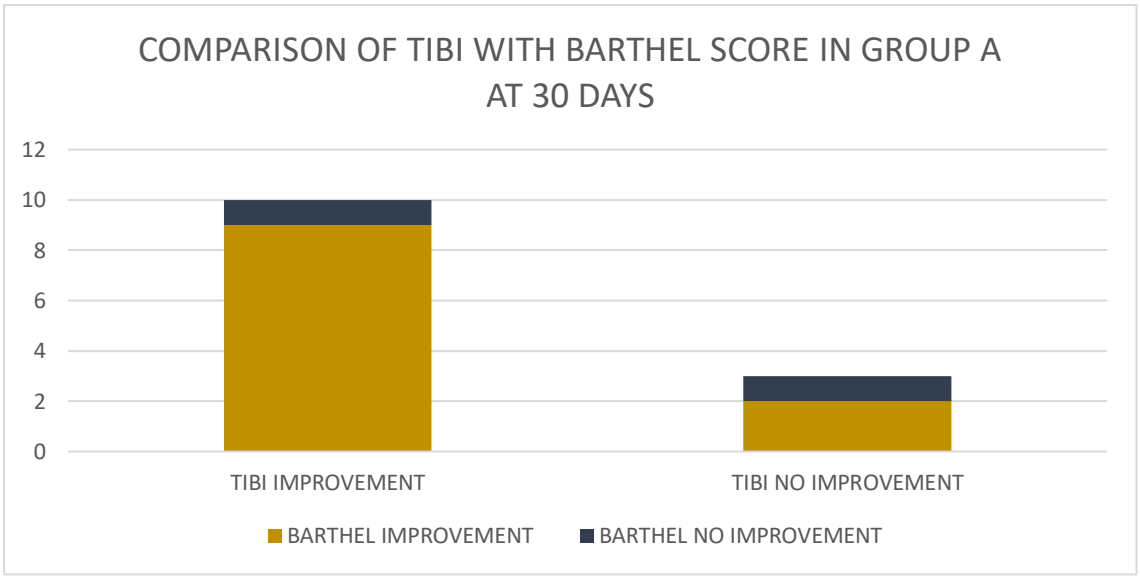
TABLE 20 C

Parameters in GROUP B	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.2820 (NS)
IMPROVEMENT IN TIBI	10	1	
NO IMPROVEMENT IN TIBI	1	1	

Level of significance P = < 0.05

S- significant NS- not significant





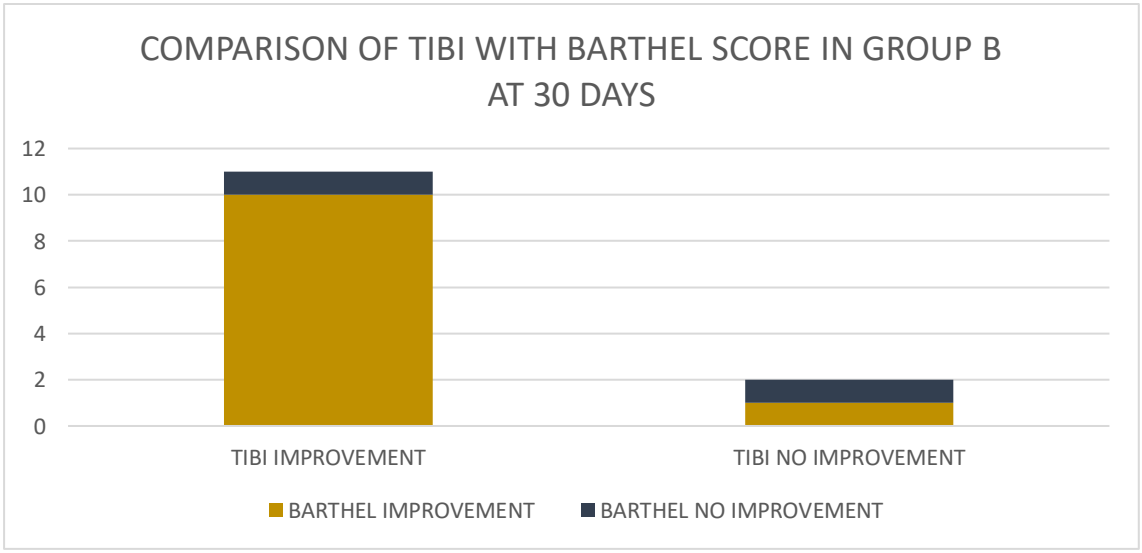


FIGURE 23: Comparison between change in TIBI to change in BI between 0-30 days

Comparison between changes in TIBI to changes in BI between 2-30 days:

Delta BI (ΔBI = BI AT 48 HOURS- BI AT 30 days)

❖ **In total**, Out of 26 patients, 22 patients had improvement in BI score at 30 days (Table 21) when compared to baseline. three patients had static BI score. one patient had worsening of BI score.

Out of 21 patients with improved TIBI, all 19 patients had improvement in BI score and 2 patients had static BI score. Out of 4 patients with static TIBI, three patients had improvement in BI score and one had static MRS and 1 patient had static BI score. One patient with worsened TIBI had worsened BI score.

❖ **In Group A**, out of 13 patients, 11 patients had improvement in BI score at 30 days (TABLE 21) when compared to baseline. One patient had static BI score and one patient had worsening of BI score.

Out of 10 patients with improved TIBI, 9 patients had improvement in BI score and one patient had static BI score. Out of 2 patients with static TIBI, 2 patients had improved BI score. One patient with worsened TIBI had worsened BI score.

❖ **In group B,** out of 13 patients, 11patients had improvement in BI score at 30 days (TABLE 21) when compared to baseline. 2 patients had worsened BI score.

Out of 11 patients with improved TIBI, all 10 patients had improvement in BI score and one patient had worsened BI score. Out of 2 patients with static TIBI, 1patients had static BI score and 1 had improvement.

TABLE 21: Comparison between change in TIBI to change in BI between 2-30 days

Comparison between Delta TIBI to Delta BI in total group between 2-30 days				
Δ	Number of patients showing TIBI improvement	Number of patients without improvement in TIBI	Number of patients showing TIBI worsening	total
Number of patients showing improvement in BI.	19	3	0	22
Number of patients without improvement in BI score	2	1	0	3
Number of patients with worsening of BI score	0	0	1	1
Comparison between Delta TIBI to Delta BI in group A between 2-30 days				
Δ	Number of patients showing TIBI improvement	Number of patients without improvement in TIBI	Number of patients showing TIBI worsening	total
Number of patients showing improvement in BI.	9	2	0	11
Number of patients without improvement in BI score	1	0	0	1
Number of patients with worsening of BI score	0	0	1	1
Comparison between Delta TIBI to Delta BI in group B between 2-30 days				
Δ	Number of patients showing TIBI improvement	Number of patients without improvement in TIBI	Number of patients showing TIBI worsening	total
Number of patients showing improvement in BI.	10	1	0	11
Number of patients without improvement in BI score	1	1	0	2
Number of patients with worsening of BI score	0	0	0	0

Comparison between changes in TIBI to changes in BI between baseline to 90 days

Delta BARTHEL (Δ BI = BI AT ADMISSION- BI AT 90 days)

❖ **In total**, out of 26 patients, 21 patients had improvement in BI score at 30 days (TABLE 22) when compared to baseline. Two patients had worsening of BI score.

Out of 21 patients with improved TIBI, all 21 patients had improvement in BI score. Out of 4 patients with static TIBI, three patients had improvement in BI score and one had static MRS and 1 patient had worsened BI score. One patient with worsened TIBI had worsened BI score.

❖ **In Group A**, out of 13 patients, 12 patients had improvement in BI score at 30 (TABLE 22) days when compared to baseline. one patient had worsening of BI score.

Out of 10 patients with improved TIBI, 10 patients had improvement in BI score. Out of 2 patients with static TIBI, 2 patients had improved B score. One patient with worsened TIBI had worsened BI score.

❖ **In group B,** out of 13 patients, 12 patients had improvement in BI score at 30 (TABLE 22) days when compared to baseline. 1 patient had worsened BI score.

Out of 13 patients 11 Patient had improvement in TIBI grade when compared to baseline. 2 patients had static TIBI without improvement. Out of 11 patients with improved TIBI, all 11 patients had improvement in BI score. Out of 2 patients with static TIBI, 1patients had static BI score and 1 had improvement.

❖ On corelating improvement in TIBI to improvement in BI, In Total population (TABLE 22 A) Out of 21 patients with improved TIBI, 21 patients had improvement in BI. Out of 5 patients with worsened TIBI, two patients had no improvement in BI.

❖ In Group A, out of 10 patients with improved TIBI, 10 patients had improvement in BI. (TABLE 22 B) Out of 3 patients with worsened TIBI, one patient had no improvement in BI.

❖ In Group B, out of 11 patients with improved TIBI, 11 patients had improvement in BI. (TABLE 22 C) Out of 2 patients with worsened TIBI, one patient had no improvement in BI.

TABLE 22: Comparison between change in TIBI to change in BI between 0-90 days

Comparison between Delta TIBI to Delta BI in total group between 0-90 days				
Δ	Number of patients showing improvement in TIBI	Number of patients without improvement in TIBI	Number of patients with worsening of TIBI	total
Number of patients showing improvement in BI	21	3	0	21
Number of patients without improvement in BI	0	0	0	0
Number of patients with worsening of BI	0	1	1	2
Comparison between Delta TIBI to Delta BI in GROUP A between 0-90 days				
Δ	Number of patients showing improvement in TIBI	Number of patients without improvement in TIBI	Number of patients with worsening of TIBI	total
Number of patients showing improvement in BI	10	2	0	12
Number of patients without improvement in BI	0	0	0	0
Number of patients with worsening of BI	0	0	1	1
Comparison between Delta TIBI to Delta BI in GROUP B between 0-90 DAYS				
Δ	Number of patients showing improvement in TIBI	Number of patients without improvement in TIBI	Number of patients with worsening of TIBI	total
Number of patients showing improvement in BI	11	1	0	12
Number of patients without improvement in BI	0	0	0	0
Number of patients with worsening of BI	0	1	0	1

TABLE 22 A

Parameters inTOTAL POPULATION	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	**P = 0.030 (S)**
IMPROVEMENT IN TIBI	21	0	
NO IMPROVEMENT IN TIBI	3	2	

TABLE 22 B

Parameters in GROUP A	IMPROVEMENT IN B SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.2307 (NS)
IMPROVEMENT IN TIBI	10	0	
NO IMPROVEMENT IN TIBI	2	1	

TABLE 22 C

Parameters in GROUP B	IMPROVEMENT IN BI SCORE	NO IMPROVEMENT IN BI SCORE	P = 0.1538 (NS)
IMPROVEMENT IN TIBI	11	0	
NO IMPROVEMENT IN TIBI	1	1	

Level of significance P = < 0.05

S- significant NS- not significant

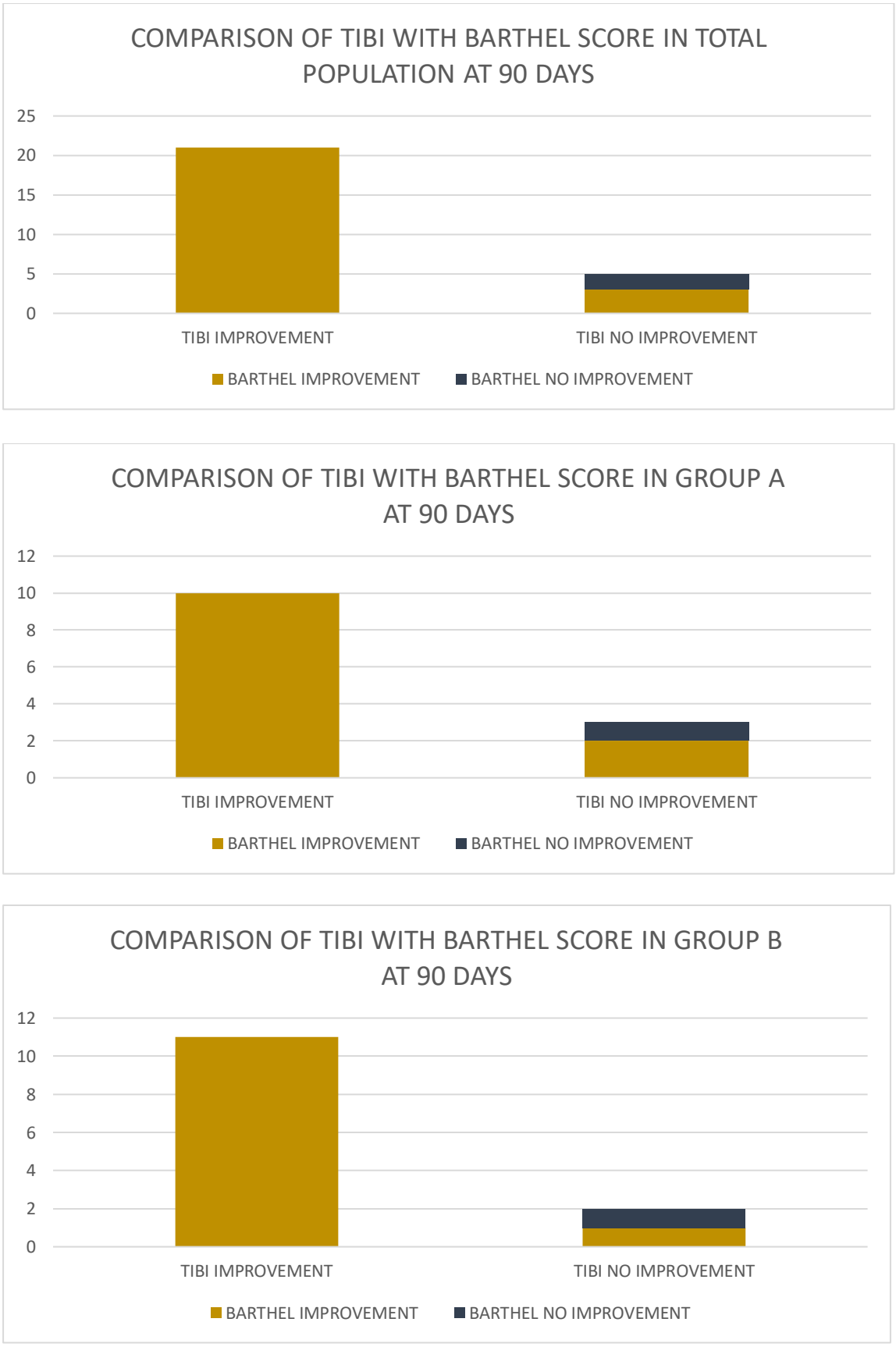


Figure 24: Comparison between change in TIBI to change in BI between 0-90 days

Comparison between changes in TIBI to changes in BI score between 30-90 days:

Delta BI (Δ BI = BI at 30 DAYS- BI at 90 days)

❖ **In total**, out of 26 patients, 23 patients had improvement in BI score at 30 days when compared to baseline (TABLE 23). 2 patients had static BI score. one patient had worsening of BI score.

Out of 21 patients with improved TIBI, all 20 patients had improvement in BI score and 1 patient had static BI score. Out of 4 patients with static TIBI, three patients had improvement in BI score and one had static BI and one patient had static BI score. One patient with worsened TIBI had static BI score.

❖ **In Group A**, out of 13 patients, 12 patients had improvement in BI score at 30 days when compared to baseline. (Table 23). One patient had static BI score and no patient had worsening of BI score.

Out of 10 patients with improved TIBI, all 10 patients had improvement in BI score. Out of 2 patients with static TIBI, 2 patients had improved BI score. One patient with worsened TIBI had static BI score.

❖ **In group B,** out of 13 patients, 11 patients had improvement in BI score at 30 days when compared to baseline (table 23). 1patient had worsened BI score. And one patient had static BI score.

Out of 11 patients with improved TIBI, all 10 patients had improvement in BI score and one patient had static BI score. Out of 2 patients with static TIBI, one patient had static BI score and one had improvement.

TABLE 23: Comparison between change in TIBI to change in BI between 30- 90 days

Comparison between Delta TIBI to Delta BI in TOTAL population between (30-90) days				
Δ	Number of patients showing improvement in TIBI	Number of patients without improvement in TIBI	Number of patients showing worsening of TIBI	total
Number of patients showing improvement in BI	20	3	0	23
Number of patients without improvement in BI	1	0	1	2
Number of patients showing worsening of BI	0	1	0	1
Comparison between Delta TIBI to Delta BI in GROUP A between 0-90 day				
Δ	Number of patients showing improvement in TIBI	Number of patients without improvement in TIBI	Number of patients showing worsening of TIBI	total
Number of patients showing improvement in BI	10	2	0	12
Number of patients without improvement in BI	0	0	1	1
Number of patients showing worsening of BI	0	0	0	0
Comparison between Delta TIBI to Delta B in GROUP B between 30-90 days				
Δ	Number of patients showing improvement in TIBI	Number of patients without improvement in TIBI	Number of patients showing worsening of TIBI	total
Number of patients showing improvement in BI	10	1	0	11
Number of patients without improvement in BI	1	0	0	1
Number of patients showing worsening of BI	0	1	0	1

Comparison of improvement in BI over different time intervals in patients with TIBI improvement at 48 hours

❖ In the total 21 patients with improved TIBI, 20 patients showed BI improvement compared to baseline (TABLE 24, 25).

❖ Twelve patients showed improvement in BI between baseline to 48 hours,

Nineteen patients showed improvement in BI between 2-30 days. Of these, 7 patients had first time improvement between 2 to 30 days while 12 patients had further improvement in BI.

Between 30 -90 days, 20 patients had improvement in BI (one patient for first time and 6 had further improvement).

❖ In GROUP A, 9/10 patients with improved TIBI (90%) showed BI improvement compared to baseline (TABLE 24, 25).

Six patients showed improvement in BI between baseline to 48 hours.

Nine patients showed improvement in BI between 2-30 days. Of these, 3 patients had first time improvement between 2 to 30 days while 6 patients had further improvement in BI.

Between 30 -90 days, 10patients showed improvement in BI (1 patient had 1st time improvement and 9 patients had further improvement in BI which was started earlier).

❖ In GROUP B, 11/11 patients with improved TIBI (100%) showed BI improvement compared to baseline (TABLE 24,25).

Six patients showed improvement in BI between baseline to 48 hours.

Ten patients showed improvement in BI between 2-30 days, 4 Patients had first time improvement in BI and 6 patients had further improvement in BI

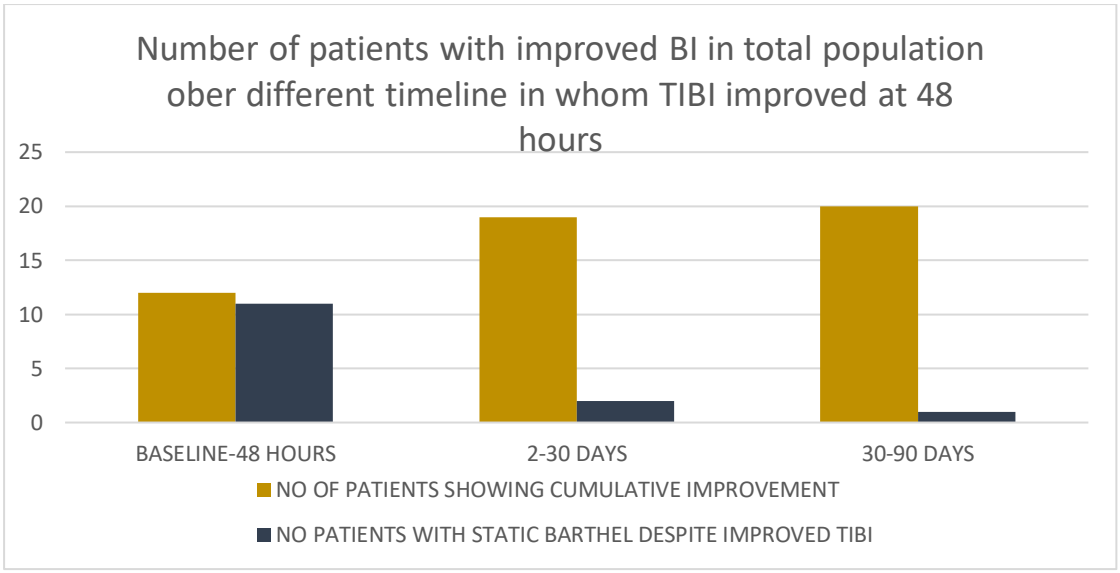
Between 30 -90 days, 10 patients had improvement in BI of which 1 patient had first time improvement in BI and nine patients had further improvement in BI which was started earlier.

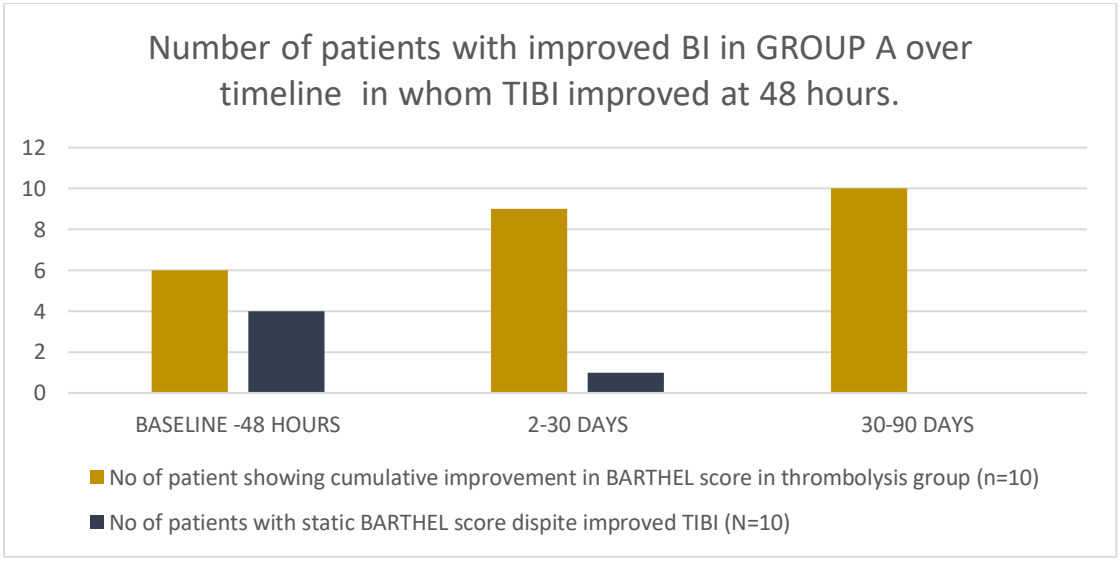
TABLE 24: Distribution of patients with improvement in BI over different time intervals in those with TIBI improvement at 48 hours

	No of patient showing 1st time improvement in BI score			No of patient showing further improvement in BI score		
	TOTAL (N=21)	GROUP A (N=10)	GROUP B (N=11)	TOTAL (N=21)	GROUP A (N=10)	GROUP B (N=11)
BASELINE - 48 HOURS	12	6	6	0	0	0
2-30 DAYS	7	3	4	12	6	6
30-90 DAYS	2	1	1	18	9	9

TABLE 25: Distribution of patients with cumulative improvement in BI over different time intervals in those with TIBI improvement at 48 hours (same as MRS)

	No of patient showing cumulative improvement in TOTAL population (N=26)	No of patient showing cumulative improvement in BI score in GROUP A (N=10)	No of patient showing cumulative improvement in BI score in GROUP B (N=11)
BASELINE -48 HOURS	12	6	6
2-30 DAYS	19	9	10
30-90 DAYS	20	10	10





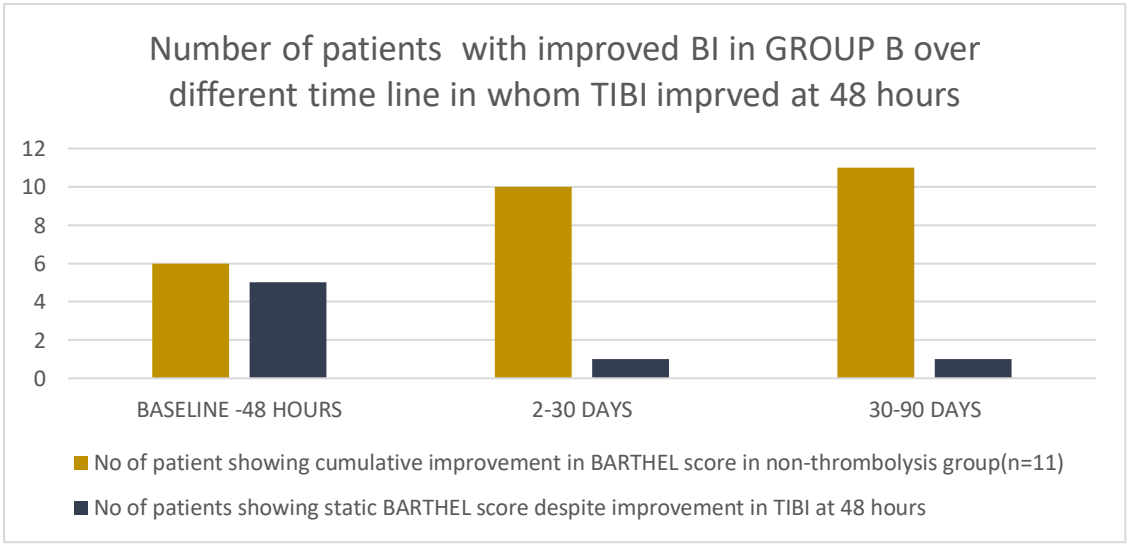


FIGURE 25: Distribution of patients with improvement in BI over different time intervals in those with TIBI improvement at 48 hours

DISCUSSION

This study was a prospective observational study done in the Jodhpur, the second largest district of Rajasthan with population of 4,140,093 with gender ratio is 916 females per 1000 of males (estimates as per Aadhar uidai.gov.in Dec 2020 data). The study aimed to look into the role of TCD in characterising AIS and its possible role in prognostication. Some important observations were made which may be of clinical relevance in the treatment of AIS specially with lack of such studies from the Indian subcontinent.

Despite the small sample size, the demographic data revealed similarities with previous Indian studies. The mean age of presentation was 68.41 ± 14.82 years in the total cohort without significant difference between Group A and Group B, compared to the study done by Sylaja et al in which mean age of stroke presentation was 58.3±14.7 years (60) In a study by Kaur et al, the mean age was 60 ± 10 years (59) . while by Ojha et al it was even younger at 49 years.(59, 60) The late age of presentation in our population compared to the studies mentioned can be probably explained by the relatively less stressful life in a tier 2 city like Jodhpur and surrounding districts in Rajasthan compared to the lifestyle of metro cities. Majority of the population have agriculture-based occupations and so they are involved in physical activities compared to the sedentary lifestyle prevalent in metro cities.

Gender distribution was lopsided with male: female ratio of 3.25: 1. In the other studies by Sylaja et al, Kaur et al and Ojha et al, the male population comprised of 67%, 62% and 59% respectively. (60–62) This strikingly high male predominance in the study cohort may be due to social norms and beliefs of the local population with a higher preference to take a sick male family member to hospital over female member.

Hypertension (58%), hyperhomocystinemia (35%), dyslipidaemias and diabetes (each 23.52%), obesity (20.58%) and tobacco addiction (29.50%) were common risk factors. Similar findings are observed in the study done by Sylaja et al, Kaur et al, Ojha et al and Ram C et al.(60–63). Amongst the risk factors, hyperhomocystinemia were seen significantly amongst the population of Jodhpur. Similar high incidence of hyper homocystinemia (74%) in the Rajasthan State was observed in the study done by Ramrakhiyani et al in the population of western India in Jaipur, city.(64)

In the total group, mean NIHSS score at the time of admission were 8.35 ±5.36, which is similar when compared to previous study by Sylaja et al in which median NIHSS was 10 (range 5-15)(60). In the study group, mean MRS and mean BI were 3.64 ±1.5 and 8.34 ± 7.96, respectively.

In total study group, 85.31 % had large vessel occlusive stroke. In the studies done by Sylaja et al and Patel et al, large vessels occlusive stroke cases comprised 42% and 86% respectively.(60,65) Our study findings are similar to that by Patel et al in which the population cohort was from Gujarat, western India. In total population 79.41 % had anterior circulatory stroke and 20.5% of patient had posterior circulatory stroke. In the study done by Kannan et al between January 2018 to December 2018, similar findings were observed as prevalence of anterior circulation stroke was higher (88.27%) when compared to posterior circulation stroke. (66)

Out of 34 patients, 47% underwent thrombolysis in our study. Sylaja et al and Khurana et al also reported a thrombolysis rate of 13% and 31.81%, respectively.(58,64). The rate of thrombolysis was significantly high in our population compared to these studies. (60),(64). Though there are locally prevalent common cultural and custom beliefs preferring non-medical treatment over modern medical care in the population and

leading to relatively poor health selecting behaviour in villages, the high thrombolysis rate in our centre is an important observation. This may be due to some of the reasons outlined below. The catchment area of our institute is approximately 200 to 300 km^2. Population density of Jodhpur is between 100-300/ square meter compared to 550-1000/ square meter in the cities involved in the previous studies. (68) figure 26. Therefore, traffic congestion is significantly lower in Jodhpur like tier 2 city compared to metro cities. Secondly, over the last 4 years, we have been able to implement a rapid acting Standard Operating Protocol for stroke in the hospital ER. As can be appreciated, the ictus to door time in the In Group A, the mean ictus to door time was 109 ± 60.417 minutes and median was 85 minutes (Range 15-250 minutes) and even in group B the mean ictus to door time was 557 minutes ± 420.371 minutes and median was 480 minutes (range 30-1290 minutes) for those who coming in 24 hours. In Group A median door to needle time was 120 minutes (range 16 to 213 minutes). We have an integrated stroke management team comprising department of neurology, Interventional radiology, Emergency medicine and General Medicine. Once a patient comes to ER in window period, all the departments are informed via WhatsApp "STROKE CARE GROUP". All the respective attending physicians come together immediately to decide the further plan of thrombolysis and/ mechanical thrombectomy. This integrative approach and use of appropriate technology has cutdown the in-hospital delay for management. Third reason is selection bias. Our study had recruited cases of AIS of 24 hour or less while in other studies recruitment duration was up to 2 weeks thereby changing the population denominator. (60)

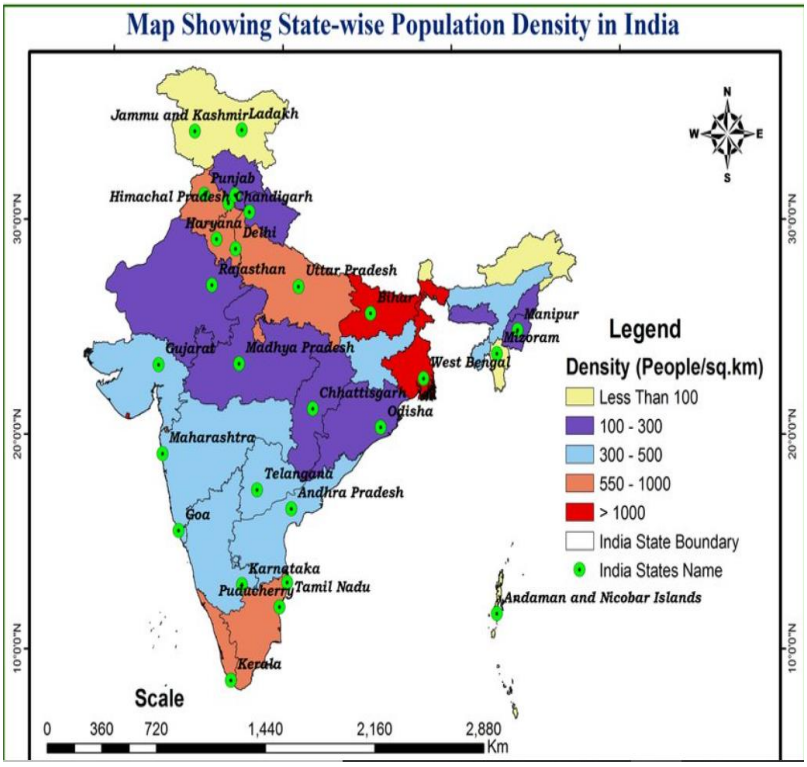


FIGURE 26: State wise population density in INDIA (year 2020) [Reference: (68)]

Amongst anterior circulation strokes, the mean ASPECTS was 8.23± 2.14. Stroke etiologic subtypes were large vessels atherosclerosis LVA (44.11%), cardio-embolic CE (24.21%),small vessels disease SVD (11.76%), other definite (5.88%), and undetermined (8.88%). In the study by Patel et al, the stroke etiologic subtypes were LVA (33%), CE (13%), SVD (29%), other definite (6%), and undetermined (18%). (65) In the study by Dash et al from Delhi, the stroke etiologic subtypes were LVA (4.7%), CE (14%), SVD (6.8%), other definite (17.3%), and undetermined (57%).(69) Thus, our study findings are similar to the study done at Gujarat, western India.(65)

The primary objective of this study was to assess the hemodynamic changes in the cerebral circulation within first 2-3 days of AIS using TCD. In our study, 8 (23%) patients had window failure. Window failure rate were similar to other studies done by Lin Y et al – window failure rate was 28.8 % and in study by Purkayastha et al window

failure was 15%. Age, gender, bone thickness and poor skill are the major reasons for inadequate insonation window.(70–72) .

TIBI flow is representative of residual flow determined by TCD for major cerebral vessels. In 1994 Alexandrov et al had worked on intracranial blood flow velocity in AIS and assessed factors for prediction of prognosis of stroke.(73) They used peak systolic velocity and flow direction to predict four types of TCD patterns like ***normal, stenotic, occlusive and collateral*** pattern. Serial TCDs were done at the time of admission and after 2 weeks. 86% of the patients had recanalization by the 2 weeks (73). In 1998 Toni D et al. observed prediction of improvement or deterioration in ischemic stroke by performing serial TCD study. (74)) They classified TCD findings as follows: ***normal***; ***middle cerebral artery (MCA) asymmetry*** (asymmetry index between affected and contralateral MCAs below -21%); and ***MCA no-flow*** (absence of flow signal from the affected MCA in the presence of ipsilateral anterior and posterior cerebral artery signals through the same acoustic window). Serial TCD examinations were done at 6, 24, and 48 hours after stroke onset. (74) During same period, the ***TIBI grading system (Appendix 6)*** by TCD for arterial occlusion was developed by Demchuk et al. (25)) Later, a further study by Demchuk et al (23) showed that improvement in TIBI score is suggestive of improvement in flow across the vessels. (23) In a population of 109 AIS patients thrombolysed with tPA, TIBI flow grading was done at admission and at 24 hours. Improvement in TIBI flow grade at 24 hours was predictive of early recovery and clinical severity. Mean age was 68±16 years and median NIHSS score before administration of tPA (pre-tPA) was 17.5. Pre-tPA NIHSS scores were higher in patients with TIBI grade 0 than TIBI grade 4 or 5 flow. TIBI flow improvement (compared to baseline at 24 hours) to grade 4 or 5 occurred in 35% of patients (19/54) with an initial grade of 0 or 1 and in 52% (12/23) with initial grade 2

or 3. The 24-hour NIHSS scores were higher in follow-up in patients with TIBI grade 0 or 1 than those with TIBI grade 4 or 5 flow. TIBI flow recovery correlated with NIHSS score improvement.(25) Our study showed that improvement in TIBI score at 48 hours is significantly correlated **(P = 0.019)** with improvement in clinical severity, i.e., **NIHSS** at **48 hours,** irrespective of the treatment of the ischemic stroke (medical management versus thrombolysis/mechanical thrombectomy).

Burgin et al developed TCD criteria for recanalization, using various aspects of the TIBI. With use of these criteria, TCD has excellent correlation with angiography for complete recanalization (sensitivity 91%, specificity 93%). (75). Repeat CT angiography is not always feasible and not a cost-effective option to perform in all the patients to look for changes in flow pattern to predict the clinical and functional outcome. However, TCD can be repeated at bedside and provide valuable dynamic real-time flow parameters which can guide the ongoing management and can also predict functional outcome without increasing the cost of hospital stay.

To the best of our knowledge none of the studies till date have compared TIBI flow grade changes to disability score and functional independence score using MRS and BI score. Our study found that TIBI flow grades improvement (minimum 1 to maximum 2 grade changes) over 48 hours are significantly associated with improvement in NIHSS, MRS and BI in the study population, at different time intervals after AIS upto 90 days. (Figure 27 and 28.)

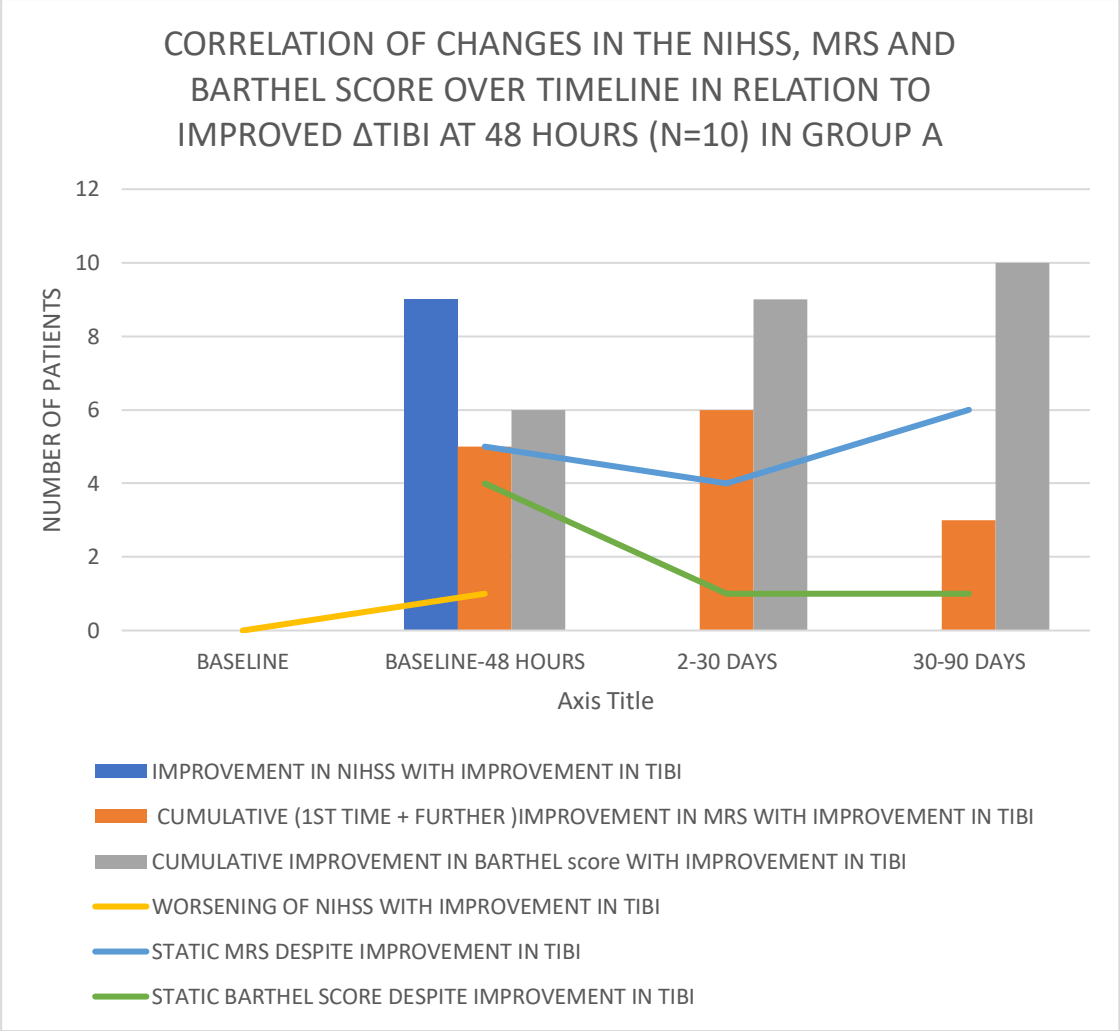


Figure 27: Correlation of changes in clinical and functional outcome over various timelines in relation to improved TIBI at 48 hours in group A.

At 90 days follow up, of 80.76 % patients whose TIBI flow grade had improved at 48 hours, 85.71% patients had improvement in **MRS**. Out of these, 94.43% had improvement in first **30 days (P = 0.09)** and 55.55 % had improvement within 48 hours of ictus. This finding suggests improvement in TIBI grade can predict MRS improvement consistently. Majority improvement could be predicted up to 30 days of ictus. Similar observations were made in GROUP A and GROUP B as shown in (TABLE 17-18), though not significant. This is because of low power of study due to smaller sample size.

Similarly, **at 90 days** follow up, 100% patients had improvement in **BI** if TIBI flow grade had improved at 48 hours **(P= 0.03).** Out of these, 90.47% had improvement in first 30 days and 57.55 % had improvement within 48 hours of ictus. This finding suggests improvement in TIBI grade can predict BI improvement consistently. Majority improvement could be predicted up to 30 days after ictus. Similar observations were made in GROUP A and GROUP B as shown in TABLE 24-25) though not significant because of lower sample size.

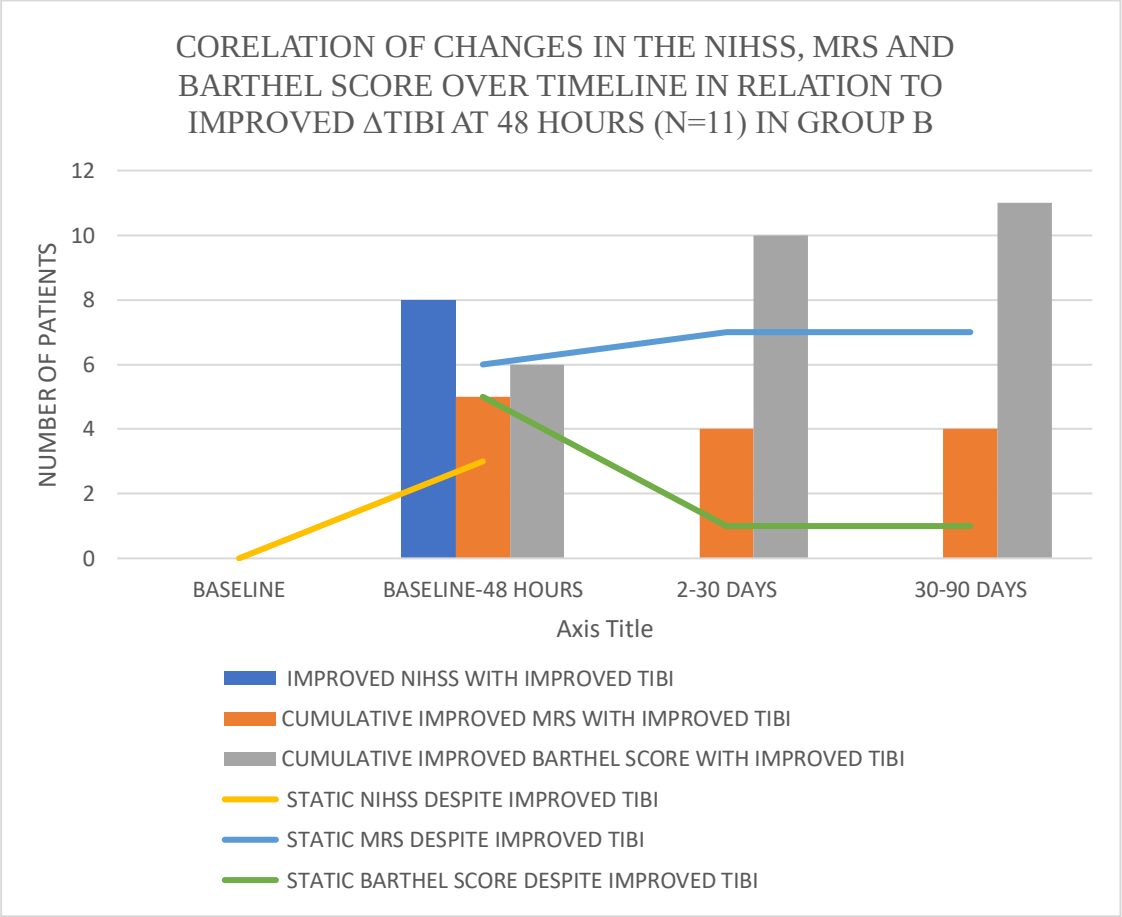


Figure 28: Correlation of changes in clinical and functional outcome over various timeline in relation to improved TIBI at 48 hours in group B

Prognosis is a medical term for predicting the likely or expected development of a disease, including whether the signs and symptoms will improve or worsen (and how quickly) or remain stable over time; expectations of quality of life, such as the ability

to carry out daily activities; the potential for complications and associated health issues; and the likelihood of survival (including life expectancy). (76) The goal of estimating prognosis is to improve clinical decision making and, ultimately, patient outcomes. Stroke is a disease associated with significant functional disability, social dysfunction and impaired mental health to the patient. After discharge, home care is primarily dependent on the care giver (in India mostly family member). Thus, stroke is associated with social dysfunction and economic stress for the family and can affect mental health of the care giver too.

Hence, a strong predictor of disability and functional independency is a much-desired need in a disease like stroke for various reasons. It increases the confidence of the caregiver and physician in care during the post stroke phase. A prediction of good long-term prognosis can change the behaviour of the patients toward his disease. Using the concept of positive biofeedback on psychology, it can help in improving overall future well-being of the patient.(77) A strong predictor also identifies the population for rehabilitation research with new strategies. This study was one such attempt in the same direction and highlights the fact that serial TCD testing and observed dynamic changes can predict short-term in-hospital clinical improvement and long-term disability and functional independency status (using MRS and BI scoring). However smaller population group was limitation in this study and the findings need to be reproduced in a bigger cohort should be studied in the future.

LIMITATIONS

Potential limitations of this studies are as follow:

- The smaller number of patients was associated with lower power of the study. Due to the COVID pandemic, the number of patients recruited fell short. In addition, 3 patients' TCD study could not completed at 48 hours and so they were not included in the study.
- TIBI classification related limitations were also noted. TIBI grade 0 (or absent flow) could have been inappropriately concluded because of technical problems
- Inadequate bony windows and window failures added to attrition of patients.
- TCD data acquisition and interpretation is a technical skill and so needs consistent practice. Intra and inter-rater variability is known to occur. Some of the patients with technical failures could be improved with further practice.
- Further limitation was lack of information regarding importance of TIBI in arterial segments other than those affected by ischemia. While TCD can directly insonate proximal vascular structures such as M1 MCA, A1 anterior cerebral artery, and P1-P2 posterior cerebral artery, it can only indirectly provide information about more distal vascularity.
- Parameters which predict the improvement in TIBI can't be analysed due to smaller population group in this study and the findings need to be reproduced in a bigger cohort should be studied in the future.

CONCLUSIONS

In acute ischemic stroke patients, serial improvement in the TCD flow gradings are significantly correlated with improvement in clinical severity and can predict early and late disability status and functional independence irrespective of treatment given at admission. It is relatively inexpensive, repeatable, and its portability offers increased convenience over other imaging methods, allowing for continuous bedside monitoring. Though the current indications in adults and children include detection of vasospasm in sickle cell disease, subarachnoid haemorrhage (SAH), intra- and extracranial arterial stenosis and occlusion, brain stem death, head injury, raised ICP, intraoperative monitoring, impaired vasomotor function, and cerebral micro-embolism in right to left cardiac shunts, our study has highlighted the fact that it can predict clinical severity, early and late disability status and functional independence in AIS. Parameters which predict the improvement in TIBI can't be analysed due to smaller population group in this study and the findings need to be reproduced in a bigger cohort should be studied in the future.

BIBILOGRAPHY

1. Khurana S, Gourie-Devi M, Sharma S, Kushwaha S. Burden of Stroke in India During 1960 to 2018: A Systematic Review and Meta-Analysis of Community Based Surveys. Neurol India. 2021;69(3):547.
2. Spilker J, Kongable G, Barch C, Braimah J, Brattina P, Daley S. Using The NIH Stroke Scale to Assess Stroke Patients. Journal of Neuroscience Nursing. 1997 Dec;29(6):384–92.
3. Adams HP, Davis PH, Leira EC, Chang KC, Bendixen BH, Clarke WR. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). Neurology. 1999 Jul 1;53(1):126–126.
4. Shah S, Vanclay F, Cooper B. Improving the sensitivity of the Barthel Index for stroke rehabilitation. J Clin Epidemiol. 1989 Jan;42(8):703–9.
5. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. Stroke. 1988 May;19(5):604–7.
6. Demchuk AM, Felburg RA, Alexandrov A v. Clinical Recovery from Acute Ischemic Stroke after Early Reperfusion of the Brain with Intravenous Thrombolysis. New England Journal of Medicine. 1999 Mar 18;340(11):894–5.
7. Feigin VL, Lawes CM, Bennett DA, Barker-Collo SL, Parag V. Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. Lancet Neurol. 2009 Apr;8(4):355–69.
8. The Lancet. 2017 Dec;390(10111):e49.

9. Ram CVS, Kumar S, Renjen PN, Kumar GP, Swaminathan J, Reddy CR, et al. Risk factors predisposing to acute stroke in India: a prospective study. J Hypertens. 2021 Nov;39(11):2183–9.
10. German Stroke Study Collaboration. Predicting outcome after acute ischemic stroke: An external validation of prognostic models. Neurology. 2004 Feb 24;62(4):581–5.
11. König IR, Ziegler A, Bluhmki E, Hacke W, Bath PMW, Sacco RL, et al. Predicting Long-Term Outcome After Acute Ischemic Stroke. Stroke. 2008 Jun;39(6):1821–6.
12. Weimar C, König IR, Kraywinkel K, Ziegler A, Diener HC. Age and National Institutes of Health Stroke Scale Score Within 6 Hours After Onset Are Accurate Predictors of Outcome After Cerebral Ischemia. Stroke. 2004 Jan;35(1):158–62.
13. Schlegel D, Kolb SJ, Luciano JM, Tovar JM, Cucchiara BL. Utility of the NIH Stroke Scale as a Predictor of Hospital Disposition. Stroke. 2003 Jan;34(1):134–7.
14. Rundek T, Mast H, Hartmann A, Boden-Albala B, Lennihan L, Lin IF. Predictors of resource use after acute hospitalization: The Northern Manhattan Stroke Study. Neurology. 2000 Oct 24;55(8):1180–7.
15. Banks JL, Marotta CA. Outcomes Validity and Reliability of the Modified Rankin Scale: Implications for Stroke Clinical Trials. Stroke. 2007 Mar;38(3):1091–6.
16. Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. The Lancet. 2000 May;355(9216):1670–4.
17. Aviv RI, Mandelcorn J, Chakraborty S, Gladstone D, Malham S, Tomlinson G. Alberta Stroke Program Early CT Scoring of CT Perfusion in Early Stroke

Visualization and Assessment. American Journal of Neuroradiology. 2007 Nov 1;28(10):1975–80.

18. Alwalid O. MCA - Alberta stroke program early CT score (ASPECTS) illustration. In: Radiopaedia.org. Radiopaedia.org; 2019.
19. Park JS, Lee JM, Kwak HS, Chung GH. Predictive value of CT angiography source image ASPECTS in patients with anterior circulation acute ischemic stroke after endovascular treatment: ultimate infarct size and clinical outcome. J Neurointerv Surg. 2019 Apr;11(4):342–6.
20. Bhatia R, Bal SS, Shobha N, Menon BK, Tymchuk S, Puetz V. CT Angiographic Source Images Predict Outcome and Final Infarct Volume Better Than Noncontrast CT in Proximal Vascular Occlusions. Stroke. 2011 Jun;42(6):1575–80.
21. Junejo H ur R, Yusuf S, Zeb R, Zeb U, Zeb AA, Ali A. Predictive Value of CT Brain Perfusion Studies in Acute Ischemic Infarct Taking MRI Stroke Protocol As Gold Standard. Cureus. 2021 Jul 20;
22. ANCHAL GUPTA, PAWAN GARG, PUSPINDER KHERA, SAMHITA PANDA. Multiphase computed tomography angiography (mCTA) derived source images in acute ischemic stroke: Beyond collaterals. Can it obviate the need for computed tomography perfusion (CTP)? Clin Neurol Neurosurg. 2022;222.
23. Akif Topcuoglu M. Transcranial Doppler ultrasound in neurovascular diseases: diagnostic and therapeutic aspects. J Neurochem. 2012 Nov;123:39–51.
24. Akopov S, Whitman GT. Hemodynamic Studies in Early Ischemic Stroke. Stroke. 2002 May;33(5):1274–9.
25. Demchuk AM, Burgin WS, Christou I, Felberg RA, Barber PA, Hill MD, et al. Thrombolysis in Brain Ischemia (TIBI) Transcranial Doppler Flow Grades

Predict Clinical Severity, Early Recovery, and Mortality in Patients Treated With Intravenous Tissue Plasminogen Activator. Stroke. 2001 Jan;32(1):89–93.

26. Aaslid R, Markwalder TM, Nornes H. Noninvasive transcranial Doppler ultrasound recording of flow velocity in basal cerebral arteries. J Neurosurg. 1982 Dec;57(6):769–74.
27. Moppett IK, Mahajan RP. Transcranial Doppler ultrasonography in anaesthesia and intensive care. Br J Anaesth. 2004 Nov;93(5):710–24.
28. R. A. Vienna, R. Aaslid. “The Doppler principle applied to measurement of blood flow velocity in cerebral arteries,” in Transcranial Doppler Sonography,. Springer, New York, NY, USA, . 1986;22–38.
29. H. A. Nicoletto, M. H. Burkman. “Transcranial Doppler series part II: performing a transcranial Doppler,.” Am J Electroneurodiagnostic Technol. 2009;49:14–27.
30. Moppett IK, Mahajan RP. Transcranial Doppler ultrasonography in anaesthesia and intensive care. Br J Anaesth. 2004 Nov;93(5):710–24.
31. Tsivgoulis G, Alexandrov A v., Sloan MA. Advances in transcranial doppler ultrasonography. Curr Neurol Neurosci Rep. 2009 Jan 16;9(1):46–54.
32. Marinoni M, Ginanneschi A, Forleo P, Amaducci L. Technical limits in transcranial Doppler recording: Inadquate acoustic windows. Ultrasound Med Biol. 1997 Jan;23(8):1275–7.
33. White H, Venkatesh B. Applications of transcranial Doppler in the ICU: a review. Intensive Care Med. 2006 Jul 10;32(7):981–94.
34. H. A. Nicoletto, M. H. Burkman. “Transcranial Doppler series part III: interpretation,.” Am J Electroneurodiagnostic Technol. 2009;49(3):244–59.
35. R. G. Gosling, D. H. King. “Arterial assessment by Doppler shift ultrasound,.” Proc R Soc Med. 1974;67(6):447–9.

36. H. A. Nicoletto, M. H. Burkman. “Transcranial Doppler series part IV: case studies,.” Am J Electroneurodiagnostic Technol. 2009;49(4):342–60.

37. Homburg AM, Jakobsen M, Enevoldsen E. Transcranial doppler recordings in raised intracranial pressure. Acta Neurol Scand. 2009 Jan 29;87(6):488–93.

38. Rigamonti A, Ackery A, Baker AJ. Transcranial Doppler monitoring in subarachnoid hemorrhage: a critical tool in critical care. Canadian Journal of Anesthesia/Journal canadien d’anesthésie. 2008 Feb;55(2):112–23.

39. Arenillas JF, Molina CA, Montaner J, Abilleira S, González-Sánchez MA, Álvarez-Sabín J. Progression and Clinical Recurrence of Symptomatic Middle Cerebral Artery Stenosis. Stroke. 2001 Dec;32(12):2898–904.

40. Christou I, Felberg RA, Demchuk AM, Grotta JC, Burgin WS, Malkoff M, et al. A Broad Diagnostic Battery for Bedside Transcranial Doppler to Detect Flow Changes With Internal Carotid Artery Stenosis or Occlusion. Journal of Neuroimaging. 2001 Jul;11(3):236–42.

41. Ducrocq X, Braun M, Debouverie M, Junges C, Hummer M, Vespignani H. Brain death and transcranial Doppler: Experience in 130 cases of brain dead patients. J Neurol Sci. 1998 Sep;160(1):41–6.

42. Moreno JA, Mesalles E, Gener J, Tomasa A, Ley A, Roca J, et al. Evaluating the outcome of severe head injury with transcranial Doppler ultrasonography. Neurosurg Focus. 2000 Jan;8(1):1–7.

43. Pennekamp CWA, Moll FL, de Borst GJ. The potential benefits and the role of cerebral monitoring in carotid endarterectomy. Curr Opin Anaesthesiol. 2011 Dec;24(6):693–7.

44. Müller M, Voges M, Piepgras U, Schimrigk K. Assessment of Cerebral Vasomotor Reactivity by Transcranial Doppler Ultrasound and Breath-Holding. Stroke. 1995 Jan;26(1):96–100.

45. Bernd Ringelstein E, Droste DW, Babikian VL, Evans DH, Grosset DG, Kaps M, et al. Consensus on Microembolus Detection by TCD. Stroke. 1998 Mar;29(3):725–9.

46. Panerai RB. Assessment of cerebral pressure autoregulation in humans - a review of measurement methods. Physiol Meas. 1998 Aug 1;19(3):305–38.

47. Kenton AR, Martin PJ, Abbott RJ, Moody AR. Comparison of Transcranial Color-Coded Sonography and Magnetic Resonance Angiography in Acute Stroke. Stroke. 1997 Aug;28(8):1601–6.

48. Kluytmans M, van der Grond J, van Everdingen KJ, Klijn CJM, Kappelle LJ, Viergever MA. Cerebral Hemodynamics in Relation to Patterns of Collateral Flow. Stroke. 1999 Jul;30(7):1432–9.

49. Tissue Plasminogen Activator for Acute Ischemic Stroke. New England Journal of Medicine. 1995 Dec 14;333(24):1581–8.

50. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). The Lancet. 1998 Oct;352(9136):1245–51.

51. del Zoppo GJ, Poeck K, Pessin MS, Wolpert SM, Furlan AJ, Ferbert A, et al. Recombinant tissue plasminogen activator in acute thrombotic and embolic stroke. Ann Neurol. 1992 Jul;32(1):78–86.

52. Should Thrombolytic Therapy Be the First-Line Treatment for Acute Ischemic Stroke? New England Journal of Medicine. 1997 Oct 30;337(18):1309–13.

53. Wildermuth S, Knauth M, Brandt T, Winter R, Sartor K, Hacke W. Role of CT Angiography in Patient Selection for Thrombolytic Therapy in Acute Hemispheric Stroke. Stroke. 1998 May;29(5):935–8.

54. Kenton AR, Martin PJ, Abbott RJ, Moody AR. Comparison of Transcranial Color-Coded Sonography and Magnetic Resonance Angiography in Acute Stroke. Stroke. 1997 Aug;28(8):1601–6.

55. Camerlingo M, Casto L, Censori B, Ferraro B, Gazzaniga GC, Mamoli A. Transcranial doppler in acute ischemic stroke of the middle cerebral artery territories. Acta Neurol Scand. 2009 Jan 29;88(2):108–11.

56. Razumovsky A v., Gillard JH, Bryan RN, Hanley DF, Oppenheimer SM. TCD, MRA and MRI in acute cerebral ischemia. Acta Neurol Scand. 2009 Jan 29;99(1):65–76.

57. Demchuk AM, Christou I, Wein TH, Felberg RA, Malkoff M, Grotta JC, et al. Accuracy and Criteria for Localizing Arterial Occlusion With Transcranial Doppler. Journal of Neuroimaging. 2000 Jan;10(1):1–12.

58. Heiss WD, Grond M, Thiel A, von Stockhausen HM, Rudolf J, Ghaemi M, et al. Tissue at Risk of Infarction Rescued by Early Reperfusion: A Positron Emission Tomography Study in Systemic Recombinant Tissue Plasminogen Activator Thrombolysis of Acute Stroke. Journal of Cerebral Blood Flow & Metabolism. 1998 Dec 31;18(12):1298–307.

59. Hackworthy RA, Sorensen SG, Fitzpatrick PG, Barry WH, Menlove RL, Rothbard RL, et al. Dependence of assessment of coronary artery reperfusion during acute myocardial infarction on angiographic criteria and interobserver variability. Am J Cardiol. 1988 Sep;62(9):538–42.

60. Sylaja PN, Pandian JD, Kaul S, Srivastava MVP, Khurana D, Schwamm LH. Ischemic Stroke Profile, Risk Factors, and Outcomes in India. Stroke. 2018 Jan;49(1):219–22.

61. Paramdeep Kaur, Jeyaraj Pandian, Gagandeep Singh, Rajinder Bansal, Birinder Paul, Monika Singla. Gender Difference in Stroke: Are They Different in India? Neurology. 2016 Apr 5;86.

62. T Ojha P, Basak S, Aglave V, Yadav J. Incidence of stroke in adults according to age, sex and subtypes in urban Indian population. Neurology and Neuroscience Reports. 2020;3(1).

63. Ram CVS, Kumar S, Renjen PN, Kumar GP, Swaminathan J, Reddy CR. Risk factors predisposing to acute stroke in India: a prospective study. J Hypertens. 2021 Nov;39(11):2183–9.

64. Neetu Ramrakhiani, Dinesh K Sharma, Ramfal Dubey, Pushkar Gupta, Apoorva Shanrma. Clinical Profile, Risk Factors and Outcomes in Patients with Cerebral Venous Sinus Thrombosis: A Study from Western India. . The Journal of the association of physicians of the India. 2019 Sep;67:49–53.

65. Avani R Patel, Amar R Patel, Soham Desai. The Underlying Stroke Etiology: A Comparison of Two Classifications in a Rural Setup. Cureus. 2019 Jul;11.

66. Kannan V, Justin C, Prashanth PRS, Alexander N. Clinical prevalence of stroke in a tertiary care hospital in Southern India. Int J Res Med Sci. 2021 Feb 25;9(3):838.

67. Khurana D, Das B, Kumar A, Kumar S. A. Temporal Trends in Intravenous Thrombolysis in Acute Ischemic Stroke: Experience from a Tertiary Care Center in India. Journal of Stroke and Cerebrovascular Diseases. 2017 Jun;26(6):1266–73.

68. Murugesan B, Karuppannan S, Mengistie AT, Ranganathan M, Gopalakrishnan G. Distribution and Trend Analysis of COVID-19 in India: Geospatial Approach. Journal of Geographical Studies. 2020 Apr 15;4(1):1–9.

69. Deepa Dash, Ashu Bhashin, Avadh Kumar Pandit, Manjari Tripathi. Risk factors and etiologies of ischemic strokes in young patients: a tertiary hospital study in north India. J Stroke. 2014 Sep;

70. Lin YP, Fu MH, Tan TY. Factors Associated with No or Insufficient Temporal Bone Window Using Transcranial Color-coded Sonography. J Med Ultrasound. 2015 Sep;23(3):129–32.

71. Sushmita Purkayastha. Transcranial Doppler Ultrasound: Technique and Application. semin neurology. 2013 Jan;

72. Marinoni M, Ginanneschi A, Forleo P, Amaducci L. Technical limits in transcranial Doppler recording: Inadquate acoustic windows. Ultrasound Med Biol. 1997 Jan;23(8):1275–7.

73. Alexandrov A v, Bladin CF, Norris JW. Intracranial blood flow velocities in acute ischemic stroke. Stroke. 1994 Jul;25(7):1378–83.

74. Toni D, Fiorelli M, Zanette EM, Sacchetti ML, Salerno A, Argentino C. Early Spontaneous Improvement and Deterioration of Ischemic Stroke Patients. Stroke. 1998 Jun;29(6):1144–8.

75. Burgin WS, Malkoff M, Felberg RA, Demchuk AM, Christou I, Grotta JC, et al. Transcranial Doppler Ultrasound Criteria for Recanalization After Thrombolysis for Middle Cerebral Artery Stroke. Stroke. 2000 May;31(5):1128–32.

76. Nature Publishing Group.

77. Jeste D v., Palmer BW, Rettew DC, Boardman S. Positive Psychiatry. J Clin Psychiatry. 2015 Jun 24;76(06):675–83.

78. National Institutes of Health, National Institute of Neurological Disorders and Stroke. Stroke Scale.

79. “Modified Rankin Scale for Neurologic Disability”. MDCalc. Retrieved 2015-02-17.

80. Barthel index-Physiopedia. In.

81. Heather A Nicoletto, Marilyn H Burkman. Transcranial Doppler series part II: performing a transcranial Doppler. Am J Electroneurodiagnostic Technol. 2009 Mar;49.

82. Bathala L, Mehndiratta M, Sharma V. Transcranial doppler: Technique and common findings (Part 1). Ann Indian Acad Neurol. 2013;16(2):174.

ANNEXURE

APPENDIX 1 The National Institute Of Health Stroke Scale-NIHSS(78)

Category	Score	Time	Score
1a. Level of Consciousness (LOC) (Alert, drowsy, etc.)	0 = 1 = 2 = 3 =	Alert Drowsy Stuporous Coma	
1b. LOC Questions (Month, age)	0 = 1 = 2 =	Answers both correctly Answers one correctly Incorrect	
1c. LOC Commands (Open/close eyes, make fist & let go	0 = 1 = 2 =	Obeys both correctly Obeys one correctly Incorrect	
2. Best Gaze (Eyes open - pt follows examiner's fingers or face)	0 = 1 = 2 =	Normal Partial gaze palsy Forced deviation	
3. Visual (Introduce visual stimulus/threat to pt's visual field quandrants. Cover 1 eye and hold up fingers in all 4 quadrants.)	0 = 1 = 2 = 3 =	No visual loss Partial hemianopsia Complete hemianopsia Bilateral hemianopsia	
4. Facial Palsy (Show teeth, raise eyebrows and squeeze eyes tightly shut.)	0 = 1 = 2 = 3 =	Normal Minor Partial Complete	
5a. Motor Arm - Left (Elevate extremity to 90 degrees and score drift/ movement. Count to 10 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion (Explain)	
5b. Motor Arm - Right (Elevate extremity to 90 degrees and score drift/ movement. Count to 10 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion (Explain)	
6a. Motor Leg - Left (Elevate extremity to 30 degrees and score drift/ movement. Count to 5 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion	
6b. Motor Leg - Right (Elevate extremity to 30 degrees and score drift/ movement. Count to 5 out loud and use fingers for visual cue.)	0 = 1 = 2 = 3 = 4 = NT=	No drift Drift Can't resist gravity No effort against gravity No movement Amputation, joint fusion (Explain)	
7. Limb ataxia (Finger to nose, heal down shin)	0 = 1 = 2 =	Absent Present in one limb Present in two limbs	
8. Sensory (Pin prick to face, arms, trunk, and legs -compare sharpness side to side, or no feeling at all.)	0 = 1 = 2 =	Normal Partial loss Severe loss	
9. Best Language (Name items, describe picture, and read sentences. Don't forget glasses if they normally wear them.)	0 = 1 = 2 = 3 =	No aphasia Mild to moderate aphasia Severe aphasia Mute	
10. Dysarthria (Evaluate speech clarity by pt reading or repeating words on list.)	0 = 1 = 2 = NT	Normal articulation Mild to moderate dysarthria Near to unintelligible or worse Intubated or other physical barrier	
11. Extinction and Inattention (Use information from prior testing or double simultaneous stimuli testing to identify neglect. Face, arms, legs and visual fields.)	0 = 1 = 2 =	No neglect Partial neglect Complete neglect	
NT= Not Testable acceptable as noted above			
TOTAL SCORE:			

APPENDIX 2 MODIFIED RANKIN SCALE-MRS

Score	Definition
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
3	Moderate disability. Requires some help, but able to walk unassisted
4	Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent
6	Dead

REFRENCE: "Modified Rankin Scale for Neurologic Disability". MDCalc. Retrieved 2015-02-17. (79)

APPENDIX 3 BARTHEL SCORE(80)

Barthel Index of Activities of Daily Living

Instructions: Choose the scoring point for the statement that most closely corresponds to the patient's current level of ability for each of the following 10 items. Record actual, not potential, functioning. Information can be obtained from the patient's self-report, from a separate party who is familiar with the patient's abilities (such as a relative), or from observation. Refer to the Guidelines section on the following page for detailed information on scoring and interpretation.

The Barthel Index

Bowels
0 = incontinent (or needs to be given enemata)
1 = occasional accident (once/week)
2 = continent
Patient's Score: _____

Bladder
0 = incontinent, or catheterized and unable to manage
1 = occasional accident (max. once per 24 hours)
2 = continent (for over 7 days)
Patient's Score: _____

Grooming
0 = needs help with personal care
1 = independent face/hair/teeth/shaving (implements provided)
Patient's Score: _____

Toilet use
0 = dependent
1 = needs some help, but can do something alone
2 = independent (on and off, dressing, wiping)
Patient's Score: _____

Feeding
0 = unable
1 = needs help cutting, spreading butter, etc.
2 = independent (food provided within reach)
Patient's Score: _____

Transfer
0 = unable – no sitting balance
1 = major help (one or two people, physical), can sit
2 = minor help (verbal or physical)
3 = independent
Patient's Score: _____

Mobility
0 = immobile
1 = wheelchair independent, including corners, etc.
2 = walks with help of one person (verbal or physical)
3 = independent (but may use any aid, e.g., stick)
Patient's Score: _____

Dressing
0 = dependent
1 = needs help, but can do about half unaided
2 = independent (including buttons, zips, laces, etc.)
Patient's Score: _____

Stairs
0 = unable
1 = needs help (verbal, physical, carrying aid)
2 = independent up and down
Patient's Score: _____

Bathing
0 = dependent
1 = independent (or in shower)
Patient's Score: _____

Total Score: _____

(Collin et al., 1988)

Scoring:

Sum the patient's scores for each item. Total possible scores range from 0 – 20, with lower scores indicating increased disability. If used to measure improvement after rehabilitation, changes of more than two points in the total score reflect a probable genuine change, and change on one item from fully dependent to independent is also likely to be reliable.

Sources:

- Collin C, Wade DT, Davies S, Horne V. The Barthel ADL Index: a reliability study. *Int Disabil Stud*. 1988;10(2):61-63.
- Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. *Md State Med J*. 1965;14:61-65.
- Wade DT, Collin C. The Barthel ADL Index: a standard measure of physical disability? *Int Disabil Stud*. 1988;10(2):64-67.

1

Guidelines for the Barthel Index of Activities of Daily Living

General

- The Index should be used as a record of what a patient ***does***, NOT as a record of what a patient ***could do***.
- The main aim is to establish degree of independence from any help, physical or verbal, however minor and for whatever reason.
- The need for supervision renders the patient not independent.
- A patient's performance should be established using the best available evidence. Asking the patient, friends/relatives, and nurses will be the usual source, but direct observation and common sense are also important. However, direct testing is not needed.
- Usually the performance over the preceding 24 – 48 hours is important, but occasionally longer periods will be relevant.
- Unconscious patients should score '0' throughout, even if not yet incontinent.
- Middle categories imply that the patient supplies over 50% of the effort.
- Use of aids to be independent is allowed.

Bowels (preceding week)

- If needs enema from nurse, then 'incontinent.'
- 'Occasional' = once a week.

Bladder (preceding week)

- 'Occasional' = less than once a day.
- A catheterized patient who can completely manage the catheter alone is registered as 'continent.'

Grooming (preceding 24 – 48 hours)

- Refers to personal hygiene: doing teeth, fitting false teeth, doing hair, shaving, washing face. Implements can be provided by helper.

Toilet use

- Should be able to reach toilet/commode, undress sufficiently, clean self, dress, and leave.
- 'With help' = can wipe self and do some other of above.

Feeding

- Able to eat any normal food (not only soft food). Food cooked and served by others, but not cut up.
- 'Help' = food cut up, patient feeds self.

Transfer

- From bed to chair and back.
- 'Dependent' = NO sitting balance (unable to sit); two people to lift.
- 'Major help' = one strong/skilled, or two normal people. Can sit up.
- 'Minor help' = one person easily, OR needs any supervision for safety.

Mobility

- Refers to mobility about house or ward, indoors. May use aid. If in wheelchair, must negotiate corners/doors unaided.
- 'Help' = by one untrained person, including supervision/moral support.

Dressing

- Should be able to select and put on all clothes, which may be adapted.
- 'Half' = help with buttons, zips, etc. (*check!*), but can put on some garments alone.

Stairs

- Must carry any walking aid used to be independent.

Bathing

- Usually the most difficult activity.
- Must get in and out unsupervised, and wash self.
- Independent in shower = 'independent' if unsupervised/unaided.

(Collin et al., 1988)

APPENDIX 4 Insonation characteristics of the cerebral vasculature

Insonation characteristics of the cerebral vasculature.

Depth Adult MFV Artery	Acoustic window	Probe angle	(mm)	Flow direction	Resistance	(cm/sec)
ECICA	Retromandibular	Superior-medial	45–50	Away	Low	30 ± 9
MCA	Middle transtemporal	Straight/Anterior - superior	30–65	Toward	Low	55 ± 12
ACA	Middle transtemporal	Straight/Anterior - superior	60–75	Away	Low	50 ± 11
PCA—segment 1	Posterior transtemporal	Straight/Posterior	60–70	Toward	Low	39 ± 10
PCA—segment 2	Posterior transtemporal	Straight/Posterior - superior	60–70	Away	Low	40 ± 10
BA	Suboccipital	Superior	80–120	Away	Low	41 ± 10
VA	Suboccipital	Superior lateral	60–75	Away	Low	38 ± 10
OA	Transorbital	Straight	45–55	Toward	High	21 ± 5
Supraclinoid ICA	Transorbital	Superior	65–80	Away	Low	41 ± 11
Parasellar ICA	Transorbital	Inferior	65–80	Toward	Low	47 ± 14

ECICA: extracranial internal carotid artery, MCA: middle cerebral artery, ACA: anterior cerebral artery, PCA: posterior cerebral artery, BA: basilar artery, OA: ophthalmic artery). Adapted from Nicoletto and Burkman. Permission obtained; copyright owner ASET (American Society of Electroneurodiagnostic Technologists), the Neurodiagnostic Society.(81)

APPENDIX 5 NORMATIVE DATA FROM INDIAN HISTORICAL CONTROL

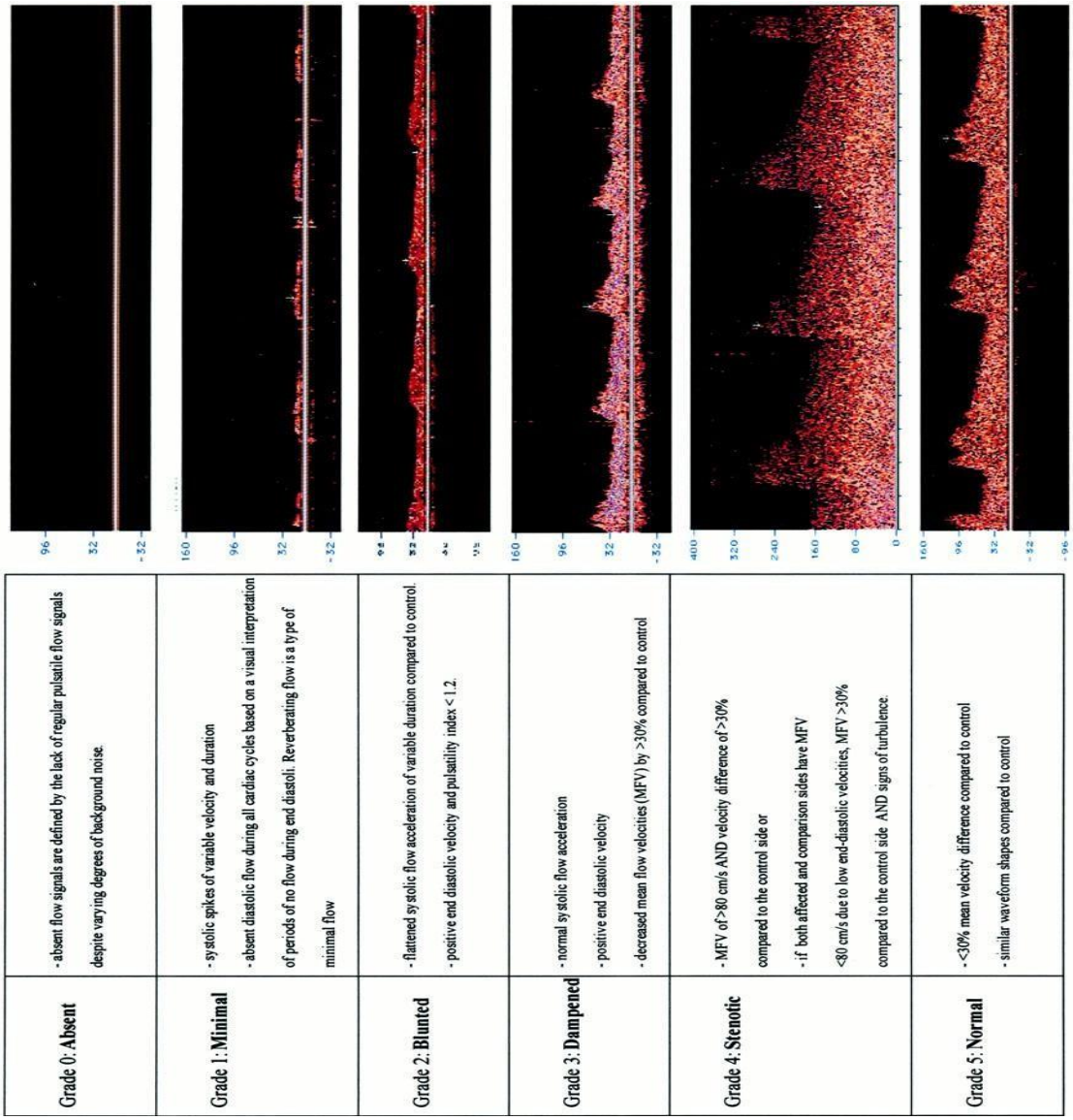
Artery	Normal MFV (cm/s)	MFV cut-off for 50% stenosis (cm/s)
M1-M2 MCA	< 80	> 100
A1 ACA	< 80	Not established, proposed > 90
ICA Siphon	< 70	> 90
PCA	< 50	Not established, proposed > 70
VA	< 60	> 70
BA	< 50	> 70

ACA: Anterior cerebral artery; BA: Basilar artery; ICA: Internal carotid artery; MCA: Middle cerebral artery; MFV: Mean flow velocity; PCA: Posterior cerebral artery; VA: Vertebral artery

Reference:

Bathala L, Mehndiratta MM, Sharma VK. Transcranial doppler: Technique and common findings (Part 1). Ann Indian Acad Neurol. 2013 Apr;16(2):174-9. (82)

APPENDIX 6 THROMBOLYSIS IN BRAIN ISCHEMIA TIBI SCORE



Grade 0: **Absent**	- absent flow signals are defined by the lack of regular pulsatile flow signals despite varying degrees of background noise.
Grade 1: **Minimal**	- systolic spikes of variable velocity and duration - absent diastolic flow during all cardiac cycles based on a visual interpretation of periods of no flow during end diastoli. Reverberating flow is a type of minimal flow
Grade 2: **Blunted**	- flattened systolic flow acceleration of variable duration compared to control. - positive end diastolic velocity and pulsatility index < 1.2.
Grade 3: **Dampened**	- normal systolic flow acceleration - positive end diastolic velocity - decreased mean flow velocities (MFV) by >30% compared to control
Grade 4: **Stenotic**	- MFV of >80 cm/s AND velocity difference of >30% compared to the control side or - if both affected and comparison sides have MFV <80 cm/s due to low end-diastolic velocities, MFV >30% compared to the control side AND signs of turbulence.
Grade 5: **Normal**	- <30% mean velocity difference compared to control - similar waveform shapes compared to control

Reference: Demchuk AM, Burgin WS, Christou I, Felberg RA, Barber PA, Hill MD et al. Thrombolysis in brain ischemia (TIBI) transcranial Doppler flow grades predict clinical severity, early recovery, and mortality in patients treated with intravenous tissue plasminogen activator. Stroke. 2001 Jan;32(1):89-93.

INFORMED CONSENT FORM

CORRELATION OF HEMODYNAMIC CHANGES BY TRANSCRANIAL DOPPLER WITH FUNCTIONAL OUTCOME IN ACUTE PRIMARY ISCHEMIC STROKE PATIENTS.

Name of investigating student: DR. PRATIK K. PATEL
MOBILE NO.9537156400

Patient/volunteer identification no:

_____

I,_____S/O Or D/O_____

_____

R/O _____

Give my full, free, voluntary consent to be a part of the study: "CORRELATION OF HEMODYNAMIC CHANGES BY TRANSCRANIAL DOPPLER WITH FUNCTIONAL OUTCOME IN ACUTE PRIMARYISCHEMIC STROKE PATIENTS", the procedure and nature of which has been explained to me in my own language to my full satisfaction. I confirm that I have had the opportunity to ask questions. I understand that my participation is voluntary and I am aware of my right to opt out of the study at any time without giving any reason. I understand that the information collected about me and any of my medical records may be looked at by responsible individual from_____(company name) or from regulatory authorities. I give permission for these individuals to have access to my records.

Place: Signature/Left thumb impression

This is to certify that the above consent has been obtained in my presence.

Date:

_____

Place: Signature of PG student

Witness 1 sign
Name:_____
Address:_____

Witness 2 sign
Name:_____
Address:_____

परियोजना का शीर्षक प्राइमरी स्ट्रोक मरीज़ में ट्रान्स्क्रनिअल डोप्पलर द्वारा लिए हेमोदीनामिक फेरफार का कार्यात्मक परिणाम से सह सम्बन्ध।

मुख्य अन्वेषक: डॉ प्रतीक पटेल

मे.....अेस/ओ या

डी/ओ.....आर/ओ.....

9537156400

.....

अध्ययन का हिस्सा बनने के लिये मेरी स्वतत्र, स्वैच्छीक सहमति देता/देती हु । इस अध्ययन की प्रकिया तथा प्रकृति के बारे मे मुझे मेरी परी सतूष्टि के लीये अपनी भाषा मे समजाया गया है । मे पुष्टि करता हु के मुझे प्रश्न पुछने का अवसर मिला है । मे समजता हु की मेरी भागीदारी स्वैच्छीक है और मुजे कोसी भी कारन दिये बीना इस अध्ययन स बहार निकलन का अधिकार है ।

मे समजता हु के मेरे और मेरे मेडीकल रेकोर्ड के बारे मे एकत्रित की गइ जानकारी को .....(कपनी का नाम) या विनियामक प्राधिकरणो से जिम्मेदार व्यकित द्वारा देखा जा सकता है । मे इन लोगो को मेरी रेकोर्ड तक पहोचने की अनुमति देता हु.

दिनाक :

हस्ताक्षर.....

यह प्रमाणित करने के लिये मेरी उपस्थितिमे उपरोकत सहमति प्राप्त की गइ है ।

दिनाक :

पी.जी. छात्र के हस्ताक्षर.....

गवाहः १)..... **नामः.....**

हस्ताक्षर **पताः**

गवाहः २)..... **नामः.....**

हस्ताक्षर **पताः**

PATIENT INFORMATION SHEET

Title of thesis: Correlation of hemodynamic changes by transcranial doppler in acute primary ischemic stroke Patients with functional outcome

Name of PG student: DR. PRATIK K. PATEL

The crude stroke prevalence in different parts of India ranged from 44.29 to 559/100,000 persons during the 2000 TO 2020. The cumulative incidence of stroke in India ranged from 105 to 152/100,000 persons per year during the past two decades in different parts of the country.

With the advent of thrombolysis therapy; functional, clinical and radiological outcome in stroke patients has improved and so the need of prognostic markers and various scales to predict the various outcomes. TCD is a convenient, low-cost, and rapidly repeatable test compared to MR and CT in suspected ischemic stroke.

I have been explained in my own understanding language that they are doing this study to see if the test TCD which is non- invasive, affordable, more widely and easily available can help in prognosis of stroke patients.

I have also been informed that I can refuse to participate further and can withdraw myself from study at any time.

The data obtained from me will be used for the purpose of the study only. All my records will be kept confidential.

भाग लेने वालो के लिये सुचना पत्र

थीसिस का शीर्षक: एक्यूट प्राइमरी इस्केमिक स्ट्रोक में ट्रांसक्रानियल डॉपलर द्वारा हेमोडायनामिक परिवर्तनों का सहसंबंध, कार्यात्मक परिणाम वाले रोगी

पीजी छात्र का नाम: डॉ। प्रतीक के. पटेल

2000 से 2020 के दौरान भारत के विभिन्न हिस्सों में क्रूड स्ट्रोक का प्रसार 44.29 से 559/100,000 व्यक्तियों के बीच था। थ्रोम्बोलिसिस थेरेपी के आगमन के साथ; स्ट्रोक के रोगियों में कार्यात्मक, नैदानिक और रेडियोलॉजिकल परिणाम में सुधार हुआ है और इसलिए विभिन्न परिणामों की भविष्यवाणी करने के लिए रोगनिरोधी मार्करों और विभिन्न पैमानों की आवश्यकता है। संदिग्ध इस्केमिक स्ट्रोक में एमआर और सीटी की तुलना में टीसीडी एक सुविधाजनक, कम लागत वाला और तेजी से दोहराने योग्य परीक्षण है।

मुझे मेरी अपनी समझ की भाषा में समझाया गया है कि वे यह अध्ययन यह देखने के लिए कर रहे हैं कि क्या परीक्षण टीसीडी जो गैर-इनवेसिव, सस्ती, अधिक व्यापक और आसानी से उपलब्ध है, स्ट्रोक के रोगियों के पूर्वानुमान में मदद कर सकता है।

मुझे यह भी सूचित किया गया है कि मैं आगे भाग लेने से मना कर सकता हूँ और किसी भी समय अध्ययन से स्वयं को अलग कर सकता हूँ।

मुझसे प्राप्त आंकड़ों का उपयोग केवल अध्ययन के प्रयोजन के लिए ही किया जाएगा। मेरे सभी रिकॉर्ड गोपनीय रखे जाएंगे

PATIENT PROFORMA

BASIC PATIENT DETAILS	
DATE	
NAME	
AGE	
GENDER	
PHONE NO.	
ADDRESS	
REGISTRATION NO.	
DATE OF ADMISSION	

SOCIO-DEMOGRAPHIC DETAILS		
EDUCATION		
	ILLITERATE	
	PRIMARY SCHOOL	
	SECONDARY SCHOOL	
	HIGHSCHOOL	
	GRADUATE AND ABOVE	
	SPECIFY	
OCCUPATION		
SOCIO ECONOMIC STATUS		
PREGNANCY STATUS		
	PREGNANT	
	NOT PREGNANT	
	NOT APPLICABLE	

DISEASE SPECIFIC DETAILS

PRESENTING COMPLAINS	
DURATION OF ILLNESS	
RISK FACTORS	HYPERTENSION DM OBESITY DYSLIIDEMIA TOBACO INTAKE ALCOHOL
TREATMENT HISTORY	ANTI HYERTENSIVE ANTI PLATELET ANTI COAGULANT LIPID LOWERING AGENTS OHA/INSULIN
GENERAL PHYSICAL EXAMINATION P BP PERIPHRAL PULSE:RIGHT/LEFT RADIAL : ULNAR : DP : TP :	

NEUROLOGICAL EXAMINATION	
HIGHER MENTAL FUNCTION	
CRANIAL NERVES	
MOTOR SYSTEM	
SENSORY SYSTEM	
CEREBELLUM	
DIAGNOSIS	
NIHSS	
MRS	
BERTHAL	

STROKE NEUROIMAGING	
CT BRAIN	
CT ANGIOGRAHY	

TCD PROFILE

AT 2HOUR OF ADMISSION	48 HOUR AFTER ADMISSION

RIGHT ARTERY	MFV (CM/SEC)	PI	SPV	DPV	TIBI	MFV (CM/SEC)	PI	SPV	DPV	TIBI
MCA M1 M2										
ACA A1										
ICA SIPHON										
PCA										
VA										
BA										

AT 2HOUR OF ADMISSION	48 HOUR AFTER ADMISSION

LEFT ARTERY	MFV (CM/SEC)	PI	SPV	DPV	TIBI	MFV (CMSEC)	PI	SPV	DPV	TIBI
MCA M1 M2										
ACA A1										
ICA SIPHON										
PCA										
VA										
BA										

FUNCTIONAL OUTCOME FOLLOW UP:

MRS	AT THE TIME OF ADMISSION	DAY 2	DAY 30	DAY 90

NIHSS	AT THE TIME OF ADMISSION	DAY 2

BERTHAL SCORE	AT THE TIME OF ADMISSION	DAY 2	DAY 30	DAY 90

अखिल भारतीय आयुर्विज्ञान संस्थान, जोधपुर
All India Institute of Medical Sciences, Jodhpur
संस्थागत नैतिकता समिति
Institutional Ethics Committee

No. AIIMS/IEC/2021/ 3508 Date: 12/03/2021

ETHICAL CLEARANCE CERTIFICATE

Certificate Reference Number: **AIIMS/IEC/2021/3343**

Project title: **"Correlation of hemodynamic changes by transcranial doppler with functional outcome in acute primary ischemic stroke patients"**

Nature of Project:	**Research Project Submitted for Expedited Review**
Submitted as:	**D.M. Dissertation**
Student Name:	**Dr. Pratik K. Patel**
Guide:	**Dr. Samhita Panda**
Co-Guide:	**Dr. Sarbesh Tiwari**

Institutional Ethics Committee after thorough consideration accorded its approval on above project.

The investigator may therefore commence the research from the date of this certificate, using the reference number indicated above.

Please note that the AIIMS IEC must be informed immediately of:

- Any material change in the conditions or undertakings mentioned in the document.
- Any material breaches of ethical undertakings or events that impact upon the ethical conduct of the research.

The Principal Investigator must report to the AIIMS IEC in the prescribed format, where applicable, bi-annually, and at the end of the project, in respect of ethical compliance.

AIIMS IEC retains the right to withdraw or amend this if:

- Any unethical principle or practices are revealed or suspected
- Relevant information has been withheld or misrepresented

AIIMS IEC shall have an access to any information or data at any time during the course or after completion of the project.

Please Note that this approval will be rectified whenever it is possible to hold a meeting in person of the Institutional Ethics Committee. It is possible that the PI may be asked to give more clarifications or the Institutional Ethics Committee may withhold the project. The Institutional Ethics Committee is adopting this procedure due to COVID-19 (Corona Virus) situation.

If the Institutional Ethics Committee does not get back to you, this means your project has been cleared by the IEC.

On behalf of Ethics Committee, I wish you success in your research.

Dr. Praveen Sharma
Member Secretary

Member secretary
Institutional Ethics Committee
AIIMS,Jodhpur

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