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Original Article

Traumatic Intracerebral Hemorrhage Surgery versus Conservative Management: A Randomized Controlled Study

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Abstract

Introduction: In India and other developing countries, traumatic brain injuries (TBIs) are a leading cause of morbidity, mortality, disability, and socioeconomic losses. In India, incidence is 56–430 per 1 lakh population. Major intracranial hematomas encountered are extradural hematoma, subdural hematoma, and traumatic intracranial hemorrhage (TICH) due to TBI.

Materials and Methods: This study is a prospective randomized control study conducted at the Department of Neurosurgery, NIMHANS, Bengaluru. Patients of traumatic intracerebral hematoma who are in clinical equipoise from May 2017 to October 2017 were enrolled in the study. The patients were enrolled to the study who got admitted to neurosurgery casualty. The details of the patients were collected including demography, clinical findings, and radiological findings which were noted. All the patients who were considered for this study underwent computed tomography brain to confirm the diagnosis, the size, and location of the hematoma.

Results: The general demographic data with clinical profile of patients are noted in tabular format. Out of 86 patients, 30 (34.48%) patients underwent early surgery, 47 (54.65%) patients were managed conservatively, and 9 (10.4%) patients were initially managed conservatively but eventually underwent surgery. Rest all findings have been noted in tabular format for well understanding in main manuscript.

Conclusion: Even though the outcomes of the early surgery group and the initially conserved group appear similar and statistically not significant, the mortality is higher in the initially conserved group and there exists an absolute difference of 11.5% between these two groups in terms of mortality, which may suggest that early surgery is beneficial as compared to initial conservative management in the management of patients with TICH.

Key words: Brain, Hematoma, Injury

INTRODUCTION

Traumatic brain injury (TBI) is a major public health problem in India, as the incidence is increasing each year. Major intracranial hematomas encountered are extradural hematoma (EDH), subdural hematoma (SDH), and traumatic intracranial hemorrhage (TICH) due to traumatic brain injury. Traumatic intraparenchymal hemorrhage or contusions are more common than EDH and SDH, account for 20%–30% of all intracranial hematomas.[1,2] Prompt surgical removal of SDH and EDH is established and widely accepted. Traumatic ICH is clearly associated with a worse outcome, but the role of surgery remains undefined in contusions and TICH.

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Multiple traumatic ICHs are found in approximately 20% of TBI patients of all the intracranial hematomas.[3] Traumatic ICHs result from rupture of intrinsic cerebral vessels and also arise from the coalescence of multiple contusions to form a big hematoma. Most TICHs occur in the orbitofrontal and temporal lobes, as most cerebral contusions occur in the same site.[2,4,5] Deeper ICHs, in

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the basal ganglia and internal capsule, found in 2% of TBI. ICHs are most common in focal head injuries, such as perforating wounds and depressed skull fractures.[6]

Imaging will show many traumatic ICHs which will develop hours to days after the injury and might not be visible on scanning soon after injury. Delayed traumatic intracerebral hematoma is a common cause of secondary neurological deterioration and progressive increase in size has been reported in up to 51% of patients on repeated computed tomography (CT) scans in the first 24 h.

There is a need for Level I prospective randomized study in patients where the neurosurgeon is in clinical equipoise to decide for conservative or operative management without doubt. Several terms are used to describe the condition including traumatic intraparenchymal hemorrhage, traumatic intracerebral hemorrhage (TICH), and contusion.

Aim and Objective

This study aims to compare the outcomes of early surgical removal versus conservative management of traumatic intracerebral hematoma in clinical equipoise patients.

MATERIALS AND METHODS

Study Design

This study is a prospective randomized control study conducted at the Department of Neurosurgery, NIMHANS, Bengaluru.

The patients were enrolled to study who got admitted to neurosurgery casualty. The details of the patients were collected including demography, clinical findings, and radiological findings which were noted. All the patients who were considered for this study underwent CT brain to confirm the diagnosis, the size, and location of the hematoma.

Treatment Allocation

The patients with clinical equipoise were selected by an experienced neurosurgeon. Patient and/or relatives were explained about the study and the consent form was filled and signed by relatives. Patients were allocated to either early surgery group or to initial conservative management. One page form was filled which included demographic details (age and gender), hematoma characteristics (site, side, and volume), and status at allocation (Glasgow Coma Scale [GCS], pupils equal, and reacting or not).

Trial Interventions

The patients who were in clinical equipoise were included in this study. The two trial interventions were early evacuation of the hematoma, combined with appropriate best medical treatment. Moreover, the best medical treatment was combined with delayed evacuation of hematoma if required. Both groups were monitored according to standard neurosurgical practice. The patients who were randomized to early surgery underwent surgery within 12 h of allocation. The best medical treatment was management of metabolic parameters such as blood glucose, blood urea, serum creatine, sodium osmotic pressure, temperature, and blood gasses. All patients were subjected to an additional CT scan at about 5 days (±2 days) to assess the changes in hematoma size. This demonstrated the proportion of the clot removed by surgery or the changes in volume of the hematoma without surgery. Eligible patients underwent craniotomy and decompression of hematoma.

Compliance

Some patients allocated to initial conservative treatment were deteriorated and eventually underwent surgery. This group is considered as crossover.

Information was collected about the status (GCS and focal signs) of the patients through the first 3 days of their trial progress. Some patients allocated to initial conservative group deteriorated in neurological condition and/or repeat scan showed increase in size of hematoma. Only those patients underwent surgery and they were recorded as crossovers.

Patients were once again assessed at the time of discharge with respect to GCS score alive or dead. Details were recorded about further reference to other hospital for observation and general care.

Number of Patients

Patients of traumatic intracerebral hematoma who are in clinical equipoise from May 2017 to October 2017 were enrolled in the study.

Inclusion Criteria

- Patients age more than 14 and above
- CT brain shows evidence of a TICH involving the cerebrum with a total volume of more than 10 ml calculated by (width × height × length)/2 in ml
- Patients presented before 48 h of head injury.

Exclusion Criteria

- Intracranial hematoma which is surfacing (EDH or SDH) and requires surgery
- Three or more individual hematomas which fulfills inclusion criteria
- Patients CT shows cerebellar contusion
- The surgery performed after 12 h of randomization
- Patients with severe pre-existing physical or mental disability or severe comorbidity which leads to a

poor outcome even if the patient completely recovers from the head injury
- Patients permanent residence outside a study country which prevents the follow-up
- If patient and/or relative has a strong belief for one treatment.

Patient Follow-Up

The patients were followed after 3 months, after the discharge from NIMHANS. Patients were called back to the outpatient department (OPD) for follow-up which was advised in discharge summary and the patients who did not come to OPD; the follow-up was done by telephonic conversation. The follow-up pro forma (Annexure) was filled for all the patients containing the details of patients recovery, their performance at and outside the home, ability to take care of themselves, and associated symptoms using Rankin score and extended Glasgow Coma Outcome scale [Scales 1 and 2].

Randomization

For allocating patients to the early surgery group and initial conservative group, block randomization method is followed where the investigator is blind for allocation of group to either early surgery group or initial conservative group. These block randomization blocks were prepared before the start of study. The distribution of the patients to each group was equal in each block. The allocation of patients to a group is continuous or alternate. After selecting the patients in clinical equipoise, the patients are allocated into either early surgery group or initial conservative group serially according to the randomized group.

Statistical Analysis

All the clinical and imaging data available were fed into a statistical software and statistical analysis was carried out using SPSS (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Qualitative variables were summarized as numbers and percentages. Quantitative variables were tested for normality. Non-normal variables were summarized as median followed by range (max-min). Test of association between qualitative variables was done using Chi-square/Fisher's exact test. Statistical significance of quantitative variables across categorical variables was tested using Mann–Whitney *U*-test or Kruskal–Wallis tests. $P < 0.05$ was considered to be statistically significant.

Scale 1: Rankin score

0	Well, no symptoms
1	Minor symptoms not affecting lifestyle
2	Minor handicap but independent in self-care,
3	Moderate handicap, requiring a little help with activities daily living
4	Needing a lot of help with activities daily living
5	Needing constant attention day and night

Scale 2: Extended glasgow outcome scale

1	Death	D
2	Vegetative state	VS
3	Lower severe disability	SD −
4	Upper severe disability	SD +
5	Lower moderate disability	MD−
6	Upper moderate disability	MD+
7	Lower good recovery	GR−
8	Upper good recovery	GR+

RESULTS

The general demographic data with clinical profile of patients are given in Table 1. A total of 86 patients were included in our study.

Out of 86 patients, 30 (34.48%) patients underwent early surgery, 47 (54.65%) patients were managed conservatively, and 9 (10.4%) patients were initially managed conservatively but eventually underwent surgery [Table 2].

Demographic and Clinical Parameters

In our study, out of 30 patients, 16 (53.3%) were male in the early surgery group and 14 (46.7%) were female. Out of 47 patients, 34 (72.3%) were male and 13 (27.7%) were female in initial conservative group. In crossover group, out of 9 patients, 7 (77.7%) were male and 2 (22.3%) were female. *P* value for gender is 0.08 which is statistically not significant. This shows randomization is uniform and there is no bias in gender distribution [Table 1].

Table 1: Gender distribution in the study population

Group	Frequency (%)
Early surgery	
Male	16 (53.3)
Female	14 (46.7)
Total	30 (100)
Initial conservative	
Male	34 (72.3)
Female	13 (27.7)
Total	47 (100)
Crossover	
Male	7 (77.7)
Female	2 (22.3)
Total	9 (100)

Table 2: Distribution of patients; early surgery group and initial conservative group

S. No.	Group	Frequency *n*=86(%)
1	Early surgery	30 (34.5)
2	Initial conservative	47 (54.65)
3	Crossover	9 (10.46)

Age Distribution in Study Population

In our study in the early surgery group, out of 30 patients, 20 (66.6%) were in 14–50 years age band and 10 (33.3%) were in >50 years age band. Out of 47 patients in initial conservative group, 31 (72.3%) were in 14–50 years age band and 16 (27.7%) were in >50 years age band. The mean age of the patients in the early surgery group is 46±13.8 years and initial conservative group is 45.9±12.6. $P = 0.992$ is statistically not significant. Hence, the randomization is good and there is no difference in distribution in age group [Table 3].

Cause and Mechanism of Injury

Out of 30 patients, 26 (86.7%) patients were injured with road traffic accident (RTA) in the early surgery group and out of 47 patients, 36 (76.6%) patients were in initial conservative group. Three (10%) patients in the early surgery group and 4 (8.5%) patients in initial conservative group had domestic fall. One (3.3%) patient in the early surgery group and 5 (10.6%) patients in initial conservative group had fall outside the home, and in initial conservative group, 1 (2.1%) patient each had injury at work place and assaulted.

Twenty-four (80%) patients in the early surgery group and 31 (66%) patients in initial conservative group had injuries due to acceleration or deceleration mechanism. Two (6.7%) patients in the early surgery group and 7 (14.9%) patients in initial conservative group had direct impact to head. Four (8.5%) patients fell at ground level in initial conservative group. Four (13.3%) patients in the early surgery group and 4 (8.5%) patients in initial conservative group had fall from more than 1 feet height. For 1 (2.1%) patient, the details are not known in initial conservative group [Table 4].

Time to Randomization

Mean time to randomize in the early surgery group is 8.5 h with SD of 7.9, and in initial conservative group, it is 15.3 h with SD of 15.7. In the early surgery group, median is 5 h with a range of 2–30 h, and in initial conservative group, the median is 9 h with a range of 1–47 h. *P* value for time to randomization is 0.024 and it is statistically significant. It is only the mean time but the patient may arrive late may be a chance.

Secondary Insults

Four (13.3%) patients in the early surgery group and 3 (6.4%) in initial conservative group had hypoxia. Nine (30%) patients in the early surgery group and 7 (14.9) patients in initial conservative group had hypotension.

Referral Details

Twenty-six (86.7%) patients in the early surgery group and 30 (63.8%) patients in initial conservative group were referred to NIMHANS by primary health center or private hospitals. Moreover, 4 (13.3) patients in early surgery and 17 (36.2%) patients in initial conservative group directly came to NIMHANS [Table 5].

Table 3: Baseline variables

Variable	Early surgery (*n*=30)	Initial conservative (*n*=47)
Age (years)		
Median	45	45
Range	21–81	24–81
Mean (SD)	46 (13.8)	45.9 (12.6)
Age band (years) (%)		
14–50	20 (66.6)	31 (66)
>50	10 (33.4)	16 (34)
Sex (%)		
Male	16 (53.3)	34 (72.3)
Female	14 (46.7)	13 (27.7)

Table 4: Injury causes and mechanisms

Variable	Early surgery group (%) *n*=30	Initial conservative group (%) *n*=47
Cause of injury		
Road traffic accident	26 (86.7)	36 (76.6)
Fall domestic	3 (10)	4 (8.5)
Fall outside home	1 (3.3)	5 (10.6)
Work	0	1 (2.1)
Assault	0	1 (2.1)
Mechanism of injury		
Acceleration/deceleration	24 (80)	31 (66)
Direct impact	2 (6.7)	7 (14.9)
Crush	0	0
Fall from ground	0	4 (8.5)
Fall From height	4 (13.3)	4 (8.5)
Details unknown	0	1 (2.1)

Table 5: Emergency services and admission details

Variable	Early surgery (%) *n*=30	Initial conservative treatment (%) *n*=47
Time to randomization (h)		
Median	5 (2–30)	9 (1–47)
Mean (SD)	8.5 (7.9)	15.3 (15.7)
Emergency services provided for airway (%)		
None	0	0
Oxygen	30 (100)	43 (91.5)
Intubation	0	4 (8.5)
Secondary insult (%)		
Hypoxia	4 (13.3)	3 (6.4)
Hypotensive	9 (30)	7 (14.9)
Hypothermia	0 (0)	0 (0)
Cardiac arrest	0 (0)	0 (0)
Referral details		
Primary admission	4 (13.3)	17 (36.2)
Secondary admission	26 (86.7)	30 (63.8)
Pupils		
Both reactive	29 (96.7)	39 (83)
One reactive	1 (3.3)	7 (14)
Both non-reactive <4 mm	0	1 (2.1)

Clinical Parameters

GCS

The mean total GCS score for the early surgery group is 11.9 with SD of 2.3, and mean GCS score for initial conservative group is 13.14 with SD of 2. The median GCS score for the early surgery group for total GCS score is 12 with a range of 9–15 and median GCS score for initial conservative group is 14 and range of 9–15. *P* value for total GCS is 0.003 and is statistically significant. The mean total GCS in the early surgery group is 12 and in initial conservative group is 13 both these values are within the range of moderate head injury although it looks statistically significant which may not be clinically significant and this difference might be affected by the sample size of both groups which is 2:3.

The mean GCS score for the early surgery group for eye opening is 3 with SD of 0.88, and mean for initial conservative group is 3 with SD of 0.76. The median for the early surgery group for eye opening score is 3 with a range of 2–4 and median for initial conservative group is 4 and range of 2–4. The mean GCS for eye response in both the groups is same.

The mean GCS score for the early surgery group for motor response is 6 with SD of 0.5, and the mean GCS score for initial conservative group is 6 with SD of 0.41. The median GCS score for the early surgery group for motor response is 6 with a range of 5–6 and median GCS score for initial conservative group is 6 and range of 5–6. The mean GCS for motor response in both the groups is same.

The mean GCS score for the early surgery group for verbal response is 3.3 with SD of 1.2, and mean GCS score for initial conservative group is 4 with SD of 1.15. The median GCS score for the early surgery group for verbal response is 3 with a range of 2–4 and median GCS score for initial conservative group for verbal response is 4 and range of 2–4.

Hospital stay

The mean hospital stay for the early surgery group is 4.5 days with SD of 0.96 days, and mean for hospital stay in initial conservative group is 4.87 days with SD of 0.97 days. The median hospital stay for the early surgery group is 5 days with a range of 3–7 days and median hospital stay for initial conservative group is 3 days and range of 2–7 days. *P* value for the hospital stay is 0.01 which is statistically significant. This suggests that patients with surgery improved fast and got discharged early without any doubt [Table 6].

Imaging Parameters

Vol. of largest hematoma

The mean volume of largest hematoma was 16.7 ml with SD of 5.8 in the early surgery group whereas 16.1 ml with SD of 5.4 in initial conservative group. The median was 18 and range 8–27.8 in the early surgery group and the median was 15 and range 10–29 in initial conservative group. *P* value for volume of large hematoma is 0.645 and it is statistically not significant.

Location of largest hematoma

In the early surgery group, 7 (23.3) patients had in the right frontal, 6 (20%) patients in the left frontal, 2 (6.7%) patients in the right temporal, and 15 (50%) patients in the left temporal region. In initial conservative group, 11 (23.4%) patients had in the right frontal, 10 (21.3%) patients in the left frontal, 12 (25.5%) patients in the right temporal, and 14 (29.8%) patients in the left temporal region.

Second hematoma

Second hematoma was seen in 8 (26.7%) patients in the early surgery group and 6 (12.8%) in initial conservative group.

Volume of second hematoma

Mean volume of hematoma 1.5 ml with SD of 2.6 in the early surgery group and 0.62 ml with SD of 1.7 in initial conservative group. *P* value for volume of the second hematoma is 0.111 and it is not statistically significant.

Location of second hematoma

The early surgery group had 4 (13.3%) patients in the right frontal, 4 (13.3%) patients in the left frontal region. Initial conservative group had 3 (6.4%) patients in the left frontal, 1 (2.1%) patients in the right temporal, and 2 (4.3%) patients in the left temporal region [Table 7].

Management Parameters

Airway

All the patients in the early surgery group were given oxygen. Forty-three (91.5%) were given oxygen in

Table 6: For Glasgow Coma Scale at presentation for the study population

	Early surgery group		Initial conservative group	
	Mean (SD)	Median (range)	Mean (SD)	Median (range)
Total Glasgow Coma Scale	11.9 (2.3)	12 (9–15)	13.14 (2)	14 (9–15)
Eye opening	3 (0.88)	3 (2–4)	3 (0.76)	4 (2–4)
Motor response	6 (0.5)	5.5 (5–6)	6 (0.41)	6 (5–6)
Verbal response	3.3 (1.2)	3 (2–5)	4 (1.15)	4 (1–5)
Hospital stay	4.5 (0.96)	5 (3–7)	4.87 (0.97)	5.5 (4–7)

initial conservative group and 4 (8.5%) patients were intubated.

Treatment

All the patients randomized to the early surgery group underwent craniotomy and evacuation of hematoma. Patients randomized to initial conservative group were provided best medical management according to standard guidelines.

Outcomes

Outcome at the time of discharge

The median GCS score at discharge in the early surgery group is 13 with a range from 7 to 15. In initial conservative group, median GCS score is 15 and range from 7 to 15 which shows improvement in conservative group at the time of discharge.

Primary outcome at 3 months

In the early surgery group, 24 (80) patients out of 30 patients had favorable outcome and 6 (20%) had unfavorable outcome. In initial conservative group, 43 (91.5%) patients had favorable outcome and 4(8.5%) had unfavorable outcome.

Secondary outcomes at 3 months

Mortality at 3 months

At the end of 3 months, out of 30 patients in the early surgery groups, 29 (96.7%) patients are alive and in initial conservative group, 44 (93.6%) patients are alive. In the early surgery group, 1 (3.3%) patient expired and in initial conservative group, 3 (6.4) patients were expired.

Table 7: Hematoma characteristics

Variable	Early surgery (%) *n*=30	Initial conservative treatment (%) *n*=47
Volume largest hematoma (ml)		
Median (range)	18 (8–27.8)	15 (10–29)
Median (SD)	16.7(5.8)	16.1(5.4)
Location of largest hematoma		
Right frontal	7 (23.3)	11 (23.4)
Left frontal	6 (20)	10 (21.3)
Right temporal	2 (6.7)	12 (25.5)
Left temporal	15 (50)	14 (29.8)
Second hematoma		
Yes	8 (26.7)	6 (12.8)
No	22 (73.3)	41 (87.2)
Volume of second hematoma (ml)		
Median (range)	0 (0–9)	0 (0–8)
Median (SD)	1.5 (2.6)	6.2 (1.7)
Location of second hematoma		
Right frontal	4 (13.3)	0
Left frontal	4 (13.3)	3 (6.4)
Right temporal	0	1 (2.1)
Left temporal	0	2(4.3)
No second hemorrhage	22 (73.3)	41 (87.2)

Extended GOS at 3 months

The results of extended GOS in both groups are similar and comparable.

In the early surgery group, 10 (33.3%) patients had good recovery, 10 (33.3%) patients had good recovery with minimal symptoms, and upper moderate recovery is seen in 4 (13.3%) of patients. Three (10%) patients had lower moderate disability, 2 (6.7%) were in upper severe disability, and 1 (3.3%) patient expired.

In initial conservative group, 22 (46.8%) patients had good recovery, good recovery with minimal symptoms is 16 (34%), and upper moderate recovery is seen in 5 (10.6%) of patients. One (2.1%) patient had lower severe disability and 3 (6.4%) patients expired. *P* value for GOS extended at 3 months is 0.23 which is not statistically significant.

Rankin score at 3 months follow-up

In the early surgery group, 10 (33.3%) patients as they are well no symptoms, 10 (33.3%) patients have minor symptoms not affecting their lifestyle, 5 (16.7%) patients as they are minimally handicapped, and one (3.3%) patient expired.

In initial conservative group, 22 (46.8%) patients as they are well no symptoms, 16 (34%) patients have minor symptoms not affecting their lifestyle, 5 (10.6%) patients as they are minimally handicapped, and 1 (2.1%) patient needs constant attention day and night, 3 (6.4%) patients expired [Table 8 and Figures 1-3].

DISCUSSION

Guidelines for the management of traumatic intracerebral hemorrhage are not clear and no Level I prospective

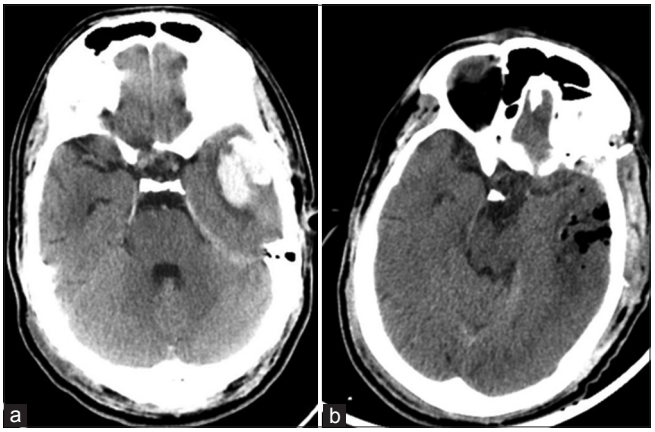

Figure 1: Patient randomized to the early surgery group. Patient presented at 7 h after injury and presentation Glasgow Coma Scale was E3M6V4. Computed tomography brain shows (a) pre-operative left temporal hematoma. (b) Post-operative good evacuation of hematoma

Table 8: Secondary outcomes at 3 months

Variable	Early surgery (%) *n*=30	Initial conservative (%) *n*=47
Mortality at 3 months		
Death (%)	1 (3.3)	3 (6.4)
Alive (%)	29 (96.7)	44 (93.6)
Glasgow Outcome Scale		
Dead	1 (3.3)	3 (6.4)
Vegetative	0	0
Severe disabled	2 (6.7)	1 (2.1)
Mod. disabled	7 (23.3)	5 (10.6)
Good recovery	20 (66.6)	38 (80.8)
Glasgow Outcome Scale extended		
Dead	1 (13.3)	3 (6.4)
Vegetative	0	0
Lower SD	0	1 (2.1)
Upper SD	2 (6.7)	0
Lower MD	3 (10)	0
Upper MD	4 (13.3)	5 (10.6)
Lower GR	10 (33.3)	16 (34)
Upper GR	10 (33.3)	22 (46.8)
Dichotomous Rankin scale score		
Unfavorable	5 (16.7)	4 (8.5)
Favorable	24 (80)	43 (91.5)
Rankin scale score		
0	10 (33.3)	22 (46.8)
1	10 (33.3)	16 (34)
2	5 (16.7)	5 (10.36)
3	4 (13.3)	0
4	0	0
5	0	1 (2.1)
Dead	1 (3.3)	3 (6.4)

studies are documented in the literature. Unlike SDH and EDH, where prompt surgical removal is established and accepted all over the world. There are trials of surgery for spontaneous ICH but no trials so far of surgery for TICH. Large intracranial hematoma with mass effect and midline shift, medium-sized hematoma with effacement of cisterns, and GCS score <8 needs early surgery. The dilemma is whether it is beneficial to perform early surgery in patients with parenchymal ICH which is one that should be addressed with high priority for the benefit of the patient. This was identified by NICE in the second edition of its guidelines for head injury.[1] The question arises whether to operate or manage conservatively in patients with clinical equipoise. This needs to be answered and to formulate standard guidelines for the management of patients in clinical equipoise. There are no prospective studies to support either surgical or conservative management.

Demographic Features

Our study is comparable to STITCH trial. We recruited our study cohort at one center (NIMHANS) for a period of 6 months. Mendelow *et al*. recruited patients from 13 countries and 31 centers for 3 years.[2] Our study

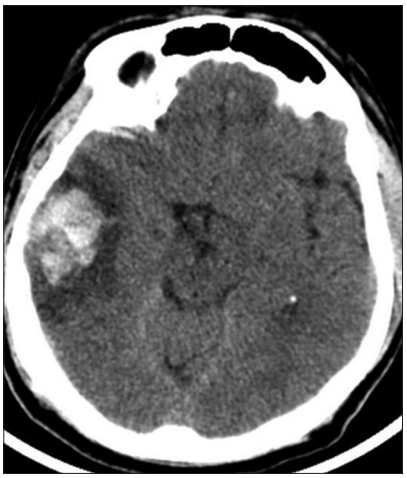

Figure 2: Patient randomized to conservative management presented after 3 h of injury. Glasgow Coma Scale was E3M6V4, computed tomography brain shows right temporal hematoma

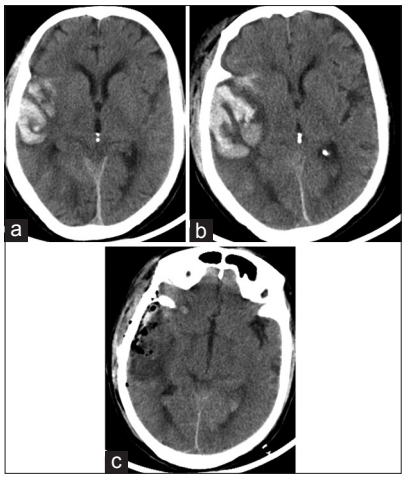

Figure 3: Patient randomized to initial conservative management and patient underwent surgery belongs to crossover group right temporal hematoma increased in size with clinical deterioration eventually underwent surgery. Patient presented 5 h after the injury. Glasgow Coma Scale (GCS) at presentation was E4M6V5 and deteriorated to GCS E3M6V3 after 5 h of randomization. (a) Computed tomography (CT) brain at the time of randomization. (b) CT brain after 5 h of randomization shows increase in size of hematoma with mass effect and midline shift to left. (c) Post-operative scan with good evacuation of hematoma and midline shift reverted

population of 86 were recruited in a relatively short period of time which is equivalent to other published series with respect to time frame. This indicates the high prevalence of intracerebral hematoma. Chang *et al*. had published his large series of 113 patients treated for a period of 3 years,[7] Alahmadi *et al*. study included 98 patients treated in 2 years.[8] Iaccarino *et al*. studied a total of 352 patients over a period of 2 years.[5]

Out of these 86 patients included in our study, 30 patients underwent surgery and 47 were managed conservatively. Mendelow *et al*., in their series, had 82 patients who underwent early surgery and 85 patients who were managed conservatively.

Our study cohort consists of a heterogeneous population with a wide age range from 21 to 81 years. Mendelow *et al*., in their series, have reported a range between 18 and 83 years. Our study has a mean age of 46 years in both groups, which is comparable to the data published by Mendelow *et al*.

Sex

Our study and the series published by Mendelow *et al*. have similar percentage of male and female patients – in a ratio of 2:1.[6] Yadav *et al*. have reported a male-to-female ratio of 2:1 and have also reported that expansion of traumatic ICH in both sexes is equal and statistically insignificant and they did not find gender as a risk factor.[9] In Alahmadi study, male-to-female ratio is 4:1. Iaccarino *et al*. study has a distribution of 3:1 male-to-female ratio.[5] Oertel *et al*. showed that male gender was so strongly associated with TICH. It may be possible that the vehicle riders are usually males, travel a lot as compared to the females, drive with alcohol consumption, hence, the incidence of trauma or RTA is common among them. Females will have the neuroprotective effects of estrogen and progesterone which reduce their likelihood of TICH.[10] Our series and other series have similar gender distribution.

Age

In our study, 60% of patients fell in the <50 years age group and 30% of patients were in >50 years age group. In Mendelow *et al*. study, there was equal distribution of patients in both age groups. Our study shows that young patients were more prone for injury. Evident by another Indian study published by Yadav *et al*., 65% of patients belong to young age.

In our study cohort, mean age in the early surgery group and initial conservative group is 46 years. Both the groups are comparable. $P = 0.992$ is statistically not significant [Table 9].

Cause of Injury and Mechanism

In our study, RTA is the most common mechanism of injury, sustained by 70% of patients, followed by other mechanisms such as fall at home and minor causes such as assaults and injury at workplace. Mendelow *et al*. reported RTA as the most common mechanism of injury, sustained by 66% of patients,[11] followed by domestic fall, assault, and injury at work place which contributed to 34%. In India, the most common cause of injury is RTAs due to poor road quality, violence of traffic rules, and inappropriate driving age.

In our study, most common mechanism of injury was acceleration or deceleration sustained by 64% of patients followed by direct impact fall at ground level and fall more than 1 m height accounting for 36% of patients. In Mendelow *et al*. study, the mechanism of injury acceleration or deceleration and direct impact has equal incidence followed by fall from ground 26%.[11] In both the studies, mechanism of injury has similar incidence.

Time to Randomization

In our study, the mean time to randomize from the time of injury is 8.5 h in the early surgery group and is 15.3 h in initial conservative group. This difference of mean duration of randomization may be due to time delay in referral of patients as a majority of the patients in our study are referred cases and also probably could be attributed to the difference in sample size of both cohorts.

Mendelow *et al*. have reported their mean time to randomization as 22 h in both groups.[12] As seen, their mean timings were delayed as compared to our study.

Iaccarino *et al*. reported a mean time period from injury to initial CT as 2 h. The second CT was obtained at an average of 9 h. The third CT was obtained at an average of 38 h.[5] This shows that there is early presentation of patients after trauma and there is high risk of expansion of hematoma. The CT scan has been repeated at regular intervals to pick up the patient for surgery before clinical deterioration evidenced by increase in size of hematoma or midline shift or increase in edema. Frowein *et al*., in their study, concluded that the 2nd and 3rd h following injuries are particularly important for the detection of hemorrhagic

Table 9: The study cohort, gender distribution, and mean age of various studies[7,9,13]

Study	Study design	No. of patients	Gender		Mean age
			Male	Female	
Chang *et al.*	Prospective retrospective	113	68	45	45
Al ahmadi *et al.*	Retrospective	98	79	19	50
Mendelow *et al.*	Prospective	170	112	46	48
Iaccarino *et al.*	Retrospective	352	256	96	55.6
Cepeda *et al.*	Retrospective	782	621	161	41
Oertel *et al.*	Prospective	96	78	18	34

lesions.[13] Oertel *et al*., in their study, have shown that results reaffirming the fact that TICH has the greatest tendency to progress early after injury, often in dramatic and rapid fashion, and hence, CT scan should be performed within 4–6 h after the first scan.[10] Hence, repeat scans should be done at regular intervals in the first 48 h.

Secondary Insults

Hypoxia raises the intracranial pressure and adds to the raised ICP which can cause fatal outcome. However, due to small fraction of patients with hypoxia, this may not contribute much to outcomes. Hypotension causes more damage to ischemic penumbra region surrounding the hematoma or contusion and equal number of patients – both the early surgery group and initial conservative group which statistically nullifies the contribution to outcome.

Mendelow *et al*., in their study, have reported a similar number of patients and there is a fair share of patients with complications between two groups which is comparable to our study.

Referral Details

In our study group, 70% of patients are referred to NIMHANS by peripheral hospital and 30% are direct admissions to NIMHANS. This is in contrast with the study conducted by Mendelow *et al*. where 40% were referred patients and 60% were primary admissions. In comparison with Mendelew *et al*., our study had more number of secondary admissions as NIMHANS is a tertiary referral center as there are limited facilities to treat head injury patients in peripheral hospitals.

Iaccarino *et al*., in their study, have shown that a majority of patients were treated in a hospital with neurosurgical unit and minor number patients treated in peripheral hospitals under neurosurgical supervision. There was no significant difference in the risk of unfavorable outcome among the patients treated in the hospitals with or without neurosurgery department.

Clinical Parameters

Total GCS

In our study, the mean GCS score in the early surgery group is 12 and in initial conservative group it is 13. In the early surgery group, the ratio of patients with mild head injury and moderate head injury is 1:2; in initial conservative group, mild head injury and moderate head injury is 1:1. This suggests that more number of patients with moderate head injury were included in the early surgery group and contributes much to good recovery as many other series found that the patients with moderate head injury benefit with surgery.

Mendelow *et al*. included mild, moderate, and severe head injury patients. In the early surgery group, the respective distribution is 2:4:1. In initial conservative group, the distribution is 1:2:1. As compared to above study, all the patients in our study belong to either moderate or mild head injury categories, as patients with GCS 3–8 with TICH need to be operated and there will not be any clinical equipoise and therefore cannot be randomized effectively.

Yadav *et al*. had a bigger fraction of moderate head injury patients with TICH of 26 ml followed by severe head injury patients with TICH of 11 ml and very minimal mild head injury patients with TICH volume of zero. This shows that the risk of expanding hematoma in patients with lower GCS score is significantly higher. Impact of GCS score has a direct correlation with the development of hematoma.

Alahmadi *et al*. have shown that poor GCS and large contusions are at increased risk of undergoing delayed surgery. The routine serial imaging for patients with small contusions and normal GCS score is less likely to alter their management after 48 h.

Iaccarino *et al*. have reported that patients with mild head injury were 40%, moderate head injury were 30%, and severe head injury were 30% at the time of admission in their series. Majority of severe head injury patients underwent surgery and so did a small number of patients with moderate and mild head injury. In initial conservative group, majority of patients had mild head injury and a small number of patients with moderate and severe head injury.

Hospital stay

In our study, it was found a median hospital stay for the early surgery group of 5 days with a range of 4–7 days. In the initially conserved group, it is 5.5 days with a range of 4–7 days. $P = 0.01$ is statistically significant. This shows that the early surgery group patients can be discharged faster as compared to patients who were initially conserved. Surgeon will be more confident of discharging patients home which reduces the financial burden on the family of patients and probably would also help patients get back to work early.

Mendelow *et al*. have reported that one-third of patients were still in the ward in the early surgery group and one-third in initial conservative group after 2 weeks. Half of the patients in the early surgery group and one-third of patients in initial conservative group were discharged. As this study included many severe head injury patients, there was a prolonged hospitalization as compared to our study.

Time Randomization to Surgery

In the early surgery group, the mean and median were same – 6 h.

Mendelow *et al*. have reported a mean of 4 h in the early surgery group and median 3 h with a range of 1–6 h. All the patients in our study were operated within 12 h of randomization and there was no violation of inclusion criteria.

Time Injury to Surgery

In the early surgery group, we had a median time to surgery of 12.5 h with a range of 3–35 h.

Mendelow *et al*., in their study, have reported that the early surgery group had a median of 23 h with a range of 16–36 h. There is a significant difference in median of both the groups and this variable cannot be compared.

Imaging Parameters

Volume of primary hematoma

In our study, mean and median volume of primary hematoma is same in both the groups and the range is also within the limits of inclusion criteria. The volume of hematoma is nearly equal and both are comparable. However, Mendelow *et al*., in their study, reported that their mean volume is 31 ml with range 11–96 ml in both the groups which is far beyond limits of clinical equipoise.

The scope of our study is limited and not to include any hematoma more than 30 ml. The literature says >50 ml of hematoma should be evacuated.

Yadav *et al*., in their study, have reported an initial TICH mean volume of 12 ml expanded to a mean volume of 33 ml, this increase was statistically significant.

Iaccarino *et al*. have reported that three-fourth of patients had a single hematoma and one-fourth of patients had more than one hematoma. About 90% of patients had small volume, 10% of patients had a volume of medium size, and small number of patients had a large volume. The analysis of variables associated with single contusions revealed that volume of single contusion is predictive for the evolution of hematoma. The mean TICH volume with midline shift was higher medium size TICH than without midline shift with small volume. Contusions <10 ml were never associated with hematoma evolution.

Location of primary hematoma

In our study cohort, 50% of patients had primary hematoma in temporal lobe and 35% in frontal lobe. In the early surgery group, 18% of patients had primary hematoma in frontal and 20% of patients in temporal lobes. In initial conservative group, 25% of patients had primary hematoma in frontal and 30% of patients in temporal region. The proportion of location of hematomas is comparable in both the groups.

In Mendelow study, in the early surgery group, 44% of patients had primary hematoma in frontal, 47% of patients had in temporal lobes, and small percent of patients in parietal and occipital regions. In initial conservative group, 50% of patients had primary hematoma in frontal, 43% of patients temporal, and small number of TICH in parietal and occipital regions. Our study and Mendelow study are comparable as the ratio of location of hematoma is more frequent in frontal and temporal lobes. This suggests the most common site of injury frontal and temporal lobes which is same in both the groups and proven in most studies.

Yadav study shows that expanding hematoma was more common in frontal and temporal regions. Majority of TICH were in frontal and temporal lobes. The expanding hematoma was seen equally in frontal and temporal regions with minimal chance in parietal region.

Second hematoma

In our study, there were small number of patients in both groups with the second hematoma and do not contribute significantly to the outcome. In Mendelow study, the second hematoma was seen in one-third of patients in both the groups.

In Yadav study, there were minimal patients with single TICH compared to large number of patients with multiple TICH. Chance of expansion of TICH is more with second or multiple contusions. In our study, there were very less number of patients having second hematoma, hence contributing less to outcome and cannot be compared.

Volume and location of second hematoma

In our study, the mean volume is 1.5 ml in the early surgery group and 0.62 ml in initial conservative group. There were small number of patients in both the groups in frontal and temporal lobes which may not contribute to outcome.

Management Parameters

Emergency services

In our study, all patients in the early surgery group received oxygen supplementation by nasal prongs in clinically permissible and optimum limits. In initial conservative group, majority of patients were given oxygen and a few patients were intubated. Some of them were intubated at peripheral hospital and referred to NIMHANS. This suggests the minimal requirement of intubation in patients with mild and moderate head injury.

Mendelow *et al*. reported that an equal numbers of patients in the early surgery group and in initial conservative group were not given any specific therapy. Majority of patients in the early surgery group and in initial conservative group were given oxygen supplementation.

A small number of patients in the early surgery group and in initial conservative group were intubated as they had severe head injury where endotracheal intubation is definitely required.

All the patients randomized to surgery underwent craniotomy and evacuation of TICH. Patients randomized to conservative management were given medical treatment as per standard neurosurgical protocols.

Outcomes

GCS at discharge

In our study, the median GCS score at discharge in the early surgery group was 13. In initial conservative group, median GCS score was 15. This showed a slight advantage in terms of GCS at discharge in conservative group. The patients in the early surgery group may have a slight lower GCS at discharge due to the post-operative stress and time needed for operative pain to be relieved. Furthermore, adjacent brain parenchyma handling during surgery needs to be accounted for. However, chances of further deterioration clinically are at a minimum as the offending TICH is evacuated.

Mendelow *et al*. recorded events at 2 weeks. Of the total number of patients in the neurosurgical wards at 2 weeks, one-third of patients were in the early surgery group and one-third of patients were in the initially conserved group. There was a significant difference in percentage of patients who expired at 2 weeks, which was 9% in the early surgery group and 20% in initial conservative group. As their study included severe head injury patients, mortality was high. In our study, there were no severe head injury patients and hence no mortality at 2 weeks follow-up.

Primary outcome at 3 months

To assess the outcomes, favorable outcome was considered with dichotomization of Rankin score which was ≤2. An unfavorable outcome was considered in case of dependency or death of the patient. We selected this in outcome analysis as the present-day focus is on clinically equipoised patients in TICH, which is not one adding years to life but to add life to years.

In our study, 80% of patients who underwent early surgery had favorable outcomes and 20% of patients had unfavorable outcome. In the initially conserved group, 92% of patients had favorable outcomes and 8% of patients had unfavorable outcome. The majority of patients had favorable outcomes and the proportions were nearly same in both the groups. Even though there is no statistical significance, there exists an "absolute benefit" of 11.49% with early surgery which makes early surgery a valid and appropriate option in the treatment of TICH.

Mendelow *et al*., in their study, reported that the early surgery had favorable outcomes in two-third of patients and one-third of patients had unfavorable outcomes. In the initially conserved group, half of the patients had favorable outcome and one-third of patients had unfavorable outcomes. There was no statistical difference in this study too in terms of comparison of outcomes. However, there existed an absolute benefit of 10.49% with early surgery.

Iaccarino *et al*. reported favorable outcomes in half of the study population, severe disability seen in one-third of patients, and small number of patients died in surgery group. In the initially conserved group, majority of patients had favorable outcomes, a small number of patients had severe disability and less number of patients expired.

The outcomes that we had in our series are in concordance with other large published series and results are comparable in terms of outcomes.

Secondary Outcomes at 3 Months

Secondary outcomes were measured with respect to mortality, extended GOS and Rankin score.

Mortality

In our series, at the end of 3 months, in the early surgery group, all patients except one were alive. In the initially conserved group, 94% of patients were alive and 6% of patients expired. The percentage mortality in the conserved group was higher, however it was not statistically significant.

In their series, Mendelow *et al*. reported that, in their early surgery group, a small number of patients expired and a majority were alive. In the initially conserved group, one-third of patients expired and two-third of patients were alive and this difference was statistically significant.

Yadav *et al*., in their study population, majority of patients with expanding hematoma were operated and among the operated, nearly half of the patients expired. There was no mortality in the conserved group and also had better grade of outcome. This study raises concerns over the advantages of surgical management that have been expressed in other large published series that have been discussed. One possible explanation is that this study involved all patients with and without clinical equipoise. Hence, this study population and randomization may not be relevant to our study cohort to draw inferences with respect to outcomes arising out of the two groups.

Extended GOS at 3 months

In our study series, the comparative analysis of results in both the groups is similar. In the early surgery group, one-

third of patients had good recovery. Another one-third of patients had good recovery with minimal symptoms. These patients went back to their normal life and are living their normal routines. Upper moderate recovery and lower moderate recovery are seen in small number of patients. These patients may take another 3 months to recover and may get back to their daily routine activities and work. Small number of patients had upper severe disability and one patient expired.

In the initially conserved group, half of the patients had good recovery. One-third of patients had good recovery with minimal symptoms. Upper moderate recovery and lower severe disability are seen in small number of patients and three patients expired. More number of patients in initial conservative group were discharged with minimal symptoms which do not affect their lifestyle as compared to the early surgery group.

Mendelow *et al*., in their study, reported that, in their early surgery group out of 82 patients, one-third of patients had good recovery with minimal symptoms. Upper moderate recovery and lower moderate recovery were seen in one-third of patients. Upper severe disability and lower severe disability were seen in one-third of patients and nearly one-fifth of patients expired. In the initially conserved group, one-third of the patients had good recovery with minimal symptoms. Upper moderate recovery and lower moderate recovery were seen in one-fourth patients. Small number of patients had upper severe disability and lower severe disability and one-third of patients expired.

The results that we have in our series are similar and comparable to that published by Mendelow *et al*. and this reiterates the fact that there is no difference in managing patients with clinical equipoise either conservatively or surgically.

Rankin score at 3 months

In our study population, and in the early surgery group, 80% of patients improved with near normal lifestyle at the end of 3 months. About 33% of patients were doing well without any symptoms, 33% of patients had minor symptoms however not affecting their lifestyle, 15% of patients were minimally handicapped, and one patient expired. All these patients may or may not have symptoms and had the potential to get back to their daily routine activities in short span of time.

In the initially conserved group, 92% of patients improved with near-normal lifestyle at the end of 3 months. About 50% of patients were doing well without any symptoms, 35% of patients had minor symptoms not affecting their lifestyle, 10% of patients were minimally handicapped, and 1 patient needed constant attention day and night, and also 3 patients had expired. On comparing the above two groups, the mortality rate was higher in the initially conserved group which may not be statistically significant but clinically contributes a lot to outcome.

In the series published by Mendelow *et al*., in their early surgery group, two-third of patients had improved with near-normal lifestyle at the end of 6 months. A quarter of the patients were doing well without any symptoms, one-third of patients had minor symptoms not affecting their lifestyle, small number of patients were minimally handicapped, and 12 patients had expired.

In the initially conserved group, half of patients had improved with near-normal lifestyle at the end of 3 months. One-fourth of patients were doing well without any symptoms, another one-fourth of patients had minor symptoms not affecting their lifestyle, small number of patients were minimally handicapped, and very less number of patients needed constant attention day and night and one-third of patients expired.

This gives the inference that even though the outcomes of the early surgery group and the initially conserved group appear similar and statistically not significant, the mortality is higher in the initially conserved group and there exists an absolute difference of 11.5% between these two groups in terms of mortality, which may suggest that early surgery is beneficial as compared to initial conservative management in the management of patients with TICH.

CONCLUSION

1. The present study demonstrates that patient with traumatic ICH in clinical equipoise, with GCS of 9–12, early surgery is indicated
2. Early surgery gives the benefit of fast recovery and better outcome
3. Patients with GCS of 14 and 15 in clinical equipoise can be managed conservatively with keen observation and regular interval imaging
4. Strategy of early surgery can be converted into reduced hospital stay, which in turn reduces the financial burden of patient's family
5. There is a scope for the development of this study into a large trial, to prove that early surgery is always better than wait and watch principle.

REFERENCES

1. Sarkar K, Keachie K, Nguyen U, Muizelaar JP, Zwienenberg-Lee M, Shahlaie K. Computed tomography characteristics in pediatric versus adult traumatic brain injury. J Neurosurg Pediatr 2014;13:307-14.
2. Zimmerman RA, Bilaniuk LT, Gennarelli T, Bruce D,

Dolinskas C, Uzzell B. Cranial computed tomography in diagnosis and management of acute head trauma. AJR Am J Roentgenol 1978;131:27-34.
3. Chesnut R, Servadei F. Surgical treatment of post-traumatic mass lesions. In: Marion DW, editor. Traumatic Brain Injury. New York: Thieme Medical; 1999. p. 81-99.
4. Rivano C, Borzone M, Carta F, Michelozzi G. Traumatic intracerebral hematomas. 72 cases surgically treated. J Neurosurg Sci 1980;24:77-84.
5. Iaccarino C, Schiavi P, Picetti E, Goldoni M, Cerasti D, Caspani M, *et al*. Patients with brain contusions: Predictors of outcome and relationship between radiological and clinical evolution. J Neurosurg 2014;120:908-18.
6. Miller J, Becker DP. Pathophysiology of head injury. In: Youmans J, editor. Neurological Surgery. Philadelphia, PA: WB Saunders; 1982. p. 1896-937.
7. Chang EF, Meeker M, Holland MC. Acute traumatic intraparenchymal hemorrhage: Risk factors for progression in the early post-injury period. Neurosurgery 2006;58:647-55.
8. Alahmadi H, Vachhrajani S, Cusimano MD. The natural history of brain contusion: An analysis of radiological and clinical progression. J Neurosurg 2010;112:1139-45.
9. Yadav YR, Basoor A, Jain G, Nelson A. Expanding traumatic intracerebral contusion/hematoma. Neurol India 2017;54:377-81.
10. Mc DA, Opeskin K. Timing of early changes in brain trauma. Am J Forensic Med Pathol 1998;19:1-9.
11. Smith C, Gentleman SM, Leclercq PD, Murray LS, Griffin WS, Graham DI, *et al*. The neuroinflammatory response in humans after traumatic brain injury. Neuropathol Appl Neurobiol 2013;39:654-66.
12. Kelley BJ, Lifshitz J, Povlishock JT. Neuroinflammatory responses after experimental diffuse traumatic brain injury. J Neuropathol Exp Neurol 2007;66:989-1001.
13. Mendelow AD, Teasdale GM, Russell T, Flood J, Patterson J, Murray GD. Effect of mannitol on cerebral blood flow and cerebral perfusion pressure in human head injury. J Neurosurg 1985;63:43-8.

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