Role of early decompressive hemicraniectomy (<24 hours) in malignant middle cerebral artery infarct

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Abstract

Introduction: Malignant middle cerebral artery territory infarct carries a mortality rate as high as 80% and produces severe disability among survivors. Decompressive hemicraniectomy is a lifesaving surgical procedure to decrease the intracranial mass effect and reduces the risk of transtentorial herniation but there are concerns that it also creates large number of survivors with severe neurological deficit.

Materials and Methods: All patients with malignant middle cerebral artery infarction fulfilling the inclusion criteria underwent surgical intervention in form of decompressive hemicraniectomy. The patients were divided into two groups: Group A (operated within 24 hours) and Group B (operated after 24 hours of stroke). The outcome of the patients was evaluated according to mRS and Barthel index.

Results: Mean mRS at discharge in patients operated within 24 hours was 4.31±0.75 whereas it was 4.54±0.52 in patients operated outside 24 hours but the difference was not significant statistically. At 3 months after discharge, mean mRS was 3.08±0.86 in Group A whereas it was 3.77±0.73 in Group B which was found to be statistically significant (p= 0.001).

Conclusion: Our study concluded that after decompressive craniectomy probability of survival significantly increased and patient with favourable outcome, mRS≤3 increases. Early decompressive craniectomy reduced mortality rates, patient had better outcome and early recovery.

Keywords: Decompressive hemicraniectomy, Malignant infarct, Herniation, Modified rankin scale, Middle cerebral artery.

Introduction

Malignant middle cerebral artery territory infarct carries a mortality rate as high as 80% and produces severe disability among survivors[1].[1,3] Decompressive hemicraniectomy is a lifesaving surgical procedure to decrease the intracranial mass effect and reduces the risk of transtentorial herniation. There also have been long-standing concerns that the decompressive hemicraniectomy creates survivors with severe neurologic disability and poor quality of life. Some studies have performed surgical decompression before clinical signs of herniation and within the first 24 hours after stroke and have reported promising results.[10] In this study we compared results of early surgery (<24 hours) versus late decompressive hemicraniectomy (beyond 24 hours) in patients of malignant middle cerebral artery infarction.

Materials and Methods

All patients presenting with malignant middle cerebral artery infarct to a tertiary care hospital from 1st March, 2015 to 31st December, 2016 fulfilling the following inclusion criteria were enrolled for this study. This is a non-randomized, prospective, a single tertiary care hospital based study.

Inclusion criteria

1. >18 years of either sex.
2. Clinical signs of infarction of the MCA territory with an NIHSS score >18 for the lesions of the non dominant hemisphere and >20 for the lesions of the dominant hemisphere.
3. Decrease in the level of consciousness to a score of >1 on item 1a of the NIHSS.
4. CT findings large hypodensity in 50% of the MCA territory with significant effacement of sulci & ventricles with midline shift.
5. In Arm (A) we included patients presenting with <24 hours of stroke onset with/without signs of herniation. In Arm (B) we included patients presenting with ≥24 hours of stroke onset with signs of herniation.

Patients with Prestroke modified Rankin scale score ≥2, GCS score <5, fixed & dilated pupils, any other coincidental brain lesion that might affect outcome, space occupying hemmorhagic transformation (i.e. hemorrhages occupying >30% of the infarcted territory with mass effect) of the infarct and life expectancy <3years due to any other general condition were excluded from the study.

Appropriate investigations including clinical and radiological evaluation were done for every patient.

Pre operatively all the patients were optimized and investigated for fitness of anesthesia which included correction of coagulation parameters and management of hypertension or hyperglycemia. All enrolled patients were subjected to a standardized decompressive hemicraniectomy as per protocol involving following steps: Large skin incision based at the ear, removal of a bone flap (diameter ≥12 cm, including the frontal, parietal, temporal, and parts of the occipital squama), removal of additional temporal bone so that the floor of the middle cerebral fossa can be decompressed and opening of the dura and insertion of an augmented dural patch consisting of either autologous periosteum and/or temporalis fascia or fascia lata. The perioperative care included antibiotic prophylaxis, DVT

prophylaxis, physiotherapy and trachesotomy if needed.

The outcome of the patients was evaluated according to mRS and Barthel index. Other parameters like hospital stay, ICU stay, need for ventilator and tracheostomy were also studied.

Results

The study included 30 patients of malignant middle cerebral artery infarction admitted between March 2015 and December 2016 with 15 patients in each group i.e. (Group A = operated within 24 hours and Group B = operated after 24 hours).

The mean age was 47.53 in group A and 50.33 in group B which was statistically non significant. ($p < 0.486$). In group A, out of total 15 patients, 9 were between the age group 46-60. In group B out of 15 patients, 10 patients were between the age group 46-60 which was statistically non-significant.

There were total 22 male patients and 8 female patients showing a male preponderance. There was no statistically significant difference in gender distribution between two groups. Out of total 30 patients 12(40%) had left sided infarct and rest 18 (60%) had right sided infarct. In Group A, 11 patients had right sided infarct and in group B, 7 patients had right sided infarct.

63.3% of patients had associated hypertension, 16.7% had Coronary Artery Disease, 26.7% had Diabetes Mellitus and 13.3% of patients had other co-morbidities [Table 1]. The two groups had statistically significant difference in distribution of coronary artery disease in two groups with all five patients present in group undergoing surgery within 24 hours.

Mean mRS at discharge in patients operated within 24 hours was 4.31±0.75 (mean±SD) whereas it was 4.54±0.52 (mean±SD) in patients operated outside 24 hours but the difference was not significant statistically. At 3 months after discharge, mean mRS was 3.08±0.86 (mean±SD) in Group A whereas it was 3.77±0.73 (mean±SD) in Group B which was found to be statistically significant ($p= 0.001$) [Table 2].

There was no statistically significant change in BI at discharge versus BI at 3 months in two groups ($p= 0.347$) [Table 3].

No statistically significant difference was found between ICU stay in two groups but the difference was significant statistically in terms of hospital stay wherein patients operated within 24 hours had a shorter stay in hospital as compared to other group.

Four patients expired during treatment, two in Group A and two in Group B.

Patients with left sided infarct had longer ICU stay and hospital stay as compared to patients with right sided infarct but the difference was not statistically significant [Table 4].

Discussion

Malignant middle cerebral artery territory infarct carries a mortality rate as high as 80% and produces severe disability among survivors.[1]

Currently, malignant hemispheric infarction is one of the main indications for decompressive hemicraniectomy when intracranial hypertension does not respond to conservative therapies.[2] About 10% or 20% of the patients with infarction in the territory of the middle cerebral artery develop hemispheric cerebral edema/swelling or malignant middle cerebral artery infarcts (MMCAI).[3]

Decompressive hemicraniectomy is a lifesaving surgical procedure to decrease the intracranial mass effect and reduces the risk of trans-tentorial herniation, therefore preventing secondary brain injury, brainstem compression and death. Immediate removal of the bone corrects the cerebral displacement, relieving the pressure exerted on the rostral midbrain structures. The rapidity of the process is difficult to be reversed by the medical methods.

The clinical course of patient with severe middle cerebral artery stroke is highly predictable. Clinical deterioration of patients with massive middle cerebral artery infarction peaks on days three to five because of increasing of brain edema, which is followed by progressive edema reduction within next two weeks. Therefore, waiting for a pupillary dilatation causes an unnecessary delay, since allowing mesencephalic ischemia to occur potentially worsens prognosis. Early identification of patients who are most likely to develop malignant edema after middle cerebral artery infarction can help in offering decompressive hemicraniectomy early.

Integration of clinical examination with early CT and MRI findings might permit determination of brain edema early after onset, thereby allowing aggressive treatment such as decompressive craniectomy before life threatening brain swelling and herniation. Predictive signs of malignant middle cerebral artery infarction observed on CT-scan (performed within 12 hours of ictus) are hypodensity in more than 50% of the middle cerebral artery territory, hyperdense middle cerebral artery and diffuse attenuation between the cortex and the white matter. A MRI diffusion-weighted imaging volume of 82 cm^3 when performed within 6 hours has a high specificity (98%) but low sensitivity (52%).[4] A MRI diffusion-weighted imaging volume of 145 cm^3 obtained before 14 hours is associated with 100% sensitivity and 94% specificity. MRI volumetric analysis appears to have a high specificity to detect patients at highest risk of developing malignant middle cerebral artery infarcts.

There also have been long-standing concerns that the decompressive hemicraniectomy creates survivors with severe neurologic disability and poor quality of life. Early hemicraniectomy reduces mortality after malignant middle cerebral artery infarction; however, it also increases the probability of survival with moderately severe disability (mRS of 4). The question arises if a mRS of 4 (unable to walk without assistance and unable to attend to own bodily needs without assistance) can be considered as a favorable outcome. Decompressive surgery is sometimes used only as a rescue therapy in the face of impending trans-tentorial herniation in selected patients. Retrospective analysis of this practice suggested that surgical decompression should be

reserved for patients who are young and have single-vessel, nondominant hemisphere strokes.[5.6] Some studies have performed surgical decompression before clinical signs of herniation and within the first 24 hours after stroke and have reported promising results.[7] Which patients should be considered for decompressive surgery and when such intervention should be undertaken remain unclear.

Further support for earlier intervention is the fact that the length of time needed for critical care therapy is significantly reduced in the group of patients treated early after severe stroke as was seen in our study. It is easy to understand that patient with anisocoria as sign for a frank herniation syndrome will have need of more advanced critical care support than those who are treated before mesencephalic ischemia can occur. This fact also accounts for the relatively better outcome in the patient group treated early.

Five randomized controlled trials concerning decompressive hemicraniectomy for malignant middle cerebral artery infarction compared role of surgery in validating indication, timing of surgery and outcome of patients - HeMMI (hemicraniectomy for malignant middle cerebral artery infarcts), HeADDFIRST (hemicraniectomy and durotomy for deterioration from infarction related swelling trial), DESTINY (decompressive surgery for the treatment of infarction of the middle cerebral artery), DECIMAL (Decompressive crainectomy in malignant middle cerebral artery infarction) and HAMLET (hemicraniectomy after middle cerebral artery infarction with life threatening Edema trial). However, all of these studies were retrospective and uncontrolled.

RCTs such as DECIMAL and DESTINY were undertaken to determine whether early hemicraniectomy offers clinically meaningful improvement in functional outcome after malignant stroke. DECIMAL study concluded that early decompressive craniectomy increased by more than half the number of patients with moderate disability and very significantly reduced (by more than half) the mortality rate compared with that after medical therapy[8]. DESTINY too showed reduced mortality in operated patients but it failed to demonstrate statistical superiority and was terminated prematurely in wake of results of joint analysis of three European trials [9].

The HAMLET study allowed delayed surgery up to 96 hours after stroke onset, and secondary outcome analyses showed that surgery within 48 hours significantly reduced the probability of severe disability or death (mRS 5 or 6), whereas delayed hemicraniectomy did not influence outcome. However, considering the small number of patients who received surgery beyond 48 hours (n 11), no final conclusion could be drawn[10].

The pooled analysis of randomized trials confirmed that decompressive surgery undertaken within 48 hours of stroke onset reduces mortality and increases the number of patients with a favorable functional outcome after malignant hemispheric infarction. However, it could not demonstrate any difference in functional outcome, comparing patients treated earlier versus later than 24 hours after symptom onset.[11]

In this study we compared results of early surgery (<24 hours) versus late decompressive hemicraniectomy (beyond 24 hours) in patients of malignant middle cerebral artery infarction. In comparison to the HAMLET trial we operated 15 patients very early i.e. < 24 hours and followed them for minimum of 3 months from the date of surgery and in the late group the other 15 patients which were operated after 24 hours and was followed for 3 months as well. The patients who were operated early showed better outcome and lesser propensities towards poor outcome (mRS of 5). In this context our results were parallel to the HAMLET which also showed greatest benefit of decompressive hemicraniectomy if surgery is performed early.

Inclusion and exclusion criteria were also as comparable with these trials and primary outcome measure was the score on modified Rankin scale (mRS) at 3 months dichotomized between favorable (0-4) and unfavorable (5 and death). Although we followed up the patients only for 3 months as compare to other studies which followed the patients upto one year but the results in our study were promising and towards a better outcome with early surgery. We had poor/unfavourable outcome only in 4 patients, two in early group and two in late group. Our results as compared to data of HAMLET/ DESTINY were much better with favorable outcome.

In the expanded meta-analysis of patients pooled from DECIMAL, DESTINY, and HAMLET, surgery conferred a protective effect on risk of death or moderate to severe disability (mRS score>4) at 12 months. Patients with an mRS score of 4 or 5may continue to enjoy meaningful interactions with their friends and family, although they likely will require 24-hour assistance indefinitely. Whether this represents an acceptable quality of life is highly subjective and will vary greatly depending on the values held by an individual patient.

In our study younger patients and those without cardiac co-morbidities showed favorable outcome and early recovery. In two prospective German studies, mortality was reduced from 78% in historical controls to 34% and 16% in surgically treated patients. Poor outcome, defined as a score lower than 60 on the Barthel index, occurred in 95% of the controls and in 50% and 16% of patients after surgery. The present study shows that after decompressive surgery the probability of survival increases from 28% to nearly 80% and the probability of survival with an mRS of ≤3 doubles. However, the probability of surviving in a condition requiring assistance from others (mRS of 4) increases more than ten times, although the risk of very severe disability (mRS of 5) is not increased. But this requires a totally dedicated team and holistic approach with inclusion of other specialties to raise the better outcome. Information about quality of life of survivors is essential for guiding such decisions.

Table 1: Comparison of associated co-morbidities in two groups

	Group				
	< 24 HRS	**> 24 HRS**	**Total**	**Chi-square value**	**P-value**
Hypertension	8	11	19	1.292	0.256
Coronary Artery Disease	5	0	5	6	0.021
Diabetes Mellitus	2	6	8	2.727	0.107
Other	3	1	4	1.154	0.299

Table 2: Comparison of mRS at discharge versus mRS at 3 months

	< 24 hours		**> 24 hours**				**95% Confidence Interval of the Difference**	
	Mean	**SD**	**Mean**	**SD**	**T**	**P-value**	**Lower**	**Upper**
mRS at Discharge	4.31	0.75	4.54	0.52	-0.911	0.371	-0.753	0.292
MRS at 3 months	3.08	0.86	3.77	0.73	-2.216	0.036	-1.337	-0.047
MRS difference	1.23	0.93	0.85	0.69	1.201	0.241	-0.276	1.046

Table 3: Comparison of BI at discharge versus 3 months

	< 24 hours		> 24 hours				95% Confidence Interval of the Difference	
	Mean	**SD**	**Mean**	**SD**	**t**	**P-value**	**Lower**	**Upper**
BI at discharge	11.54	5.16	11.92	9.47	-0.129	0.899	-6.559	5.790
BI 3 months	57.69	12.01	62.31	10.13	-1.059	0.300	-13.608	4.377
BI difference	46.15	13.09	50.38	9.00	-0.960	0.347	-13.328	4.866

Table 4: Comparison of Left Group and Right Group

	Left		**Right**				**95% Confidence Interval of the Difference**	
	Mean	**SD**	**Mean**	**SD**	**T**	**p-value**	**Lower**	**Upper**
ICU stay	9.67days	4.66	9.56	5.33	0.059	0.954	-3.763	3.985
Hospital stay	16.58days	7.69	16.11	6.25	0.185	0.855	-4.759	5.703
mRS difference	0.44	0.53	1.35	0.79	-3.103	0.005	-1.513	-0.304
BI difference	38.89	15.37	44.71	8.92	-1.229	0.231	-15.583	3.949

Conclusion

Patients treated before reversible signs of herniation had lower mortality rates was lower, better outcome, and were dependent on critical care for a shorter length of time. Our study showed that after decompressive craniectomy probability of survival significantly increases and number of patients with favourable outcome (mRS≤3) increases. Risk of very severe disability (mRS≥5) does not increase. The mortality rate in patients having cardiac co-morbidities eg, atrial fibrillation, coronary heart disease was significantly higher. Further studies are required to better elucidate quality of life outcome measures, timing of surgery, and treatment of dominant hemisphere.

Conflict of Interest: None.

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