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RESEARCH ARTICLE

OUTCOME OF DECOMPRESSIVE HEMICRANIECTOMY IN MASSIVE MIDDLE CEREBRAL ARTERY INFARCTION AND ITS PROGNOSTIC MARKERS

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ABSTRACT

Background: Malignant Middle cerebral artery territory (MCA) infarction constitutes about 10% of ischemic strokes. Though Decompressive Hemicraniectomy (DHC) has shown decreased mortality, the functional outcome and prognostic markers are still inconclusive. Objective: To determine the prognostic markers and functional outcome of Decompressive Hemicraniectomy in a series of patients with Malignant MCA Infarction. **Methods:** This was a prospective study from November 2015 to December 2017 at tertiary care hospital. Totally, 52 patients with massive MCA infarct were included in this study. All the patients were analysed elaborately both in pre-operative and post-operative period. The functional outcome was assessed with Barthel index (BI) during the follow up period of 6 months. **Results:** Out of 52 patients, 23 patients (44.2%) had favourable outcome (BI > 60). The good prognostic factors noted were age less than 45 years (60.9%), surgery done within 24 hours (73.3%), right sided infarction (60.9%). Early return of consciousness within 5 days in post-operative period and absence of clinical signs of herniation pre-operatively had statistically significant functional outcome based on BI>60 over 6 months follow up. Mortality was noted in 23.1% of patients. **Conclusion:** Decompressive hemicraniectomy is a favourable surgical treatment in patients with massive middle cerebral artery infarction. Age less than 45 years, right sided infarction, surgery done within 24 hours from ictus especially before clinical signs of herniation and postoperative regaining of consciousness within 5 days after surgery are good prognostic markers.

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INTRODUCTION

Stroke is the second-leading cause of death worldwide. Ischaemic stroke constitutes around 85% of all stroke patients (Kasner, 2001). Cerebral edema secondary to brain infarction leads to mass effect, increased intracranial pressure and tissue shift which causes rapid worsening of patient within 48 hours of infarction. The Space occupying cerebral edema more than two-third or more than 50 % to 70% of the middle cerebral artery territory is known as malignant cerebral infarction. Massive hemispheric or malignant Middle cerebral artery territory infarction constitutes about 10% of ischemic strokes (Murray, 1997; Holtkamp, 2001) These patients present with severe neurological deficits like hemiplegia, forced head and eye deviation, progressive deterioration in consciousness, aphasia, or a contralateral neglect syndrome (Holtkamp *et al*., 2001). Intensive medical management for malignant cerebral infarction in the form of mechanical ventilation, osmotic diuretics, hyperventilation and sedation were reported to be unsuccessful. Despite intensive medical management, mortality rate was reported as 80% (Kuroki *et al*., 2001; Cho, 2003).

Decompressive hemicraniectomy (DHC) is done as an emergency surgical procedure for brain edema due to several reasons, including massive middle cerebral artery (MCA) infarct. Decompressive hemicraniectomy produces compensatory space for the swollen brain and prevents the secondary damage. Though decompressive hemicraniectomy (DHC) has shown decreased mortality compared to medical management, the functional outcome of the patient post decompressive hemicraniectomy are still inconclusive (Holtkamp *et al*., 2001; Leonhardt, 1997; Gupta, 2004). Due to lack of literatures on pre and post-operative prognostic markers for Decompressive Hemicraniectomy, this procedure is less often done at the appropriate time. The objective of this study is to determine the prognostic factors associated with favourable functional outcome of decompressive hemicraniectomy in patients with malignant MCA infarction.

Objective of the study: Primary objective of this study is to determine the functional outcome of Decompressive Hemicraniectomy within a series of consecutive patients with malignant MCA infarction. Secondary objective of this study is to determine the various prognostic factors associated with

favourable functional outcome within a series of consecutive patients who underwent decompressive hemicraniectomy as treatment for malignant MCA infarction.

MATERIALS AND METHODS

Patient selection: A prospective study was done on 52 patients who presented with malignant MCA territory infarction treated with Decompressive Hemicraniectomy in our Institute of neurology, Madras medical college, Chennai. The time period was from November 2015 to December 2017. All the patients presenting with clinical deficits suggestive of MCA territory infarction were enrolled in this study. Patients fulfilling the inclusion and exclusion criteria were included to avoid many confounding factors.

Inclusion criteria: Patients presenting with clinical deficits suggestive of MCA infarction with NIHSS ≥ 16 or clinical deterioration of consciousness with score ≥ 1 on item 1a of NIHSS. Patients with Initial CT Brain or MRI showing infarct of > 50 percent of MCA territory with or without infarction in other territory. Follow-up CT or MRI study demonstrating brain swelling and a midline shift >5mm were included in this study. Patients who presents to hospital before 24 hours from the time of onset were included. Informed consent by responsible relative was obtained.

Exclusion criteria: Patients with Pre-stroke modified Rankin Scale (mRS) score ≥2 and chronic disabling neurological illness, patients with acute stroke presenting with both pupils fixed and dilated, contralateral ischemia or other brain lesion that could affect functional outcome, space-occupying haemorrhagic transformation of the infarct, other serious illness that could affect outcome of patient, known coagulopathy or systemic bleeding disorder and contraindication for anaesthesia were excluded from this study. Patients presented after 24hrs from ictus, stroke with unknown time of onset, GCS less than 5 and clinical signs of herniation before admission were also excluded.

Patient evaluation: All the patients enrolled in this study underwent complete clinical examination along with a detailed history at the time of admission. History of vomiting was given importance and considered as one of the parameter for prognosis. Patients were assessed with NIHSS scale and Glasgow coma scale (GCS) at the time of admission. Clinical signs of herniation like anisocoria, bilateral Babinski sign and deterioration of consciousness were recorded on admission and preoperatively. Imaging of Brain was done either with CT or MRI. Patients were thoroughly monitored during course of admission in both pre and post-operative period. Levels of consciousness of all patients were evaluated on the 5th postoperative day. Patients were carefully monitored post operatively for the following parameters like duration of stay in the ICU, need for mechanical ventilation, clinical status, requirement of anti-edema measures, biochemical parameters and signs of sepsis.

Assessment of functional outcome: Functional outcome was evaluated by the Barthel index (BI) and Modified Rankin Scale at the time of discharge and every month until 6 months of follow-up. Patients were divided into two groups based on Barthel index (Mahoney, 1965). Group A includes patients with favorable outcome which was defined as BI ≥60 (mild disability to good recovery) and Group B includes patients with poor outcome which was defined as BI <60(moderate to severe disability).

Statistical analysis: The collected data were entered in Excel spread sheet and analysed using STATA statistical software package release 11. We used the two sided independent sample t test to compare means across dichotomous variables and the one way ANOVA test for comparison of means across multilevel variables. Linear regression analysis were used. A type I error of 0.05 was considered for all the analyses. Frequency test including the number of participants, age and gender were analysed.

RESULTS

Totally 52 patients were analysed in this study. Among 52 patients 37 were male and 15 were female. Patients mean age of this cohort was 47.4± 13.02 years. Table 1and 2 shows baseline observations of this study. Minimum age was 15 years and maximum age was 70 years. The commonest etiological factor was large vessel atherosclerosis(55.8%) and major risk factors were alcohol (53.9%) and smoking (36.5%) shown in Table 3.The comparison of prognostic markers based on Barthel Index pre and post operatively in the two groups (Group A and Group B) are shown in Table 4 and 5 respectively. Among 52 patients, 29 patients (55.8%) were in Group B had unfavourable outcome (BI <60) and 23 patients (44.2%) were in Group A had favourable outcome (BI > 60). Out of 52 patients, 44.2% of patients were younger than 45 years, 16% were in the age group of 46-59 years and 25% were older than 60 years. Among patients aged below 45 years (60.9%) had a satisfactory favourable outcome and in patients with above 60 years (84.6%) had unfavourable outcome with a statistically significant (p=0.03) age factor. Mean preoperative GCS was 9.82 ± 2.32 and mean NIHSS on admission was 22.2 ± 4.9. Accurately, 73.3 % of patients operated within 24 hours had BI>60 at 6 months follow up, while 29.4% of patient operated after 48 hours had BI >60 at 6 months follow up which was statistically significant(p=0.02).Mean timing of surgery was 40.7 ± 20.1 hours. Out of 52 patients,60.9 % of patient with right side infarction had BI>60 at 6 months follow up and 31% patient with left side infarction had BI>60 at 6 months follow up which was statistically significant (p=0.03). Mortality was 23.1 % during the hospital stay as well as during follow up for 6 months. One patient died on 3rd month and another patient developed late onset seizures and died on 5th month. Patients with negative clinical signs for herniation preoperatively and early return of consciousness within 5 days in the post-operative period and patients without respiratory failure had statistically significant favourable functional outcome based on BI>60 over 6 months follow up. Mean duration of hospital stay was 22.5± 6.9 days. Gender distribution, involvement of additional vascular territory and post-operative infection was statistically insignificant for favourable functional outcome based on BI > 60 over 6 months follow.

DISCUSSION

Among patients with ischaemic stroke, the malignant MCA infarction was always considered as poor prognosis group. The dynamic natural of course of illness like mass effect during early 2-4 days leads to rapid clinical deterioration. Decompressive Hemicraniectomy surgery reduces the mass effect and prevents secondary damage and tissue shifts.

Table 1. Baseline variables: MCA- Middle Cerebral Artery, ACA- Anterior Cerebral Artery, CT- computed tomography

variables		n (%)
Age	<45 years	23(44.2)
	46-59 years	16(30.8)
	>60 years	13(25)
Sex	Male	37(71.2)
	female	15(28.8)
Affected side	right	23(44.2)
	left	29(55.8)
Time to operate	<24 hrs	15(28.8)
	24-48 hrs	20(38.5)
	>48 hrs	17(32.7)
VASCULAR TERRITORY	MCA	33(63.5)
	MCA and ACA	19(36.5)
Clinical signs of Herniation positive		24(46.2)
Vomiting before admission		12(23.1)
Pre-operative CT herniation		21(40.1)
Respiratory Failure post- operative		18(34.6)
Mortality		12(23.1)

Table 2. Observations of the study: SD- Standard Deviation, BI- Barthel Index, GCS- Glascow Coma Scale, NIHSS- National Institute of Health Stroke Scale

Variables	Mean ± SD
Mean age (years)	47.4±13.02
Mean pre-operative GCS	9.82± 2.32
Mean NIHSS	22.2±4.9
Mean timing of surgery (hours)	40.7±20.1
Mean duration of hospital stay (days)	22.5±6.9
Mean Barthel Index during 6 months follow up	44.9±29.4

Table 3. Etiology and risk factors

variables		N(percent)
ETI0LOGY	LARGE VESSEL ATHEROSCLEROSIS	29(55.8)
	CARDIOEMBOLISM	8(15.4)
	ICA DISSECTION	1(1.9)
	OTHER/UNKNOWN	14(26.9)
RISK FACTORS	Diabetes mellitus	17(32.7)
	Systemic Hypertension	19(36.5)
	Coronary artery disease	6(11.5)
	SMOKER	19(36.5)
	ALCOHOIC	28(53.9)

Table 4. Comparison of Pre-operative variables between two groups: MCA- middle cerebral artery, ACA- anterior cerebral artery

Variables		GROUP B BI <60 (n=29)	GROUP A BI>60 (n=23)	P VALUE
Age	<45 years	9(39.1%)	14(60.9%)	0.03
	45-60 years	9(56.2%)	7(43.8%)	
	>60 years	11(84.6%)	2(15.4%)	
Sex	Female	9(60%)	6(40%)	0.69
	Male	20(54.1%)	17(45.9%)	
Time To Operate	< 24 hrs	4(26.7%)	11(73.3%)	0.02
	24-48 hrs	13(65%)	7(35%)	
	>48 hrs	12(70.6%)	5(29.4%)	
Vascular Territory	MCA	16(48.5%)	17(51.5%)	0.16
	MCA + ACA	13(68.4%)	6(31.5%)	
Affected Side	right	9(39.1%)	14(60.9%)	0.03
	left	20(69%)	9(31%)	
Clinical signs of herniation	YES	17(70.8%)	7(29.2%)	0.04
	NO	12(42.8%)	16(57.2%)	
Pre-operative CT herniation	yes	15(71.4%)	6(28.6%)	0.06
	no	14(45.2%)	17(54.8%)	
Vomiting within 24 hours	yes	6(54.5%)	5(45.5%)	0.92
	no	23(56.1%)	18(43.9%)	

Table 5. Comparison of post-operative variables between two groups:

VARIABLES		GROUP BBI <60 (n=35)	GROUP A BI>60 (n=26)	P VALUE
RETURN OF CONSCIOUSNESS WITHIN 5 DAYS AFTER OP	YES	13(40.6%)	19(59.4%)	0.005
	NO	16(80%)	4(20%)	
RESPIRATORY FAILURE	YES	15(83.3%)	3(16.4%)	0.003
	NO	14(41.2%)	20(58.8%)	
INFECTION	YES	14(70%)	6(30%)	0.102
	NO	15(46.9%)	17(53.1%)	

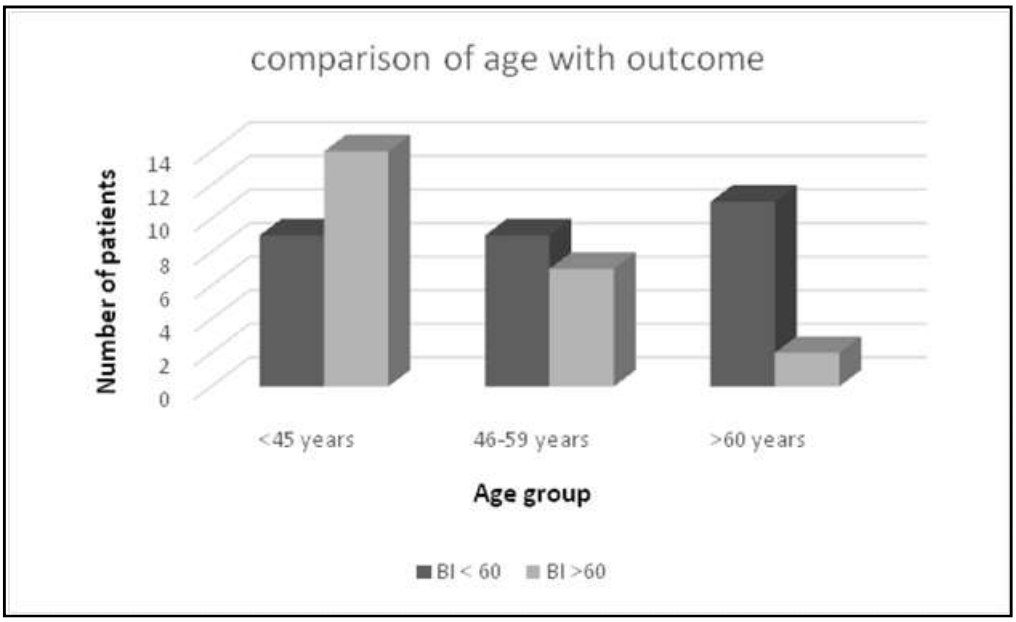

Figure 1. Comparison of age with final outcome: showing better outcome in patient's younger than 45 years

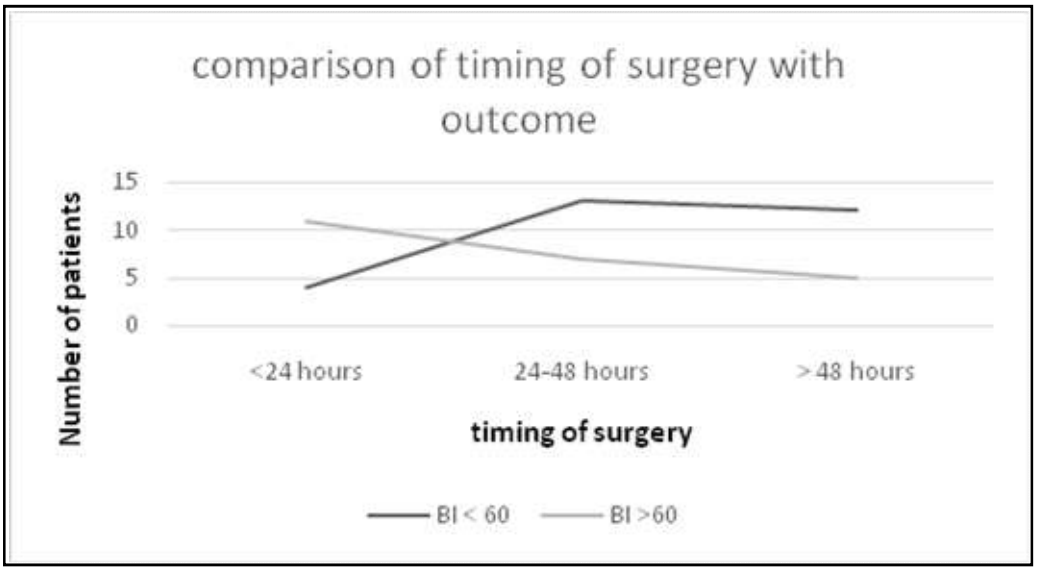

Figure 2. Comparison of timing of surgery with Barthel Index at 6 month: showing better outcome when operated within 24 hours

According to three randomized control trials (DECIMAL, DESTINY, HAMLET) early Decompressive hemicraniectomy for malignant MCA infarction reduces mortality compared to conservative medical management (Leonhardt *et al*., 1997; Gupta *et al*., 2004). Survival at one year was higher in the DHC compared with the medical management. They also showed probability of survival at one year after DHC were increased from 28% to 78%.Outcomes were measured based on mRS scale.

Among the survived patients most of them had moderate to severe disability. DESTINY and DECIMAL were stopped early due to high difference in mortality between the groups (Frank *et al*., 2014; Lu *et al*., 2014; Yang *et al*., 2015). In our study, the mortality was 23.1% which is consistent with the above three RCTs. Among 12 mortality patients, two had late onset seizures during the follow up period. In our study, 52 patients of aged between 15 to 70 years were analysed. 15 were female and 37 were male.

40 % of males and 45.9% of females had favourable outcome. Statistically gender was found to be insignificant in influencing the functional outcome. Several randomized and non-randomized studies showed that gender does not have significant impact on outcome after decompressive hemicraniectomy (Nakayama *et al*., 1994; Rieke *et al*., 1995). Mean age in our study was 47.4 ± 13.02 years with age ranging from15 years to 70 years. Majority of patients were in the age group of less than 45 years (44.2%). Accurately, 60.9 % of patients younger than 45 years, 43.8% of patients in the age group of 46 -59 years and 15.4% elder than 60 yearshad favourable outcome following DHC during six months follow up (Figure 1). Though DHC reduces mortality among all age group, outcomes were better in patients aged less than 60 years. Patients younger than 45 years in particular were found to have better functional outcome which was found to be statistically significant (p=0.03). Majority of RCTs like DECIMAL, DESTINY I, HAMLET included patients in age between 18 to 60 years. Vehedi *et al*. (2007) noted patients with above and below 50 years who had benefitted from surgery compared to conservative group. Kuroki *et al*. also showed surgery is better than conservative management even in patients above 70 years (Yang, 2015; Rieke, 1995). These studies showed 40 % of patients had moderate to severe disability at one year.

In our study, 73.3% of patientsoperated within 24 hours, 35 % of patients operated between 25 – 48 hours and 29.4% of patients operated after 48 hourshad favourable functional outcome at six months (Figure 2). DCH within 24 hours were found to be statistically significant (p=0.02) when compared with surgery after 24 hours. Mean timing of surgery in our cohort is 40.7 ± 20.1 hours. Majority of patients were operated in the time period between 24- 48 hours. Schwab *et al*. observed decompression before 24 hours had significant favourable outcome with Barthel index >60 for one year follow up (Vahedi *et al*., 2007; Hacke *et al*., 1996). Vahedi *et al*. showed there is no difference in outcome based on timing of surgery either before or after 24 hours. In our view, along with the timing, pre-operative GCS, NIHSS and clinical deterioration can be considered for a good favourable outcome. In our study, we had excluded patients presenting on admission with GCS less than 5. Mean pre-operative GCS was 9.82 ± 2.32. Outcomes was found to be better in patients with pre-operative GCS more than 9 on regression analysis. History of vomiting within 24 hours were considered as individual prognostic marker in various studies. But in our cohort, 21 % of patient had history of vomiting in history which was found out to be statistically insignificant (p=0.92). Gupta *et al*. showed that functional outcome after decompression on dominant hemisphere were similar to non-dominant hemisphere (Gupta, 2004). In Kilincer *et al*. review, there is no difference in functional outcome between domninant and non-dominant hemisphere (Kilincer *et al*., 2005; Schwab *et al*., 1998). In our study, 44.2 % of patients had right sided and 55.8 % had left sided infarction. Favourable outcome was noted in 60.9 % of patients with non-dominant hemisphere involvement as compared to 31 % of patients with dominant hemisphere infarction which was statistically significant (p=0.03). Rehabilitation in both dominant and non-dominant hemisphere involvement is hindered by several factors. In dominant hemisphere infarction aphasia is the major deterrent hindering rehabilitation. In non-dominant infarction hemineglect, depression, abulia were significant contributors hindering rehabilitation (Holtkamp *et al*., 2001; Hofmeijer, 2003).

In our view, non-dominant hemisphere infarction had better functional outcome, but side of infarction should not be considered as exclusion criteria. In our cohort, 46.2 % of patients had positive clinical signs of herniation pre-operatively. Among 24 patients with positive clinical signs of herniation, 7 (29.2%) had favourable functional outcome and found to be a significant prognostic marker affecting the outcome(p=0.04). Similarly we had found that the regaining of consciousness within 5 days during post-operative period and patients not developing respiratory failure had favourable functional outcome with significant statistical correlation (Hofmeijer, 2003; Jüttler, 2007; Vahedi *et al*., 2007). Even though involvement of additional arterial territory and infection during post-operative period increase the mortality and morbidity of the patients as reviewed in several studies (Zhao, 2012; Slezins *et al*., 2012).

We found these factors were not statistically significant markers to affect favourable functional outcome. As per our institutional experience, we observed that decomperessive hemicraniectomy as a useful surgical procedure for malignant MCA infarction. Patient aged less than 60 years especially less than 45 years, right sided hemisphere involvement, pre-operative GCS ≥9 , time of surgery within 24 hours from ictus, negative clinical signs of herniation and regaining of consciousness before 5 days in post-operative period without development of respiratory failure were considered as good prognostic factors. Since the study was conducted in consecutive series of patients and non-randomized, it was considered as one of the important limitation of this study. Hence, larger randomized studies are required to validate these findings.

Conclusion

Decompressive hemicraniectomy is a useful surgical treatment in malignant MCA infarction particularly in younger patients. Age less than 45 years, right hemisphere involvement, DCH within 24 hours from ictus before clinical signs of herniation and regaining of consciousness within 5 days after surgery were considered as good prognostic factors associated with better functional outcome.

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