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Malignant middle cerebral artery stroke management in developing world-outcome predictors

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Abstract

Background & Objectives: Malignant middle cerebral artery (MCA) stroke constituting 5% of all strokes carries a high mortality across the world. We aimed to study predictors of malignant MCA stroke outcome, especially decompressive surgery in a developing country scenario. *Methods:* This was a prospective study design where patients with malignant MCA stroke (defined as imaging-CT/MRI showing infarct involving >2/3rd MCA territory) admitted within 7 days of illness to SCTIMST, between January 2010 and December 2014 (5 years) were recruited. Clinical and imaging data, surgical details, in hospital complications and discharge outcome were collected. Follow-up data was collected at 3 and 12 months post-stroke. *Results:* We had 74 patients of malignant MCA territory strokes, 42 operated and 32 non-operated, who were comparable at baseline, except for age and stroke severity. At 3 months, deaths were more among the non-operated group (63% in non-operated vs 23% in operated group, p=0.02), while functional outcome was comparable. At 1 year follow-up, age below 60 years, lower stroke severity at onset and decompressive surgery were found to be independent predictors of good outcome. (p=0.04). Delayed surgery group, albeit small had a better 1 year outcome in comparison to the medical arm.
Conclusions: Early functional outcome in the decompression group did not differ from the medically treated patients, other than mortality benefit. However, at 1 year, patients with age<60 years, lower stroke severity and decompressive surgery had a better morbidity and mortality outcome, indicating long term benefit of this life saving procedure in developing country scenario as well.

Keywords: Malignant middle cerebral artery stroke, decompressive hemicraniectomy, functional outcome.

INTRODUCTION

Malignant MCA stroke, which constitutes a small fraction of all ischemic strokes carries a high mortality of the order of 80% with conservative management.[1-3] Decompressive hemicraniectomy is a lifesaving palliative surgery to relieve intracranial pressure in which the skull is opened and a bone flap is removed to allow the edematous brain to swell outward, thereby preventing intracranial tissue shifts and life-threatening herniation. Although there has been level one evidence on the benefit of this palliative procedure, all were from developed countries.[4-7] Short as well as long term functional outcome in malignant MCA stroke survivors also depends on comprehensive rehabilitation. In a developing country scenario like ours with very few centres in the public health care sector offering comprehensive neuro-rehabilitation, post discharge care is almost always done by the family. Therefore extrapolation of data from clinical trials where participants received a 3-6 months intensive neuro-rehabilitation may be an overestimation of the benefit of this palliative procedure, when applied to resource limited settings. With increasing prevalence of lifestyle diseases and stroke in developing countries, we are seeing more survivors with severe strokes. Hence more data about malignant MCA strokes in the current era of better intensive medical care and likely to receive a predominantly care giver based rehabilitation post discharge is required before recommending surgical management for all. This is more true in older patients and those with delayed presentation, where existing evidence is insufficient.

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Our primary aim was to identify short and long term predictors of outcomes of patients admitted with malignant MCA strokes. In addition, we also looked into the impact of the surgical procedure (decompression) in 2 subgroups, older patients (>60 years) and those undergoing late surgery (beyond 48 hours of onset) on outcome.

METHODS

The study was conducted at Comprehensive Stroke Care centre, Department of Neurology, Sree Chitra Tirunal Institute for Medical Sciences and Technology, a tertiary care centre for Neurological and Cardiovascular disorders, catering to an average of 400 inpatients in stroke unit annually, 80% of whom are ischemic stroke. Ours was a prospective study design where consecutive stroke patients admitted between Jan 2010 to December 2014 (5 years) with malignant MCA stroke, defined as infarct involving > 2/3rd of MCA territory on CT/MRI were recruited. The conduct of the study was approved by institutional ethics committee.

The inclusion criteria of the study patients were: 1. Malignant MCA strokes; 2. Age > 18 years; 3. Duration < 96 hours from onset of symptoms to the decision on need for surgical/ medical management; 4. Premorbid modified Rankin Scale (mRS) 2 or less. The exclusion criteria were: 1. Other additional arterial territory strokes – anterior/posterior cerebral artery; 2. Bi-hemispheric stroke; 3. Other serious acute medical comorbidities at admission like acute coronary syndromes, congestive cardiac failure, respiratory or hepatic failure-which can influence against decision for surgery.

All the patients admitted received intensive care in Stroke/Neurology ICU with continuous monitoring of hemodynamic and neurological status-using Glasgow coma score and NIHSS. Worsening of sensorium by 1 point drop in GCS from baseline, not explained by metabolic abnormalities or seizures, with imaging showing increasing mass effect was considered as point of intervention. All the subject's caregivers were counselled regarding the outcome of malignant MCA stroke, need for decompression and expected outcome of the procedure. There was no distinction made in Right versus left hemispheric involvement in the decision making. Main reason for opting for conservative management was age >60 years (24/32), financial constraints (4/32) and relatives inability to cope with disability long term (4/32).

Patients with good outcome was defined as mRS ≤ 3 and fair outcome was defined as mRS ≤ 4.We looked at outcome at discharge, 3 months and 12 months from the outpatient follow-up data from stroke clinic. Wherever follow-up data was incomplete, we did a telephonic follow-up of mRS.

RESULTS

Out of 1100 ischemic stroke patients admitted during the study period of 5 years, 74 who satisfied inclusion criteria were taken in this study (6.7%). Of these 42 patients had undergone decompressive hemicraniectomy in addition to medical management and 32 had received medical management alone.

On comparing the baseline characteristics, the surgical group were relatively younger and had lower stroke severity as measured by National Institute of Health Stroke scale (NIHSS) at presentation. Rest of the demographic and clinical parameters were comparable between the groups, which is given in Table 1. The most common etiology of stroke across both groups was cardioembolism. Neuroimaging data of the patients are given in Table 2.

Outcome at discharge

At discharge 27 in surgical group and 14 in medical group had a fair outcome (mRS ≤ 4) which was comparable. None had good outcome-defined as m RS ≤ 3 at discharge. There were 8 deaths in the surgical group and 14 in the medical arm, the difference being significant on univariate analysis (43.75% versus 19%). But on correction for age and baseline NIHSS scores, this difference was not statistically significant.

Long term outcome

We had follow up data for all patients in the surgical group. Three and 12 month follow up was available for 29 and 28 respectively in the medical group .Mortality was less in the surgical group at both the follow-up time points. There was no significant difference between good and fair outcome (mRS ≤ 3 or 4) between surgical and medical group at 3 months. However, at 12 months, good and fair outcome were better in the survivors undergoing decompression, after age and NIHSS adjusted analysis without an increase in survivors with severe disability (mRS 5) (Table 3 and 4).

Table 1: Baseline patient characteristics

Patient characteristics	Surgical management N=42	Medical management N=32	p value
Mean Age (in years ±SD)	51.7 ±12.7	62.6 ±16	**0.002**
Sex F:M	18:24	14:18	0.939
Medical comorbidities :			
Type 2 diabetes mellitus	14	11	0.925
HTN	22	16	0.839
Dyslipidemia	10	8	0.906
Coronary artery disease	12	8	0.732
arrhythmia	15	14	0.483
Etiology of stroke:			
Large vessel atherosclerosis	7	3	
Cardioembolic	18	17	
Other determined etiology	3	4	
Indeterminate cause	14	8	
Hemisphere involved			
Left	19	12	0.504
Right	23	20	
NIHSS on admission	16.8±3.6	19.4±4.1	**0.005**
Aphasia	18/42	14/32	0.990
GCS on admission	10±2.2	9.2 ±2.4	0.169
In-hospital complications DVT			
Infections	1 /42	0/32	1.00
	17/42(40.4%)	9/32(28.1%)	0.33
Seizures	4/ 42 (9.5%)	2/32 (6.25%)	0.609

Table 2: Imaging characteristics

Patient characteristics	Surgical group	Medical group	p value
Hemorrhagic conversion			
Nil	27/42	21/32	0.490
HI 1 and 2	6/42	7/32	
PH 1 and 2	9 /42	4/32	
Midline shift			
Nil	13/42	11	0.870
0-10mm	22/42	17	
>10mm	7/42	4	
Herniation	3/29	5/42	1.00
Vessel imaging:			
(Site of occlusion/stenosis)			
No occlusion/stenosis	4	2	
Internal carotid artery	14	11	
MCA proximal segment (M1)	13	12	
MCA distal segment (M2)	4	3	
Collateral scoring	N = 30	N = 21	
No collaterals	7	8	0.393
Collaterals < 50%	17	8	
Collaterals > 50%	6	5	

Table 3: Survivors Outcome on follow-up 3 and 12 months

Patient characteristics	Surgical group N=42 (%)	Medical group N=32 (%)	Odd ratio (95% CI)	P value for the odds ratio *
mRS at 3 months				
≤ 3	3	3		NS
≤ 4	29	8	0.36	0.09
>4	13	21	(0.11-1.19)	
mRS at 12 months				
≤ 3	12	3		0.046
≤ 4	28	6	0.25	0.04
>4	14	22	(0.07 – 0.91)	
mRS at 3 months excluding death				
≤ 4	29	8	0.22	0.16
5	2	6	(0.02 – 1.85)	
mRS at 12 months excluding death				
≤ 4	31	6	–	–
5	1	0		

Results of possible outcome predictors

Age: On analyzing patients above 60 years who underwent surgery, there was no significant difference in stroke severity at baseline .However, elderly had no significant benefit, either in terms of survival or disability with decompression as compared to younger patients.

Late surgery group: There were 13 patients who underwent decompressive hemicraniectomy (DH) beyond 48 hours after presentation. Surgical group had a significant mortality benefit at 3 and 12 months in comparison to the medical arm. Functional outcome did not differ between early and delayed surgery groups at short term .At 12 months fair outcome was more seen in the late DH group in comparison to the medical arm, independent of baseline clinical profile and stroke severity.

DISCUSSION

Decompressive hemicraniectomy for malignant MCA stroke has class I evidence in favour of mortality and morbidity benefit, though there is evidence to suggest that advances in neurocritical care management has led to an overall improvement in mortality in critically ill patients.[7,8] But these strokes leave the survivors with significant residual disability for the patient's caregivers to deal with. The caregiver / rehabilitation backup available for these patients is likely to be a major determinant in their long term outcome, which is less studied. More literature from developing countries where state run rehabilitation facilities are limited will help the treating doctors and caregivers in taking better informed decisions regarding acute and long term care of stroke survivors with moderate to severe disabilities, taking into account the strengths and limitations of our existing health care resources and caregiver support.

In our study surgical candidates were significantly younger with lower stroke severity scores at admission. This observation has been

Table 4: Mortality on follow-up at 3 and 12 months

Patient characteristics	Surgical group N=42(%)	Medical group N=32(%)	Odd ratio (95% CI)	P value for the odds ratio*
Mortality at 3 months	10/42 (26.2%)	20/29 (69%)	0.24 (0.07 – 0.77)	0.02
Mortality at 12 months	13/42 (33.3%)	22/28 (78.6%)	0.12 (0.02 – 0.77)	0.01

*P value was calculated for odd ratio after multiple logistical regression.

comparable with reports on malignant MCA stroke by other Indian authors as well.[9-11] Predictors of fair outcome reported were younger age[9-11], and midline shift <5 mm.[10] While preoperative GCS had a borderline effect on long term outcome[10], timing of the procedure had no significant impact on the same. Interestingly none of the medical comorbidities like diabetes, CAD, atrial fibrillation or hypertension had an impact on short or long term outcome, which indicates the impact of critical care services on overall improvement in patient outcome of both medical and surgical patients. Preoperative GCS over 8 and APACHE II score<13 has also been reported as predictors of good outcome predictors by some authors.[12]

In-hospital complications and hospital stay were comparable between medical and surgical patients in our patient cohort. Early deaths were more in the medical arm. However multivariate logistic regression adjusting for age and NIHSS failed to show a statistically significant mortality benefit for surgery in the early phase. Early deaths reported by other series from India ranges from 3.8%[11] to 28%.[9] However, both these series had only looked into the outcome of surgical patients. In a predominantly medically treated cohort, mortality at discharge was reported to be around 15%.[8] The reason for the higher early mortality in our cohort is not clear, except for age and predominantly cardioembolic etiology.

Survival benefit was evident in the surgical arm at 3 months itself, which was sustained at 1 year without increase in number of patients with severe disability (mRS 5) in surgical group. Others from India have also reported good QOL in survivors beyond 12 months.[9] These observations suggest that in a developing country scenario like ours, care giver based rehabilitation is not inferior to more structured comprehensive rehabilitation facilities offered in developed world and the surgical patients survive long term with less disability as compared to medically treated cohort.

All major RCTs and observational studies from our country have excluded the elderly except a few.[13,14] Age has been found to be a crucial risk factor in determining functional outcome after decompressive hemicraniectomy, with more chance for surviving with moderate to severe disability beyond 50-60 years of age.[14,15] Most of the evidence for decompressive hemicraniectomy in elderly compared decompressive hemicraniectomy in elderly versus decompressive hemicraniectomy in young, rather than decompressive hemicraniectomy in elderly versus medical management. Mortality in our older patients did not change much with surgery. This is contrary to previously reported trials where elderly undergoing surgery had a better survival at 6 months and beyond.[13] The reason for the comparable mortality in the surgical group with medical arm in elderly is difficult to explain other than age being an adverse prognosticator. Age related brain atrophy in elderly offers some degree of protection against tissue shifts.[16,17] This might have contributed to a selection bias in surgical candidates among elderly, which might have increased their overall mortality. Though older patients undergoing surgery had a fair functional outcome in comparison to medical arm, this was clearly inferior to the younger survivors. This observation has been reported by other authors as well. We believe this observation is important in practice, as the treating physicians can give a realistic picture of expected benefit while counselling the caregivers of older patients.

Data on late decompression, although less robust, have suggested no significant benefit in mortality or morbidity.[6] In resource poor settings, late presentation to tertiary hospitals are very common and more data on benefit in this patient subgroup is very important while making management decisions. In our study there were 13 patient who underwent decompressive hemicraniectomy beyond 48 hours. They had a lower mortality throughout 1 year and better functional outcome at long term. Considering that the maximum period of edema after malignant MCA stroke is between 2nd to 5th day, decompression between 48-96 hours too might be logically considered in selected cases.[18]

Considering that only 93 subjects were there in the pooled analysis of the landmark 3 RCTs, our sample number of 74 is fairly good for an observational study. We did not exclude subjects by age and believe that this would more likely reflect the ground scenario in a tertiary care centres in developing country. All our patients were discharged home. Also we had 100% follow up of the surgical group and >80% of the medical arm, which adds to the strength of the study as well. We could look into a small subgroup of patients undergoing late surgery also, to see its benefit. Our older patients undergoing surgery had a fair outcome at 1 year without significant mortality benefit, which is a novel observation.

However, our study is not without its limitations. Baseline stroke severity was less in the surgical arm, which is considered a major predictor of both short and long term outcome. However, our adjusted analysis still showed

a benefit in the surgical arm at short and long term. We also had only very few patients older than 60 years and those who underwent delayed DH, hence our results may not be generalizable in those patient subgroups.

Summarizing, DH is definitely a lifesaving surgery irrespective of the demography, in younger patients. There is also evidence for morbidity benefit at long term with this procedure, which was also seen in the delayed surgical group. Older patients undergoing surgery had a fair outcome among survivors without any significant mortality benefit. Our observations, especially regarding outcome in older patients and delayed surgical arm needs to be tested in larger studies, in developing country scenario. This will help the treating physicians while counselling the care givers regarding the realistic picture of outcome, enabling optimal use of the available health care resources.

DISCLOSURE

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