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A Cohort Study of Decompressive Craniectomy for Malignant Middle Cerebral Artery Infarction

A Real-World Experience in Clinical Practice

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Abstract: Decompressive hemicraniectomy with malignant middle cerebral artery (MCA) infarction is effective but remains underutilized. The aim of this study was to observe the utilization of this intervention in mainland China.

We included patients with malignant MCA infarction who admitted in West China Hospital between December 2007 to March 2011. The outcomes were death and favorable outcome (mRS < 4) at 1 month and 1 year. The multivariate logistic regression model was used to identify the independent predictors for outcomes.

Ten percent (219/2174) of patients with acute ischemic stroke had malignant MCA infarction and 31.1% (68/219) patients meet the criteria that ≤60 years of age and the timing to hospital <48 hours after stroke onset. Of them, 18 patients (26.5%) underwent to decompressive hemicraniectomy. In total, 31 patients (14.2%) underwent the decompressive surgery. The average age was 53 ± 12 years; median NIHSS score was 21. The case fatality rate of patients in surgery group was significantly lower than those of in nonsurgery group at 1 month and 1 year follow-ups (32.3% and 38.7% vs. 51.1% and 61.2%, respectively, $P < 0.05$). Patients in surgery group had a higher proportion of good outcome at 1 year follow-up (32.2% vs. 13.3%, $P = 0.006$). After adjusting for confounders including age, sex, NIHSS score, and GCS score on admission, decompressive hemicraniectomy was an independent predictor of good outcome for 1 year (OR = 3.44, 95% CI, 1.27–9.31).

This study shows better outcomes in the surgical group, which are consistent with findings in previous prospective randomized trials. However, this beneficial intervention remains underutilized in clinical settings.

(*Medicine* 94(25):e1039)

Abbreviations: GCS = Glasgow Coma Scale, MCA = middle cerebral artery, mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale, TIA = transient ischemic attack.

Editor: Gregory Bix.
Received: December 6, 2014; revised: May 20, 2015; accepted: May 28, 2015.
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The authors have no conflicts of interest to disclose.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000001039

INTRODUCTION

Malignant middle cerebral artery (MCA) infarction may occur in up to 10% of patients who have acute ischemic stroke and have a mortality rate of approximately 80%.[1,2] Because of the limitations of medical therapies, decompressive hemicraniectomy has been proposed for patients with space-occupying hemispheric infarction. This therapy can prevent secondary tissue damage by creating compensatory space to accommodate the swollen brain.[3–5] However, given the lack of data, neurosurgeons may be reluctant to perform this procedure. Recently, the pooled analysis of 3 small randomized trials demonstrated decompressive hemicraniectomy can reduce mortality and morbidity related to malignant infarction of the MCA.[6] It is expected that the procedure would be increased due to positive effect on outcomes. How often this therapy is effectively used in China remains unclear. The aims of the present study were to determine the proportion of patients with ischemic stroke who would have been potentially eligible for hemicraniectomy and to observe the utilization of decompressive hemicraniectomy with malignant MCA territory infarction in mainland China.

METHODS

Subjects

We included patients with acute ischemic stroke admitted consecutively to neurological wards of the West China Hospital, Sichuan University, between December 2007 and March 2011. All patients had a clinical diagnosis of stroke according to World Health Organization (WHO) criteria and intracranial hemorrhage was further excluded by CT or MRI scan in the hospital.[7] Inclusion criteria were as follows: infarction more than two-thirds the MCA territory as defined by computed tomography and/or magnetic resonance imaging; neuroradiologic evidence of local brain swelling such as midline shift of 5 mm or more indicating space-occupying edema; prestroke modified Rankin Scale (mRS) <2. Informed consent was obtained from the patients' relatives. This research project was approved by the Scientific Research Department of West China Hospital, which conformed to the local ethic criteria.

Data Collection

The following demographic and clinical data were recorded and evaluated: age, sex, location of infarction, National Institutes of Health Stroke Scale (NIHSS) scores, Glasgow Coma Scale (GCS) scores, and history of vascular risk factors such as hypertension, diabetes mellitus, hypercholesterolemia, history of transient ischemic attack (TIA), coronary heart disease, history of stroke, and smoking status.

TABLE 1. Characteristics of Patients With and Without Hemicraniectomy

	Surgery Group N = 31	Nonsurgery Group N = 188	Total N = 219	*P* Value
Male, n (%)	14 (45.2%)	87 (46.3%)	101 (46.1%)	0.908*
Age, yr	53.19 ± 11.65	63.68 ± 15.01	62.19 ± 15.01	**0.000**†
Dominant hemisphere	22 (71.0%)	100 (53.2%)	122 (55.7%)	0.065*
Median NIHSS	21	17	18	**0.018**‡
Median GCS	8	10	10	0.104‡
Risk factors, n (%)				
Hypertension	12 (38.7%)	73 (38.8%)	85 (38.8%)	0.990*
Diabetes mellitus	4 (12.9%)	25 (13.3%)	29 (13.2%)	1.000§
Atrial fibrillation	7 (22.6%)	30 (16.0%)	37 (16.9%)	0.362*
Hypercholesterolemia	1 (3.2%)	7 (3.7%)	8 (3.7%)	1.000§
Previous TIA	2 (6.5%)	3 (1.6%)	5 (2.3%)	0.148§
Coronary heart disease	2 (6.5%)	11 (5.9%)	13 (5.9%)	1.000§
Current smoker	9 (29.0%)	31 (16.5%)	40 (18.3%)	0.094*
Alcohol intake	4 (12.9%)	22 (11.7%)	26 (11.9%)	0.770§

GCS = Glasgow Coma Scale; NIHSS = National Institutes of Health Stroke Scale; TIA = transient ischemic attack.
* χ^2 test.
† Student *t* test.
‡ Mann–Whitney *U* test.
§ Fisher Exact test.

Outcome Measurements

The main outcomes were death and favorable outcome at 1 month and 1 year. Death was all-cause case fatality. Favorable outcome was defined as mRS<4.[6] Patients were followed up by telephone call, clinic interview, or letter inquiry using a structured data form.

Statistical Analysis

We compared the differences between 2 groups using *t* test, Mann–Whitney *U* test, or χ^2 test where appropriate. The multivariate logistic regression model was used to identify the independent predictors for fatality and outcome at 1 months and 1 year. For comparison, we divided the included patients as surgery group (underwent decompressive hemicraniectomy) and nonsurgery group (without surgery). ''Early'' was defined as that surgery was performed within 48 h of symptom onset and ''late'' was surgery performed after 48 h of significant deterioration.[8] All statistical analyses were performed with SPSS 18.0 (SPSS Inc, Chicago, IL) for Windows package.

RESULTS

Ten percent (219/2174) of patients with acute ischemic stroke had malignant MCA infarction. Of them, 31 patients (14.2%) underwent the decompressive surgery The average age was 53 ± 12; number of males 14; median NIHSS score was 21. A favorable outcome was achieved in 32.2% of the patients at the end of 1 year. Based on data from our center, 10% suffered from malignant infarction and 31.1% (68/219) patients did meet the criteria that they were ≤60 years of age and the timing to hospital <48 hours after stroke onset. Among 68 patients who did meet above criteria, 18 patients (26.5%) underwent to decompressive hemicraniectomy. The patients in surgery group were younger (53.19 years vs. 63.68 years; $P < 0.001$) and had a higher median NIHSS score (21 vs. 17, $P = 0.018$) on admission than nonsurgery group. The other characteristics on sex, infarct hemisphere, GCS scores, and risk factors were comparable between surgery group and nonsurgery group ($P > 0.05$) (Table 1).

Upon univariate analysis, patients in surgery group had a higher proportion of good outcome than patients in nonsurgery group in 1 year follow-up (32.2% vs. 13.3%, $P = 0.006$; OR = 3.59; 95% CI, 1.50–8.62). The case fatality rate of patients in surgery group was significantly lower than those of in nonsurgery group in 1 month and 1 year follow-ups (32.3% and 38.7% vs. 51.1% and 61.2%, respectively, $P < 0.05$) (Table 2). After adjusting for confounders including age, sex, NIHSS score, and GCS score on admission, decompressive hemicraniectomy was an independent predictor for 1-year good outcome (OR = 3.44, 95% CI, 1.27–9.31) (Table 3).

In surgery group, the characteristics in sex, infarct hemisphere, NIHSS score, and GCS score were comparable between ''early'' hemicraniectomy and ''late'' hemicraniectomy ($P > 0.05$) (Table 4). The patients ≤60 years of age have a lower median NIHSS score and GCS score (20 and 9 vs. 24 and 5; *P*, 0.039 and 0.023) than the patients >60 years of age (Table 5).

There were no significant differences on case-fatality rate after 1 month and 1 year (28.6% and 28.6% vs. 35.3% and 47.1%, $P > 0.05$) between ''early'' surgery and ''late'' surgery. There was no significant difference on functional outcome after 1 year ($P > 0.05$) (Table 4). There were no significant differences on case-fatality rate after 1 month and 1 year (26.1% and 30.4% vs. 50.0% and 62.5%, $P > 0.05$) or on functional outcome after 1 year between patients younger than 60 years old and patients older than 60 years old (Table 5).

DISSCUSSION

Our study showed that 10% (219/2174) patients admitted for acute ischemic stroke had malignant MCA infarction in according with previous studies and 31.1% (68/219) patients did meet the criteria that they were ≤60 years of age and the timing to hospital <48 hours after stroke onset. However, only 31 patients (14.2%) underwent decompressive hemicraniectomy.

TABLE 2. Outcomes at 1 Month and 1 Year Follow-Up of Patients With and Without Hemicraniectomy

	Surgery Group N = 31	Nonsurgery Group N = 188	*P* Value	OR 95% CI
Survival after 1 mo			**$P = 0.008$***	**OR = 2.84 (1.28, 6.34)**
Alive	21 (67.7%)	82 (48.9%)		
Dead	10 (32.3%)	106 (51.1%)	**$P = 0.014$***	**OR = 2.61 (1.20, 5.70)**
Survival after 1 yr				
Alive	19 (61.3%)	71 (38.8%)	**0.003†**	**OR = 3.59 (1.50, 8.62)**
Dead	12 (38.7%)	117 (61.2%)	**mRS 0–3 vs 4–6**	
mRS score after 1 yr			**$P = 0.006$‡**	**OR = 3.20 (1.47, 6.97)**
Median	4	6		
Range	2–6	2–6	**mRS 0–4 vs 5–6**	
mRS 2	1 (3.2%)	1 (0.5%)	**$P = 0.002$***	
mRS 3	9 (29.0%)	21 (12.8%)		
mRS 4	6 (19.4%)	25 (12.8%)		
mRS 5	3 (9.7%)	24 (12.8%)		
mRS 6	12 (38.7%)	117 (61.2%)		

mRS = modified Rankin Scale. Adjusted for age, sex, NIHSS score, GCS score on admission.
* χ^2 test.
† Mann–Whitney *U* test.
‡ Fisher Exact test.

The rate of hemicraniectomy is very low. The procedure for hemicraniectomy was also underutilized in the world.[9,10] There is almost certainly a multifactorial cause, such as clinicians do not consider mRS < 4 as a favorable outcome although it was considered a favorable outcome in the pooled analysis[11] or relatives of patients hesitate to receive the surgery or spiritual reasons, financial concerns, etc. In addition, the proportion of patients meeting criteria for hemicraniectomy is low, which needs to be improved by early evaluation and expansion of the clinical indications of hemicraniectomy. Future studies should investigate population-based eligibility and appropriate patient selection for hemicraniectomy in the ''real world'' situation..

TABLE 3. Multivariate Logistic Regression for Outcomes at 1-Mo and 1-Yr Follow-Up

	Adjusted OR	95% CI	*P*
Survival after 1 mo			
Age (>60 yr)	0.912	0.509, 1.634	0.757
Sex	0.828	0.471, 1.456	0.511
NIHSS	0.904	0.832, 0.981	**0.016**
GCS	0.996	0.866, 1.145	0.955
Surgery/nonsurgery	3.609	1.494, 8.717	**0.004**
Survival after 1 yr			
Age (>60 yr)	0.644	0.357, 1.163	0.144
Sex	0.707	0.398, 1.257	0.238
NIHSS	0.892	0.818, 0.972	**0.009**
GCS	0.957	0.830, 1.105	0.551
Surgery/nonsurgery	2.998	1.268, 7.091	**0.012**
Good outcome after 1 yr			
Age (>60 yr)	0.314	0.128, 0.774	**0.012**
Sex	1.153	0.514, 2.583	0.730
NIHSS	0.931	0.820, 1.056	0.266
GCS	1.072	0.873, 1.317	0.507
Surgery/nonsurgery	3.441	1.272, 9.308	**0.015**

GCS = Glasgow Coma Scale, NIHSS = National Institutes of Health Stroke Scale.

In the present series, the case-fatality rates for 1 month and 1 year after surgery were 32.3% and 38.7%, respectively; these are comparable with previous reports.[12,13] However, data on functional outcome showed more heterogeneous in previous studies.[4,14,15] Our study suggests both fatality and functional outcomes may be better after surgery. In fact, the surgical group did better despite having a significantly higher NIHSS on presentation while the nonsurgical group was clinically ''better'' on presentation, they did clinically ''worse'' on follow-up.

Compared to the pooled analysis,[6] patients in our study: were older (25% patients were aged more than 60 years); were selected for surgery late after symptom onset (17 patients underwent surgery after 48 h). We found hemicraniectomy can improve both survival rate and functional outcomes. There still exists controversy on the cut-off point of age to perform surgery.[16–18] In a meta-analysis, age is the only prognostic factor for poor outcome.[19] Arac et al carried out an extensive review of the literature to find that the outcome was much worse in patients over 60 years of age compared to that under 60 years of age.[14] We found that patients over 60 years of age had a worse function outcome but had no significant difference in case fatality rates between patients younger than 60 years old and patients older than 60 years old. But, Kuroki et al described that the decompressive surgery outcome is better than the conservative treatment even in patients older than 70 years old.[20] The Chinese randomized trial recruited 29 elderly subjects between the ages of 60–80 and showed that decompressive hemicraniectomy can reduce mortality and increase the chances of surviving with no severe disability (mRS = 4) in elderly patients.[21] Recently, 112 patients 61 years of age or older (median, 70 years; range, 61–82) with malignant middle-cerebral-artery infarction were assigned to either conservative treatment or hemicraniectomy, and the result showed hemicraniectomy increased survival without severe disability among patients 61 years of age or older.[22] From the data available, elder patients will benefit from the decompressive surgery.

Some studies have reported that the timing of surgery is not correlated with the functional outcome of patients;[23,24] however, early surgical intervention has been regarded as an

TABLE 4. Comparison Between ''Early'' and ''Late'' in Surgery Group

	Early Group (≤48 h) N = 14	Late Group N = 17	(>48 h) Total N = 31	Statistics
Male, n (%)	6 (42.9%)	8 (47.1%)	14 (45.2%)	1.000‡
Age, yr	54.14 ± 11.52	52.41 ± 12.05	53.19 ± 11.65	0.688*
Dominant hemisphere	9 (64.3%)	13 (76.5%)	22 (71.0%)	0.693‡
Median NIHSS	20	21	21	0.265†
Median GCS	9	8	8	0.193†
Survival after 1 mo				1.000‡
Alive	10 (71.4%)	11 (64.7%)	21 (42.9%)	OR = 1.36 (0.30, 6.28)
Dead	4 (28.6%)	6 (35.3%)	10 (42.9%)	
Survival after 1 yr				0.461‡
Alive	10 (71.4%)	9 (52.9%)	19 (45.2%)	OR = 2.22 (0.50, 9.96)
Dead	4 (28.6%)	8 (47.1%)	12 (54.8%)	
mRS score after 1 yr				mRS 0–3 vs 4–6
Range	2–6	2–6	2–6	$P = 1.000$‡
mRS 2	0 (0.0%)	1 (5.9%)	1 (3.2%)	OR = 1.33 (0.29, 6.04)
mRS 3	5 (35.7%)	4 (23.5%)	9 (29.0%)	mRS 0–4 vs 5–6
mRS 4	4 (28.6%)	2 (11.8%)	6 (19.4%)	$P = 0.285$‡
mRS 5	1 (7.1%)	2 (11.8%)	3 (9.7%)	OR = 2.57 (0.60, 11.06)
mRS 6	4 (28.6%)	8 (47.0%)	12 (38.7%)	

GCS = Glasgow Coma Scale, mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale.
* Student *t* test.
† Mann–Whitney *U* test.
‡ Fisher Exact test.

important factor for better functional outcome by other studies.[25–27] Our study included that 17 patients underwent to decompressive hemicraniectomy beyond 48 hours and showed that there were not significant differences between within 48 hours and beyond 48 hours on case-fatality rate and functional outcome. Of course, it may be related to the limited power (N = 31).

The present study has several limitations. First, this is a retrospective hospital-based study and may be subject to selection bias. One could imagine that patients too ill for surgery or patients whose families opted for pallitive care or hospice skew the ''nonsurgical'' group to sicker patients with ipso facto poorer mRS and mortality rates. Second, patients' selection for decompressive craniectomy is not confined to criteria of

TABLE 5. Comparison Between Patients ''≤60 years'' and ''>60 years'' in Surgery Group

	Surgery Group (≤60 y) N = 23	Surgery Group (>60 y) N = 8	Total N = 31	Statistics
Male, n (%)	10 (43.5%)	4 (50.0%)	14 (45.2%)	1.000†
Dominant hemisphere	16 (69.6%)	6 (75.0%)	22 (71.0%)	1.000†
Median NIHSS	20	24	21	**0.039***
Median GCS	9	5	8	**0.023***
Survival after 1 mo				0.381†
Alive	17 (73.9%)	4 (50.0%)	21 (67.7%)	OR = 2.83 (0.53, 15.04)
Dead	6 (26.1%)	4 (50.0%)	10 (32.3%)	
Survival after 12 mo				0.206†
Alive	16 (69.6%)	3 (37.5%)	19 (61.3%)	OR = 3.81 (0.71, 20.53)
Dead	7 (30.4%)	5 (62.5%)	12 (38.7%)	
mRS score after 12 mo				mRS 0–3 vs 4–6
Range	2–6	2–6	2–6	$P = 0.222$†
mRS 2	1 (4.3%)	0 (0.0%)	1 (3.2%)	OR = 4.50 (0.47, 42.97)
mRS 3	8 (34.8%)	1 (12.5%)	9 (29.0%)	mRS 0–4 vs 5–6
mRS 4	5 (21.8%)	1 (12.5%)	6 (19.4%)	$P = 0.113$†
mRS 5	1 (4.3%)	2 (25.0%)	3 (9.7%)	OR = 4.67 (0.77, 28.41)
mRS 6	8 (34.8%)	4 (50.0%)	12 (38.7%)	

GCS = Glasgow Coma Scale, mRS = modified Rankin Scale, NIHSS = National Institutes of Health Stroke Scale.
* Mann–Whitney *U* test.
† Fisher Exact test.

≤60 years of age and the timing to hospital <48 hours after stroke onset. In addition, there may be some sort of selection bias by the surgeons for decompressive craniectomy. However, it reflects decompressive craniectomy for malignant middle cerebral artery infarction in a real-world experience. Whether a patient could perform the surgery is determined by surgeons in daily clinical practice. The decision-making process balances evidence, patient preference, and clinical expertise.

This study shows better outcomes in the surgical group, which are consistent with findings in previous prospective randomized trials. However, this beneficial intervention remains underutilized in clinical settings.

ACKNOWLEDGMENT

This research was supported by the Science and Technology Infrastructure Projects of Sichuan Province (No. 2012JCPT008).

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