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Original Article

The Outcome Following Decompressive Craniectomy or Conservative Treatment for Malignant Middle Cerebral Artery Infarction

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Abstract

Background: At present, malignant middle cerebral artery (MCA) infarction has a high morbidity and mortality rate worldwide. The aims of this study were to identify the mortality rate, to determine the value of decompressive craniectomy in patients who were presented with malignant middle cerebral artery (MCA) infarction, to compare functional outcome in elderly patients with younger patients and identify significant risk factors related to the mortality.

Method: Medical records of patients with malignant middle cerebral artery (MCA) infarction treated in Bhumibol Adulyadej Hospital between January 2008 and April 2011 were reviewed. A total of 82 patients with complete medical records and radiographic imagines were included in this study. The area of infarction was determined by the ABC/2 method and the degree of herniation was determined with Ambient cistern effacement and shift of the midline. The Glasgow Coma Scale score was assessed for neurologic status at admission, at operative time (in surgery group), and at one-week time after infarction. All patients were assessed with the modified Rankin Scale (RS) at discharge and at 3 months after infarction.

Results: The mortality rate of patients with malignant middle cerebral artery (MCA) infarction at discharge was 45% and 3 months after infarction was 48.8%. At discharge, there was a significant difference in the mortality of patients with malignant middle cerebral artery (MCA) infarction in conservative group and surgery group [(17/50 (34%) versus 20/32 (62.5%)), p = 0 .011]. Also at 3 months after infarction, there was a significant difference in mortality in the conservative group and the surgery group [(19/50 (38.0%) versus 21/32 (65.6%)), p = 0.015]. There was a significant high mortality rate in the surgery group with age≤ 60 years. Dyslipidemia and ischemic heart disease were risk factors of malignant middle cerebral artery (MCA infarction related death with an odd ratio 1.419 (95%CI 0.504-4.00) and 2.00 (95%CI 0.345-11.578) respectively.

Conclusion: The mortality rate of patients with malignant middle cerebral artery (MCA) infraction treated at our hospital was nearly 50% and the rest of the patients were dependent. There was a significant high mortality rate in the surgery group with age≤ 60 years which could be explained by the severity of thedisease. In addition, the more underlying diseases, the higher the mortality rate will be.

Keywords: **malignant MCA infarction, decompressive craniectomy, decompressive surgery in elderly**

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Introduction

Decompressive craniectomy procedures have been used to relieve increased ICP and cerebral edema caused by a variety of pathological events. In a classic article in 1905, Cushing was the first to report the use of this procedure. Since then, the surgical decompression has been reported as a treatment option worldwide. In 1968, Greenwood used surgical intervention (decompressive hemicraniectomy as well as resection of necrotic parenchyma) in the treatment of such cases, which decreased the mortarity rate to below 50%. In 1981 Rengachary and coworkers reported the first successful cases in which straightforward craniectomy was undertaken, without resection of necrotic brain tissue. Since that study, many studies have been reported in the treatment of massive cerebral ischemia (Table 1)[7].

In 2007 The American Heart Association launched Guidelines for the Early Management of Patients With Ischemic Stroke. The recommendation was "Decompressive surgery for malignant edema of the cerebral hemisphere may be life-saving, but the impact of morbidity is unknown. Both the age of the patient and the side of the infarction (dominant versus non-

Table 1 Summary of clinical studies in which decompressive croniectomy was completed in patients with massive supratentorial infarct*

Authors & Year	No. of Cases	Time to Surgery	Tissue Re-Section	Mean Patients Age (yrs)	Outcome
Greenwood, 1968	9	1-21 days	yes	49.86	survivors: 3 w/severe disability, 3 w/moderate & acceptable neurological deficit
Kjellberg & Prieto, 1971	1†	Not given	no	not given	death
Ivamoto, et al., 1974	1	3 days	yes	49	mild disability; depression
Rengachary, et al., 1981	3	2-5 days	no	31	2 w/persistent hemiplegia (1 severely disabled); one w/only a mild hemisensory deficit
Young, et al., 1982	1	2 days	yes	59	hemiparesis
Kondziolka & Fazl, 1988	3	1-5 days	no	43.7	3 w/independent function 7 mild deficits
Delashaw, et al., 1990	9	< 1-7 days	no	57	1 died of nonnenrological causes; 8 survived (BI scores; 4.60-95, 4<60) 5 patients would undergo op again w/out hesitation; 3 would undergo again w/ some reservation
Jourdan, et al, 1993	7	2-3 days	no	43.8++	5 survivors; all independent, 4 w/residual hemiparesis inter-fering w/ambulation, 2 w/ residual aphasia but normal comprehension; depression present in 2
Rieke, et al, 1995	32	1-5 days (mean 39 hrs)	no	48.8	21 survivors; mean BI = 62.6; (15 ≥ 60, 1 excellent, 5 ≤ 60); of 6 survivors w/dominant hemisphere infarct, 5 w/incomplete aphasia; mean IcU stay 13.3 days
Carter, et al., 1997	14	< 1-19 dyas	yes	49.2	3 died of nonneurological causes; mean BI = 63 (8 > 60.3 < 60); mood disturbances were significant; all had problems w/social reintegration; 6 would undergo op again 3 maybe, 2 would not
Schwab, et al., 1998	31	< 1 day (mean 21 hrs)	no	50.3	26 survivors; mean BI = 68.8 (range 60-90) mean ICU stay 7.4 days
Yoo, et al., 1999	2$	not given	no	29	good outcome on Glasgow Outcome Scale in both

*Cases associated with concomitant disease such as an intracranial aneurysm were excluded, Abbreviations; BI = Barthel Index/ ICU = intensive care unit.
†A bifrontal craniectomy was performed.
++The age of one patient was not reported.
§A bilateral craniectomy was performed.

Table 2 Literature review of decompressive craniectomy for malignant MCA infarction in patients? > 60 years of age*

Authors & Year	No. of patients	No. of Lesions Rt MCA	No. of Lesions Lt MCA	Patients w/Early Op (< 24 hrs)	Mean Time to FU (mos)	No. w/Good Outcome/No. Who Survived	No. of Deaths/ No. in Study	Main Outcome Score
Carter et al., 1997	3	3	0	1	12	1/3	0/3	BI
Walz et al., 2002	4	3	1	1	NA	NA	4/4	BI
Leonhardt et al., 2002	9	9	0	1/9	12	0/6	2/8**	BI
Holkamp et al., 2001	7	5	2	/37	7	0/3	4/7	BI
Delashaw et al., 1990	3	3	0	1/3	16	1/3	0/3	BI
Rieket et al., 1995	6	6	0	3/6	11	2/3	3/6	BI
Harscher et al., 2006	14	13	1	5/14	12.3	1/3	11/14	BI
Kilincer et al., 2005	13	8	5	4/13	6	0/4	9/13	mRS
Yao et al., 2005	12	9	3	0	5/75	1/8	4/12	BI

***FU = follow-up; NA = not available**

****One patient dropped out of this study.**

dominant hemisphere) may affect decisions about surgery. Although the surgery may be recommended for treatment of seriously affected patients, the physician should advise the patient's family about the potential outcomes, including survival with severe disability (Class IIa, Level of Evidence B"[9].

In 2007, there were 3 prospective, multicenter, randomized, controlled, clinical trials launched: DECIMAL (DEcompressive Craniectomy In MALignant middle cerebral artery infarction), DESTINY (DEcompressive Surgery for the Treatment of malignant INfarction of the middle cerebral arterY), and HAMLET (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial). The meta-analysis of these trials concluded that early decompressive craniectomy (within 4 days after onset) significantly reduced mortality in large hemispheric stroke and increased the number of patients with moderate disability in patients among 18-55 years of age[2,3,6].

In 2005 Yu Yao and colleagues, Launched the article: Is decompressive craniectomy for malignant middle cerebral artery territory infarction of any benefit for elderly patients? and in 2009, A. Arac and colleague launched a review artricle: Assessment of the outcome following decompressive craniectomy for malignant middle cerebral artery infarction in patients older than 60 years of age. These studies concluded that decompressive craniectomy in elderly reduced mortality in large hemispheric stroke but increased the number of patients with severe disability in patients older than 60 years of age[1,4]. (Table 2)[1].

Recently, there have been a large number of cases with malignant MCA infarction in Bhumibol Adulyadej Hospital. However, the outcome following decompressive craniectomy and conservative treatment has never been statistically analyzed. This article aimed to identify the mortality rate, to determine the value of decompressive craniectomy in patients who presented with malignant middle cerebral artery (MCA) infarction, to compare functional outcome in elderly patients with younger patients and identify significant risk factors related to the mortality in Bhumibol Adulyadej Hospital.

Patients and Methods

1. Patient selection

Medical records of patients with malignant middle cerebral artery (MCA) infarction treated in Bhumibol Adulyadej hospital between January 2008 and April 2011 were reviewed. A total of 82 patients with complete medical records and radiographic imagings were included in this study. The criteria for malignant MCA territory infarction was the area of infarction of more than 50% of the MCA territory as defined by computed tomography with an acute onset of corresponding clinical signs and symptoms. The area of infarction was determined by the ABC/2 method[8] (Figure 1) and the degree of herniation was determined with ambient cistern effacement and shift of the midline (an infarct

Table 3 Characteristics of the Study Population.

Variables	Surgery gr. Value (%) n=32	Conservative gr. Value (%) n=50
Sex		
M9 (28.1)	20 (40.0)	
F 23 (71.9)	30 (60.0)	
Mean age in yrs.	60.78 (14.18)	70.0 (13.82)
range	60.0 (28-86)	70.5 (41-99)
Infarction characteristics (no. of patiens)		
Hemispheric location		
Right 9non-dominant)	18 (56.3)	23 (46.0)
Left (dominant)	13 (40.6)	25 (50.0)
Bilateral infarction	1 (3.1)	2 (4.0)
MCA23 (71.9)	40 (80.0)	
MCA+ACA	4 (12.5)	5 (10.0)
MCA+PCA	1 (3.1)	5 (10.0)
ICA (MCA+ACA+PCA)	4 (12.5)	0 (0.0)
Stroke everity		
Mean GCS score		
at admission	10.16 (3.38)	10.92 (2.64)
at operative time	7.20 (2.16)	N/A
at one-week time	8.63 (2.41)	10.78 (3.04)
Time from onset to hospital (hours)		
mean ± SD	13.16 (22.47)	11.55 (17.8)
median (range)	3.5 (1-96)	2.5 (1-72)
Time from onset to surgery (hours)		
mean ± SD	39.41 (29.57)	N/A
median (range)	24 (2-120)	
Causes of infarction (no. of patients)		
cardioembolic	19 (59.4)	29 (58.0)
intracranial atherosclerosis	13 (40.6)	21 (42.0)
CT findings		
Volume of infarction (mm^3)		
mean ± SD	260.56 (76.89)	155.92 (103.43)
median (range)	262 (120-429)	131.5 (54-570)
Ambient cistern effacement (no. of patients)	28 (87.5)	4 (8.0)
Midine shift ≥ 5 mm. (no. of patients)	29 (90.6)	3 (60.0)
mean midline shift ± SD	10.06 (5.23)	1.76 (0.43)
Length of stay (days)		
mean ±SD	24.32 (18.14)	22.49 (26.36)
median (range)	18 (2-58)	11 (2-137)
Medical co-morbidities (no. of patients)	27 (84.4)	36 (92.0)
Hypertension	20 (62.5)	31 (62.0)
Dyslipidemia	5 (15.6)	14 (28.0)
Atrial fibrillation	16 (50.0)	25 (50.0)
Valvular heart disease	6 (18.8)	8 (16.0)
Ischemic heart disease	2 (6.3)	4 (8.0)
Diabetes mellitus	12 (37.5)	12 (24.0)
Hyperthyroidism	2 (6.3)	0 (0.0)
Chronic kidney disease	0 (0.0)	3 (6.0)
Stroke in the young	0 (0.0)	0 (0.0)
Old cerebral or cerebellar infarction	0 (0.0)	14 (28.0)
Complications	24 (75.0)	32 (64.0)
hemorrhagic infarction	8 (25.0)	8 (16.0)
myocardial infarction	3 (9.4)	1 (2.0)
pneumonia	19 (59.4)	20 (40.0)
sepsis	10 (31.3)	15 (30.0)
renal failure	8 (25.0)	6 (12.0)

volume of 200 mm^3 having a 91% accuracy for predicting malignant behavior[10]). All of these patients were first treated using standardized conservative management including controlling optimum blood pressure, hyperosmolar treatment, and so on. Decompressive craniectomy was used as second-line treatment in cases of significant neurologic deterioration, such as further decrease of consciousness to stupor or the development of anisocoria and GCS less than 8 or significantly drop more than 2 points from the admission. All underlying diseases of each patient and medications were recorded to be evaluated as the risk factors, such as hypertension, dyslipidemia, atrial fibrillation, valvular heart disease, ischemic heart disease, diabetes mellitus, hyperthyroidism, chronic kidney disease, stroke in the young, and old cerebral or cerebellar infarction.

2. Operative technique

Decompressive craniectomy was done by removing parts of the frontal, parietal, temporal, and occipital squama, resulting in a large bone flap (diameter > 12 cm). A star-shaped durotomy was done then opened centered on the flap. A homologous temporal fascia

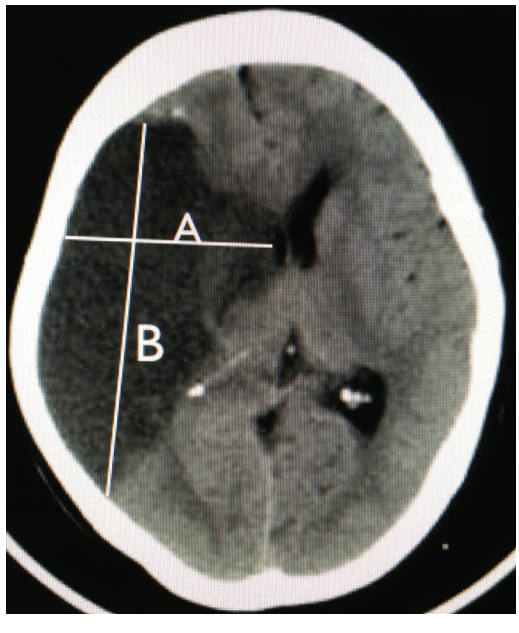

Figure 1 ABC/2 method. First, the largest diameter (A) of the infarct and its largest perpendicular diameter (B) were measured with a caliper. Then, the vertical diameter (C) was determined by summing the thickness of the slices in which the lesion was visible. Infarct volume was calculated according to the formular $.5 \times A \times B \times C$

was placed into the incision for volume-enlarged dural repair[4].

3. Patient evaluation

The Glasgow Coma Scale score was assessed for neurologic status at admission, at operative time (in surgery group), and at one-week time after infarction. All patients were assessed for the modified Rankin Scale (RS) at discharge and at 3 months after infarction. Modified Rankin Scale*

0 = No symptoms at all

1 = No significant disability despite symptoms; able to carry out all usual duties and activities

2 = Slight disability; unable to carry out all previous activities, but able to look after own affairs without assistance

3 = Moderate disability requiring some help, but able to walk without assistance

4 = Moderate severe disability; unable to walk without assistance and unable to attend to own bodily needs without assistance

5 = Severe disability; bedridden, incontinent, and requiring constant nursing care and attention

*van Swieten, J. C., Koudstaal, P. J., Visser, M. C., Schouten, H. J., van Gijn, J. (1988). Interobserver agreement for the assessment of handicap in stroke patients. Stroke, 19, 604607.

4. Statistical analysis

Statistical analyses were performed using SPSS software (standard version 17.5; SPSS, Inc.). Continuous variables were reported as the means ± SD and median (minimum and maximum range). Categorical variables were recorded using numbers and percentages. A comparison of the mean values was perform using the student t-test. Categorical variables were compared using Chi-square tests. A probability value of 0.05 was considered significant.

Results

Study population

Characteristics of the study population consisted of 82 patients (29 men and 53 women), are presented in Table 3.

In comparison of patient's characteristics between surgery and conservative groups by *t-test*, there was significant difference in age, GCS at one-week time, shift of the midline, volume of infarction, mRS at discharge, and mRS at 3 months after onset (Table 4).

The variables which were found to be significantly related mortality between surgery and conservative group were age ≤ 60 years, presence of hemorrhagic infarction, and presence of one or more underlying diseases (Table 6).

Dyslipidemia and ischemic heart disease were significant risk factors of malignant middle cerebral artery (MCA) infarction relating to death with odd

Table 4 The t-test table of patients' characteristics and outcome

Variables	Srugery gr. Value n=32	Conservative gr. value n=50	P value
Age	60.78 ±14.180	70.04 ± 13.821	0.004
Onset time to hospital	13.16 ±22.473	11.55 ±17.8	0.720
GCS at admission	10.16 ±3.38	10.90 ±2.636	0.268
GCS at one-week time	8.36 ±2.41	10.78 ±3.037	0.004
Valume of infarction	260.56 ± 76.885	155.92 ±103.427	0.000
Midline shift	10.06 ± 5.23	4.25 ±4.712	0.002
Hospital stay	24.32 ± 18.141	22.49 ± 26.364	0.735
mRS at discharge	5.59 ± 0.56	5.06 ± 0.913	0.004
mRS at 3 months	5.50 ± 0.803	4.98 ± 1.078	0.022
Time of onset to dead	23.33 ± 20.740	23.06 ± 21.754	0.968

Table 5 Outcome of the patients at discharge and at 3 months after conset in surgery and conservative group.

Variables	Surgery gr. Value (%) n=32	Conservative gr. value (%) n=50
Mortality	21/32 (65.6%)	19/50 (38%)
age ≤ 60	12/21 (57.1%)	4/19 (21.1%)
age > 60	9/21 (42.9%)	15/19 (78.9%)
Time from onset to death		
mean±SD	23.33 (20.74)	23.06 (21.75)
median (range)	14 (2-60)	10 (3-58)
Cause of death (no. of patients)		
brain herniation	6 (18.8)	5 (10.0)
sepsis10 (31.3)	10 (20.0)	
renal failure	1 (3.1)	1 (2.0)
respiratory failure	-	2 (4.0)
status epilepticus	-	-
MI	2 (6.3)	1 (2.0)
mRS score		
at discharge		
mean±SD	5.59 (0.56)	5.06 (0.91)
median (range)	6 (4-6)	5 (2-6)
at 3 months after onset		
mean±SD	5.50 (10.8)	4.98 (1.08)
median (range)	6 (3-6)	5 (3-6)

Table 6 Outcome among categorial variables

Variables	Surgery gr. (%)	conservative gr. (%)	p value
Age ≤ 60			0.047
dead	70.6	33.3	
dependent	29.4	66.7	
age > 60			0.176
dead	60	39.5	
dependent	40	60.5	
hemorrhagic infarction			0.046
dead	75	23	
dependent	25	75	
volume ≤ 200 mm^3			0.06
dead	60	28.2)	
depdent 40	71.8		
volume > 200 mm^3			0.789
dead	68.2	72.7	
dependent	31.8	27.3	
midline shift ≥ 5 mm			0.968
dead	65.5	66.7	
dependent	34.5	33.3	
underlying disease ≥ 1 disease			0.017
dead	69.2	39.5	
dependent	30.8	60.47	

ratio 1.419 (95%CI 0.504-4.00) and 2.00 (95%CI 0.345-11.578) respectively (Table 7).

Discussion

Since Harvey Cushing reported decompressive craniectomy to relieve increased ICP, there have been varieties of decompressive procedures reported to treat increased ICP worldwide, including that from malignant MCA infarction. Based on our data, we found that the younger patients with age ≤ 60 years had significant higher mortality rate in the surgery group compared to the conservative group. This may be explained by the severity of disease that the mean volume of the infarction (> 200 mm^3) in the younger patients was higher than the mean in the elderly group. And from the drop of mean GCS at operative time (7.20 ± 2.16) from 10.16 (3.38) at the admission time may suggest that the patients who had neurological deterioration also have had supratentorial herniation in the same time before surgery.

Table 7 Risk factors of malignant middle cerebral artery (MCA) infarction relating to death

Variables	Surgery gr. Value (%) n=32	Conservative gr. value (%) n=50	Odd ratio (95% CI)
Medical co-morbidities			
(no. of patients)	27 (*4.4)	46 (92.0)	0.263 (0.051 - 1.353)
Hypertension	20 (62.5)	31 (62.0)	0.642 (0.261-1.580)
Dyslipidemia	5 (15.6)	14 (28.0)	1.419 (0.504-4.0)
Atrial fabrillation	16 (50.0)	25 (50.0)	1.0 (0.421-2.377)
Valvular heart disease	6 (18.8)	8 (16.0)	0.361 (0.09-1.107)
Ischemic heart disease	2 (6.3)	4 (8.0)	2.0 (0.345-11.578)
Diabetes mallitus	12 (37.5)	12 (24.0)	0.580 (0.222-1.519)
Hyperthyroidism	2 (6.3)	0 (0.0)	0.463 (0.040-5.320)
Chronic kidney disease	0 (0.0)	3 (6.0)	-
Old cerebral or cerebellar infarction	0 (0.0)	14 (28.0)	0.943 ± 288-02.979)

However, for the elderly patients age > 60 years, we found that there was no different outcome between surgical and conservative groups which may be from the mean volume of infarction less than 200 mm^3 and aging brain atrophy. Given that the elderly tend to recover poorly and end up with a bed ridden status or death from nasocomial infection, in addition, our data suggested that most patients in both groups die because of infection leading to sepsis from hospital acquired pneumonia and urinary tract infection, our recommendation is to provide better hospital care especially more awareness in aseptic protocols.

Based on our data, it is interesting that the presence of underlying diseases plays a significant role in the mortality rate in surgery group compared to conservative group. Even single medical co-morbidity significantly increases mortality rate in surgery group [18/26 (69.2%) (p value 0.017)]. With this data, for

the patients with co-morbidity undergoing surgical decompression, we can provide the prognosis to the patient's family.

Moreover, the other significant risk factor related to death in surgery group from our data is the presence of hemorrhagic infarction as it causes much more increases ICP resulting supratentorial herniation compared with MCA infarction alone. Dyslipidemia and ischemic heart disease were risk factors of malignant middle cerebral artery (MCA) infarction related to death with odd ratio 1.419 (95%CI 0.504-4.00) and 2.00 (95%CI 0.345-11.578) respectively.

Author's recommendation

Based on our data and that from the available literature, the patients with malignant MCA infarction who tend to have benefit from early decompressive craniectomy include ...

- Age less than 60 years
- Have no underlying disease
- Infarct volume more than 200 mm^3, with the cistern compression or midline shift more than 5 mm., appeared on radiographic imaging such as CT or MRI
- GCS at admission less that 10

Conclusion

The mortality rate of patients with malignant middle cerebral artery (MCA) infraction treated in our hospital was nearly 50%. Unfortunately, the rest of patients were dependent. There was a significantly high mortality rate in surgery group with age ≤ 60 years which could be explained by more severity of the disease. In addition, the more underlying diseases, the higher the mortality will be.

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