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Clinical Outcome of the Patients Treated Surgically for Malignant Middle Cerebral Artery Infarction (MMCAI) at Sawanpracharak Hospital

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Abstract This study the relationship of factors associated with clinical outcome in surgical groups of malignant middle cerebral artery infarction (MMCAI). The data were retrospectively collected from surgically treated at Sawanpracharak Hospital between September 2012 and September 2023. All patients diagnosis malignant middle cerebral artery infarction (MMCAI). Decompressive hemicraniectomy (DHC) is one of the surgical options to treat. Patients who had history of disabling, neurological disease, stroke, secondary parenchymal hemorrhage, comorbidities preventing the surgery from being conducted such as renal and hepatic failure, use of warfarin and any coagulopathies, contraindication of the general anesthesia and surgery, pregnancy and any intracranial mass lesion were excluded from this study. This study was categorizes the treatment outcomes into 2 categories: (1) survive, (2) dead were collected. In this study, there was statistically significant association between clinical outcome and Glasgow coma scale (GCS) on admission, GCS on consultation, midline shift, sepsis and length of stay. Correlation coefficient between independent variable with functional outcome of MMCAI patients. This research used independent variable which statistically significant; GCS on admission, GCS on consultation, midline shift, hospital stay and sepsis. Duration onset to operating room (day3) was the important factor in the clinical even though there is no statistically significant. After coefficient independent variable on clinical outcomes of MMCAI patients was done the present study found that there was statistically significant association between functional outcome and GCS on consultation, duration onset to OR (day3), hospital stay and sepsis. The present study found that analysis of factors which affect on clinical outcomes of MMCAI patients were GCS on consultation, duration onset to OR(day3), hospital stay and sepsis.

***Keywords*:** **malignant middle cerebral artery infarction; decompressive hemicraniectomy; Glasgow coma scale; Glasgow outcome scale**

Introduction

The World Health Organization defines ischemic stroke as the "sudden onset of deficient neurological symptoms" attributed to a brain disorder caused by a circulatory disorder lasting longer than 24 h[1] when the ischemic event is associated with brain edema and

refractory intracranial hypertension, affecting 2/3 of the middle cerebral artery area, the cerebrovascular accident (CVA) is characterized as malignant middle cerebral artery infarction (MMCAI). Life-threatening MMCAI occurs in up to10% of all stroke patients,[2,3] and has a mortality rate 50-80%.[4] The main cause of death in patients with MMCAI is focal brain edema, with resultant compartment shift and cerebral herniation[5]. The prognosis is usually poor despite maximal intensive care treatment.[5,6] Several medical therapies have been proposed to reduce development of brain edema and intracranial pressure, such as hyperventilation, osmotic therapy and barbiturate administration.[4,7,8]

As the only therapy, decompressive hemicraniectomy (DHC) is one of the surgical options to treat brain edema, and lessens the risk of brain herniations and death has been proposed for patients with space-occupying hemispheric infarction, seeking to relieve the high intracranial pressure.[5,9] DHC includes the temporary removal of some bone fragments (e.g., frontal, temporal and parietal bone), followed by duraplasty procedure to provide space for the brain. Therefore, the therapy seeks to create a compensatory space to accommodate the brain and normalize intracranial pressure, reverting brain tissue shifts[5]. It has been suggested that the prognostic factors of DHC patients with MMCAI vary, including age of patient, brain herniation degree and preoperative neurological status. Patients younger than 60 years undergoing surgery as early as possible have more satisfactory results,[10] and it has been reported that early DHC is related to lower neurological deficits and an earlier return to activities of daily life[11], patients who delayed surgery were associated with a poor outcome.[12]

Material and Method

A retrospective analysis of patients who were admitted to the Department of Surgery and Medicine at Sawanpracharak hospital, Nakhonsawan province between September 2012 and September 2023 was conducted. The research proposal was reviewed and approved by the Ethics Committee, Sawanpracharak Hospital, Nakhonsawan. In all patients suspected of stroke, computerized tomography (CT) scan of the brain was done on arrival at the hospital. All CT scan findings were evaluated by a neurosurgeon, neurologist and a radiologist.

The inclusion criteria for MMCAI in this study was first time massive middle cerebral artery infarction, ischemic signs (hypodensity in MCA territory) on subsequent cerebral computed tomography (CT) scan involving at least 2/3 or the MCA territory and signs of local swelling (effacement of the sulci, compression of the lateral ventricle). Patients who had history of disabling, neurological disease, stroke, secondary parenchymal hemorrhage, comorbidities preventing the surgery from being conducted such as renal and hepatic failure, use of warfarin and any coagulopathies, contraindication of the general anesthesia and surgery, pregnancy and any intracranial mass lesion were excluded from this study.

Personal data including sex, age vital sign, admission ward, major risk factors (e.g., hypertension, diabetes mellitus, heart disease, previous stroke, hyperlipidemia), minor risk factors (e.g., smoking, alcoholic consumption, chronic renal disease), Glasgow coma scale (GCS) on admission, GCS on consultation, midline shift (MS), infarction area volume, duration onset to consultation (D1), duration consultation to operating room [OR] (D2), duration onset to OR

(D3), operating time, intraoperative blood loss, length of stay, hemorrhagic infarction, brain edema, pneumonia, convulsion, renal failure, sepsis, post-operative rebleeding and Glasgow outcome scale (GOS) in this study was categorizes the treatment outcomes into 2 categories: (1) survive, (2) dead, were collected.

All MMCAI patients were surgically treated. Furthermore, those with post-operative rebleeding were appropriately surgically treated.

STATA SE18 was used for statistically analysis. The characteristics of the subjects were described in terms of frequency, percentage and mean standard deviation. Students t-test was used for comparison of continuous quantitative variable and Chi-square test were used for discrete data. The association between the groups was measured using the odds ratio with 95% confidence interval for every prognostic factors. Only variables with a p-value <0.05 in the separate analysis were selected and studied in the binary logistic regression analysis. For all statistical tests, a value of $p<0.05$ was considered statistically significant. Correlation coefficient between independent variables with functional outcome of MMCAI patients were also studied.

Results

There were 211 consecutive MMCAI patients admitted to the Department of Surgery and Medicine at Sawanpracharak Hospital, Nakhonsawan province between September 2012 and September 2023. The age of the patients ranged from 39-89 years old, one-hundred eleven patients were male (52.61%), the mean agea of those who survived and died were 61.76±11.65 and 64.11±11.29, respectively. Glasgow coma scale (GCS) on admission (hr) was [survive11.68±2.85, dead 10.52±2.87]; GCS on admission (mild 36.50%, moderate 41.23% and severe 22.23%); GCS on consultation (hr) [survive 8.63±2.62, dead 7.20±2.10]; GCS on consultation (mild 5.69%, moderate 25.59% and severe 68.72%); and rt-PA on admission (26.54%). Midline shift (MS) mm [survive 8.84±3.52, dead 10.30±3.71], MS 5-10 mm 64.45% MS >10 mm 35.55%. Attending physician (Medicine 45.02%, Neuro-medicine 34.60% and Neuro-surgery 33.18%). Admission ward (Medicine 38.86%, Neuro-surgery 30.81%, Stroke unit 27.96% and Neurosurgical ICU 2.37%). Duration onset to consultation (day1) (hr) [Survive 34.02±40.28, dead 36.85±46.167] duration consultation to operating room (day2) (hr) [survive 10.83±16.17, dead 9.99±24.17] duration onset to operating room (day3) (hr) [survive 55.97±41.22, dead 60.05±51.86]. Regarding operating time of the patients (min) [Survive 65.10±27.83, dead 59.95±25.71]. The CT characteristics of the patients were ischemic area (mm^3) [survive 273.15±70.52, dead 278.95±59.06]. Eleven (5.51%) had episode of convulsion. And eight (3.79%) had rebleeding post-operatively. One-hundred and one (47.87%) patients had pneumonia and fifty-three (25.12%) had sepsis. Length of stay (day) [survive 19.02±27.39, dead 9.28±11.17]. In this study, there was statistically significant association between clinical outcome and mean GCS on admission ($p<0.05$), GCS on admission ($p<0.05$), mean GCS on consultation ($p<0.05$), GCS on consultation ($p<0.05$), mean midline shift ($p<0.05$), midline shift ($p<0.05$), sepsis ($p<0.05$) and length of stay ($p<0.05$) (Table 1).

Table 1 Demographic features, clinical characteristics, disease factors and treatment factors of MMCAI patients (n=211)

Demographic features		Study groups (n=211)		p-value
		Survive (n=101)	Dead (n=110)	
Sex (no) percentage	Male	59 (28.0)	52 (19.9)	0.105
	Female	42 (19.9)	58 (27.5)	
Mean age (yr)		61.76±11.65	64.11±11.291	0.139
Mean GCS on admission (hr)	11.68±2.849	10.52±2.873	0.003	
GCS on admission (hr)	Mild (13-15)	45 (44.6%)	32 (29.1%)	0.016
	Moderate (9-12)	41 (40.6%)	46 (41.8%)	
	Severe (<8)	15 (14.9%)	32 (29.1%)	
Mean GCS on consultation (hr)		8.63±2.622	7.20±2.098	<0.001
GCS on consultation (hr)	Mild (13-15)	9 (8.9%)	3 (2.7%)	0.002
	Moderate (9-12)	34 (33.7%)	20 (18.2%)	
	Severe (<8)	58 (574)	87 (79.1%)	
rt-PA	Yes	29 (13.7)	27 (12.8)	0.493
	No	72 (34.1)	83 (39.3)	
Mean Midline shift (mm.)		8.84±3.518	10.30±3.714	0.004
Midline shift	MS 5-10	72 (71.2%)	64 (58.2%)	0.047
	MS >10	29 (28.7%)	46 (41.8%)	
Attending physician (no) percentage	Medicine	40 (19.0)	55 (26.1)	0.316
	Neuro-surgery	37 (17.5)	33 (15.6)	
	Neuro-medicine	24 (11.4)	49 (23.2)	
Admission ward (no) percentage	Med	33 (15.6)	49 (23.2)	0.194
	Surge	33 (15.6)	32 (15.2)	
	Stroke unit	31 (14.7)	28 (13.3)	
	Sub ICU	4 (1.9)	1 (0.5)	
Duration onset to consult (hr)	34.02±40.275	36.85±46.167	0.637	
Duration consult to operating room(OR) (hr)		10.83±16.173	9.99±24.165	0.769
Duration onset to to operating room(OR) (hr)		55.97±41.224	60.05±51.856	0.531
Operating time (min)	65.10±27.830	59.95±25.706	0.164	
Ischemic area (mm^3)		273.15±70.522	278.95±59.095	0.517
Rebleed (no) percentage	Yes	3 (1.4)	5 (2.4)	0.550
	No	98 (46.4)	105 (49.8)	
Pneumonia (no) percentage	Yes	47 (22.3)	54 (25.6)	0.710
	No	54 (25.6)	56 (26.5)	
Convulsion (no) percentage	Yes	3 (1.4)	8 (3.8)	0.160
	No	98 (46.4)	102 (48.3)	
Sepsis (no) percentage	Yes	6 (2.8)	47 (22.3)	<0.001
	No	95 (45.0)	63 (29.9)	
Length of stay (day)		19.02±27.385	9.28±11.172	0.001

This research used independent variable which statistically significant; GCS on admission, GCS on consultation, midline shift, hospital stay and sepsis. Duration onset to operating room (day3) was the important factor in the clinical even though not statistical significant (Table 2). The factors affecting clinical outcome of the patients were GCS on consultation, duration onset to OR (day3), length of stay and sepsis ($p<0.05$) (Table 3). Factors significantly affected clinical outcome of the patients were GCS on consultation, duration onset to OR [day3] hospital stay, and sepsis ($p<0.05$) (Table 4).

Table 2 Correlation coefficient between independent variable with functional outcome of MMCAI patients

Factor	GCS admit	GCS consult	MS	Hospital stay	Sepsis	Duration 3
Glasgow coma scale admit	1.000					
Glasgow coma scale consult	0.588	1.000				
MS	-0.053	-0.274	1.000			
Hospital stay	-0.008	0.050	-0.115	1.000		
Sepsis	0.011	0.058	0.335	0.032	1.000	
Duration 3	0.271	0.299	0.009	0.168*	0.220	1.000

* p<.05

Table 3 Coefficient logistic regression analysis on clinical outcomes of MMCAI patients

Factor	B	S.E.	Wald	df	p-value	Exp (B)	95% C.I for Exp (B)	
							Lower	Upper
GCS admit	0.077	0.079	0.934	1	0.334	1.080	0.924	1.261
GCS consult	0.231	0.113	4.212	1	0.040	1.260	1.010	1.571
MS	-0.054	0.052	1.066	1	0.302	0.947	0.855	0.050
Hospital stay	0.111	0.025	19.707	1	0.000	1.117	1.064	1.173
Sepsis	-3.362	0.610	30.383	1	0.000	0.035	0.010	0.115
Duration 3	-0.014	0.006	5.764	1	0.016	0.986	0.975	0.977
Constant	-2.117	1.005	4.435	1	0.035	0.120		

Table 4 Analysis of factors which affect on clinical outcomes of MMCAI patients

Factor	B	S.E.	Exp(B)	p-value
GCS consult	0.317	0.091	1.374	0.001
Duration3(day3)	-0.014	0.005	0.968	0.009
Hospital Stay	0.115	0.025	1.121	<0.001
Sepsis	-3.393	0.619	0.034	<0.001
Constant	-2.484	0.657	0.083	<0.001

Cox & Snell R^2 = 0.377, Nagellkerke R^2 =0.503, Percentage correct = 81.50

Discussion

MMCAI which space occupying brain edema is the leading cause of mortality in the first week following stroke.[13] The annual incidence is between 10-20 per 100,000 people and females are more commonly affected.[14] The prognosis is generally poor and mortality had been reported in up to 80%.[4] In the present study, the overall mortality rate was 52.13% which is similar to the reported by the previous study. The mean age of the present study was 62.90±11.50 years. Age has been reported to be the most important pretreatment prognostic factor.[15] In this study, there was no significant association between age with functional outcome. Timing of surgery is another crucial factor for hemicraniectony in MMCAI. Clinical studies have provided evidence for a benefit of early surgery.[16-18]

These have been numerous attempts to identify outcome predictors for MMCAI. Several models had been proposed and validated to help clinicians in predicting mortality and functional outcome.[19-22] The following independent factors were significantly associated with outcome: history of hypertension or heart disease, increased baseline white blood cell count, early CT hypodensity of the MCA territory and involvement of additional vascular territories, old age patients, female sex, diabetes mellitus, clinical signs of herniation and timing of surgery.

Glasgow coma scale (GCS) was developed in 1974 by Teasdale G and Jennett B was utilized world-wide.[23] Glasgow outcome Scale (GOS) first described in 1975 by Jennett B and Bond M used for evaluating outcomes of the patients. GCS and GOS are used to evaluated severity and treatment outcome worldwide. The admission GCS was a well-known predictor of outcome in MMCAI. The GCS score was a standard neurological assessment tool that because of its reproducibility and reliability.[24] GCS on admission was statistically significant association between with functional outcome ($p<0.05$) and GCS on consultation was statistically significant association with functional outcome ($p<0.05$). With regard to radiological variables based on CT imaging a significant association between midline shift as the predictor of functional outcome ($p<0.05$).

Bem junior[25] shows that surgical approach in <12 hr had better outcome, Soltani suggest that early decompressive craniectomy (DC) in patients with MMCAI can decrease mortality and improved the functional outcome.[17] The present study found 70% of the patients who had early DC (<12hr) were survive.

Sepsis was well known to occur at the onset at most comatose patients. In the present study, there was significant association between sepsis with functional outcome ($p<0.05$). In addition, the present study showed that length of stay was significant association with functional outcome ($p<0.05$).

Correlation coefficient between independent variable with functional outcome of MMCAI patients who had operative treatment [GCS on admission, GCS on consultation, midline shift, length of stay and sepsis] were statistically significant. Logistic regression analysis in this study found that GCS on consultation, sepsis, length of stay and duration onset to operating room were significant association with functional outcome. Factors which association with MMCAI patients who had operative treatment were GCS on consultation ($p<0.05$) patients who had better GCS will had better outcome, hospital stay ($p<0.05$)

patients who had longer hospital stay will had better outcome, patients who reduce onset to OR one hour will increased change to survive 96.8% ($p<0.05$) and patients who has no clinical sepsis will increased change to survice 3.4% ($p<0.05$).

Conclusion

Malignant middle cerebral artery infarction (MMCAI) is generally associated with poor prognosis and high mortality rate. Decompressive hemicraniectomy (DHC) is one of the surgical options to treat. Early DHC is related to lower neurological deficits and an earlier return to activities of daily life, patients who delayed surgery were associated with a poor outcome. Patients who had better GCS on consultation will had better outcome. Patients who reduce onset to OR will increased change to survive. Patients who has no clinical sepsis will increased change to survice and patients who had longer hospital stay will had better outcome.

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บทคัดย่อ: การศึกษานี้มีวัตถุประสงค์เพื่อศึกษากลุ่มผู้ป่วย malignant middle cerebral artery infarction (MMCAI) ที่ได้รับการผ่าตัดถึงผลการรักษาและปัจจัยที่มีผลต่อการรักษา เป็นการศึกษาย้อนหลังของผู้ป่วย MMCAI จำนวน 211 รายที่รับไว้ในโรงพยาบาลสวรรค์ประชารักษ์ระหว่างเดือนกันยายน 2555 ถึงเดือนกันยายน 2566 ผู้ป่วยทั้งหมดได้รับการวินิจฉัยว่าเป็นโรค MMCAI และได้รับการผ่าตัดรักษาโดยวิธีการทำ decompressive hemicraniectomy (DHC) ผู้ป่วยที่มีภาวะทุพพลภาพ ผู้ป่วยโรคหลอดเลือดสมองก่อนหน้านี้ ผู้ป่วยมีเลือดออกในเนื้อสมอง ผู้ป่วยโรคเรื้อรัง เช่น โรคไตวาย โรคตับ ผู้ป่วยที่ได้รับยา warfarin และยาต้านการแข็งตัวของเลือดอื่น ๆ ผู้ป่วยที่มีข้อห้ามในการดมยาสลบและการผ่าตัด ผู้ป่วยท้อง และผู้ป่วยที่มีก้อนเนื้อในสมองไม่นับรวมในการรักษานี้ การศึกษานี้แบ่งกลุ่มผู้ป่วยเป็น 2 กลุ่มตามผลการรักษา คือ กลุ่มรอดชีวิตและกลุ่มเสียชีวิต ผลการศึกษาพบว่าปัจจัยที่มีผลต่อการรักษานี้ประกอบด้วย GCS เมื่อผู้ป่วยแรกรับในโรงพยาบาล ($p<0.05$) GCS เมื่อรับการปรึกษาจากต่างแผนก ($p<0.05$) ระยะการเคลื่อนที่ของสมองผ่านแนวกลาง ($p<0.05$) ภาวะติดเชื้อในกระแสเลือด ($p<0.05$) และระยะเวลาการรักษาตัวในโรงพยาบาล ($p<0.05$) การศึกษาค่าสัมประสิทธิ์สหสัมพันธ์ระหว่างปัจจัยที่มีผลต่อการรอดชีวิตของผู้ป่วย พบว่า ความสัมพันธ์ระหว่างต่อแปรอิสระที่มีผลต่อการรอดชีวิตของผู้ป่วยมีความสัมพันธ์กันไม่เกิน 0.80 จึงไม่มีปัญหาตัวแปรอิสระมีความสัมพันธ์กันเชิง multicollinearity สามารถใช้ตัวแปรอิสระเหล่านี้ในการวิเคราะห์ความถดถอยโลจิสติกส์ได้ คือเลือกตัวแปรอิสระที่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติเข้าสมการ ได้แก่ Glasgow come scale (GCS) เมื่อผู้ป่วยแรกรับในโรงพยาบาล GCS เมื่อรับการปรึกษาจากต่างแผนก ระยะทางการเคลื่อนที่ของสมองผ่านแนวกลาง ภาวะติดเชื้อในกระแสเลือดและระยะเวลาในการรักษาตัวในโรงพยาบาล รวมถึงตัวแปรที่มีความสำคัญถึงแม้จะไม่มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติ ได้แก่ ระยะเวลาตั้งแต่เกิดเหตุจนถึงการผ่าตัดรักษา (Duration3) หลังจากการวิเคราะห์ด้วยค่าสัมประสิทธิ์ของการวิเคราะห์สมการถดถอยโลจิสติกส์ พบว่า ปัจจัยที่มีผลต่อการรอดชีวิตของผู้ป่วยประกอบด้วย GCS เมื่อรับการปรึกษาจากต่างแผนก มีภาวะติดเชื้อในกระแสเลือด ระยะเวลาตั้งแต่เกิดเหตุจนถึงการผ่าตัดรักษา (D3) และระยะเวลาในการรักษาตัวในโรงพยาบาล และการวีเคราะห์ตัวแบบปัจจัยที่มีผลต่อการรอดชีวิตของผู้ป่วย พบว่า ปัจจัยที่มีความสัมพันธ์กับผลการรอดชีวิตของผู้ป่วย MMCAI ที่รักษาด้วยการผ่าตัดประกอบด้วย GCS เมื่อรับการปรึกษาจากต่างแผนก ภาวะติดเชื้อในกระแสเลือด ระยะเวลาตั้งแต่เกิดเหตุจนถึงการผ่าตัดรักษา (D3) และระยะเวลาในการรักษาตัวในโรงพยาบาล

คำสำคัญ: **ผู้ป่วย malignant middle cerebral artery infarction; การทำ decompressive hemicraniectomy; แบบวัด Glasgow coma scale; แบบวัด Glasgow outcome scale**