Outcome predictors of open embolectomy in middle cerebral artery occlusion

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Running title: Statistical analysis of MCA embolectomy outcome
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Abstract

Object: The purpose of this paper was to analyze the outcome of the patients with acute middle cerebral artery (MCA) occlusion treated by the open embolectomy.

Methods: A clinical chart review was retrospectively conducted for 30 patients who had suffered MCA occlusion and were treated with the open embolectomy. According to Glasgow outcome scale, the patients' outcome at discharge was divided in two groups: favorable outcome (good recovery and moderate disability) or unfavorable outcome (severe disability, vegetative state, and dead). The following variables between the favorable and unfavorable outcome were analyzed: age, sex, Glasgow Coma Scale on admission, affected side, occlusion site, occlusion time, atrial fibrillation on electrocardiogram, fibrinolysis, aphasia, hemiparesis, and hemorrhagic infarction after surgery.

Results: Outcome of 30 patients was the favorable one in 16 patients (good recovery in 9 and moderate disability in 7) and the unfavorable one in 14 patients (severe disability in 12, vegetative state in 1, and 1 patient died). The M1 occlusion and fibrinolysis performance were more frequent in the unfavorable outcome group than the favorable one. Logistic regression analysis with a stepwise method indicated that the only occlusion site was independently associated with the unfavorable outcome. The occlusion time over 360 minutes was not predictor of the unfavorable outcome.

Discussion: The outcome of patients with MCA occlusion treated by the open embolectomy depends on the occlusion site and the fibrinolysis performance in the present study. The M1

occlusion is also the independent risk factor of the unfavorable outcome. However, the occlusion time itself has no relation to the unfavorable outcome. These results indicate that therapeutic time windows vary in individuals probably due to the collateral blood flow.

Introduction

We recently reported the efficacy of the open embolectomy in patients with the acute middle cerebral artery (MCA) occlusion.[5] Although rapid restoration of the cerebral blood flow is the principle goal for ischemia, it is our impression that the only restoration time may not be an important outcome predictor of the MCA occlusion. Because the therapeutic time window may vary among individuals due to the collateral blood blow.[5;6;9]

In the present study, we analyze outcome predictors of the open embolectomy and clarify whether the occlusion time is involved in the outcome.

Patients and Methods

Indications and surgical techniques for the open MCA embolectomy were previously reported in detail.[5] Briefly, the patient had severe neurological deficits with and without cognitive dysfunction due to the MCA (the horizontal M1 segment or the M2 division) occlusion. Intra-arterial fibrinolysis did not succeed sufficiently. Computed tomography (CT) after fibrinolysis or angiography showed no low density area at the affected MCA territory. The open embolectomy was carried out through the fronto-temporal craniotomy.

Patient population: From October 1997 to December 2006, 30 patients (72.2 ± 8.2 years old) were treated with the open embolectomy and retrospectively analyzed using the clinical data. Clinical condition on admission and outcome at discharge were evaluated according to the Glasgow Coma Scale (total score) and Glasgow Outcome Scale, respectively. The affected sides were 10 patients in the right and 20 in the left. The M1 and M2 occlusion were observed in 21 and 9 patients, respectively. Twenty one of 30 patients underwent the local intra-arterial fibrinolysis with urokinase. In the majority of remaining cases, fibrinolysis was not performed because of difficulty in accessing a microcatheter to the MCA. The average time to flow restoration after ictus (the occlusion time) was 372.7 6 ± 120.0 minutes ranging from 168 to 800 minutes. All patients had the full recanalization based on the postoperative angiograms. When CT on postoperative day 1 showed no hemorrhagic transformation, the patients received warfarin to prevent recurrence. The asymptomatic and symptomatic hemorrhagic infarction happened in 1 and 2 patients, respectively. One patient underwent the decompressive surgery for the hemorrhagic transformation. Two patients among three patients with hemorrhagic infarction underwent the intra-arterial local fibrinolysis. The patients' outcome was divided in two categories: favorable outcome (good recovery and moderate disability) or unfavorable outcome (severe disability, vegetative state, and dead) and compared two groups.

Statistical Analyses: We performed all analyses using SPSS statistical software (Dr. SPSS II, SPSS Inc). Comparisons of demographic data and clinical variations between favorable and unfavorable groups were performed by Student's t test, Chi-square test, and Mann-Whitney's U test. Variables were then entered in a stepwise logistic regression model to determine the independent effect of each variable on outcome. Values of $P<0.05$ were considered significant.

Results

Sixteen patients had favorable outcome (good recovery in 9 and moderate disability in 7) at discharge, while 14 patients (severe disability in 12, vegetative state in 1, and 1 patient died) did not (Table 1). The occlusion site and the fibrinolysis were associated with the unfavorable outcome significantly (Table 1). The occlusion time was not significantly different in the favorable and unfavorable outcomes (340.8 ± 98.7 versus 409.3 ±

134.8, P = 0.120). Other demographic data such as age, Glasgow Coma Scale score in admission, the occlusion side, and the hemorrhagic infarction had also no relation to the outcome (Table 1). Logistic regression analysis with stepwise method was used to determine independent predictors of the unfavorable outcome. Variables tested were the presence of global aphasia, the presence of severe hemiparesis, the M1 occlusion, the fibrinolysis performance, the occlusion time over 360 minutes, and the symptomatic hemorrhagic transformation. Logistic regression analysis revealed that only the M1 occlusion was the predictor of unfavorable outcome (P = 0.031, odds ratio: 24.7, 95% CI: 1.34 to 455.1). The occlusion time over 6 hours was not the predictor of the poor outcome (P = 0.707, odds ratio: 1.75, 95% CI: 0.096 to 31.9).

Discussion

In 1956, the open embolectomy for MCA occlusion was firstly reported by Welch.[12] Although there were some reports of the open embolectomy, its role remains contraversial.[2;3;6;7;9;10] In the present study, we attempted to provide additional information with respect to patient selection and prognostic factors.

Meyer et al.[9] concluded that the collateral flow was the best predictor of outcome after the open embolectomy. We completely agree with their conclusions. However, it is difficult to estimate the sufficient collateral blood flow preoperatively. Additionally, it is unknown how long the ischemic penumbra can be tolerated. Although cerebral blood flow studies including single photon emission computed tomography (SPECT) are very useful to evaluate the regional blood flow, it is not easy to perform the preoperative SPECT routinely because of time consuming and emergency environment. Currently, we use the finding of no low density area on the follow-up CT after fibrinolysis or angiography as the surgical indicator for the open embolectomy.[5] We judge the presence or absence of sufficient collateral blow flow based on the follow-up CT findings. However, all patients underwent the open embolectomy did not have the favorable outcome. Further study of the reliable indicator such as perfusion magnetic resonance imaging should be conducted to improve outcome.

Since the endovascular techniques and devices are developed, intra-arterial thrombolytic therapies include chemical and mechanical methods.[1;4] Recently, Levy and colleagues[8] reported that treatment with a self-expanding stent placement with concomitant administration of IIb/IIIa inhibitors contributed to the achievement of recanalization in all M1 occlusions.

The local and/or systemic thrombolytic agent application into the ischemic brain tissue and the reperfusion injury on blood brain barrier are the risk factors for the hemorrhagic transformation. Although the hemorrhagic transformation was not associated with the outcome, the fibrinolysis was one of the risk factors in our study. The present study excluded the patients successfully treated with the fibrinolysis. Therefore, the thrombolytic agent would have some effects for outcome if the fibrinolysis doses not succeed.

In Japan, intravenous recombinant tissue plasminogen activator (IV rt-PA) within 3 hours of ischemic stroke onset was approved in October 2005. The present study did not include the patients treated with the IV rt-PA. The number of patients treated with IV rt-PA rapidly increases in Japan. However, some of patients did not improve only with IV rt-PA therapy. Therefore, it is a problem how to treat the patients who do not respond to the IV rt-PA. Further examinations should be needed whether the open embolectomy can be one of the treatment option after the insufficient effect of the IV rt-PA.

In the present study, the M1 occlusion comparing with the M2 occlusion was only the independent risk factor of poor outcome. This reason will be the involvement of the lenticulostriate arteries, which are terminal vessels with poor collaterals.

The recanalization therapy has been the time limitation because the brain ischemia will result in the cerebral infarction. The time limit of the recanalization of MCA blood flow has been believed to be within 360 minutes because the restoration of flow after 360 minutes produced severe neurological deficits and cerebral infarction.[6;11] However, in the present study, the occlusion time itself and the occlusion time over 360 minutes were not associated with the unfavorable outcome. These results strongly suggest that the collateral blood flow varies in individuals and the open embolectomy can be effective even over 360 minutes after ictus if CT after angiography or insufficient fibrinolysis demonstrates no low density area in the affected MCA territory.

Table 1. Characteristics of 30 patients treated with open embolectomy.

Clinical Characteristics	Number of Patients (%)		*P* value
	Favorable outcome n = 16 (53.3%)	Unfavorable outcome n = 14 (46.7%)	
Sex			0.919*
female	6 (37.5)	5 (35.7)	
male	10 (62.5)	9 (64.3)	
Age (yr, mean ± SD)	73.8 ± 8.9	70.4 ± 7.2	0.276†
GCS score (mean ± SD)	11.4 ± 2.0	12.2 ± 2.7	0.334†
Side			0.075**
right	3 (18.8)	7 (50.0)	
left	13 (81.3)	7 (50.0)	
Occlusion site			0.012**
M1	8 (50.0)	13 (92.9)	
M2	8 (50.0)	1 (7.1)	
Aphasia			0.062**
none	3 (18.8)	7 (50.0)	
motor	3 (18.8)	3 (21.4)	
sensory	1 (6.3)	0	
global	9 (56.3)	4 (28.6)	
Hemiparesis			0.094**
none	2 (12.5)	0	
mild	1 (6.3)	0	
severe	13 (81.3)	14 (100.0)	
Atrial fibrillation			0.472**
no	4 (25.0)	2 (14.3)	
yes	12 (75.0)	12 (85.7)	
Fibrinolysis			0.012**
no	8 (50.0)	1 (7.1)	
yes	8 (50.0)	13 (92.9)	
Occlusion time (minutes)	340.8 ± 98.7	409.3 ± 134.8	0.120†
Hemorrhagic infarction			
none	16 (100)	11 (78.6)	0.055**
asymptomatic	0	1 (7.1)	
symptomatic	0	2 (14.3)	

*: Chi-square test, †: Unpaired Student's t-test, **: Mann-Whitney’s U test

Table 2. Results of logistic regression analysis between favorable and unfavorable outcome in the patients surgically treated with the open embolectomy.

	Probability value / Odds ratio (95% CI)
Occlusion site (M1 or M2)	0.014 / 39.08 (2.12-720.2)
Global aphasia (yes or no)	0.381 / 0.333 (0.028-3.903)
Fibrinolysis (yes or no)	0.013 / 42.67 (2.24-814.3)
Occlusion time (less than 360 minutes or over 360 minutes)	0.016 / 5.464 (0.43-69.04)

CI: confidence interval

Reference List

1. Becker KJ, Brott TG: Approval of the MERCI clot retriever: a critical view. Stroke 36:400-403, 2005

2. Gagliardi R, Benvenuti L, Guizzardi G: Acute operation in cases of middle cerebral artery occlusion. Neurosurgery 12:636-639, 1983

3. Garrido E, Stein BM: Middle cerebral artery embolectomy. Case report. J.Neurosurg. 44:517-521, 1976

4. Gobin YP, Starkman S, Duckwiler GR, et al: MERCI 1: a phase 1 study of Mechanical Embolus Removal in Cerebral Ischemia. Stroke 35:2848-2854, 2004

5. Horiuchi T, Nitta J, Sakai K, et al: Emergency embolectomy for treatment of acute middle cerebral artery occlusion. J.Neurosurg. 106:257-262, 2007

6. Kakinuma K, Ezuka I, Takai N, et al: The simple indicator for revascularization of acute middle cerebral artery occlusion using angiogram and ultra-early embolectomy. Surg.Neurol. 51:332-341, 1999

7. Khodadad G: Middle cerebral artery embolectomy and prolonged widespread vasospasm. Stroke 4:446-450, 1973

8. Levy EI, Mehta R, Gupta R, et al: Self-expanding stents for recanalization of acute cerebrovascular occlusions. AJNR Am.J.Neuroradiol. 28:816-822, 2007

9. Meyer FB, Piepgras DG, Sundt TM, Jr., et al: Emergency embolectomy for acute occlusion of the middle cerebral artery. J.Neurosurg. 62:639-647, 1985

10. Muramoto M, Kim F, Kim I: [Thrombectomy of the middle cerebral artery (author's transl)]. No Shinkei Geka 9:733-738, 1981

11. Okada Y, Shima T, Oki S, et al: Experimental microsurgical embolectomy after middle cerebral artery embolization in the dog. J.Neurosurg. 58:259-266, 1983

12. Welch K: Excision of occlusive lesions of the middle cerebral artery. J.Neurosurg. 13:73-80, 1956