

Functional Outcomes of Decompressive Craniectomy in Patients with Malignant Middle Cerebral Artery Infarction and Their Association with Preoperative Thalamus Deformation: An Analysis of 12 Patients

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Abstract

Objective Decompressive craniectomy (DC) in patients with malignant middle cerebral artery (MCA) infarction is known to decrease the mortality rate. However, the functional outcomes (communication and oral intake) of this procedure remain unclear. Most patients with malignant MCA infarction exhibit a loss of consciousness, which may be principally governed by the thalamus. We herein investigated the functional outcomes of DC at 90 days after the onset of malignant MCA infarction and their association with preoperative thalamus deformation, which can occur due to pressure and edema.

Methods Twelve of 2,692 patients with acute cerebral infarction were diagnosed with malignant MCA infarction and underwent DC. We evaluated preoperative thalamus damage using brain computed tomography and its association with communication and oral intake abilities and the modified Rankin Scale (mRS) and Barthel index scores at 90 days after stroke onset.

Results The mRS score at 90 days was 0-4 in five patients. Seven patients could communicate immediately after surgery, while five could do so by 90 days. Five patients were able to resume the oral intake of food at 90 days. All patients with preoperative thalamus deformation showed a poor recovery, while those with absent or slight preoperative thalamus deformation showed a good recovery.

Conclusion Patients with preoperative thalamus deformation caused by pressure and edema show a poor oral intake and communication abilities after DC, suggesting that preoperative thalamus deformation is a predictor of poor functional outcomes after DC in patients with malignant MCA infarction.

Key words: malignant middle cerebral artery infarction, decompressive craniectomy, functional outcomes, thalamus deformation sign

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Introduction

Malignant middle cerebral artery infarction (MMCAI) is an infarct of the middle cerebral artery (MCA) territory and shows severe cerebral edema as well as herniation. MMCAI may also involve the anterior cerebral artery (ACA) and/or

posterior cerebral artery (PCA) territories. MMCAI is a potentially lethal clinical condition with poor outcomes and a mortality rate of approximately 80% without surgical treatment (1-4). Decompressive craniectomy (DC) is increasingly being performed in patients with malignant brain ischemia to avoid the harmful consequences of cerebral edema and increase in the intracranial pressure (5-7), and this procedure

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has been consistently associated with a decrease in the mortality rate to approximately 30% (8-11). DC is recommended for patients with MMCAI in the Japanese stroke guideline (grade A) (12), although the outcomes remain unclear. In general, most clinical studies have used the modified Rankin Scale (mRS) and Barthel index (BI) scores as indicators of functional disorders after DC in patients with ischemic infarction. However, even if the mRS score is 5 and/or BI is 0 after DC, some patients may exhibit the ability to communicate and eat. Therefore, only the mRS or BI may be inappropriate for the evaluation of individuals undergoing DC for MMCAI.

The reticular formation in the brainstem, ascending reticular activating system, nonspecific thalamus nuclei, and thalamocortical projections should be intact and functional for a fully conscious state (13). In particular, the thalamus plays an important role in maintaining consciousness. Most patients with MMCAI exhibit a decrease level of consciousness, and cerebral herniation results in preoperative thalamus deformation caused by pressure and edema. Therefore, we hypothesized that the severity of thalamus deformation of MMCAI patients at the time of onset may affect the outcomes after DC.

In this study, we investigated the communication and oral intake abilities and motor function at 90 days after the onset of MMCAI in 12 patients who underwent DC. In addition, we analyzed the association of these outcomes with preoperative thalamus deformation.

Materials and Methods

Between April 2007 and July 2014, 2,692 patients with acute cerebral infarction were admitted to our hospital. Among these, 12 MMCAI patients underwent DC that was performed according to clinical signs and symptoms, such as progressive disturbance in consciousness, anisocoria, and cerebral herniation, on computed tomography (CT).

We collected data regarding age, sex, clinical type, location of the infarct, National Institutes of Health Stroke Scale (NIHSS) scores at the time of admission, Japan Coma Scale scores at the time of onset and before surgery, and the interval (hours) between admission and DC. In addition, we analyzed the volume of the infarct area, length of the midline shift, and thalamus deformation before surgery using brain CT. The communication and oral intake abilities and the mRS and BI scores were recorded at 90 days after stroke onset.

Brain CT images with a 5 mm thickness were obtained parallel to the orbitomeatal (OM) line. To measure the infarct volume, we analyzed the hypodense area on CT images using the ABC/2 technique, which is generally used to measure the volume of an intracerebral hemorrhage. In this technique, A is the maximum diameter of the low-density area, B is the diameter of 90 degrees to A, and C is the number of CT slices with infarction multiplied by the slice thickness (14). We determined the presence and severity of

thalamus deformation at the level of the anterior horn of the lateral ventricle and pineal gland. The affected thalamus was compared with the contralateral one, and the thalamus deformation sign (TDS) was scored using a subjective scale as follows: 0, no deformation; 1, mild deformation; and 2, severe deformation. Two authors (Y.K. and I.D.) assessed the volume of the infarct and TDS grade independently. For the infarct volume, we used the average value measured by the two authors. If the TDS level was different between two authors, then the two authors discussed the difference and reached a consensus for the final result in each patient. A good recovery was defined as the ability to communicate even by gesturing after DC and at 90 days after stroke onset, in addition to oral intake at 90 days. Patients who did not exhibit a good recovery were classified as the poor recovery group.

Statistical analysis

Age, the interval between stroke onset and DC, the mean infarct volume on CT images, and the mean length of the midline shift were compared between the good and poor recovery groups using Student's t-tests; the status of preoperative thalamus deformation was compared using the χ^2 test; and the NIHSS scores at admission and the mRS scores at 90 days were compared using the Wilcoxon test. All statistical analyses were performed using the PASW Statistics 18.0 software program (SPSS Science, Chicago, USA). Data are expressed as the means \pm standard deviations or median. A p-value of <0.05 was considered to be statistically significant.

Results

The Table demonstrates the characteristics of the 12 patients included in this study. There were six men and six women with a mean age of 61.9 ± 11.3 years (range, 38-75 years) at the time of onset. Infarction was caused by cardiac embolism in 10 patients and arterial dissection in two.

The mRS score at 90 days after stroke onset was 0-4 in five patients. The location of the infarct, as confirmed by magnetic resonance imaging, was the MCA in five patients and the ACA and MCA in seven. Infarction was right-sided in 10 patients and left-sided in two. The median NIHSS score at the onset of cerebral infarction was 18.5, the mean interval between stroke onset and DC was 34.4 ± 12.1 hours, the mean infarction volume on CT images was 393 ± 88 cm³, and the mean length of deviation from the midline was 10.6 ± 4.3 mm. Seven patients were able to communicate immediately after surgery, while five could do so by 90 days after stroke onset. Five patients exhibited a recovery of oral food intake at 90 days. The median mRS and BI scores at 90 days after onset were 5 and 0, respectively. With regard to the groups stratified by recovery, the age of patients in the good recovery group was 56.7 ± 12.1 years, while that of patients in the bad recovery group was 69.2 ± 4.6 years; this difference was significant ($p < 0.05$). There were no differ-

Table. Characteristics of Patients Who Underwent Decompressive Craniectomy after Malignant Middle Cerebral Infarction.

age	sex	Clinical type	Infarction area	JCS at admission	JCS at surgery	Infarction side	NIHSS at admission	Time to operation	Internal/external decompression	Infarct volume (cm ³)	Midline shift (mm)	TDS	Thalamus deformity	Communication after surgery	Communication at 90 days	Oral intake at 90 days	mRS score at 90 days	Barthel index score at 90 days	Notes
66	M	CE	MCA	100	200	lt	20	24	I	412	7	1	-	P	P	P	4	20	motor aphasia
43	F	CE	ACA+MCA	200	200	lt	19	40	I	409	13	1	-	P	P	P	3	95	motor aphasia
68	M	CE	ACA+MCA	1	100	rt	15	44	I	421	12	0	-	P	P	P	4	60	
67	M	AD	MCA	1	300	rt	40	24	I	400	12	2	+	IP	IP	IP	5	0	DC, pneumonia, tracheostomy
38	F	CE	ACA+MCA	2	30	rt	12	12	E	390	6	0	-	P	P	P	3	55	
75	F	CE	ACA+MCA	100	200	rt	24	44	I	369	14	2	+	IP	IP	IP	5	0	DC, pneumonia, tracheostomy
64	F	CE	ACA+MCA	2	100	rt	14	24	I	411	8	2	+	IP	IP	IP	5	0	DC, pneumonia, tracheostomy
64	F	AD	MCA	0	sedation	rt	40	60	I+E	260	15	1	-	P	P	IP	5	0	DC, pneumonia, tracheostomy
65	M	CE	MCA	0	100	rt	18	31	E	237	0	0	-	P	IP	IP	6	0	Recurrence of stroke at 42 days
73	F	CE	ACA+MCA	30	200	rt	22	40	I	506	13	2	+	IP	IP	IP	5	0	DC, pneumonia
53	M	CE	MCA	1	30	rt	13	31	E	356	14	0	-	P	P	P	3	75	
67	M	CE	ACA+MCA	20	200	rt	12	39	E	556	14	2	+	IP	IP	IP	6	0	brain hernia
61.9 ± 11.3 (mean ± SD)						lt: 2 rt: 10		18.5 (median)	34.4 ± 12.1 (mean ± SD)	I: 7 E: 4 I+E: 1	393 ± 88 (mean ± SD)	10.6 ± 4.3 (mean ± SD)		P: 7 IP: 5	P: 6 IP: 6	P: 5 IP: 7	5 (median)	0 (median)	

AD: arterial dissection, AF: atrial fibrillation, CE: cardiac embolism, M: male, F: female, mRS: modified Rankin Scale, NIHSS: National Institutes of Health Stroke Scale, ICA: internal carotid artery, MCA: middle cerebral artery, ACA: anterior cerebral artery, TDS: thalamic deformation sign, I: internal decompression/E: external decompression, DC: disturbed consciousness, P: possible, IP: impossible

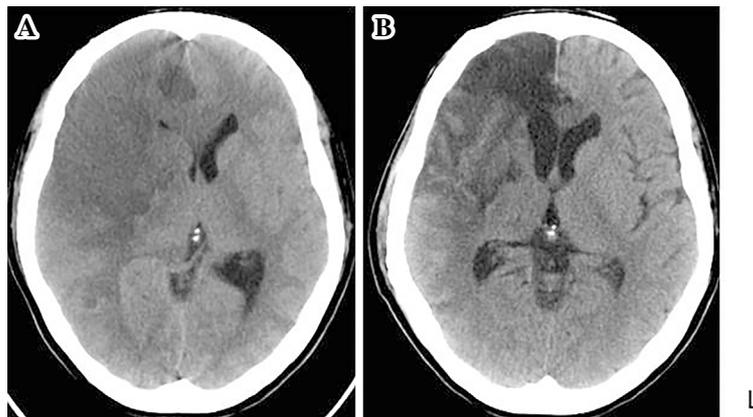


Figure 1. Case 1. 38-year-old woman. A: A grade 0 thalamus deformation sign (TDS) at the time of surgery. B: No thalamus deformation is observed 2 months after decompressive craniectomy (DC). The patient could communicate and eat, with a modified Rankin Scale (mRS) score of 3 at 90 days after the onset.

ences in the median NIHSS score at the time of onset, interval between stroke onset and DC, volume of the infarct on CT images, or length of midline deviation between the two groups. All patients in the poor recovery group showed severe thalamus deformation at the preoperative stage, while those in the good recovery group showed absent or mild thalamus deformation (Fig. 1-3).

Discussion

We investigated the functional outcomes of DC at 90 days after the onset of MMCAI and their association with preoperative thalamus deformation in 12 patients. All patients

with preoperative thalamus deformation showed a poor recovery, while those with absent or slight preoperative thalamus deformation showed a good recovery. Patients who exhibited a good recovery after DC tended to be younger. Previous studies reported that DC in patients with MMCAI improves the survival rate at 1 year and the mRS and BI scores (15-18). All these studies included patients aged >65 years, similar to the cohort included in our study.

The BI and mRS are the most common clinical indices for the measurement of outcomes. A favorable outcome is generally defined as a BI score of >60 or an mRS score of ≤2 (19). However, not only physical disability but also social interaction, occupational activities, communication

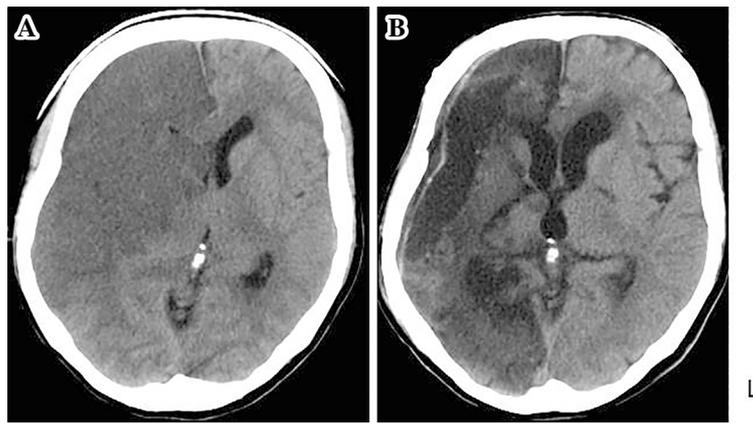


Figure 2. Case 2. 64-year-old woman. A: A grade 2 thalamus deformation sign (TDS) before DC surgery. B: A low-density area is observed in the thalamus at 2 months after DC. The patient underwent tracheostomy due to pneumonia and was unable to communicate or eat. Her modified Rankin Scale (mRS) score was 5 at 90 days after the onset.

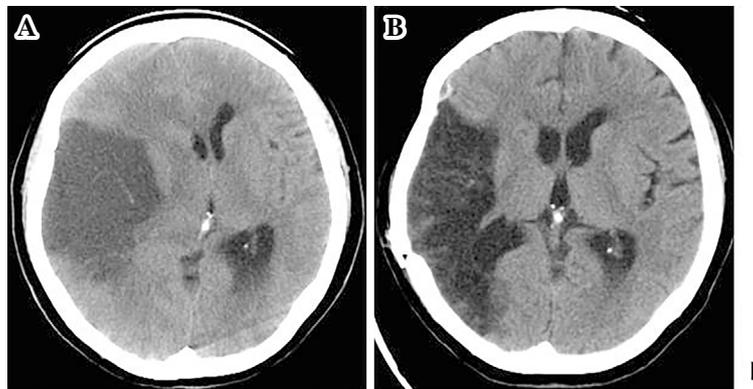


Figure 3. Case 3. 64-year-old woman. A: A grade 1 thalamus deformation sign (TDS) before surgery. B: The low-density area in the thalamus disappeared at 2 months after DC. The patient underwent tracheostomy due to pneumonia and was unable to eat, although she could communicate using hand gestures. Her modified Rankin Scale (mRS) score was 5 at 90 days after the onset.

skills, and cognitive and emotional functions must be evaluated in stroke patients. We consider that good communication and oral intake abilities after craniectomy in patients with MMCAI indicate a good recovery and treatment success, even if the mRS score is 5 and BI score is 0. In fact, language comprehension was poor in patients who underwent left-sided DC. However, the communication abilities assessed by objective means were maintained, even in the presence of aphasia, in patients who underwent left-sided DC.

The prediction of malignant cerebral infarction is extremely important in patients with MMCAI who are scheduled to undergo DC. In previous studies, severe cerebral edema was predicted according to certain factors, including an NIHSS score of 20, embolism in the terminal portion of the internal carotid artery, retching/vomiting within 24 hours after stroke onset, leukocytosis, an infarct volume more than 50% of the MCA territory on CT images, the involvement of other blood vessels (ACA or PCA) (20, 21), and an infarct volume of $>145 \text{ cm}^3$ on diffusion-weighted imaging

(DWI) (22). In the present study, older age and preoperative disturbance of consciousness were associated with a poor prognosis. In addition, severe deformation of the thalamus on the CT images was associated with the prognosis of MMCAI patients undergoing DC. We consider that preoperative thalamus deformation is a useful predictor of postoperative disturbance in consciousness of MMCAI patients. In particular, a grade 0 or grade 1 TDS indicated reversible damage of the thalamus improvement of consciousness after surgery and a better prognosis. However, the direct relationship between preoperative thalamus deformation and the prognosis after DC remains unknown. Although the direct relationship of the thalamus deformation and prognosis remains unclear, the thalamus dysfunction may decrease the level of consciousness and cause aspiration pneumonia after the onset of MMCAI. In fact, most patients with a poor prognosis developed pneumonia after DC.

There are several limitations associated with our study. In addition to a relatively small number of cases and our retrospective analysis, DC was not performed using the rigorous

protocols of prospective studies. Additionally, a functional and physiological analysis of the thalamus was not carried out.

In conclusion, patients with preoperative thalamus deformation caused by MMCAI showed poor oral intake and communication abilities after DC, suggesting that preoperative thalamus deformation is a useful predictor of the functional outcomes after DC in patients with MMCAI. To the best of our knowledge, no report has demonstrated the usefulness of TDS for the evaluation of the prognosis in MMCAI after DC. Therefore, further analyses are necessary to clarify the present results.

The authors state that they have no Conflict of Interest (COI).

References

- Hacke W, Schwab S, Horn M, Spranger M, De Georgia M, von Kummer R. 'Malignant' middle cerebral artery territory infarction: clinical course and prognostic signs. *Arch Neurol* **53**: 309-315, 1996.
- Moulin DE, Lo R, Chiang J, Barnett HJ. Prognosis in middle cerebral artery occlusion. *Stroke* **16**: 282-284, 1985.
- Ropper AH, Shafran B. Brain edema after stroke. Clinical syndrome and intracranial pressure. *Arch Neurol* **41**: 26-29, 1984.
- Berrouschot J, Sterker M, Bettin S, Koster J, Schneider D. Mortality of space-occupying ('malignant') middle cerebral artery infarction under conservative intensive care. *Intensive Care Med* **24**: 620-623, 1998.
- Vahedi K, Vicaute E, Mateo J, et al. Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL Trial). *Stroke* **38**: 2506-2517, 2007.
- Juttler E, Schwab S, Schmiedek P, et al. Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY): a randomized, controlled trial. *Stroke* **38**: 2518-2525, 2007.
- Hofmeijer J, Kappelle LJ, Algra A, Amelink GJ, van Gijn J, van der Worp HB. Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAMLET]): a multicentre, open, randomised trial. *Lancet Neurol* **8**: 326-333, 2009.
- Pillai A, Menon SK, Kumar S, Rajeev K, Kumar A, Panikar D. Decompressive hemicraniectomy in malignant middle cerebral artery infarction: an analysis of long-term outcome and factors in patient selection. *J Neurosurg* **106**: 59-65, 2007.
- Rieke K, Schwab S, Krieger D, et al. Decompressive surgery in space-occupying hemispheric infarction: results of an open, prospective trial. *Crit Care Med* **23**: 1576-1587, 1995.
- Schwab S, Steiner T, Aschoff A, et al. Early hemicraniectomy in patients with complete middle cerebral artery infarction. *Stroke* **29**: 1888-1893, 1998.
- Robertson SC, Lennarson P, Hasan DM, Traynelis VC. Clinical course and surgical management of massive cerebral infarction. *Neurosurgery* **55**: 55-61; discussion 61-62, 2004.
- The Joint Committee on Guidelines for the Management of Stroke. Japanese Guidelines for the Management of Stroke. Kyowa Kikaku, Ltd, Tokyo, 2015 (in Japanese).
- Plum F, Posner JB. The Diagnosis of Stupor and Coma. FADC, Philadelphia, 1980.
- Kothari RU, Brott T, Broderick JP, et al. The ABCs of measuring intracerebral hemorrhage volumes. *Stroke* **27**: 1304-1305, 1996.
- Arac A, Blanchard V, Lee M, Steinberg GK. Assessment of outcome following decompressive craniectomy for malignant middle cerebral artery infarction in patients older than 60 years of age. *Neurosurg Focus* **26**: E3, 2009.
- Gupta R, Connolly ES, Mayer S, Elkind MS. Hemicraniectomy for massive middle cerebral artery territory infarction: a systematic review. *Stroke* **35**: 539-543, 2004.
- Juttler E, Unterberg A, Woitzik J, et al. Hemicraniectomy in older patients with extensive middle-cerebral-artery stroke. *New Engl J Med* **370**: 1091-1100, 2014.
- Zhao J, Su YY, Zhang Y, et al. Decompressive hemicraniectomy in malignant middle cerebral artery infarct: a randomized controlled trial enrolling patients up to 80 years old. *Neurocrit Care* **17**: 161-171, 2012.
- Sulter G, Steen C, De Keyser J. Use of the Barthel index and modified Rankin scale in acute stroke trials. *Stroke* **30**: 1538-1541, 1999.
- Kasner SE, Demchuk AM, Berrouschot J, et al. Predictors of fatal brain edema in massive hemispheric ischemic stroke. *Stroke* **32**: 2117-2123, 2001.
- Krieger DW, Demchuk AM, Kasner SE, Jauss M, Hantson L. Early clinical and radiological predictors of fatal brain swelling in ischemic stroke. *Stroke* **30**: 287-292, 1999.
- Oppenheim C, Samson Y, Manai R, et al. Prediction of malignant middle cerebral artery infarction by diffusion-weighted imaging. *Stroke* **31**: 2175-2181, 2000.