The Outcome Predictors of Malignant Large Infarction and the Functional Outcome of Survivors Following Decompressive Craniectomy

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■ OBJECTIVE: **Cerebral infarction is a common cause of disability. Malignant large infarction (MLI) is a catastrophic event, and there is no effective medical treatment. This study aimed to assess the outcome predictors of MLI and to analyze the impact of decompressive craniectomy (DC) on the functional outcome of survivors.**

■ METHODS: **This study comprised 213 MLI cases. Outcome was evaluated with modified Rankin Scale (mRS) at 1-year follow-up, and various parameters were tested for MLI outcome predictors. The impact of DC on functional outcome was examined after being further stratified into good survival (mRS score = 0, 1, 2, 3), poor survival (mRS score = 4, 5), and mortality (mRS score = 6) groups.**

■ RESULTS: **Standard medical treatment only was used in 106 cases, and both medical treatment and DC were used in 107 cases. With multiple logistic regression analysis, age, motor response at deterioration/operation, and DC were identified as independent outcome predictors of MLI ($P = 0.027$, $P < 0.001$, $P < 0.001$). Compared with the sole standard medical treatment, additional DC resulted in a better outcome (odds ratio [OR] =19.95; 95% confidence interval [CI], 7.61–52.27; $P < 0.001$). Further analysis of functional outcome revealed that DC significantly increased the chance of good survival as opposed to poor survival (OR = 20.04; 95% CI, 6.05–66.32; $P < 0.001$) and death (OR = 43.72; 95% CI, 13.21–144.72; $P < 0.001$).**

■ CONCLUSIONS: **In this study, DC performed on a young patient with motor response of localizing pain or better was linked with a better outcome. DC not only reduced mortality and increased the number of good survivals but also, most importantly, decreased the number of poor functional outcome survivals.**

INTRODUCTION

Cerebral infarction is a common cause of disability. Although large infarction (LI) accounts for <10%–15% of all ischemic strokes, it is the leading cause of mortality in the acute stage and a major cause of severe disability after ischemic strokes.[1-4] LI generally refers to a cerebral infarction involving more than one half to two thirds of the middle cerebral artery (MCA) territory.[3,5] LI cases with early clinical deterioration or involvement of complete MCA territory are frequently termed malignant large infarction (MLI).[2] With intensive medical treatment, reported mortality rates of MLI were approximately 80%.[2,6]

Decompressive craniectomy (DC) for MLI was rarely performed before 2000 mainly because of the concern that it might increase survival but with overwhelming neurologic impairment and handicap. However, there has been an increased interest in DC since 2000 as a result of studies showing that in addition to mortality reduction, there might also be a chance of outcome

Key words
- Decompressive craniectomy
- Functional outcome
- Malignant large infarction
- Outcome predictor

Abbreviations and Acronyms
CI: Confidence interval
CT: Computed tomography
DC: Decompressive craniectomy
LI: Large infarction
MLI: Malignant large infarction
MCA: Middle cerebral artery
MRI: Magnetic resonance imaging
mRS: Modified Rankin Scale
OR: Odds ratio

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improvement.[7-13] Nevertheless, the evidence was far from definitive, especially regarding the functional outcome of survivors, and it remains a very controversial and debated topic in stroke management communities. The objective of this study was to evaluate the impact of various MLI variables on outcome. We also analyzed the clinical role of DC in MLI cases focusing on the functional outcome of survivors.

MATERIALS AND METHODS

In agreement with our national and hospital rules, approval for this study from the institutional review board of Chang Gung Memorial Hospital was granted (104-2574B). From December 1996 to February 2005, 213 MLI cases treated at Chang Gung Memorial Hospital-Linkou that fully complied with the selection criteria were enrolled in this study. All recruited patients were admitted to a stroke unit or intensive care unit, and at least 2 brain computed tomography (CT) scans were performed for each studied case; the first one was performed in the emergency department, and the second one was performed when neurologic deterioration was detected. The inclusion criteria for this study included 1) a minimum ischemic involvement of 50% of the MCA territory on brain CT scan or magnetic resonance imaging (MRI) at deterioration, 2) CT/MRI evidence of intracranial mass effect with minimum midline shifting of 4 mm at the level of septum pellucidum or pineal body at deterioration, and 3) clinical deterioration with either worse consciousness or anisocoria with loss of light reflex during standard medical treatment. Worse consciousness was defined as a 2-point decrease of Glasgow Coma Scale score or 1-point decrease of motor response. The motor response was scored from 1 to 6: M1, no response to painful stimuli; M2, extension to painful stimuli; M3, abnormal flexion to painful stimuli; M4, flexion to painful stimuli; M5, localizing painful stimuli; and M6, obeying orders. Exclusion criteria for cases from this study included 1) a preexisting disability with modified Rankin Scale (mRS) score ≥ 3, 2) a known coagulopathy or use of thrombolytic agents, and 3) any concomitant severe disease that might disturb the assessment of outcome. All enrolled patients were managed with standard medical treatment. Because there was continuing debate about the functional outcome of survivors, opposing attitudes about surgical treatment for MLI existed among neurologists and neurosurgeons in our institute before 2005. Therefore, after detailed discussion with family members, the recruited MLI patients were randomly chosen to receive additional decompressive craniectomy according to the different attitude of the physician on duty.

Standard Medical Therapy

All patients were admitted to a stroke unit or intensive care unit. The patient's head was kept elevated by 30°. All patients were maintained in a mild fluid restriction state with 1800 mL of daily fluid in the first week. Intravenous antihypertensive agents were administered when blood pressure was >220/120 mm Hg. Body temperature was kept <38°C, and blood glucose level was maintained at <180 mg/dL. Endotracheal intubation was performed to maintain adequate tissue oxygenation in patients with clinical deterioration or signs of respiratory insufficiency. Hyperventilation was used only in an emergency with the target level of arterial partial pressure of carbon dioxide (Pa_{CO_2}) of 30–35 mm Hg. Osmotherapy with mannitol or glycerol was initiated when there was evidence of mass effect. Mannitol 0.25–0.5 g/kg body weight was administered every 4–6 hours. Glycerol 250 mL was administered intravenously 4–6 times a day. During osmotherapy, blood osmolarity was maintained at approximately 300–320 mOsm/L.

Surgical Treatment

DC was performed within 3 hours of clinical deterioration. The operation consisted of a craniectomy extending at least 12 cm in the anteroposterior direction and 10 cm in the superoinferior direction that was large enough to match the infarcted area. Additional temporal bone removal was performed so that the floor of the middle cerebral fossa could be fully explored and decompressed. The dura mater was opened, and an augmented patch was inserted to further relieve the elevated intracranial pressure. Patients who survived surgery underwent a secondary cranioplasty 2 months after DC.

Analyses of Outcome Predictors of MLI and Impact of DC on Functional Outcome

Variables including demographic (age and sex) and clinical (initial motor response, motor response at deterioration/operation, time to deterioration/operation, deterioration with pupil change, deterioration with change in consciousness, and DC) characteristics were recorded and evaluated as outcome predictors. Univariate analysis was performed first to assess each factor. Factors with statistically significant difference in the first stage were subsequently adopted for the multivariate analysis to identify the independent outcome predictors. The impact of DC on outcome was further analyzed in regard to good survival, poor survival, and mortality.

Outcome Assessment

Outcome was assessed with mRS at 1-year follow-up. Outcome was first dichotomized into good (mRS score 0–3) and poor (mRS score 4–6). To compare and contrast functional outcome of survivors between surgical and nonsurgical groups, outcome assessment was further divided into 3 groups: good survival (mRS score 0–3), poor survival (mRS score 4–5), and death (mRS score 6).

Statistical Analysis

We used Student t-test for continuous variables and χ^2 test for dichotomized variables in the univariate and multivariate analyses. A multiple logistic regression was applied to identify independent outcome predictors of MLI. When the functional outcomes were further divided into good survival, poor survival, and death, a multinomial logistic regression was employed to examine the impact of DC after adjusting for confounding variables. All statistical analyses were 2-sided, and a P value < 0.05 was considered statistically significant.

RESULTS

Among 213 patients included in this study, 103 were men and 110 were women. Age range was 44–84 years (average 63.85 years). Of 213 patients with MLI, 106 were treated with standard medical therapy (49.8%), and 107 were treated with both standard medical