Hemicraniectomy for Malignant Middle Cerebral Artery Syndrome: A Review of Functional Outcomes in Two High-Volume Stroke Centers

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Background and Purpose: Despite recent landmark randomized controlled trials showing significant benefits for hemicraniectomy (HCT) compared with medical therapy (MT) in patients with malignant middle cerebral artery infarction (MMCAI), HCT rates have not substantially increased in the United States. We sought to evaluate early outcomes in patients with MMCAI who were treated with HCT (cases) in comparison to patients treated with MT due to the perception of procedural futility by families (controls). *Methods:* We retrospectively evaluated consecutive patients with acute MMCAI treated in 2 tertiary care centers during a 7-year period. Pretreatment National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) at 3 months were documented. Functional independence (FI) and survival without severe disability (SWSD) were defined as mRS of 0-2 and 0-4, respectively. *Results:* A total of 66 patients (37 cases and 29 controls) fulfilled the study inclusion criteria (mean age 59 ± 15 years, 52% men, median admission NIHSS score: 19 points [interquartile range {IQR}: 16-22]). Cases were younger (51 ± 11 versus 68 ± 13 years; $P < .001$) and tended to have lower median admission NIHSS than controls (18 [IQR:16-20] versus 20 [IQR:18-23]; $P = .072$). The rates of FI and SWSD at 3 months were higher in cases than controls (16% versus 0% [$P = .031$] and 62% versus 0% [$P < .001$]), while 3-month mortality was lower (24% versus 77%; $P < .001$). Multivariable Cox regression analyses adjusting for potential confounders identified HCT as the most important predictor of lower risk of 3-month

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mortality (hazard ratio: .02, 95% confidence interval: .01-0.10; $P < .001$). *Conclusions:* HCT is a critical and effective therapy for patients with MMCAI but cannot provide a guarantee of functional recovery. **Key Words:** Malignant ischemic stroke—large vessel occlusion—hemicraniectomy—functional independence—survival without severe disability—mortality.
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Introduction

Stroke is one of the most debilitating diseases in the United States, being the fifth leading cause of death, and one of the major cause of disability. Stroke kills nearly 130,000 Americans each year, which is 1 of every 20 deaths in the United States.[1-3] Ischemic stroke is much more common than hemorrhagic stroke, and occlusion of the middle cerebral artery (MCA) or one of its branches is one of the more common causes of it. Malignant middle cerebral artery territory infarction (MMCAI) exerts mechanical force on surrounding tissue structures by progressive brain edema, mainly vasculature and cerebrospinal fluid, leading to rising of intracranial pressure (ICP). The rise of ICP further deteriorates the condition by compromising cerebral blood flow and tissue shift, and transtentorial and uncal herniation, causing brain stem dysfunction.[4-8]

Hemicraniectomy (HCT) is an established procedure for the management of malignant brain edema and increased ICP, both of which play a vital role to complicate the course of MMCAI.[9] Recent landmark randomized controlled clinical trials and meta-analyses documented substantial survival and functional outcome benefits in patients who underwent HCT as compared to those who received medical therapy (MT).[10-12] However, the utilization of the procedure has not substantially increased in the United States over the years, as it is commonly difficult for patients' families to reconcile the wishes of the patient with the possibility of a poor functional outcome. In view of the former considerations, we sought to evaluate early outcomes in patients with MMCAI who were treated with HCT (cases) in comparison to patients treated with MT due to the perception of procedural futility by families (controls).

Methods

Patient Selection

We evaluated in a retrospective cohort study design consecutive patients with acute MMCAI treated in 2 tertiary care centers (University of Tennessee Health Science Center, Memphis, Tennessee; and Attikon University Hospital, Athens, Greece) during a 7-year period (2009-2015). Details regarding our international multicenter collaborate group have been previously published.[13-15]

Consecutive patients were identified by the International Classification of Diseases code searches of health records. Patients were included in this study if (1) they were aged 18-75 years, (2) stroke located within the MCA territory either alone or in combination with other vascular territory infarcts, and (3) imaging studies including computed tomography or magnetic resonance imaging demonstrating an infarct involving larger than 70% of the MCA territory. We excluded patients with stroke limited to non-MCA territories. This study was approved by the ethics committee of participating institutions.

Clinical variables of interest including age, race, gender, medical history of hypertension, hyperlipidemia, coronary artery disease, atrial fibrillation, cigarette smoking, systolic and diastolic blood pressures, and other clinical presentations were obtained from medical records. Pretreatment National Institutes of Health Stroke Scale (NIHSS, NIHSS at discharge, and modified Rankin scale [mRS]) at 3 months were obtained per institutional protocol in all patients with acute ischemic stroke. The mRS ranges from 0 (no symptoms) to 6 (death), with intermediate values (1-5) representing increasing functional and cognitive disability. Poor functional outcome was defined as an mRS score of 4 (moderately severe disability), 5 (severe disability), or 6 (death). Outcome measures in our study included (1) functional independence (FI) defined as mRS of 0-2, (2) survival without severe disability (SWSD) defined as mRS 0-4, and (3) death.

Medical Management

Patients with MMCAI were best managed in a neuroscience intensive care unit due to a possible need for intubation, mechanical ventilation, and various other procedures to prevent complications. All patients received MT according to the current American Heart Association recommendations for acute ischemic stroke.[16] In brief, medical management is typically the same as is applied for stroke in general which mainly target to regulate cerebral perfusion and to minimize cerebral metabolic demands. Malignant stroke was usually managed by elevation of the head of bed, osmotherapy with mannitol or hypertonic saline, sedation, hypothermia, deep sedation, controlled hyperventilation, and maintenance of adequate oxygen and blood supply. The use of muscle relaxants was left at the discretion of the treating physician. Monitoring of ICP was also left at the discretion