Research Article

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Early versus late surgical decompression in patients with malignant middle cerebral artery infarction

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Abstract

Objective: Malignant cerebral edema accompanying ischemic stroke is life threatening. Decompressive hemicraniectomy (DHC) has been suggested as an alternative or adjunct therapeutic strategy for cerebral edema in order to decrease mortality and enhance functional outcomes because medical treatment alone is mostly insufficient. The aim of this study was to determine the efficacy of early DHC in patients with malignant middle cerebral artery (MCA) infarction.

Methods: A retrospective, single-center, cohort study was conducted on a consecutive sample of 96 patients who underwent DHC due to MCA infarction. We assessed the influence of early DHC (<24 hours after the onset of symptoms) versus late DHC (>24 hours after the first signs of herniation) on mortality and functional outcome. Outcomes were evaluated in terms of 1-month mortality and the modified Rankin Scale (mRS) score (with favorable outcome defined as mRS ≤3) at the 3rd month follow-up.

Results: The age of the patients ranged from 18 to 80 years, with a mean age of 53.98±12.01 years and 58.87±11.6 years in the early and late-DHC groups, respectively. The 1-month mortality rate was 20.3% in the early-DHC group and 50% in the late-DHC group (p=0.006). The mortality rate was significantly higher in the late-DHC group. At the 3rd month follow-up, the percentage of patients with an mRS≤3 was 31.3% in the early-DHC group and 9.4% in the late-DHC group (p=0.035). The difference was statistically significant.

Conclusion: This study demonstrated that early-DHC may decrease mortality and improve functional outcomes in patients with malignant MCA infarction.

Keywords: Decompressive hemicraniectomy, cerebral edema, stroke, malignant MCA infarction

INTRODUCTION

Up to 10% of acute ischemic stroke cases have malignant middle cerebral artery (MCA) infarction, which is characterized by a life-threatening, space-occupying cerebral edema, with a mortality rate of 80% (1, 2).

Conventional medical treatment of elevated intracranial pressure (ICP) consists of hyperventilation, mannitol, diuretics, and barbiturate coma (3). However, these management strategies have inadequate supporting evidence and their effect on patient outcomes remains uncertain (4, 5). Decompressive hemicraniectomy (DHC) has been suggested as an alternative or adjunct therapeutic strategy for space-occupying cerebral edema because medical treatment is not always effective. Despite utmost medical care, the mortality rate of malignant MCA infarction approaches 80% without surgical intervention (6). Decompressive hemicraniectomy (DHC) is a well-established procedure for the treatment of malignant brain edema. The effect of DHC in malignant MCA infarction has been established by three randomized clinical trials: DESTINY, HAMLET, and DECIMAL (7-9). The age limit for inclusion was 60 years for all three controlled trials. Recently, the DESTINY II trial evaluated the effects of hemicraniectomy on patients older than 60 years (10). The influence of DHC in decreasing unfavorable outcome and death after MCA infarction is measured using the modified Rankin Score (mRS) (10, 11).

Patient selection for DHC is based on neurologic findings, patient baseline characteristics, stroke presentation, imaging interpretation, and time from onset of symptoms to surgery (12).

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We aimed to compare the effects of early DCH and late DHC in reducing mortality and unfavorable outcome rates of patients with malignant MCA infarcts. We investigated the impact of early DHC (<24 hours after the onset of symptoms, based on initial clinical condition and CT findings) versus late DCH (>24 hours after the first signs of reversible herniation) on mortality and functional outcome.

METHODS

A retrospective, single-center, cohort study was conducted on a consecutive sample of 96 patients who underwent DHC due to MCA infarction in our stroke center between January 2011 and February 2016. Patients were evaluated for recanalization treatment. Patients either solely underwent intravenous recombinant tissue-type plasminogen activator (i.v.rt-PA) treatment or underwent mechanical thrombectomy following i.v.rt-PA, if indicated. Patients with large MCA infarcts received standard treatment in accordance with current guidelines.

We assessed the impact of early decompressive surgery (<24 hours the onset after symptoms, based on the patient's clinical condition and CT findings at admission) versus late surgery (>24 hours after the first signs of reversible herniation) on mortality and functional results.

Demographic data, National Institutes of Health Stroke Scale (NIHSS) score on admission, evel of consciousness prior to surgery, timing of surgery, type of imaging modality used for vascular evaluation, presurgical radiologic findings, 1-month mortality, and functional outcomes on the modified Rankin scale (mRS) at the 3rd month follow-upwere recorded.

Malignant MCA infarction was defined as an infarction affecting at least 50% of the MCA territory on CT, with or without additional findings of ipsilateral cerebral artery occlusion. The clinical assessment of patients was based on the NIHSS score (13).

Patients who received DHC due to the hemorrhagic transformation of ischemic stroke, patients with severe head trauma, anoxic brain injury, subarachnoid hemorrhage with vasospasm, contralateral ischemia, coagulopathy, bleeding disorder or any other condition that could potentially affect the outcome, and patients with pre-stroke mRS ≥2 were excluded from the study. The study protocol was approved by the local ethics committee.

Clinical outcome at 3 months was determined using the mRS score. Poor outcome was defined as a mRS score of 4-6 and favorable outcome was defined as a mRS score of 0-3. The primary endpoint was a favorable outcome 3 months after surgery, defined as mRS ≤3.

Stroke etiology was categorized according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria after diagnostic tests were concluded (14). Follow-up computed tomography (CT) at 24 hours was assessed for the presence of hemorrhagic transformation, which was graded as hemorrhagic infarction (HI) or parenchymal hemorrhage (PH) according to the European-Australasian Acute Stroke Study (ECASS) classification. The presence of small petechiae along the edges of the infarct was defined as HI1. The presence of confluent petechiae within the infarcted area without a space-occupying effect was defined as HI2. The presence of blood clots in ≤30% of the infarcted area with a slight space-occupying effect was defined as PH1. The presence of blood clots in >30% of the infarcted area with a substantial space-occupying effect was defined as PH2 (15). According to the Safe Implementation of Thrombolysis in Stroke Monitoring Study (SITS-MOST) criteria symptomatic intracranial hemorrhage was described as a local or remote PH2 at the 22 to 36-hour CT scan accompanying deterioration in the NIHSS ≥4 points from baseline or any intracranial hemorrhage resulting in death (16).

Symptomatic intracranial hemorrhage, severe infections, and pulmonary embolism following decompressive surgery were defined as major complications. Asymptomatic hemorrhagic transformations, hydrocephalus, sinking flap syndrome, seizures, and non–life-threatening infections, or deep vein thrombosis were classified as minor complications. Surgical decompression was performed by removing a large flap of bone (at least 12 cm in diameter; always including the frontal, temporal, and parietal and occipital squama) and performing duraplasty. Surviving patients underwent cranioplasty after 6 months using acrylic material. All patients were mechanically ventilated and treated in the intensive care unit. In both patient groups, early management of ischemic stroke was carried out according to standard clinical guidelines (17).

Ethical approval all procedures involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. We declare that this study has been approved by the local ethics committee of Eskişehir Osmangazi University. Informed consent written informed consent was obtained from patients and parents of the patients who participated in this study.

RESULTS

A total of 96 patients met the inclusion criteria. The patient characteristics in each outcome category are presented in Table 1.

The age of the patients ranged from 18 to 80 years. The mean age was 53.98±12.01 years in the early-DHC group and 58.87±11.6 in the late-DHC group (p=0.057). The prevalences of comorbid diseases such as hypertension (p=0.999), atrial fibrillation (p=0.456), previous stroke (p=0.218), and smoking (p=0.999) were similar between the early- and late-DHC groups.

Table 1.Baseline characteristics, outcomes, and complications of patients with malignant middle cerebral artery

Characteristics		Early DHC (n=64)	Late DHC (n=32)	p
Sex	Female	26 (40.6%)	13 (41.9%)	0.999
	Male	38 (59.3%)	19 (61.2%)	
Age, years		53.98±12.01	58.87±10.6	0.057
NIHSS score on admission median (IQR)		19 [12 – 25]	19 [12 – 24]	0.056
Mean time from symptom onset to surgery, h (SD)		16 [6 – 37]	36 [26 – 56]	<0.001
Current smoking		27 (42.2%)	13 (40.6%)	0.999
Hypertension		27 (42.2%)	14 (43.8%)	0.999
Diabetes mellitus		19 (29.7%)	12 (37.5%)	0.589
Hypercholesterolemia		22 (%34,4)	10 (31.3%)	0.939
Atrial fibrillation		17 (26.6%)	6 (18.8%)	0.456
Previous stroke		4 (6.3%)	4 (12.5%)	0.218
Stroke etiology, n (%)	Large artery disease	25 (39.1%)	17 (53.1%)	0.311
	Cardioembolism	29 (29.7%)	6 (18.8%)	
	Other determined etiology	4 (6.3%)	2 (6.3%)	
	Unknown etiology	13 (20.3%)	7 (21.9%)	
	Dissection	3 (4.7%)	-	
Symptomatic hemorrhage		6 (9.4%)	2 (6.3%)	0.602
Minor complications		14 (21.9%)	2 (6.3%)	0.100
Major complications		7 (10.9%)	-	0.091
Outcome, n (%)				
Modified Rankin Scale 0– 3		20 (31.3%)	3 (9.4%)	0.035
Modified Rankin Scale 4-6		43 (67.2%)	29 (90.6%)	0.024
Mortality, n (%)		13 (20.3%)	16 (50.0%)	0.006

Cerebral infarctions involved the MCA (71.8%), ICA (12.5%) or both (15.6%). The mean NIHSS score was 18.1±4.8. There were no clinically significant differences between the baseline demographic and clinical characteristics of the early-DHC and late-DHC groups.

The interval between admission and surgery ranged between 6-56 hours (mean= 22.80±12.49 hours).

The etiology of stroke was atherosclerosis in 52 patients, cardioembolism (due to atrial fibrillation, valvular disease or hypertrophic cardiomyopathy) in 35 patients, internal carotid artery dissection with secondary MCA occlusion in 3 patients, and unknown in 6 patients. Stroke etiologies of the two groups were similar. Six (10.3%) of the 64 patients in the early-DHC group and 4 (12.5%) of the 32 patients in the late-DHC group showed signs of uncal herniation prior to DHC (p>0.05).

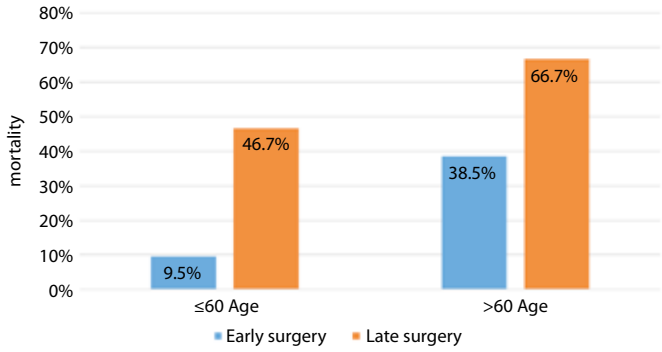
Of the 96 patients enrolled in the trial, 67 (69.7%) survived. The mean duration between symptom onset and surgery was 36 hours in the late-DHC group and 16 hours in the early-DHC group. Mortality rates were 20.3% (13/64) and 50% (16/32) in the early-DHC and late-DHC groups, respectively. Mortality was significantly reduced in the early-DHC group compared to the late-DHC group (p=0.006).

At the 3rd month follow-up, 31.3% of the patients in the early-DHC group and 9.4% of patients in the late-DHC group had an mRS ≤3 (p=0.035). Favorable outcome rates at the 3rd month follow-up were higher in the early-DHC group than in the late-DHC group (p=0.035).

The number of patients presenting with dominant hemispheric stroke was 29/64 (45.3%) in the early-DHC group and 14/32 (43.8%) in the late-DHC group. In total, 6 patients had major complications and 14 patients experienced minor complications. The two groups did not differ in terms of major complications after DHC (p>0.05). Of the 6 patients with major complications, 3 were in the early-DHC group. The major complications were septicemia in 3 patients and brain abscess in 3 patients. One patient in the early-DHC group and two patients in the late-DHC group developed brain abscess. Two patients died of septicemia.

Minor complications such as seizure, deep vein thrombosis, and pneumonia without septicemia were not statistically significantly different between the two groups (p=0.100). The two groups did not differ significantly in terms of asymptomatic intracranial hemorrhage complications following DHC (p=0.491).

Figure 1. Mortaliy rate in early and late decompressive surgery



In the early-DHC group, 1-month mortality was reduced from 61.9% to 38.1% in patients aged ≤60 years of age when DHC was performed within 24 hours after the onset of symptoms, but there was no significant difference in functional outcome and mortality (p>0.05). However, mortality was higher in patients older than 60 years (46.2% vs. 19.3%; p=0.01) (Figure 1).

Among patients aged over 60 years, there were no significant differences in mortality between the early- and late-DHC groups (38.1% and 20%, p>0.05). There was no significant difference in functional outcomes at 3 months (p>0.05).

The NIHSS on admission did not affect primary outcomes; however, the NIHSS prior to surgery was significantly associated with mRS scores of 4-6 (p<0.001) and death (p<0.001).

Seventeen (17.7%) patients were treated with i.v.rt-PA, whereas 22 (22.9%) patients were treated with i.v.rt-PA and endovascular approach. Before early decompressive surgery, 57 (59.3%) patients received standard treatment. The two groups did not differ in terms of major and minor complications following DHC (p>0.05).

DISCUSSION

Malignant cerebral edema accompanying ischemic stroke is life-threatening. Despite optimal medical treatment, malignant MCA infarction causes severe morbidity and mortality (18, 19). Some series have reported mortality rates reaching up to 80% in patients who do not undergo decompressive surgery. Therefore, DHC should be considered to mitigate the mass effect of the swollen cerebral or cerebellar tissues. The aim of DHC is to alleviate the pressure of the edematous brain tissue by removing a bone flap and the dura mater underneath. Though prior studies claimed that DHC did not enhance functional recovery and quality of life, recent studies demonstrated partial improvement, even in cortical symptoms such as aphasia (20).

A systematic review comprising 129 studies on the use of DHC for MCA infarction showed that there were no differences between early and late DHC groups in terms of outcomes. On the other hand, reduced mortality rates were reported for patients receiving DHC within 24 hours of ictus (21). In our study, patients who received surgery within 24 hours were defined as the early-DHC group, and patients who underwent surgery later than 24 hours were defined as the late-DHC group. Both functional outcomes and mortality were found to be associated with early-DHC intervention (p=0.035 and p=0.006). This study aimed to evaluate the effect of hemicraniectomy on functional outcomes and mortality.

Over the past 10 years, 3 randomized trials were published on the effects of decompression surgery in malignant MCA infarction. In the DECIMAL trial of 38 patients, mortality at 1 week was 5% in the DHC group and 67% in the medical treatment group. At 4-weeks mortality rate was 16% in the DHC group and 33% in the medical treatment group and a significant reduction in mortality was observed (7). In the DESTINY trial with 32 randomized patients, the 1-month mortality rate was 12% in the DHC group and 53% in the medical treatment group. In the HAMLET trial with 64 patients, the 14-day mortality rate was 16% in the decompression group and 56% in the non-decompression group (8). In a prospective pooled analysis of the DECIMAL, DESTINY, and HAMLET trials, a significant reduction in mortality was shown in the DHC group. However, when evaluated in the context of functional outcomes (defined as mRS ≤ 3), no significant differences were observed (22).

In the present study, favorable outcome was defined as a mRS ≤3, and outcome was significantly better in the early-DHC group (31.3% of the early DHC vs. 9.4% in the late group; p=0.035).

Patient age is an important prognostic factor in this procedure. The mean ages of our patients were 53.98 and 58.87 years in the early- and late-DHC groups, respectively. It is known that outcomes are generally better in young patients. In the literature, the mean age values in patient groups with better outcomes are mostly below 50 years (23, 24).

The maximum duration between symptom onset and the start of treatment was 36 hours in the DESTINY study, 24-96 hours in the HAMLET study, and 48 hours in the DECIMAL study. In our study, the group that underwent surgery within 24 hours was defined as the early-DHC group.

Though some studies showed no statistically significant difference between early (0-23 hours) and late (24-48 hours) surgery in terms of mortality, recent studies indicated that early surgery had a lower rate of complications (25). In contrast, some studies stated that early DHC decreased mortality but did not differ significantly from late-DHC in terms of favorable outcomes. In our study, the mortality and unfavorable outcome rates of the early-DHC group were statistically significantly lower than in the late-DHC group.

In the literature, surgery has been shown to provide better results in terms of mortality in younger patients with malignant MCA infarction (26). A statistically significant decrease in the mortality rate was detected in the subgroup analysis of patients aged below 60 years, but no significant differences were observed in terms of functional outcomes (p=0.006). The overall mortality was higher among patients aged over 60 years (46.2% vs. 19.3%; p=0.01).

In our study, 17 (17.7%) patients were treated with i.v.rt-PA, whereas 22 (22.9%) patients were treated with i.v.rt-PA and endovascular approach. We found that the standard treatment group, i.v.rt-PA treatment group, and combined i.v.rt-PA and endovascular treatment group did not differ in terms of minor and major complications (such as infections, seizures, asymptomatic and symptomatic intracerebral hemorrhage, deep vein thrombosis) between. These results were similar to our previous study, where we found no significant differences between the outcomes of patients who did and did not receive thrombolytics before surgical intervention (26).

One of the limitations of our study is that diffusion-weighted magnetic resonance imaging infarct volumes were not evaluated. Early infarction volume is suggested as predictive of malignant ischemic edema and should be evaluated for the selection of patients. Another limitation is that, in our study, only 1-month mortality and 3-month functional outcomes were recorded, whereas the main trials assessed the same outcomes with a 1-year follow-up period. The longer follow-up duration of these trials may justify the different outcomes.

CONCLUSION

This study demonstrated that early DCH may prolong survival and improve functional outcomes in selected patients with malignant MCA infarction. It should be kept in mind that proper patient selection and early surgical intervention may provide good functional outcomes.

Ethics Committee Approval: We declare that this study has been approved by the local ethics committee of Eskişehir Osmangazi University.

Informed Consent: Written informed consent was obtained from patients and parents of the patients who participated in this study.

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