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Original Article

What is the optimum time to decompressive surgery in the patients with malignant middle cerebral artery infarction?

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Abstract

Aim: In the patients with malignant middle cerebral artery (MCA) infarctions, the mortality was as high as 70% with conservative treatment. Decompressive craniectomy (DC) was shown to decrease mortality especially in 48 hours. We aimed to investigate both the effect of decompression time and the size of craniectomy on the mortality in this patient group.

Material and Methods: 45 adult patients underwent to DC due to malignant MCA infarction were evaluated in this study. The demographic and clinical features were recorded retrospectively. The patients were splitted into three groups: Group 1, DC in the first 24 hours; group 2, in 24-48th hours; group3, in 48-96th hours of the admission. The size of craniectomy was the same as the infarct (standard), or it was two centimeters larger than the size of infarct (larger).

Results: Of all patients, 53.3% (n=24) was female; and mean age of the sample was 67.38±4.76. 66.7% (n=30) of the patients died due to malign MCA infarction. The size of craniectomy was larger in 26.7% (n=12), and was standard in the others. Mean time to surgery was 43.07±29.87 hours. Mortality rate was minimum in group 2 (p=0.01). The patients undergoing to larger craniectomy survived longer than the others, but the difference was non-significant (p=0.06).

Conclusion: We suggested that not the approach of "surgery as soon as possible" but the surgery between 24-48th hours of the admission would be the optimal approach. This issue is especially important, because earlier or later interventions not only have a less benefit on the outcome but also may lead several unnecessary complications.

Keywords: Middle cerebral artery infarction; decompressive surgery; decompressive craniectomy.

INTRODUCTION

Malignant stroke is one of the reasons of acute brain injury. MCA infarctions may occur less frequently and approximately in 1-10% of supratentorial stroke (1). Ischemic cell death may result from brain edema causing increased intracranial pressure in these patients. Ischemic edema in a large part of cerebral hemisphere was shown to considerably increase the mortality (2). Acute edema causing devastating results is predictive on mortality. In survivors, acute edema generally culminates in herniations having several neurological implications. Both infarct itself and acute edema may lead to clinical signs and symptoms such as hemiplegia, hemiparesis, cognitive dysfunction, cranial nerve palsy, papilledema, or convulsions (3,4).

Conventional management strategies aiming at reducing ICP consist of several head elevation, osmotic agents, controlled hyperventilation, and hypothermia (4). However, several studies showed us that mortality was as high as 70% with conservative treatment in the patients suffered from malignant MCA infarctions (5,6). Moreover, in the most of the survivors of these patients were shown to have chronic disabilities post injury.

Beyond conventional treatment, decompressive craniectomy (DC), defined as removal of cranium and subsequent durotomy/duroplasty, has become one of the treatment strategies in these patients, especially aiming at reducing the intracranial pressure (7-10). Besides, both medical and decompression treatment aims to restore regional perfusion, correct midline shift, and reduce brainstem pressure (2). Indeed, DC may be chosen in any disease situation causing increased intracranial pressure (11,12). DC was shown to have important effects on

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mortality in the patients with malign MCA infarct especially if performed in the first 48 hours of the event (13-15). This method was shown to significantly reduce the mortality in these patients especially before neurological signs and symptoms were developed (16). However, in some studies showed nonsignificant benefit with DC in these patients (17). Several factors such as patient age and timing of surgery were studied to if affect the success/outcome of the surgery or not (18).

To our knowledge, size of craniectomy has not yet been evaluated adequately, as a contributor to the success of DC in the literature. We aimed to investigate both the effect of decompression time and the size of craniectomy on the mortality and the morbidity after DC in the patients with malignant MCA infarction

MATERIAL and METHODS

The patients underwent to DC due to malignant MCA infarction were evaluatedinthis study. The patients were followed inseveral clinics of neurochirurgy of Adiyaman University Medical Faculty, Adiyaman University medical faculty and Adiyaman State Hospital, between March 2010 and June 2018. The data of the patients were collected from the electronic recordings and analyzed retrospectively. This study was approved by local ethics committee (Adiyaman University School of Medicine, Local Ethics Committee; Date: 16.04.2019; Number: 2019/3-7). In addition, a written informed consent was obtained from the patients whose tissues were used.

The patients diagnosed with malignant MCA infarction according to neurological and radiological examination were evaluated. The adult patients with malignant MCA infarction who underwent to decompressive surgery to decrease shift and intracranial pressure were included in our study. All the patients included in the study had symptoms of MCA infarction. The patients with multiple localized infarcts, or who underwent to surgery due to in-car and off-road traffic accident, fall, syncope or the complications of previous surgical operations were excluded from the study.

Basic demographic and clinical features of the patients were recorded and analyzed. Glasgow Coma Scale (GCS), neurological findings (such as monoplegia, hemiplegia), the size of craniectomy, timing of surgery, and the duration of hospitalization of the all patients were recorded and analyzed. The patients were grouped as having hemiplegia or monoplegia, or not. They were also grouped as the location of infarct: right or left. Anterior-posterior x-rays and computed tomography imaging of the patients were evaluated. Computed tomography (CT) imaging was repeated at each day in the first week, and at every 3 days in the second week. The change of brain image was depicted in figure 1. To delineate infarction more precisely, magnetic resonance imaging in the most of the patients, and digital subtraction angiography in some were also evaluated. Because these patients should be followed as in-patient for a long time, the patients were followed up for all the hospital stay, and the mortality rate was evaluated in this period.

A total of 45 patients were divided into 3 groups according the timing of surgery after the admission: Group 1, DC in the first 24 hours; group 2, DC in 24-48th hours; group 3, DC in 48-96th hours of the admission. The patients in group 1 were treated immediately with intravenous mannitol 1x100 mL and dexamethasone 1x8mg on admission; and after the clinical stabilization was established, DC was performed in these patients. The patients in group 2 were undergone to DC in 24-48th hours of the admission, after treatment with mannitol 4x100 mL and dexamethasone 4x4mg for 24 hours. The patients in group 3 were undergone to DC in 48-96th hours of the admission, after treatment with mannitol 4x100 mL and dexamethasone 4x4mg for 48 hours. The size of craniectomy was adjusted according to the size of infarction detected in the cranial CT imaging. In some patients, craniectomy was performed at the same size as the infarct (standard); however, in the others, the size of craniectomy was 2 cm larger than the size of infarct (larger, Figure 2).

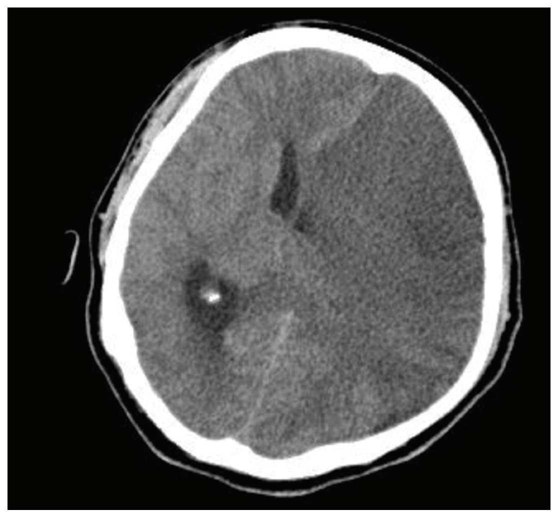

Figure 1. Preoperative axial CT imaging demonstrating malignant MCA infarction, parenchymal edema, and 2 cm shift in the parenchyma in a 31 year-old patient

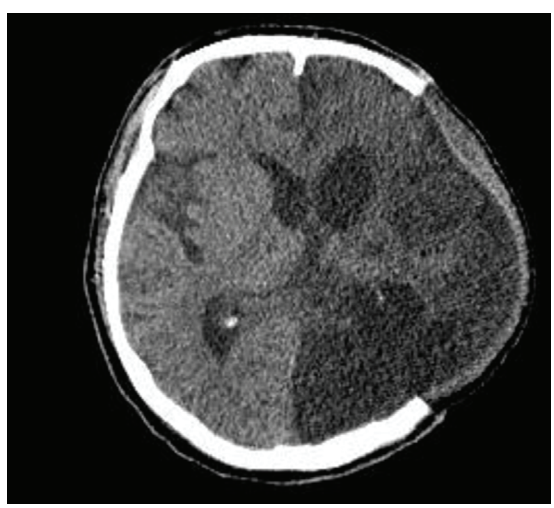

Figure 2. Postoperative axial CT imaging in the same patient demonstrating the correction of shift, and minimum parenchymal edema

Surgical technique
The patient was positioned in dorsal decubitus. Head was elevated and rotated as to be parallel to the floor. The extremities were stretched downward along the body. Chlorhexidine and alcoholchlorhexidine were applied. The surgical incision was demarcated from the parietal region to the temporal bone. After the towels were placed, skin was incised. The ipsilateral temporal artery and the frontal branch of the facial nerve were preserved. The temporal muscle fascia was incised. The temporal muscle was detached from the bone and then craniotomy was performed with a craniotome by preserving the frontal sinuses. Hemostasis was established and the bone plate was detached. Dura was opened towards parietal lobe and anchored to the bone edge. Brain was irrigated with warm saline. Duraplasty was performed with fascia lata or aponeurotic galea. Continuous stich and biological glue were applied and closed draining system was placed. Bone flap was inserted under the muscular fascia of ipsilateral hemiabdomen.

Statistical Analysis
SPSS 25.0 (IBM Corparation, Armonk, New York, United States) was used for statistical analysis. The conformity of the data to normal distribution was evaluated with Shapiro-Wilk test, homogeneity of variance was evaluated with Levene's test. When comparing groups, One-Way Anova (Robuts Statistic: Brown-Forsythe) test was used forage; Kruskal-Wallis H Test Monte Carlo stimulation technique for GCS; Fisher-Freeman-Holton test Monte Carlo Stimulation technique for gender, mortality, hemiplegia, monoplegia, location of lesion and the size of craniectomy. Patients were evaluated according to the age, gender, GCS, hemiplegia, monoplegia, location of lesion and craniectomy. Cox regression analysis with enter method was used to measure the effects of prognostic factors on timing of surgery and mortality. Quantitative variables were depicted as mean ± standard deviation (SD) / minimum-maximum and median (minimum-maximum) in the tables. Categorical variables were shown as n (%). Variables were evaluated with 95% confidence level, and p<0.05 was accepted as significant.

Results

Of all patients, 53.3% (n=24) was female; and mean age of the sample was 67.38 ± 4.76. The number of patients was 14 (31.1%), 14 (31.1%), and 17 (37.8%) in group 1, group 2, and group 3, respectively. 66.7% (n=30) of the patients died due to malign MCA infarction, 33.3% (n=15) of them survived. 60% (n=27) of the patients had right sided, 40% (n=18) had left sided MCA infarction. All the patients had motor and sensorial defects preoperatively. Hemiplegia, hemiparesis and monoplegia were detected in 84.1% (n=37), 17.7% (n=8) and 14% (n=6) of the patients, respectively. 48.8% (n=22) of the patients suffered from epileptic seizures necessitating the usage of antiepileptic treatment. The size of craniectomy was larger than infarct area in 26.7% (n=12) of the patients; however, it was the same as the infarct size in 73.3% (n=33) of the patients. Mean GCS score of the patients was 6.60±1.07, and all the patients had a GCS score equal to or less than 8. Preoperative and postoperative mean GCS scores were 5 and 9, respectively. Mean time to surgery after admission was 43.07±29.87 hours. Demographic and clinical features of the patients were demonstrated in Table 1.

Gender distribution, and mean age and GCS score were similar in 3 groups. There were no significant differences between the groups according to the clinical findings such as hemiplegia, monoplegia, and location of infarct or size of craniectomy. 11 (78.6%), 5(35.7%), and 14 (82.4%) of the patients in group 1, group 2, and group 3, respectively, died during disease process. There was significant difference between 3 groups according to mortality rate (p=0.010), and mortality was minimum in group 2 in which the patients underwent to DC in 24-48th hours of the event (Table 2).

Given the timing of surgery, age, gender or GCS score had no significant role on mortality. Cox regression analysis detected that the patients undergoing to larger size of craniectomy survived longer than the others, but the result was nonsignificant (p=0.06; OR: 0.233, 95.0% CI: 0.050-1.086). As a result, none of the clinical factors had a significant predictive role on mortality (p>0.05) (Table 3).

Table 1. Demographic and clinical features of the patients

	n	%
Groups		
Group 1	14	31.1%
Group 2	14	31.1%
Group 3	17	37.8%
Gender		
Female	24	53.3%
Male	21	46.7%
Mortality		
Alive	15	33.3%
Exitus	30	66.7%
Hemiplegia		
Absent	7	15.9%
Exist	37	84.1%
Monoplegia		
Absent	37	86.0%
Exist	6	14.0%
Location of lesion		
Right MCA	27	60.0%
Left MCA	18	40.0%
Size of Craniectomy		
Larger	12	26.7%
Standard	33	73.3%
	Mean±SD	**Median (Min-Max)**
Age	67,38±4,76	68 (58 - 80)
GCS score	6,60±1,07	7 (5 - 9)
Time to surgery (hours)	43,07±29,87	33 (6 - 92)

Min.: minimum, Max.: Maximum, SD: Standard Deviation

Table 2. Demographic and clinical features of the patient groups.

	Group 1 (n=14)	Group 2 (n=14)	Group 3 (n=17)	P Value
	Mean±SD. / Min.-Max.	Mean±SD. / Min.-Max.	Mean±SD. / Min.-Max.	
Age	67.71±5.73 / 58-80	67.43±4.40 / 60-75	67.06±4.45 / 60-75	0.932 [a]
	Median (Min.-Max.)	Median (Min.-Max.)	Median (Min.-Max.)	
GCS	7 (5 - 8)	6 (5 - 8)	7 (5 - 9)	0.313 [kw]
	n (%)	**n (%)**	**n (%)**	
Gender				
Female	6 (42.90)	7 (50.00)	11 (64.70)	0.507 [ff]
Male	8 (57.10)	7 (50.00)	6 (35.30)	
Mortality				
Alive	3 (21.40)	9 (64.30)	3 (17.60)	0.010 [ff]
Exitus	11 (78.60)	5 (35.70)	14 (82.40)	
Hemiplegia				
Absent	2 (14.30)	2 (15.40)	3 (17.60)	0.999 [ff]
Exist	12 (85.70)	11 (84.60)	14 (82.40)	
Monoplegia				
Absent	10 (83.30)	11 (78.60)	16 (94.10)	0.501 [ff]
Exist	2 (16.70)	3 (21.40)	1 (5.90)	
Location of lesion				
Right MCA	8 (57.10)	8 (57.10)	11 (64.70)	0.871 [ff]
Left MCA	6 (42.90)	6 (42.90)	6 (35.30)	
Size of craniectomy				
Larger	4 (28.60)	4 (28,60)	4 (23.50)	0.999 [ff]
Standard	10 (71.40)	10 (71.40)	13 (76.50)	

[a] OneWay ANOVA (RobutsStatistic:Brown-Forsythe), [ff]FisherFreemanHalton Test(Monte Carlo), [kw]Kruskall-Wallis H Test (Monte Carlo), Min: Minimum, Max: Maximum, SD: StandardDeviation.

Table 3. Cox regression analysis showing the predictors of mortality in the patients.

	B	SE	P Value	Odds Ratio	95,0% CI for Odds Ratio	
					Lower	Upper
Age	0.029	0.050	0.566	1.029	0.933	1.135
Gender	0.132	0.482	0.784	1.141	0.444	2.935
GCS	-0.063	0.239	0.793	0.939	0.587	1.501
Hemiplegia	-0.383	0.652	0.557	0.682	0.190	2.450
Monoplegia	-0.305	0.771	0.692	0.737	0.163	3.336
Location of lesion	-0.470	0.460	0.306	0.625	0.254	1.538
Size of Craniectomy	-1.457	0.785	0.064	0.233	0.050	1.086

Cox Regression (Enter Model), B: Regression coefficients, SE: Standard error, CI: Confidence Interval.

DISCUSSION

Of all patients, 53.30% (n=24) was female and mean age was 67.38 ± 4.76. 60% (n=27) of the patients had right sided, 40% (n=18) had left sided MCA infarction. All the patients had motor and sensorial defects preoperatively, and 48.80% (n=22) needed antiepileptic treatment. The size of craniectomy was larger than infarct area in 26.7% (n=12) of the patients; however, it was the same as the infarct size in the others. Mean GCS score of the patients was 6.60±1.07. Mean time to surgery after admission was 43.07 ± 29.87 hours. Of all patients, 66.70% (n=30) died due to malign MCA infarction, 33.3% (n=15) of them survived. 11 (78.60%), 5(35.70%), and 14 (82.40%) of the patients in group 1, group 2, and group 3, respectively, died during disease process. There was significant difference between 3 groups according to mortality rate (p=0.01), and mortality was minimum in the patients underwent to DC in 24-48th hours of the event/admission. Cox regression analysis detected that the patients undergoing to larger size of craniectomy survived longer than the others, but the result was nonsignificant. Moreover, none of the clinical factors had a significant predictive role on mortality.

Miller et al. investigated the importance of size and site of craniectomy in the replica skull (19). They increased and monitored the intracranial pressure via a balloon in their model. Then, they performed sequential progressive craniectomy to decrease ICP when a threshold of increased ICP was reached. They found that the most effective size was 8.3 cm for DC, but a size of 7.5 cm was adequate to decrease ICP. They also found that the location of craniectomy was nonsignificant if the size of craniectomy was ≥7.5cm or ≤3.5 cm. However, when the size was 4.5 or 5.5 cm, anterior flaps were shown to be more effective in decreasing ICP. In another study analyzing the predictors of the mortality in the patients with swollen MCA infarct, they were grouped according to the mean size of craniectomy: 13.1 cm(n=14) vs 12.5 cm (n=31) (20). There was no significant difference between two groups according to the mortality. Also in regression analysis, craniectomy size was not found as a predictor for mortality. In our study, including real patients, the craniectomy larger than infarct size improved survival, but this effect was statistically nonsignificant. We could not monitor intracranial pressure, and also did not analyze the effect of the size of craniectomy on decreasing ICP.

Several studies in the literature revealed that functional disabilities and death were reduced by DC (8,17,21-24). But, in the same studies, the mortality rate was shown not to decrease in the patients with favorable outcome (25). Paliwal et al. investigated the effect of DC on functional outcome of Asian patients with acute malignant MCA ischemic stroke (15). Of a total of 75 patients, underwent to DC, early surgery (inter quartile range 15-31 hours) was performed in 67%, late surgery (IQR 52-90 hours) in the others. In 64 % of the patients undergoing early surgery had right MCA infarct. In this study, right sided MCA infarct (p=0.006) and early decompressive craniectomy (p=0.041) were shown to be predictors of favorable outcome at 6 months. In a meta-analysis of 7 studies, Slezin et al. analyzed 12 month outcome of 338 patients with malignant MCA infarct (26). These studies revealed that the surgery performed between 48-96th hours of the admission would not improve the outcome in this patient group. Several other studies demonstrated that DC later than 48 hours of event would not improve mortality rate or unfavorable outcome (8, 22). Similarly, we found that early DC had significant effect on mortality. We revealed that the surgery performed earlier, but in between 24-48 hours, improved survival in our patients. We found that not the approach of "surgery as soon as possible" but the surgery between 24-48th hours of the admission would be the optimal approach. However, in the study of Paliwal et al., early surgery consisted of the patients undergoing surgery with a median of 23 hours (15). The optimal time to surgery was not certain according to many studies in the literature (27). We know that all the patients with MCA infarction would not develop clinical and/or imaging findings of herniation or mass effect. In the first study, 65 % of the patients with MCA infarct worsened significantly (28); however, the other patients survived at 3 weeks follow-up. Hence, such an approach of "surgery as soon as possible" might lead some risks for the patients (29,30). Studies analyzing the patients undergoing earlier decompressive surgery may cause some bias, because these patients would already survive or have favorable outcome based on first trial (28). In some studies, no differences were found between the patients undergoing to DC before 48 hours and those undergoing to surgery later than 48 hours according to the outcome (13,31). In general, when performing these studies, we should narrow the intervals to truly evaluate the effect of timing of surgery. An analysis of several randomized controlled trials showed no differences of outcome and mortality between the patients undergoing to surgery in 24 hours of event and those having surgery in 24-45 hours of event (21). Regarding to these analyses and our results, we advocate the approach that optimum timing for decompressive surgery is between 24 and 48 hours of the event, but not the approach of "surgery as soon as possible". This issue is especially important, because earlier or later interventions not only have least benefit on outcome but also may lead several unnecessary complications.

In the study of Paliwal et al., another contrast to ours was that the location of the infarct was predictive on the outcome at 6 months in their study (15). We could not show any differences between the patients having right and left sided infarcts according to mortality. In one study, besides the location of infarct, other radiological findings were analyzed in malignant MCA syndrome (32). Optic nerve sheath diameter and the ratio of optic nerve sheath diameter/eyeball transverse diameter were found to be higher in malignant MCA syndrome comparing to nonmalignant syndrome. But, these parameters did not have any impact on outcome. In our study, we did not analyze other radiological parameters than the location of infarct. Again, in another study, the location of infarct was shown not to have significant impact on the outcome of the patients (33). Future studies will clarify some specific points in imaging of these patients, which make us to select the correct patients for decompressive surgery.

Gender was found not to have any significant impact on mortality in the patients undergoing DC. Similar to our findings, Sundseth et al. showed that there was no significant difference between male and female patients according to mortality (20). Because hemiplegia or monoplegia may cause the secondary complications and may point to an important infarct, they create a significant morbidity. Actually, the presence of paralysis of one or more extremities might also make us to think that this finding might be associated with mortality. However, we did reveal that the patients with hemiplegia or monoplegia did have a similar mortality rate to the others. This might be explained by impact of a lot of factors in the patients with malignant MCA infarct undergoing to DC. The stress of surgery, accompanying infections, organ failure and the other factors may mask the impact of the paralysis on the mortality of these patients.

Early decompressive surgery was shown in several randomized controlled trials analyzing the patients ≤60 years of age (22,35,36). Several reports other than excluded the older patients >60 years (36). In our study, we did not limit the patients according to age, and we included the patients older than 60 years. Another studies also revealed that DC decreased mortality in the patients older than 60 years (23,37,38). All these studies were stopped earlier due to probable benefit of the surgery in the patients with malignant MCA infarct. Moreover, several studies also showed that DC together with decreasing mortality, increased the number of patients with disability (8,23,24,38). Same studies suggested that older age was an important predictor of functional disability in the patients undergoing DC. Moreover, in one study, older age was found to be one of the most important predictors of poor functional outcome, although early or late decompressive surgery did not have any impact on outcome (13). In one national survey analyzing the practice of stroke physicians and neurosurgeons, at least the half of the neurosurgeons and the more of stroke physicians were shown to advocate DC in the patients older than 60 years. As a result, survival with a major functional disability is the possible result of decompressive surgery in the patients with malign MCA infarct. The older patients should be carefully selected for decompressive surgery, and their family or caregivers should be informed about the surgery.

Intracranial pressure was not observed, and thereby the effect of the craniectomy size on decreasing ICP could not be analysed. This is a limitation of the present study. In addition to in this study, we did not analyze the other radiological parameters than the location of infarct. Some studies in the literature also studied several radiological findings of the patients. As a strength of our study, we analyzed the timing of DC in narrow intervals. We divided the patients as time to surgery in <24 hours, 24-48 hours and >48 hours. As a result of our analysis, different from the other investigations, we revealed that not the approach of “surgery as soon as possible” but the surgery between 24-48th hours of the admission would be the optimal approach. In addition, we did not limit the patients according to age, and also included the patients older than 60 years.

CONCLUSION

We found that the craniectomy larger than infarct size improved survival, but this effect was statistically nonsignificant. We also found that early DC had significant effect on mortality. The surgery performed earlier, but in between 24-48 hours, was shown to improve the survival in our patients. As a conclusion, we suggested that not the approach of “surgery as soon as possible” but the surgery between 24-48th hours of the admission would be the optimal approach. This issue is especially important, because earlier or later interventions not only have a less benefit on the outcome but also may lead several unnecessary complications. We could not show any differences between the patients having right and left sided infarcts according to mortality. We also did reveal that the patients with hemiplegia or monoplegia did have a similar mortality rate to the others. Future investigations including more clinical and radiological parameters will clarify the uncertain issues about the surgery.

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