

Decompressive craniectomy is a life-saving procedure in malignant MCA infarction

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ABSTRACT

الأهداف: لدراسة مؤشرات ووقت ونتائج قطع القحف المخفف للضغط (DC) الذي يتم إجراؤه في حالات احتشاء الشريان الدماغى الأوسط الخبيث (MCA) في مركز الرعاية الثالثية الخاص بنا.

المنهجية: اشتملت دراسة سلسلة حالات بأثر رجعي للمرضى الذين خضعوا لل DC بسبب احتشاء MCA الخبيث في مدينة الملك عبد العزيز الطبية، الشؤون الصحية بوزارة الحرس الوطني، الرياض، خلال الفترة من يناير 2012م حتى ديسمبر 2018م. جمعنا كذلك البيانات الديموغرافية، والسرييرية، والإشعاعية، والسكتة الدماغية وتقييم المضاعفات المتعلقة بالجراحة ونتائج الخروج.

النتائج: ثمانية عشر مريضاً (متوسط العمر: 50±10 عام)، من بينهم 13 (72%) من الرجال، خضعوا لل DC خلال فترة الدراسة. من بين المرضى، كان 9 (50%) مصابين بسكتة شديدة (NIHSS 16–25)، و 10 (56%) مصابين باحتشاء MCA بالجهة اليمنى، و 11 (61%) تلقوا إما تحلل الخثرة في الوريد أو استئصال الخثرة داخل الأوعية الدموية أو معاً. تضمنت مؤشرات الجراحة التدهور السريري في 16 (89%) مريضاً، اتساع الحدقة المائل لوحظ في 11 (61%) مريضاً، وعلامات ارتفاع الضغط داخل الجمجمة في 6 (33%) مريضاً. أجريت الجراحة في غضون 48 ساعة في 14 (78%) من المرضى. كان متوسط مدة الإقامة في وحدة العناية المركزة 15±7 أيام. سبعة (39%) مرضى خرجوا إلى منازلهم و نقل 3 (17%) إلى وحدة إعادة تأهيل للمرضى المنومين، وتوفي 2 (11%) من المرضى. كان لدى جميع المرضى مضاعفات مرتبطة بالسكتة الدماغية. أصيب واحد (6%) من المرضى بتسرب السائل النخاعي، و 3 (17%) أصيبوا بمتلازمة الجلد الزائد الغارق وعدوى الجرح، و 2 (11%) أصيبوا بورم دموي فوق الجافية.

الخلاصة: أن قطع القحف المخفف للضغط منقذ للحياة في مرضانا الذين يعانون من احتشاء MCA الخبيث. خضع معظم المرضى لعملية جراحية في غضون 48 ساعة. خرج أكثر من ثلث المرضى إلى منازلهم، بينما حدثت الوفيات في مريضين فقط. إضافة إلى ذلك، كانت المضاعفات المرتبطة بالسكتة الدماغية والجراحة منتشرة في مجموعتنا.

Objectives: To investigate the indications, timings, and outcomes of decompressive craniectomy (DC) performed for malignant middle cerebral artery (MCA) infarctions at our tertiary care center.

Methods: This retrospective case series involved patients who underwent DC for malignant MCA infarction at King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, between January 2012 and December 2018. Demographic,

clinical, and radiological data were collected, and stroke- and surgery-related complications and discharge outcomes were assessed.

Results: Eighteen patients (mean age: 50±10 years), of whom 13 (72%) were men, underwent DC during the study period. Of the patients, 9 (50%) had severe stroke (NIHSS 16–25), 10 (56%) had right MCA infarction, and 11 (61%) received either intravenous thrombolysis or endovascular thrombectomy or their combination. Indications for surgery included clinical deterioration as seen in 16 (89%) patients, ipsilateral pupillary dilatation as seen in 11 (61%) patients, and signs of raised intracranial pressure in 6 (33%) patients. Surgery was performed within 48 h in 14 (78%) patients. The mean Intensive Care Unit stay was 15±7 days. Seven (39%) patients were discharged home and 3 (17%) were transferred to an inpatient rehabilitation unit, and 2 (11%) patients died. All patients had stroke-related complications; one (6%) patient developed cerebrospinal fluid leak, 3 (17%) had sunken skin flap syndrome and wound infection each, and 2 (11%) developed epidural hematoma.

Conclusion: The DC was life-saving in our patients with malignant MCA infarction. Most of the patients had surgery within 48 hours. More than one-third of the patients were discharged home, while mortality occurred in only 2 patients. Moreover, stroke- and surgery-related complications were common in our cohort.

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Stroke is one of the leading causes of death and adult disability worldwide.^{1,2} The burden of stroke is increasing and is a significant challenge for health care systems across the globe.² Ischemic stroke due to occlusion of proximal middle cerebral artery (MCA), usually involve large portions of a hemisphere and may cause space-occupying cerebral edema, leading to rapid neurological deterioration and cerebral herniation.^{2,3} Nearly 35 years ago, Hacke et al⁴ coined the term “malignant” for acute and complete MCA territory infarction involving a space-occupying cerebral edema and subsequently a considerably rapid neurological deterioration and herniation. Malignant MCA infarction involves more than 50% of and often the entire MCA territory.³⁻⁵ In the early phase of malignant MCA infarction, cytotoxic edema develops followed by the development of vasogenic edema.³ Approximately 1-10% of all MCA strokes can turn into malignant MCA infarction with a mortality risk of up to 80% within the first week.^{2,3} Acute brain swelling occurring within 48 hours results in elevated intracranial pressure (ICP) or brain herniation, which in turn leads to the deterioration of consciousness or death usually within the first week.^{2,3,6} The clinical predictors of malignant transformation include high NIHSS (National Institute of Health Stroke Scale) score, young age, female gender, as well as history of hypertension, ischemic heart disease, and congestive heart failure.^{2,6} The radiological predictors of malignant transformation are >66% perfusion deficit, >50% involvement of MCA territory on initial CT scan, and combined involvement of internal carotid artery and MCA, among many others.⁶

Control of ICP remains an important challenge in patients with severe post-stroke or post-traumatic brain edema. The medical management for raised ICP include head-of-bed elevation, hyperventilation, osmotic therapy, and sedation.^{6,7} Although osmotic therapy has failed to improve treatment outcomes, it can be used to bridge time until definitive surgical treatment can be performed.³ Systemic hypothermia in raised ICP due to malignant MCA infarction has been associated with multiple complications without any clear benefit on outcome.⁶

Trephination, an ancient treatment method of brain diseases, may be the earliest form of decompressive craniectomy.⁸ Decompressive craniectomy (DC) was

described more than a century ago, but it did not receive acceptance for most of the 20th century.^{8,9} One of the earliest reports on DC for malignant MCA infarction was published in 1951.¹⁰ A pooled analysis of three randomized trials conducted in the early part of this century showed for the first time the benefit of early DC in malignant MCA infarction.¹¹ These 3 initial European trials, namely, DECIMAL, DESTINY, and HAMLET, were the first to prove that DC was associated with decreased mortality and with the increased number of patients with favorable outcome.¹¹⁻¹⁴ The mortality rates decreased from 78% in historical controls to as low as 16% in surgically treated patients, with the number needed to treat (NNT) as low as 2 for survival with mRS (modified Rankin Scale) of ≤ 4 .¹³

The DC involves the removal of a part of the skull referred to as bone flap; along with opening of dura to accommodate brain swelling.^{8,9} In malignant MCA infarction, only unilateral decompression, also termed as decompressive hemicraniectomy, is performed.⁸ The DC allows an edematous brain tissue to herniate outside, thus preventing neuronal damage in other regions of the brain.^{2,8} A meta-analysis of 8 randomized trials and 4 observational studies confirmed the mortality benefit of DC in malignant MCA infarction.⁷ Patients and caregivers were satisfied with their QALY despite the disability of the patients; however, professionals did not consider surgery as favorable treatment due to the high disability rates post-surgery.⁷

There is one prior published study about decompressive craniectomy in malignant MCA infarction from Saudi Arabia describing 6 patients undergoing DC.¹⁵ Our study aimed to investigate the indications, timings, and outcomes of DC performed for malignant MCA infarctions at our tertiary care center. We believe that this work will add to the limited literature about this condition from the region.

Methods. This retrospective case series involved patients who underwent DC for malignant MCA infarction at the King Abdulaziz Medical City, Ministry of National Guard Health Affairs, Riyadh, KSA. Our institution is a tertiary care center with a comprehensive stroke unit. This study was approved by the Institutional Review Board of the King Abdullah International Medical Research Center, Riyadh, KSA, and it was conducted from January 2012 to December 2018. Patients were identified from hospital discharge records. Patients of any gender aged >18 years and with malignant MCA infarction treated with DC during the study period were included. Those who had DC for brain

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Table 1 - Demographic features and vascular risk factors of patients who underwent decompressive craniectomy.

Patient characteristics	Total (n=18) n (%)
<i>Demographics</i>	
Age in years (mean ± SD)	50 ± 10
<i>Gender</i>	
Male	13 (72)
Female	5 (28)
<i>Vascular Risk Factors</i>	
Hypertension	8 (44)
Diabetes mellitus	6 (33)
Dyslipidemia	5 (28)
Atrial fibrillation	4 (22)
Current smoker	6 (33)
Past smoking history	5 (28)
Coronary artery disease	1 (6)
Obesity	3 (17)

Table 3 - Stroke- and surgery-related complications in patients who underwent decompressive craniectomy.

Stroke-related Complication	n (%)
Hemorrhagic transformation	9 (50)
Recurrent stroke	4 (22)
Respiratory tract infection	10 (56)
Urinary tract infection	7 (39)
Sepsis	4 (22)
Deep vein thrombosis	5 (28)
Pulmonary embolism	2 (11)
Seizures/Epilepsy	5 (28)
Pressure ulcers	3 (17)
Myocardial infarction	2 (11)
Tracheostomy tube placement	7 (39)
Gastrostomy tube placement	5 (28)
Death	2 (11)
<i>Surgery-related Complications</i>	
Wound infection	3 (17)
Epidural hematoma	2 (11)
Subdural hygroma	1 (6)
Sunken skin flap syndrome	3 (17)
Cerebrospinal fluid leak	1 (6)
Bone resorption	0 (0)

injury or other indications were excluded. Patients who had involvement of more than one vascular territory in acute infarction were not considered for DC.

In our center, the decision of DC in malignant MCA infarction is made through multidisciplinary approach. The treating neurologist, intensivist and neurosurgeon make a consensus decision after discussion with family and obtaining informed consent. The clinical criteria for consideration of decompressive craniectomy

Table 2 - Stroke severity and common symptoms at presentation of patients who underwent decompressive craniectomy.

NIHSS score	n (%)
<i>Stroke Severity</i>	
5–15	8 (44)
16–25	9 (50)
>25	1 (6)
<i>Presenting Symptoms</i>	
Unilateral weakness	18 (100)
Speech or language dysfunction	11 (61)
Gaze preference	9 (50)
Altered level of consciousness	9 (50)
Seizure	4 (22)
Vomiting	1 (6)
Sudden headache	1 (6)

include good premorbid status of the patient, clinical worsening characterized by decrease in Glasgow Coma Scale or increase in NIHSS score within 48 hours of presentation, signs of raised intracranial pressure characterized by increasing headache, nausea, vomiting, decrease in level of alertness, or ipsilateral dilatation of the pupil. Radiological criteria for malignant MCA infarction include established full territory MCA infarction, midline shift and mass effect within 48 hours of presentation.

Demographic, clinical, and radiological data were collected from paper-based and electronic medical records. Stroke severity was assessed based on the NIHSS score at initial presentation and at discharge and based on the modified Rankin Scale (mRS) score at discharge. The statistical software package SPSS Statistics (SPSS Inc., Chicago, Illinois) version 21.0 was used for statistical analysis.

Due to the small number of patients, comparative analysis could not be performed; hence, only descriptive statistics are reported herein. Categorical data are presented as counts and percentages, whereas numerical data are presented as means±standard deviation.

In order to determine the previous literatures on DC for malignant MCA infarction in Saudi Arabia, PubMed and google scholar were searched using the terms of decompressive craniectomy in Saudi Arabia. We found one prior study of 6 patients who underwent DC for malignant MCA infarction in Saudi Arabia.¹⁵ Additionally, we found one study about the physician awareness of DC for malignant MCA infarction from Saudi Arabia and one case report of DC in a patient with malignant MCA infarction related to COVID-19 from Saudi Arabia.

Results. During the study period, a total of 3,075 patients were admitted to the stroke service of our institution. Eighteen patients, of whom 13 (72%) were men, underwent DC during the study period. The patient mean age was 50 ± 10 (range: 33–65) years. Majority of the patients (16 or 89%) presented within 6 h of symptom onset, and the mean NIHSS score in our cohort was 16 ± 3 . Of the patients, 9 (50%) had severe stroke at presentation (NIHSS 16–25), 8 (44%) presented with moderately severe stroke (NIHSS 5–15), and one patient had an NIHSS score of >25 . All patients had a focal weakness at presentation; 11 (61%) patients experienced speech and language difficulties, and gaze preference and altered level of consciousness was seen in 9 (50%) patients each. Four (22%) patients had seizure at the onset of stroke. Sudden severe headache was reported by only one (6%) patient. Hypertension was the most common risk factor in 8 (44%) patients, followed by diabetes and current smoking in 6 (33%) patients each. Five (28%) patients had dyslipidemia and past smoking history, and 4 (22%) had atrial fibrillation. Table 1 presents the demographic features and vascular risk factors, and Table 2 shows the stroke severity and common presenting symptoms in our cohort.

Acute ischemic stroke was treated with intravenous (IV) thrombolysis alone in one (6%) patient, with the combination of IV thrombolysis and endovascular thrombectomy (ET) in one (6%) patient, and with ET alone in 9 (50%) patients. Of those patients who had ET alone, 8 received a small dose (5–18 mg) of intra-arterial alteplase (tPA). Seven (39%) patients were not candidate for acute thrombolysis, and 10 (56%) patients underwent surgery for right hemispheric infarction. The indications for surgery included clinical deterioration as seen in 16 (89%) patients, ipsilateral dilatation of pupil as seen in 11 (61%) patients, and signs of raised ICP as seen in 6 (33%) patients. Moreover, radiological progression was seen in 17 (94%) patients. Surgery was performed within 48 h of symptom onset in 14 (78%) patients, out of which 2 (11%) had surgery within 12 h of symptom onset. The mean ICU stay was 15 ± 7 days.

Seven (39%) patients were discharged home, 3 (17%) were transferred to an inpatient rehabilitation unit, 4 (22%) were transferred to other facilities, 2 (11%) had prolonged hospitalization, and 2 (11%) died. One (6%) patient was fully independent at discharge (mRS 0–2) and 15 (83%) had moderate to severe disability (mRS 3–5). One (6%) patient had an NIHSS score of 0–5 at discharge, 10 (56%) had an NIHSS score of 6–15, and 5 (28%) had an NIHSS score of ≥ 16 at discharge. All patients had one or more stroke-related complications as described in Table 3. Surgery-related complications

included CSF leak in 1 (6%) patient, sunken skin flap syndrome and wound infection in 3 (17%) patients each whereas 2 (11%) patients had epidural hematoma. Due to our small sample size, comparative analysis according to age, gender, hemisphere involved, or stroke severity at presentation could not be performed.

Discussion. The DC has become a treatment of choice in malignant MCA infarction. Multiple randomized trials and meta-analysis have confirmed not only the benefit in mortality of DC, but also the patient satisfaction with the outcomes of surgery.^{7,16–18} Although physicians believe that this surgery may not be worthwhile given the associated high disability rates post-surgery, patients and caregivers express their satisfaction with the quality of life post-DC.^{7,19} We did not study the patient satisfaction component; however, significant mortality benefits of DC were observed in our patients. Natural history of malignant MCA infarction suggests mortality of nearly 80% in patients with malignant MCA infarction.¹¹ In our cohort, only 2 patients died, representing a mortality rate of nearly 11%, which is close to or better than the initial pooled analysis of randomized trials.¹¹ In the prior study from Saudi Arabia, 50% of the patients died within 3 months and the remaining had median mRS of 4.5.¹⁵ Most of our patients had moderate to severe disability at the time of discharge as reported in the previous trials;¹¹ nevertheless, nearly 40% of them were discharged home.

In our cohort, the mean age was 50 years, and majority of the patients were male. This is consistent with the patients in the early randomized trials and the published literature, wherein most of the treated patients were aged <60 years, as well.^{11,15–16} In many studies, the upper age limit was 55–65 years.^{7,17} In a review of 382 patients, the mean age was 50 years, and 59% of the patients were male.¹⁹ The age of >60 years has been reported to be associated with increased mortality and poor functional outcomes in patients undergoing DC for malignant MCA infarction, particularly those above 70 years of age.^{20–22}

The greatest benefit of decompressive surgery is seen when it is performed within 48 h of symptom onset.^{7,16} However, a recent study has found that the outcomes of DC performed within and beyond 48 hours were not different.²³ The majority of our patients underwent DC in less than 48 hours, and approximately 20% underwent surgery beyond 48 hours from symptom onset, quite similar to the randomized trials.¹¹ We did not compare the outcomes based on the timing of surgery due to our small sample size. Most of our patients displayed clinical

or radiological deterioration within 48 h, as is known from previous literature.²⁴ Moreover, patients who undergo surgery within 24 h have better outcomes than those who undergo surgery within 24–48 h or beyond 48 h.²⁵ Some data have suggested that ultra-early DC (i.e., DC performed within 6 h of symptom onset) may have additional beneficial effect.²⁶ Meanwhile, more than half of our patients had a surgery on their non-dominant hemisphere. Studies have shown that there is no significant difference in the functional outcome of DC whether a surgery was performed in the dominant hemisphere or in the non-dominant hemisphere.^{27,28} Many of our patients had IV thrombolysis or ET prior to DC. Many of those who had ET also received intra-arterial alteplase. It has been shown that intra-arterial thrombolysis prior to DC does not affect the outcome and does not increase the surgical complications.²⁹

The DC is associated with a variety of complications, which may include hemorrhagic complications, infectious or inflammatory complications, or cerebrospinal fluid (CSF) compartment-related complications.¹⁸ Surgical complications do not only occur in the early post-operative phase; they may continue to occur up to several months after the procedure.³⁰ In our small cohort, we observed both surgery- and stroke-related complications. Hemorrhagic transformation was seen in half of our patients. In a Canadian study, hemorrhagic transformation was seen in 59% of the investigated patients; however, it did not affect the overall outcome and discharge disposition.³¹ In our cohort, wound infection and sunken skin flap syndrome were seen as surgical complications, followed by epidural hematoma and subdural hygroma formation. The CSF leak was also seen in one patient. Stroke-related complications, including respiratory or urinary tract infection, post-stroke seizure or epilepsy, and recurrent stroke, were quite common in our cohort. Many patients required tracheostomy and/or gastrostomy tube placement.

The DC was a life-saving procedure for our patients. Only 2 patients died and thus the survival rate in our series was >80%. Despite the moderate to severe disability in the survivors, more than one-third of them were discharged home compared to the 27% patient discharge rate in one study.³¹ Using historical controls as basis, we not only observed the survival benefit of DC in our patients, but we also found that despite their disability, patients may be discharged home and be placed under the care of their loved ones. Due to our small sample size, we could not compare the discharge outcomes and discharge disposition according to age groups or gender. Moreover, due to lack of long-term follow up, we could not determine the psychosocial impact of DC.

Our study has some limitations. Being a single-center study, the total number of patients was rather small and hence comparative analysis could not be performed. We did not conduct long-term follow up on our patients given that many of those who underwent DC were not eligible to continue medical care at our institution after discharge due to an institutional policy. One of the strengths of our study is that it is the first of its kind in the region, and it will contribute to the scientific literature on decompressive craniectomy in the management of stroke.

In conclusions, DC was a life-saving procedure performed in our patients with malignant MCA infarction. While most of our patients had moderate or severe disability at the time of discharge, one patient was fully independent functionally at the time of discharge and more than one-third of the patients were discharged home. Moreover, stroke- and surgery-related complications were common in our cohort.

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