

# Decompressive craniectomy versus conservative treatment: limits and possibilities in malignant stroke

Craniectomia descompressiva *versus* tratamento conservador: limites e possibilidades no AVC maligno

Isaac Holanda Mendes MAIA<sup>1</sup>, Thaissa Pinto de MELO<sup>2</sup>, Fabrício Oliveira LIMA<sup>1</sup>, João José de Freitas CARVALHO<sup>1</sup>, Francisco José Arruda MONT'ALVERNE<sup>1</sup>, Edson LOPES JÚNIOR<sup>3</sup>, Marcelo Bezerra DIÓGENES<sup>4</sup>, Thaís Saraiva Leão CUNHA<sup>4</sup>, Bárbara Matos Almeida QUEIROZ<sup>4</sup>, Marina Franciss TAMIETTI<sup>4</sup>, Fernanda Martins MAIA<sup>1</sup>

## ABSTRACT

**Background:** Malignant infarction of the middle cerebral artery (MCA) occurs in a subgroup of patients with ischemic stroke and early decompressive craniectomy (DC) is one of its treatments. **Objective:** To investigate the functional outcome of patients with malignant ischemic stroke treated with decompressive craniectomy at a neurological emergency center in Northeastern Brazil. **Methods:** Prospective cohort study, in which 25 patients were divided into two groups: those undergoing surgical treatment with DC and those who continued to receive standard conservative treatment (CT). Functionality was assessed using the modified Rankin Scale (mRS), at follow-up after six months. **Results:** A favorable outcome (mRS $\leq$ 3) was observed in 37.5% of the DC patients and 29.4% of CT patients ( $p=0.42$ ). Fewer patients who underwent surgical treatment died (25%), compared to those treated conservatively (52.8%); however, with no statistical significance. Nonetheless, the proportion of patients with moderate to severe disability (mRS 4–5) was higher in the surgical group (37.5%) than in the non-surgical group (17.7%). **Conclusion:** In absolute values, superiority in the effectiveness of DC over CT was perceived, showing that the reduction in mortality was at the expense of increased disability.

**Keywords:** stroke; brain edema; decompressive craniectomy.

## RESUMO

**Introdução:** O infarto maligno da artéria cerebral média (ACM) ocorre em um subgrupo de pacientes com acidente vascular cerebral (AVC) isquêmico e a craniectomia descompressiva (CD) precoce é um de seus tratamentos. **Objetivo:** Investigar o desfecho funcional de pacientes com acidente vascular cerebral isquêmico maligno submetidos à craniectomia descompressiva em um centro de emergência neurológica do nordeste do Brasil. **Métodos:** Nesta coorte prospectiva, os pacientes foram divididos em dois grupos: aqueles submetidos a tratamento cirúrgico com craniectomia descompressiva (CD) e aqueles que mantiveram tratamento conservador (TC) padrão. A funcionalidade foi avaliada por meio da Escala de Rankin modificada (ERm) ao final de seis meses de seguimento. **Resultados:** Evidenciou-se desfecho favorável (ERm $\leq$ 3) em 37,5% dos pacientes craniectomizados e em 29,4% dos pacientes não craniectomizados ( $p=0,42$ ). A mortalidade foi menor no grupo de pacientes que se submeteram a tratamento cirúrgico (25%) do que entre aqueles tratados conservadoramente (52,8%), porém sem significância estatística. Por outro lado, a proporção de pacientes com incapacidade moderada a grave (ERm 4–5) foi maior no grupo cirúrgico (37,5%) do que no grupo não cirúrgico (17,7%). **Conclusão:** Em valores absolutos, percebeu-se superioridade na eficácia do tratamento cirúrgico sobre o conservador, mostrando que a redução de mortalidade se dá à custa de aumento da incapacidade funcional.












**Palavras-chave:** acidente vascular cerebral; edema encefálico; craniectomia descompressiva.

<sup>1</sup>Hospital Geral de Fortaleza, Serviço de Neurologia, Fortaleza CE, Brazil.

<sup>2</sup>Hospital Geral de Fortaleza, Serviço de Enfermagem, Fortaleza CE, Brazil.

<sup>3</sup>Hospital Geral de Fortaleza, Serviço de Neurocirurgia, Fortaleza CE, Brazil.

<sup>4</sup>Universidade de Fortaleza, Centro de Ciências da Saúde, Fortaleza CE, Brazil.

Isaac Holanda Mendes MAIA  <https://orcid.org/0000-0001-5482-9736>; Thaissa Pinto de MELO  <https://orcid.org/0000-0003-4905-0714>; Fabrício Oliveira LIMA  <https://orcid.org/0000-0002-0383-4145>; João José de Freitas CARVALHO  <https://orcid.org/0000-0002-1070-5552>; Francisco José Arruda MONT'ALVERNE  <https://orcid.org/0000-0003-0362-257X>; Edson LOPES JÚNIOR  <https://orcid.org/0000-0001-5106-9006>; Marcelo Bezerra DIÓGENES  <https://orcid.org/0000-0002-6204-889X>; Thaís Saraiva Leão CUNHA  <https://orcid.org/0000-0002-6763-3107>; Bárbara Matos Almeida QUEIROZ  <https://orcid.org/0000-0001-8519-4729>; Marina Franciss TAMIETTI  <https://orcid.org/0000-0003-0534-3523>; Fernanda Martins MAIA  <https://orcid.org/0000-0001-6548-7268>

**Correspondence:** Isaac Holanda Mendes Maia; Hospital Geral de Fortaleza; Rua Ávila Goulart, 900 – Papicu; 60175-295 Fortaleza CE, Brazil; E-mail: isaacholanda@hotmail.com

**Conflict of interest:** There is no conflict of interest to declare.

Received on August 1, 2019; Received in its final form on November 27, 2019; Accepted on January 8, 2020.



Mortality in extensive ischemic stroke (EIS) in the territory of the middle cerebral artery (MCA) can reach up to 80% according to some controlled studies<sup>1,2</sup>. Transtentorial herniation is the most common cause of death<sup>3</sup>. In view of this scenario, the selection of patients for early prophylactic decompressive craniectomy (DC) surgery is an essential measure in the treatment of acute neurovascular syndrome in emergency neurological services worldwide<sup>4</sup>.

EIS is said to be malignant when there is neurological deterioration secondary to extensive cerebral infarction and consequent encephalic edema, which in turn usually occurs between the second and fifth day after the stroke<sup>5,6,7</sup>. The patient may present clinical signs of intracranial hypertension, such as headache, nausea, vomiting, anisocoria, epileptic crisis, mental confusion, lowering of consciousness level and coma<sup>8,9,10</sup>.

Two forms of malignant ischemic stroke management are recognized: isolated conservative treatment (CT) and surgical treatment associated to clinical measures, such as osmotherapy with mannitol or hypertonic saline<sup>11,12,13,14</sup>. The first multicenter randomized controlled trials that sought to evaluate the benefit of DC surgery were the HAMLET (Hemicraniectomy After Middle cerebral artery infarction with Life-threatening Edema trial) in 2006, the DECIMAL (DEcompressive Craniectomy In Malignant MCA Infarction) and the DESTINY I (Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery) in 2007. They established benefits in the survival of patients under 60 years of age undergoing early surgical decompression for malignant stroke, when compared to CT. However, such studies did not assess the quality of life of these survivors. Often, the survival of patients undergoing DC was accompanied by serious sequelae, such as tetraparesis, aphasia, chronic pain and depression. The choice of treatment in the EIS has become a real dilemma for neurologists, neurosurgeons and intensive care specialists, mainly with the advent of new knowledge from so-called Palliative Medicine<sup>15,16,17</sup>. Therefore, this study aimed to evaluate the functional outcome of patients with malignant ischemic stroke treated in a neurological emergency center in the Northeast of Brazil, submitted to DC surgery or not.

## METHODS

This was a prospective cohort study, in which all patients with MCA malignant ischemic stroke treated by the neurological emergency service of the General Hospital of Fortaleza City, Ceará State, Brazil, from November 1<sup>st</sup>, 2015 to December 30<sup>th</sup>, 2016, were evaluated. The inclusion criteria were diagnosis of ischemic stroke with an ictus of 48 hours or less, an extensive ischemic area measured with cranial CT (>50% of MCA territory), neurological deterioration and clinical signs of intracranial hypertension.

The initial sample of 29 patients was divided into two groups: 10 patients who were treated with DC surgery and 19 who continued receiving gold-standard conservative treatment in the stroke unit, with the support of the specialized multidisciplinary team, including neurologists, nurses, physiotherapists, occupational therapists, speech therapists and dentists. Two patients from the craniectomized group and two patients from the non-craniectomized group were lost from the follow-up, thus providing a final sample of 25 individuals.

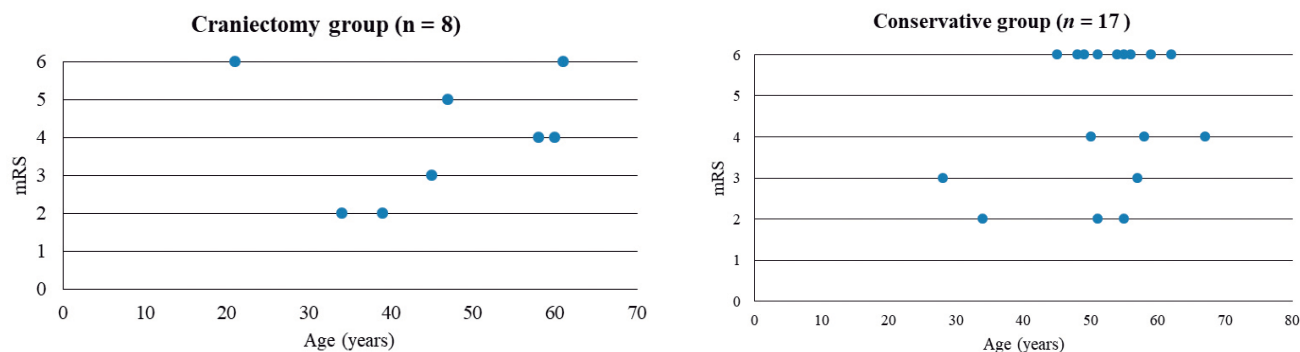
The patients were monitored by the Neurology and Neurosurgery team during hospitalization and reassessed by telephone, after six months, by the Neurology team. The functional status of both groups was compared to the modified Rankin Scale (mRS). The favorable functional outcome of mild impairment (mRS 0-3) was adopted as the primary outcome. A mRS between 4 and 5 represents moderate to severe disability, which together with an mRS of 6, comprised the total of unfavorable outcomes. The magnitude of the neurological deficit was quantified with the standard National Institutes of Health Stroke Scale (NIHSS), stratified as mild (0-10), moderate (11-18) and severe (>18). The level of consciousness was measured with the Glasgow Coma Scale (GCS) score, as severe ( $\leq 8$ ), moderate (between 9 and 12) and mild (between 13 and 15).

Data were analyzed using the IBM SPSS version 23 software. Absolute and relative frequencies were calculated for the qualitative variables and mean and standard deviation for the quantitative variables. The quantitative measures were evaluated for normality using the Shapiro-Wilk test. Student's t-test, the Mann-Whitney test and the chi-squared test were used to examine the association between variables. The results were presented in graphs and tables. For all the inferential procedures used, a significance level of 5% was adopted.

## RESULTS

In the sample analyzed, most patients with EIS in both groups were women, representing 70.6% of the patients that received the conservative treatment and 50% of the patients that underwent craniectomy. Ages ranged from 21 to 67, with the majority corresponding to the age group between 21 and 59 (75.0% in CD group and 88.2% in CT group), as presented in Figure 1. Regarding origin, 62.5% of the surgical patients and 70.5% of the non-surgical patients lived in Fortaleza City, as presented in Table 1.

The most prevalent risk factors in both populations were systemic hypertension, sedentary lifestyle and smoking. Most patients treated in the referral service were sedentary (n=20). Smoking ranked as the second risk factor (n=16), followed by systemic hypertension (n=15), as shown in Table 1. Some patients presented more than one factor. Regarding the



**Figure 1.** Distribution by age of patients treated conservatively and surgically in a neurological emergency center after malignant ischemic stroke.

**Table 1.** Sociodemographic and etiological profile of the patients affected by malignant ischemic stroke of a neurological emergency center.

Variable	Group			
	Craniectomy		Conservative	
Sex				
Male	4	50.0	5	29.4
Female	4	50.0	12	70.6
Age group				
21-60	6	75.0	15	88.2
≥60	2	25.0	2	11.8
Origin				
Fortaleza City	5	62.5	12	70.5
Metropolitan region	2	25.0	0	0
Countryside of the state	1	12.5	5	29.5
Associated factor				
Systemic hypertension	5	62.5	11	64.7
Diabetes mellitus	1	12.5	4	23.5
Dyslipidemia	1	12.5	3	17.6
Previous stroke	0	0	3	17.6
Sedentary lifestyle	7	87.5	13	76.5
Family history of stroke	3	37.5	6	35.6
Chagas disease	0	0	2	11.8
Oral contraceptive use	0	0	1	5.9
Obesity	1	12.5	1	5.9
Congestive heart failure	1	12.5	5	29.4
Arrhythmia	1	12.5	1	5.9
Traumatic brain injury	1	12.5	0	0
Valvopathies	0	0	1	5.9
Migraine	1	12.5	2	11.8
Smoker	3	37.5	13	76.5
Previous Rankin				
0-1	8	100	16	94.1
4	0	0	1	5.9
Mechanism				
Cardioembolic	3	37.5	5	29.5
Cryptogenic	5	62.5	11	64.7
Large vessels	0	0	1	5.8

previous functionality, evaluated with the modified Rankin Scale (mRS), Table 2 shows that most patients had no significant disability and that all the patients that had craniectomy were functionally independent regarding activities of daily living. One individual in the surgical group (3.5%) had a moderately severe disability (mRS=4) prior to the stroke.

Most patients were able to reach the neurological referral service within the therapeutic window period for intravenous thrombolytic administration (4.5 hours after onset of symptoms), totaling 11 cases (38%). Nine patients (31%) arrived between 4.5-8 hours after the onset of symptoms, and nine (31%) patients arrived with an interval of more than 8 hours. Only one patient received thrombolytic therapy with alteplase. According to the etiological investigation of the stroke, 16 cases of the total sample had no defined etiology.

Seven patients had cardioembolic etiology and only one case presented large vessels mechanism (Table 1).

Regarding the clinical manifestations at the time of admission, all the patients presented motor and sensory symptoms. Twenty patients presented speech changes and visual changes. In addition, 64% of the patients had altered levels of consciousness. Only five patients had headaches, three had a seizure episode, and vomiting was reported in 20% of the cases (Table 3). At admission, 25% of the craniectomized patients and 23.5% of non-craniectomized patients arrived at the hospital with a Glasgow Coma Scale score considered severe (GCS<8); 62.5% of the surgical patients and 35.3% of the non-surgical patients had a moderate score (9-12), and 12.5% of the craniectomized patients and 41.2% of the non-craniectomized patients presented a mild GCS

**Table 2.** Clinical profile of the patients affected by malignant ischemic stroke of a neurological emergency center.

Variable	Group			
	Craniectomy (n=8)		Conservative (n=17)	
	n	%	n	%
Onset of symptoms-admission				
≤4.5 hours	2	25.0	6	35.3
4.5-6 hours	0	0	5	29.4
>6 hours	6	75.0	6	35.3
Side affected				
Right	2	25.0	9	52.9
Left	6	75.0	8	47.0
Glasgow Coma Scale score -admission				
Serious	2	25.0	4	23.5
Moderate	5	62.5	6	35.3
Mild	1	12.5	7	41.2
NIHSS score - admission				
Moderate	3	37.5	8	47.1
Serious	5	62.5	9	52.9
Banford score - admission				
LACS	1	12.5	0	0
PACS	0	0	4	23.5
TACS	7	87.5	13	76.5
Thrombolysis				
Yes	0	0	0	0
No	8	100	17	100
Presence of anisocoria	3	37.5	4	23.5
Final Rankin score				
0-3	3	37.5	5	29.4
4-6	5	62.5	12	70.6
Physiotherapy time				
≥3 months	4	66.7	6	35.3
<3 months	2	33.3	11	64.7

(13-15). Regarding the magnitude of the neurological damage calculated by the NIHSS score, no individual was classified as mild NIHSS (0-10), 11 patients had moderate NIHSS (11-18), and the majority of patients (n=14) had NIHSS considered severe >18). In relation to the cerebral hemisphere involved, the majority of craniectomized patients had their left side affected (n=6), whereas most of conservative patients had their right hemisphere more affected (n=9) (Table 1).

Regarding the functionality of the patients with malignant stroke at the 6-month follow-up, Figure 2 shows the percentage of all functional outcomes according to the mRS, whereas Table 4 divides the two groups into favorable outcome (mRS 0-3), unfavorable outcome (mRS 4-5) and death (mRS=6). Most patients who received conservative treatment evolved to death (52.8%). In addition, 37.5% (3/8) of the craniectomized patients and 29.4% (5/17) of the non-craniectomized patients achieved a favorable outcome of mild disability (mRS 0-3), whereas 37.5% (3/8) of the patients in the craniectomized group and 17.6% (3/17) of the non-craniectomized group had moderate to severe disability (mRS 4-5) after six months. Mortality (mRS=6) was 2.1% (2/8) among surgical patients and 52.9% (9/17) among those treated

conservatively. Of those who died, 81.8% presented a cause of death related to brain herniation. One patient died of sudden cardiac arrest 10 months after discharge. The mean time between the stroke and death was 6.8 days.

## DISCUSSION

The average age of patients in our sample was 50.0±10.9, whereas in the study by Vital et al.<sup>18</sup> it was 63 (32-83). Patients were allocated to the groups within 48 hours of the stroke, with this time being 30 hours for the DECIMAL study, 96 hours for the HAMLET, 36 hours for the DESTINY I and 48 hours for the DESTINY II. The mean time between the onset of symptoms and admission to the emergency room was 7 hours (range 2-25). In the studies by Bongiorno et al.<sup>19</sup> at the Hospital de Clínicas de Porto Alegre, Brazil, the average was 13.2±1.4 hours. The mean NIHSS admission score in the DECIMAL study was 22.5 for the surgery group and 23.4 for the non-surgery group, whereas in the present sample it was 20.7 and 19.9, respectively, showing that the patients of the present study were in a less serious condition upon arrival at the neurological referral service.

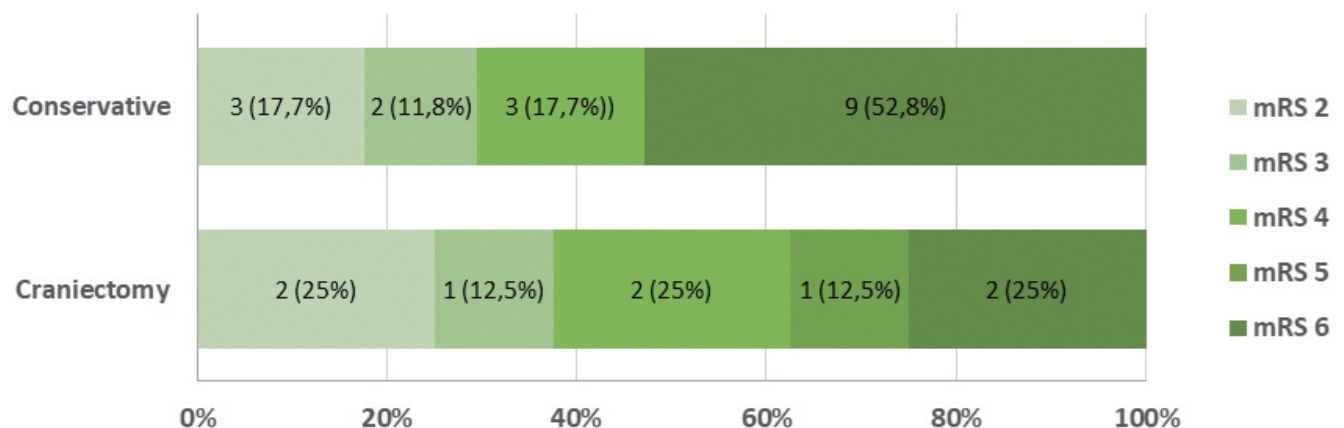
In the study by Mattos et al.<sup>20</sup>, patients with GCS<8 in the preoperative examination showed a tendency for poor outcomes, which represented a quarter of the craniectomized patients in the present study. The mean ictus-craniectomy interval for the patients of the present study was 39.7

**Table 3.** Clinical manifestation of patients with malignant ischemic stroke treated at a neurological emergency center.

Clinical manifestation	n	%
Motor	25	100
Sensitive	25	100
Aphasia	20	80
Visual	20	80
Consciousness	16	64
Headache	5	20
Vomiting	5	20
Convulsive crisis	3	12
Hemineglect	4	16

**Table 4.** Stratification of the modified Rankin Scale at the end of the 6-month follow-up in patients with ischemic stroke treated in a neurological emergency center.

Variables	Craniectomy	Conservative	p-value
RANKIN	0-3	3 (37.5)	5 (29.4)
	4-5	3 (37.5)	3 (17.7)
	6	2 (25.0)	9 (52.9)



**Figure 2.** Functional capacity measured with the mRS after 6 months in two therapeutic groups (Decompressive Craniectomy vs. Conservative) of patients with malignant ischemic stroke.

hours, whereas in the DECIMAL it was 20.5 hours (interval between 7 and 43 hours). In studies on MCA hemispheric infarction, Fiorot Junior et al.<sup>21</sup> published that the mean age of patients was 59.1±18.0, whereas in our sample it was 50.0±10.9, with 46.6±13.2 in the DC group and 51.8±9.3 in the CT group. When risk factors were analyzed, 31.0% of the craniectomized patients and 22% of the non-craniectomized DECIMAL patients were hypertensive, whereas in the present study these figures were 62% and 64.7%, respectively, thus showing an unsatisfactory control of modifiable risk factors, such as hypertension.

The cardioembolic mechanism was the most prevalent in the present sample, found in 37.5% in the surgical group and 29.5% in the non-surgical group. The mean time between symptom onset and therapeutic decision among patients with hemispheric infarction in the study by Fiorot Junior et al.<sup>21</sup> was 33 hours for craniectomized patients and 37 hours for non-craniectomized patients, whereas, in our study, 26.5 and 31 hours, respectively. In the DESTINY I study, these values were 24.4 ± 6.9 and 23.8 ± 7.8 hours, showing that the time for making decisions about the type of treatment in our hospital is similar to international data.

In the analysis of functionality between the two therapeutic groups, the present study showed that the favorable outcome (mRS 0–3) after 6 months was better among the patients who underwent DC surgery when compared to those on CT, numerically corresponding to 37.5% (3/8) of the craniectomized patients compared to 29.4% (5/17) of the non-craniectomized patients. The proportion of patients

with moderate to severe disability (mRS 4–5) was higher in the surgical group (37.5%) than in the non-surgical group (17.7%), proving that survival is accompanied by a reduction in functionality. Furthermore, the number of deaths (mRS=6) among the patients who underwent DC (25% mortality) was lower when compared to those on CT (52.9% mortality). Studies of DC in patients with traumatic brain injury showed that the procedure, even after clinical signs of brain herniation, can still lead to better functional outcomes compared to conservative treatment<sup>22</sup>. Although this has not shown such benefit in stroke studies, in our sample, even with a rate of 37.5% of patients in the CD group with anisocoria, CD brought a favorable outcome (mRS) for 37.5% of them. In the international literature, the DESTINY I study, with the inclusion of 32 patients, revealed a statistically significant reduction in mortality: 15 (88%) of the 17 patients randomized to hemicraniectomy versus 7 (47%) of the 15 patients randomized to conservative therapy survived after 30 days (p<0.02).

In the study by Kim et al.<sup>23</sup> on the attitude of patients as to their disability after MCA hemispheric stroke, 55% of patients considered an mRS score of 3 to be the worst disability acceptable.

In sum, it is concluded that although DC surgery is a procedure that reduces mortality, the increased survival is accompanied by serious functional disability. Accordingly, it is important for the medical team to inform family members about the risks, susceptibilities and likely postoperative functional outcome for patients, considering that many of them will require lifelong special and individualized care.

## References

- Mohan Rajwani K, Crocker M, Moynihan B. Decompressive craniectomy for the treatment of malignant middle cerebral artery infarction. *Br J Neurosurg*. 2017 Aug;31(4):401-9. <https://doi.org/10.1080/02688697.2017.1329518>
- Das S, Mitchell P, Ross N, Whitfield PC. Decompressive hemicraniectomy in the treatment of malignant middle cerebral artery infarction: a meta-analysis. *World Neurosurg*. 2019 Mar;123:8-16. <https://doi.org/10.1016/j.wneu.2018.11.176>
- Algethamy HM, Samman A, Baeesa SS, Almekhlafi MA, Al Said YA, Hassan A. Decompressive hemicraniectomy for malignant middle cerebral artery infarction-Experience from the Western Province of Saudi Arabia. *Neurosciences (Riyadh)*. 2017 Jul;22(3):192-7. <https://doi.org/10.17712/nsj.20173.20170051>
- Rahme R, Curry R, Kleindorfer D, Khoury JC, Ringer AJ, Kissela BM, et al. How often are ischemic stroke patients eligible for decompressive hemicraniectomy? *Stroke*. 2012 Feb;43(2):550-2. <https://doi.org/10.1161/STROKEAHA.111.635185>
- Treadwell SD, Thanvi B. Malignant middle cerebral artery (MCA) infarction: pathophysiology, diagnosis and management. *Postgrad Med J*. 2010 Apr;86(1014):235-42. <https://doi.org/10.1136/pgmj.2009.094292>
- Wartenberg KE. Malignant middle cerebral artery infarction. *Curr Opin Crit Care*. 2012 Apr;18(2):152-63. <https://doi.org/10.1097/MCC.0b013e32835075c5>
- Staykov D, Gupta R. Hemicraniectomy in malignant middle cerebral arter infarction. *Stroke*. 2011; 42:513-6. <https://doi.org/10.1161/STROKEAHA.110.605642>
- Huttner HB, Schwab S. Malignant middle cerebral artery infarction: clinical characteristics, treatment strategies, and future perspectives. *Lancet Neurol*. 2009 Oct;8(10):949-58. [https://doi.org/10.1016/S1474-4422\(09\)70224-8](https://doi.org/10.1016/S1474-4422(09)70224-8)
- Wijdicks EFM, Sheth KN, Carter BS, Greer DM, Kasner SE, Kimberly WT, et al. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2014 Apr;45(4):1222-38. <https://doi.org/10.1161/01.str.0000441965.15164.d6>
- Torbey MT, Bosel J, Rhoney DH, Rincon F, Staykov D, Amar AP, et al. Evidence-based guidelines for the management of large hemispheric infarction a statement for health care professionals from the Neurocritical Care Society and the German Society for Neuro-Intensive Care and Emergency Medicine. *Neurocrit Care*. 2015 Feb;22(1):146-64. <https://doi.org/10.1007/s12028-014-0085-6>
- Hauer E-M, Stark D, Staykov D, Steigleder T, Schwab S, Bardutzky J. Early continuous hypertonic saline infusion in patients with severe cerebrovascular disease. *Crit Care Med*. 2011 Jul;39(7):1766-72. <https://doi.org/10.1097/CCM.0b013e318218a390>

12. Akins PT, Axelrod YV, Arshad ST, Guppy KH. Initial conservative management of severe hemispheric stroke reduces decompressive craniectomy rates. *Neurocrit Care*. 2016 Aug;25(1):3-9. <https://doi.org/10.1007/s12028-016-0270-x>
13. Simard JM, Sahuquillo J, Sheth KN, Kahle KT, Walcott BP. Managing malignant cerebral infarction. *Curr Treat Options Neurol*. 2011 Apr;13(2):217-29. <https://doi.org/10.1007/s11940-010-0110-9>
14. Zweckberger K, Juettler E, Bösel J, Unterberg WA. Surgical aspects of decompressive craniectomy in malignant stroke: Review. *Cerebrovasc Dis*. 2014;38(5):313-23. <https://doi.org/10.1159/000365864>
15. Hofmeijer J, Amelink GJ, Algra A, van Gijn J, MacLeod RM, Kappelle LJ, et al. Hemicraniectomy After Middle cerebral artery infarction with Life-threatening Edema Trial (HAMLET). Protocol for a randomised controlled trial of decompressive surgery in space-occupying hemispheric infarction. *Trials*, 2006;7:29. <https://doi.org/10.1186/1745-6215-7-29>
16. Vahedi K, Vicaud E, Mateo J, Kurtz A, Orabi M, Guichard JP, et al. Sequential-design, multicenter, randomized, controlled trial of early decompressive craniectomy in malignant middle cerebral artery infarction (DECIMAL trial). *Stroke*. 2007;38(9):2506-17. <https://doi.org/10.1161/STROKEAHA.107.485235>
17. Jüttler E, Schwab S, Schmiedek P, Unterberg A, Hennerici M, Woitzik J, et al. Decompressive Surgery for the Treatment of Malignant Infarction of the Middle Cerebral Artery (DESTINY I): a randomized, controlled trial. *Stroke*. 2007 Sep;38(9):2518-25. <https://doi.org/10.1161/STROKEAHA.107.485649>
18. Vital RB, Hamamoto Filho PT, Luvizutto GJ, Ducati LG, Braga GP, Nunes HRdC, et al. Decompressive hemicraniectomy in a South American Population – morbidity and outcomes analysis. *PLoS ONE*. 2016 Jan;11(1): e0146747. <https://doi.org/10.1371/journal.pone.0146747>
19. Bongjorni GT, Hockmuller MCJ, Klein C, Antunes ACM. Decompressive craniotomy for the treatment of malignant infarction of the middle cerebral artery: mortality and outcomes *Arq Neuropsiquiatr*. 2017 Jul;75(7):424-8. <https://doi.org/10.1590/0004-282X20170053>
20. Mattos JP, Joaquim AF, Almeida JP, Albuquerque LA, Silva EG, Marengo HA, et al. Decompressive craniectomy in massive cerebral infarction. *Arq Neuropsiquiatr*. 2010;68(3):339-45. <https://doi.org/10.1590/s0004-282x2010000300002>
21. Fiorot Junior JA, Silva GS, Cavalheiro S, Massaro AR. Use of decompressive craniectomy in the treatment of hemispheric infarction. *Arq Neuropsiquiatr*. 2008;66(2A):204-8. <https://doi.org/10.1590/s0004-282x2008000200012>
22. Shah A, Almenawer S and Hawryluk G. Timing of decompressive craniectomy for ischemic stroke and traumatic brain injury: a review. *Front Neurol*. 2019;10:11. <https://doi.org/10.3389/fneur.2019.00011>
23. Kim B-J, Hong YR, Han Y, Hwang Y-H, Ohk B, Park J. Age-Dependent Attitudes of Ischemic Patients towards Disability after Decompressive Hemicraniectomy for Malignant Middle Cerebral Artery Infarction, *World Neurosurgery* (2018). doi: 10.1016/j.wneu.2018.02.050.