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Original Article Decompressive craniectomy index: Does the size of decompressive craniectomy matter in malignant middle cerebral artery infarction?

Thiago Pereira Rodrigues<sup>1</sup>, Mariana Athaniel Silva Rodrigues<sup>2</sup>, Leonardo Favi Bocca<sup>1</sup>, Feres Eduardo Chaddad-Neto<sup>1</sup>, Sergio Cavalheiro<sup>1</sup>, Edson Amaro Junior<sup>2</sup>, Gisele Sampaio Silva<sup>3</sup>, Italo Capraro Suriano<sup>1</sup>, Ricardo Silva Centeno<sup>1</sup>

<sup>1</sup>Department of Neurology and Neurosurgery, Federal University of Sao Paulo, <sup>2</sup>Department of Radiology, Albert Einstein Hospital, <sup>3</sup>Academic Research Organization, Hospital Albert Einstein, São Paulo, Brazil.

E-mail: \*Thiago Pereira Rodrigues - thiagopereirarodrigues@yahoo.com.br; Mariana Athaniel Silva Rodrigues - mariathaniel@gmail.com; Leonardo Favi Bocca - leobocca5@gmail.com; Feres Eduardo Chaddad-Neto - fereschaddad1@gmail.com; Sergio Cavalheiro - sergiocavalheironeuro@gmail.com; Edson Amaro Junior - edson.junior@einstein.br; Gisele Sampaio Silva - giselesampaio@hotmail.com; Italo Capraro Suriano - suriano.ops@terra.com.br; Ricardo Silva Centeno - ricardoscenteno@gmail.com



\*Corresponding author: Thiago Pereira Rodrigues, Department of Neurology and Neurosurgery, Federal University of Sao Paulo, São Paulo, Brazil.

thiagopereirarodrigues@yahoo. com.br

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# ABSTRACT

**Background:** Malignant middle cerebral artery (MCA) infarction is associated with high mortality, mainly due to intracranial hypertension. This malignant course develops when two-thirds or more of MCA territory is infarcted. Randomized clinical trials demonstrated that in patients with malignant MCA infarction, decompressive craniectomy (DC) is associated with better prognosis. In these patients, some prognostic predictors are already known, including age and time between stroke and DC. The size of bone flap was not associated with long-term prognosis in the previous studies. Therefore, this paper aims to further expand the analysis of the bone removal toward a more precise quantification and verify the prognosis implication of the bone flap area/whole supratentorial hemicranium relation in patients treated with DC for malignant middle cerebral infarcts.

**Methods**: This study included 45 patients operated between 2015 and 2020. All patients had been diagnosed with a malignant MCA infarction and were submitted to DC to treat the ischemic event. The primary endpoint was dichotomized modified Rankin scale (mRS) 1 year after surgery (mRS $\leq$ 4 or mRS>4).

**Results:** Patients with bad prognosis (mRS 5–6) were on average: older and with a smaller decompressive craniectomy index (DCI). In multivariate analysis, with adjustments for "age" and "time" from symptoms onset to DC, the association between DCI and prognosis remained.

**Conclusion:** In our series, the relation between bone flap size and theoretical maximum supratentorial hemicranium area (DCI) in patients with malignant MCA infarction was associated with prognosis. Further studies are necessary to confirm these findings.

Keywords: Cerebral volumetry, Decompressive craniectomy, Intracranial pressure, Malignant middle cerebral artery infarction

# INTRODUCTION

Malignant middle cerebral artery (MCA) infarction is a neurological condition associated with high morbidity and mortality, mainly due to intracranial hypertension secondary to cerebral

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edema.<sup>[18]</sup> This malignant course develops after a large ischemic stroke of at least two-thirds of MCA territory, comprising up to 15% of total MCA strokes and with mortality rates reaching 80% without surgical treatment.<sup>[3]</sup> Several randomized clinical trials (RCTs) have demonstrated that in patients with malignant MCA infarction, decompressive craniectomy (DC) was associated with lower mortality when performed early, increasing quality-adjusted life years, although at high costs.<sup>[7,10,19]</sup>

Prognostic predictors in patients who underwent DC after malignant MCA infarction have been explored by several authors since the DECIMAL trial, the first multicenter RCT published in 2007.<sup>[19]</sup> Daou *et al.*<sup>[4]</sup> in 95 patients series with malignant MCA infarction that underwent DC found: midline shift >10 mm, previous history of stroke, history of diabetes mellitus, time between stroke and DC, preoperative pupillary dilatation, and stroke in dominant hemisphere as poor prognostic predictors. von Olnhausen *et al.*<sup>[21]</sup> in 46 patients series found: infarct of basal ganglia, high preoperative blood glucose level, and low preoperative Glasgow Coma Scale as poor prognostic factors. Paliwal *et al.*<sup>[15]</sup> found early DC (performed within 48 h from stroke onset) and right MCA infarction as good prognostic predictors.

Previous series of patients with malignant MCA infarction that underwent DC analyzed the size of bone flap. Olnhausen *et al.*<sup>[21]</sup> measured the length and the height of bone flap in postoperative head CT, using length, height, and length X height in statistical analyses, found no association between those measurement and prognosis. Neugebauer *et al.*<sup>[14]</sup> in a retrospective series compared standard DC with an extended DC. They found that in the extended DC group, in-hospital mortality due to cerebral herniation was lower. However, overall in-hospital mortality was not statistically different and they did not measure long-term results. Wagner *et al.*<sup>[22]</sup> found that suboptimal decompressive (<12 cm in diameter) was associated with hemorrhages on the border of craniectomy and, thus, with a higher mortality rate.

Studies in patients with traumatic brain injury (TBI) showed that large craniectomy bone flap was associated with better clinical outcome<sup>[13]</sup> and better postoperative intracranial pressure control.<sup>[16]</sup>

Importantly, the method to measure the DC size has been mainly based on bone flap diameter.<sup>[1,7,9,10,14,19]</sup> Recently, Schur *et al.*<sup>[16]</sup> described a new method to calculate the craniectomy bone flap. In this method, the skull hemicircumference is calculated contralateral to the DC side (in the same axial CT slice), and the flap circumference is estimated using mathematical formulas. Therefore, each patient had a ratio of flap circumference/cranial hemicircumference and, thus, the cranial size was considered in these calculations. They applied this method in patients with TBI and demonstrated

that larger bone flap (ratio >65%) achieved better intracranial pressure (ICP) control. This concept of "taking the patient's head size in account" proposed by Schur *et al.* is fundamental, but using just one axial CT slice for performing these calculations is not ideal. At present, using open-source softwares, we can directly measure complex shape areas.

Therefore, this paper aims to further expand the analysis of the bone removal toward a more precise quantification and verify the prognosis implication of the bone flap area/whole supratentorial hemicranium relation in patients treated with DC for malignant middle cerebral infarcts.

## MATERIALS AND METHODS

## Patients' selection

This retrospective study was approved by the Institutional Review Board and was performed following the Declaration of Helsinki. All subjects enrolled into this study gave signed consent (in case of decreased level of consciousness, patient's relatives signed informed consent), and all data were anonymized at source. We enrolled consecutive patients from a single tertiary hospital between 2015 and 2020, with primary admission diagnosis of malignant MCA infarction and age  $\geq$ 18 years at admission, and requiring DC as clinical treatment for the primary condition.

The diagnosis of malignant MCA infarction was made through a comprehensive analysis of multiple factors, including initial CT scan ischemic areas, National Institutes of Health Stroke Scale (NIHSS), tomographic signs of mass effect, age, and past medical history. Then, a multidisciplinary team including a neurologist assistant, a neurosurgery assistant, a neuroradiologist, and a critical care assistant, made the final decision about whether it has the potential to develop a malignant course or not. In patients that malignant courses were expected, DC was performed as soon as possible. In this study, malignant MCA infarction diagnosis included patients with a large infarction in vascular territory of MCA including or not another vascular territory (anterior cerebral artery or posterior cerebral artery).

Clinical and radiological data were collected from the electronic medical records and image server, and included age, sex, laterality of infarction, time from onset of symptoms until DC, NIHSS score, vascular territory's area, medical history, alteplase use, brain endovascular procedures before DC, midline shift (MLS) peak time, and modified Rankin scale (mRS) after 1 year.

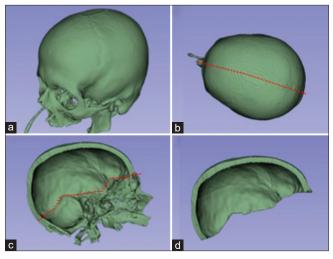
## Surgical procedure

All procedures were performed by board certified neurosurgeons from our hospital neurosurgical department. Two types of skin flaps were made, according to surgeon's personal preference: a large inverted question mark or "T" type skin flap (Kempe's incision<sup>[12]</sup>). After craniectomy, the dura was incised, and then, an expansion duraplasty using pericranium was made. As an institutional protocol, the craniectomy should be as large as possible, with special attention to decompression of the temporal lobe.

## Image analysis

All CT examinations performed during patients' clinical care were analyzed and processed in the software 3D Slicer (v. 4.10 – www.slicer.org), an open-source software.<sup>[5]</sup> CT scanner acquisition settings were: KPv: 120; matrix size:  $512 \times 512$ ; and slice thickness: 2.5 mm, manufacturer Philips, Netherlands.

Manual bone segmentation of all supratentorial hemicranium was performed using the sagittal suture, internal occipital protuberance, groove for transverse sinus, the intersection between the middle fossa floor and the lateral wall, and the intersection between anterior cranial fossa floor and lateral/anterior wall as the borders. This area was considered maximum theoretical supratentorial hemicranium bone flap [Figure 1]. Coregistration between preoperative and postoperative CT examinations was performed with subtracted postoperative volume from preoperative volume considered as bone flap removed in DC procedure (superficial/external area as skull removed area) [Figure 2]. A decompressive craniectomy index (DCI) was calculated



**Figure 1:** Bone segmentation of preoperative C.T. examination. (a) All cranial bone segmented. (b) The red-dotted line represents a cut passing through external occipital protuberance, sagittal suture, and internasal suture. (c) A left-sided hemicranium with the red-dotted line representing a cut that passes through internal occipital protuberance, groove for transverse sinus, intersection between the middle fossa floor and the lateral wall, and the intersection between anterior cranial fossa floor and lateral/anterior wall. (d) The maximum theoretical hemispheric hemicranium bone flap.

based on the ratio between the bone flap area and the maximum theoretical supratentorial hemicranium area using the "segment statistics module" provided by Slicer 3D.

Transverse CT in aligned to orbitomeatal line was used for the measurement of maximum craniectomy diameter.

# Statistical analysis

The categorical variables were described as numbers of cases and percentages, and the quantitative variables were characterized as means  $\pm$  standard deviations.

For comparison between groups (favorable or unfavorable), continuous variables were compared with Mann–Whitney U-test, while categorical variables were analyzed by Fisher's exact test.

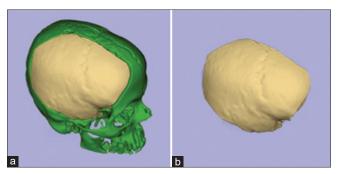
A multivariate logistic regression model was performed, using the "enter" method, to identify if DCI was independently associated with worse outcome, with adjustment for age and time from symptoms onset to DC.

The correlation between maximum craniectomy diameter and DCI, and between age and DCI was tested using Pearson's correlation test. The interaction between significant variable in the regression model was checked using Wald test.

For the statistically significant association, P < 0.05 was used (for multivariate model inclusion, we use P < 0.1). All analyses were performed using the statistical program IBM Statistical Package for the Social Sciences version 26.

## RESULTS

We included 45 patients who underwent a DC after the diagnosis of a malignant MCA infarction in our hospital from 2015 to 2020. The mean age at DC was 52.8 years. The mean time between the ischemic ictus and DC was 42.1 h. Isolated MCA infarction occurred in 25 patients; MCA plus ACA occurred in nine patients; MCA plus ACP occurred in six patients; and MCA plus ACA plus ACP occurred in five



**Figure 2:** Bone flap area calculation. (a) Coregistration of preoperative and postoperative C.T. examinations. (b) Subtracting postoperative C.T. examination from preoperative C.T. examination obtained exactly the bone flap defect.

patients. Regarding skin flap, large inverted question mark was more frequent than "T" type (26 vs. 19 patients). All patients had NIHSS scores higher than 13 [Table 1].

In comparison between groups, patients with bad prognosis (mRS 5–6) were on average: older (P = 0.009) and with a smaller DCI (P = 0.022). Other factors did not significantly differ between favorable (n = 25) versus unfavorable (n = 20) group, which included sex, infarction side, intravenous thrombolysis using time from symptoms onset to DC (P = 0.091), ASPECTS score, admission glucose level, and peak of MLS [Table 2].

In the multivariate model, we included three factors that met the criteria (P < 0.1 in univariate analysis): age (P = 0.009), time from symptoms onset to DC (P = 0.091), and DCI (P = 0.022). Bone flap area was excluded from the multivariate model because of multicollinearity issues [Table 3].

The Pearson's correlation between DCI and maximum craniectomy diameter was 0.594 (P < 0.001) and the scatter plot is shown in Figure 3 (showing how the DCI correlates with MAXIMUM craniotomy diameter). Based on the regression line of the scatter plot, the maximum craniectomy diameter of 12 cm correlates with DCI  $\approx$  0.575.

The interaction between age and DCI in regression model was ruled out (Wald test = 0.609, P = 0.435).

**Table 1:** General characteristic of the patients (*n*=45).

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Characteristic	Value (%)
Men	23 (51.1)
Mean age (years)	52.8±11.19*
Mean time from symptom onset to DC (hours)	42.1±29.65*
Mean NIHSS score <sup>[2]</sup> (admission)	19±3*
DC on left hemisphere	19 (42.2)
Infarction site restricted to ipsilateral MCA territory	25 (55.6)
Infarction site in MCA territory plus ACA or PCA	20 (44.4)
Admission glucose level (mmol/L)	$8.84 \pm 4.68^{*}$
Skin incision type	
Large inverted question mark	26 (57.9)
"T" type (Kempe's incision)	19 (42.2)
ASPECTS	
ASPECTS 0	13 (28.9)
ASPECTS 1	7 (15.6)
ASPECTS 2	15 (33.3)
ASPECTS 3–6	10 (22.1)
Stroke treatment used before DC	
Intravenous alteplase	13 (28.9)
Intra-arterial thrombolysis OR thrombectomy	9 (20)
mRS after 1 year	
mRS 3	16 (35.6)
mRS 4	9 (20)
mRS 5	2 (4.4)
mRS 6 (death)	18 (40)
MCA: Middle cerebral artery, ACA: Anterior cerebral arte	ery,

MCA: Middle cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, DC: Decompressive craniectomy,

mRS: Modified Rankin scale. \*Mean values are presented  $\pm$  SD

The analysis of dichotomized outcomes according to DCI cutoffs is shown in Figure 4.

#### DISCUSSION

In this study, we evaluated all patients who underwent a DC after a malignant MCA infarction in a single center from 2015 to 2020. In this series, we identified three possible predictors: age, time from symptoms onset to DC (P = 0.069), and the relation between bone flap area and maximum theoretical supratentorial hemicranium area DCI.

Age as a predictive factor in patients with malignant MCA infarction that underwent DC was already demonstrated by several authors. In Carter *et al.*<sup>[2]</sup> series, all the patients under 50 years old had a good functional outcome versus just 3 of 6 old patients. Holtkamp *et al.*<sup>[8]</sup> reported a series of 12 patients >55 years old submitted to DC. None of these patients had a good functional prognosis (mRS < 4). In Destiny II study,<sup>[11]</sup> after 12 months, just 6% of patients older than 60 years of age had mRS  $\leq$  3 versus 43% in the younger group.

Time from symptoms onset to DC has already identified as a predictive factor by the previous studies. Schwab *et al.*,<sup>[17]</sup> in a series of 63 patients, reported that the early decompressive group (<24 h after symptoms onset) had a better outcome. In Vibbert *et al.*,<sup>[20]</sup> series that included 64 patients, a subgroups analysis demonstrated that patients operated in 48 h from symptom onset had better prognosis than patients operated after 48 h from symptoms onset.

Craniectomy bone flap size was also previously evaluated in literature. von Olnhausen *et al.*<sup>[21]</sup> evaluated the bone flap length, height, and area (length × height). The method to measure length and height was the largest measure in the axial plane (length) and in the coronal plane (height). They found

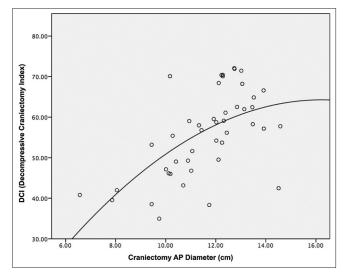


Figure 3: Correlation between decompressive craniectomy index and maximum craniectomy diameter. AP: Anteroposterior

Table 2: Outcome group comparison (favorable vs. unfavorable).						
	Favorable outcome, mRS≤4, <i>n</i> =25	Unfavorable outcome, mRS>4, <i>n</i> =20	P value	Total, <i>n</i> =45		
Sex						
Male	11	12	0.373ª	23		
Female	14	8		22		
Age						
Median (IQR)	47 (43-53.5)	58.5 (49.75-65)	$0.009^{b}$	52 (44-61)		
Infarction side						
Left	8	11	0.142ª	19		
Right	17	9		26		
Intravenous thrombolysis						
Yes	6	7	>0.515ª	13		
No	19	13		32		
Time from symptoms onset to DC (hours)						
Median (IQR)	30 (20-44)	42.5 (25-73.75)	0.091 <sup>b</sup>	36 (21-49.5)		
ASPECTS						
Median (IQR)	1 (0-2)	2 (1-2.75)	0.315 <sup>b</sup>	2 (0-2)		
Admission glucose level (mmol/L)						
Median (IQR)	6.88 (5.99-8.54)	9.24 (5.75-12.59)	0.157 <sup>b</sup>	7.21 (5.99-9.85)		
Peak of MLS (mm)						
Median (IQR)	6.44 (2.43-9)	7.48 (4.33-12.07)	0.242 <sup>b</sup>	6.64 (3.85-10.72)		
Bone flap area (cm <sup>2</sup> )						
Median (IQR)	163.83 (143.79-179.36)	145.25 (126.93-165.02)	$0.044^{b}$	158.25 (134.46-168.70		
Decompressive craniectomy index* (%)						
Median (IQR)	58.74 (53.69-70.09)	49.38 (43.91-59.43)	$0.022^{b}$	57.17 (46.95-63.68)		

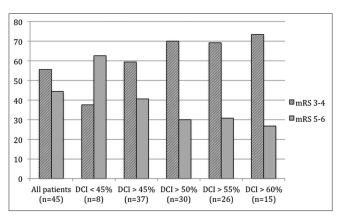
\*Decompressive craniectomy index: Bone flap area/maximum theoretical supratentorial hemicranium area. <sup>a</sup>Fisher's exact test, <sup>b</sup>Mann–Whitney *U*-test, MLS: Midline shift, IQR: Interquartile range

Table 3: Multivariate analysis (binary logistic regression).						
	Odds ratio	95% CI	P-value			
Age Hours from symptoms onset to DC Decompressive	0.912 0.973 1.117	0.842-0.988 0.945-1.002 1.019-1.224	0.024 0.069 0.018			
craniectomy index* (%) *Decompressive craniectomy index: Bone flap area/maximum theoretical						

supratentorial. DC: Decompressive craniectomy, NIHSS: National Institutes of Health Stroke Scale, CI: Confidence Interval

no significant association between these measurements and prognosis. Wagner *et al.*<sup>[21]</sup> described a series of 60 patients. In this series, they analyzed hemicraniectomy-associated lesions (hemorrhages and infarct). There was a significant relation between the size of craniectomy and the occurrence of hemicraniectomy-associated hemorrhagic lesion, and the occurrence of these hemorrhagic lesions was associated with higher mortality rate. The size of craniectomy was also measured using the diameter of bone defect in postoperative CT examinations.

In this series, for the purpose of analyzing bone flap area, we employed an open-source graphic software and, thus, we



**Figure 4:** Dichotomized outcomes according to decompressive craniectomy index cutoffs.

measured the area of the bone flap. This measurement took into account the curvature and the shape. Furthermore, we also considered the bone area of supratentorial hemicranium. The high relation between bone flap area and maximum theoretical supratentorial hemicranium area, that is, DCI, was significantly associated with good prognosis. Despite the fact that high DCI was significantly associated with better prognosis, the odds ratio was low: 1.117, therefore, the magnitude of the effect was low. We think that other unevaluated factors could also be predictive factors.

In our opinion, most of neurosurgeons agree that size matters in DC and the minimal craniectomy diameter established by Wagner *et al.*<sup>[22]</sup> (12 centimeters) is worldwide accepted. The occurrence of progressive cerebral herniation in patients who underwent DC for malignant MCA infarction was previously reported.<sup>[6]</sup>

In our series, we had a low frequency of therapeutic thrombolysis (28.9% of intravenous alteplase use and 20% of intra-arterial or mechanical thrombectomy). It happened mainly because of two factors: delayed time between initial ictus and arrival at hospital, and the fact that most of our patients arrived at our hospital coming from other hospitals that do not have stroke team and, therefore, are not able to implement thrombolysis therapies.

This retrospective study has several limitations. First, it is based on a small sample size in a single institution. Second, because of the limited number in this series, we could not define a precise cutoff for DCI.

Apart from the discussion about whether to perform or not the DC in patients with malignant MCA infarction (that in our view is well-established in literature), we think that technical aspects emphasizing how to perform a DC in patients with malignant MCA infarction should be better evaluated.

Concisely, in this study, we described a method to calculate craniectomy bone flap area. Considering the maximum theoretical supratentorial hemicranium area and the craniectomy bone flap area, we obtained the DCI. Then, in a 45 patients' series of malignant MCA infarction that underwent DC, we found three prognostic predictors: age, hours from symptoms onset to DC, and DCI.

## CONCLUSION

In our series, the relation between bone flap size and theoretical maximum supratentorial hemicranium area DCI in patients with malignant MCA infarction was associated with prognosis. Further studies are necessary to confirm these findings.

## Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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## **Conflicts of interest**

There are no conflicts of interest.

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