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Large Size Hemicraniectomy Reduces Early Herniation in Malignant Middle Cerebral Artery Infarction

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Key Words
Decompressive surgery · Hemicraniectomy · Malignant middle cerebral artery infarction · Space-occupying edema

Abstract
Background: Decompressive hemicraniectomy (DHC) reduces mortality and improves outcome after malignant middle cerebral artery infarction (MMI) but early in-hospital mortality remains high between 22 and 33%. Possibly, this circumstance is driven by cerebral herniation due to space-occupying brain swelling despite decompressive surgery. As the size of the removed bone flap may vary considerably between surgeons, a size too small could foster herniation. Here, we investigated the effect of the additional volume created by an extended DHC (eDHC) on early in-hospital mortality in patients suffering from MMI. ***Methods:*** We performed a retrospective single-center cohort study of 97 patients with MMI that were treated either with eDHC (n = 40) or standard DHC (sDHC; n = 57) between January 2006 and June 2012. The primary study end point was defined as in-hospital mortality due to transtentorial herniation. ***Results:*** In-hospital mortality due to transtentorial herniation was significantly lower after eDHC (0 vs. 11%; p = 0.04), which was paralleled by a significantly larger volume of the craniectomy (p < 0.001) and less cerebral swelling (eDHC 21% vs. sDHC 25%; p = 0.03). No statistically significant differences were found in surgical or non-surgical complications and postoperative intensive care treatment. ***Conclusion:*** Despite a more aggressive surgical approach, eDHC may reduce early in-hospital mortality and limit transtentorial herniation. Prospective studies are warranted to confirm our results and assess general safety of eDHC.

Introduction

Subtotal and complete infarctions of the middle cerebral artery (MCA) are usually accompanied by massive cerebral swelling. Due to the confined space within the skull, the additional swelling volume causes brain tissue shifts and an increase in intracranial pressure (ICP), which may finally result in transtentorial herniation [1]. Even under maximum medical treatment, however, these so-called 'malignant' MCA infarctions (MMI) remain associated with a mortality rate up to 80% [2, 3].

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Decompressive hemicraniectomy (DHC) with opening of the dura is a surgical procedure with the purpose of creating additional space for the swollen brain by removing large parts of the supratentorial cranium [1, 4, 5]. Meanwhile, randomized controlled trials on patients undergoing DHC for treatment of MMI have evidenced that DHC substantially reduces mortality [6, 7]. Despite the life-saving characteristic of DHC, in-hospital mortality still remains as high as 22–33% [6–9].

More than the technique of DHC, the dimensions of the removed bone flap are considered crucial, since they define the amount of additionally created volume for the swollen brain to occupy [10–14]. Using mathematical formulas, this volume can be estimated. Consequently, larger craniectomies should also create larger volumes [15, 16]. However, whether larger craniectomies also translate into a reduced rate of in-hospital mortality due to herniation or not remains unknown. Therefore, the aim of this study was to investigate the effect of an extended DHC (eDHC) compared to a standard DHC (sDHC) on early in-hospital mortality due to transtentorial herniation in patients suffering from MMI.

Methods

This single-center, retrospective cohort study was approved by the ethics committee of the Charité – Universitätsmedizin Berlin, Germany (reference number: EA1/156/14), and it included 97 patients with MMI who underwent either sDHC or eDHC in a non-randomized fashion between January 2006 and June 2012.

Patient Management

The general clinical need for DHC in the setting of MMI was determined according to the inclusion criteria of the DESTINY trials. This included a severe MCA syndrome with dense hemiplegia, head and eye deviation, hemineglect and aphasia when the dominant hemisphere was involved next to an impaired and progressively deteriorating level of consciousness over the first 24–48 h and definite infarction of two-thirds of the MCA territory with or without additional infarction of the ipsilateral anterior or posterior cerebral artery territory [8, 17]. All patients were treated according to the guidelines of the German Society of Neurosurgery. DHC was performed within 48 h after symptom onset in the majority of patients. Patients undergoing DHC after 48 h were only included if they did not present signs of transtentorial herniation before surgery. Both techniques were used according to the decision of the treating neurosurgeon. Except for various surgeons there were no further inclusion criteria.

Postoperatively, patients were transferred to our neurointensive care unit. ICP was continuously monitored on the side of the DHC and patients remained intubated and sedated until ICP was within normal ranges. A critical ICP threshold was defined as ICP >20 mm Hg for longer than 10 min and treated according to national and international guidelines with cerebrospinal fluid drainage, osmotic therapy and deep sedation. All patients had at least one routine postoperative CT or MRI scan within 24 h after surgery to rule out procedure-related complications. Additional CT scans were obtained in case of clinical deterioration and to document transtentorial herniation.

Surgical Technique of sDHC and eDHC

Surgical decompression was performed in a standardized step-by-step fashion. All patients were anaesthetized with propofol and remifentanil and a mean arterial pressure of 70–80 mm Hg was targeted. sDHC was performed as previously described [1, 4, 7, 8, 18, 19]. A large question mark-shaped curvilinear skin incision starting at the widow's peak and continuing posteriorly along the midline to the inion before turning to the ear and ending approximately 1 cm below the root of the zygoma in front of the tragus was performed. The skin, galea and temporal muscle were reflected as a single flap. Standard burr holes were placed at the root of the zygoma, behind the lambdoid suture and 1–1.5 cm lateral of the midline at the level of the bregma in order to define the inferior, posterior and medial extension of the craniectomy. Accordingly, a bone flap measuring at least 12 cm in diameter and extending along these margins to the supraorbital rim was removed. The middle cerebral fossa was additionally decompressed by removing excess bone of the temporal squama down to the temporal base. Next, the underlying dura was opened in a stellate fashion extending to the edge of the craniectomy with sparing of bridging veins. If needed, peripheral dural tack-up stitches were placed to control epidural bleeding from Pacchioni granulations. An external ventricular drain or parenchymal ICP device was inserted. Before closure, the surgical field was thoroughly irrigated with sterile saline, and the exposed brain tissue was loosely covered by the remaining dura without performing duraplasty [20].

eDHC was performed in modification of Holland and Nakaji [21] and differs from sDHC by removing a bone flap that covers the entire supratentorial hemicranium of the affected hemisphere. The landmarks outlining this extended osseous removal are the root of the zygoma (indicating the floor of the temporal fossa), the asterion (confluence of the lambdoid, occipital-mastoid and temporal-parietal sutures indicating the area of transition between the sigmoid and transverse sinus), the inion (marking the sinus confluence as the posterior margin), the midline (delineating the course of the superior sagittal sinus) and the glabella (marking the anterior margin). For exposure, a linear midline skin incision from the widow's peak continuing posteriorly 3 cm beyond the inion was performed. The skin, galea and temporal muscle were reflected as a single flap. In 2 patients, the transverse sinus was injured during the craniotomy. In these cases, the footplate of the craniotome was removed and bleeding was stopped with bone wax. The craniotomy was then completed by sparing an at least 1 cm bone ridge from the site of injury. The remaining surgical steps were performed as described above.

Analysis of Neuroimaging Data

Infarct volume and hemispheric swelling was determined directly from the postoperative CT scans or from matched diffusion weighted imaging and fluid attenuation inversion recovery sequences of the postoperative MRI scans with the aid of iPlan® Cranial planning software (BrainLAB, Feldkirchen, Germany) and VISAGE7 (Visage Imaging GmbH, Germany).

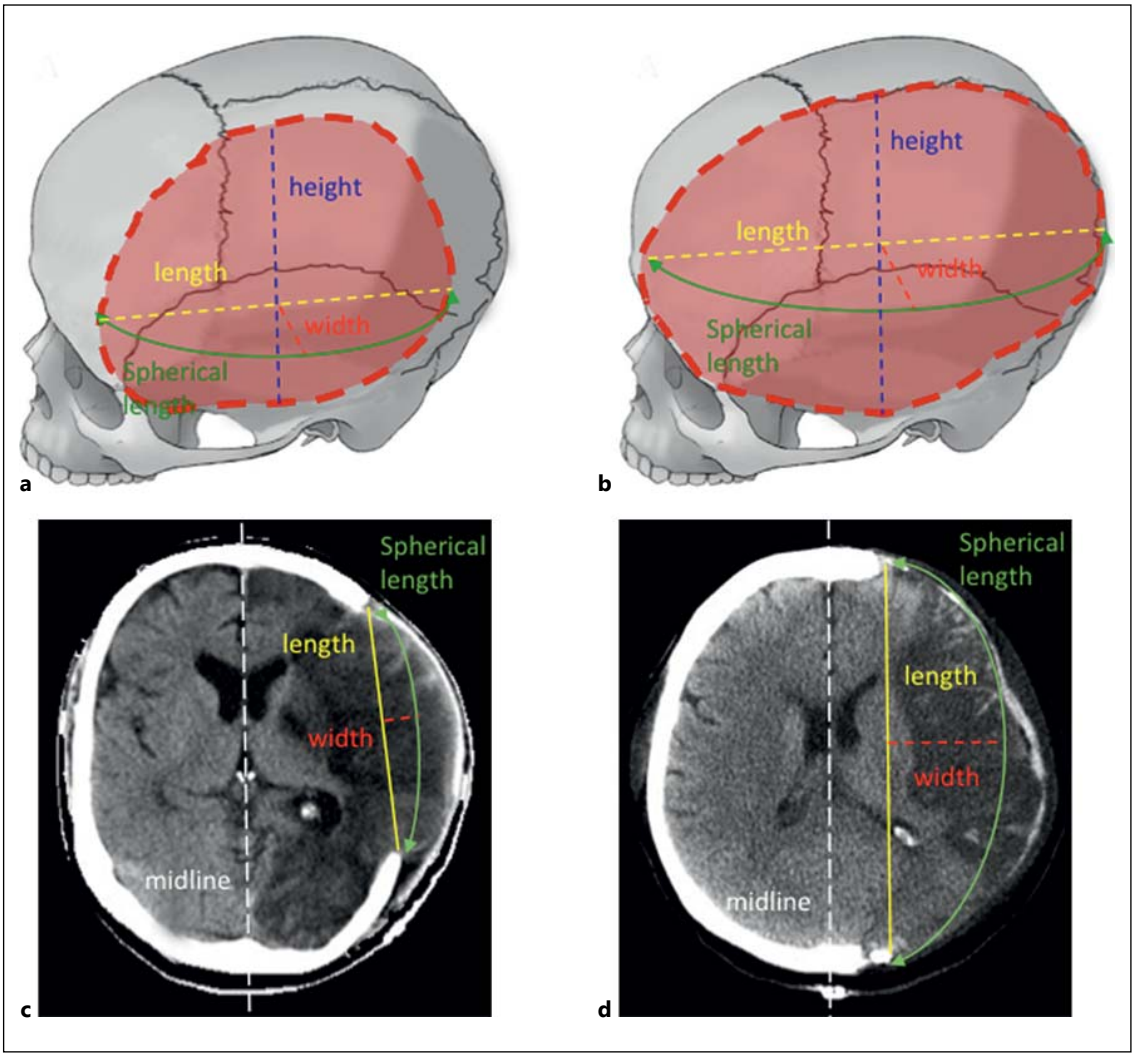

Fig. 1. Extent of bone removal and measurement of longitudinal dimensions of sDHC (left) and eDHC (right). **a** and **b** Lateral views of the craniectomy defect (red area). Length and height are measured from opposite bone edges while measurement for spherical length is taken from the convexity of the bone flap. Width is measured from an imaginary line connecting the edges of the craniectomy up to the summit of the bone flap. **c** and **d** CT scans that illustrate the difference of length and spherical length in a transverse plane.

Measurement of longitudinal dimensions is shown in figure 1. Volume gain was calculated as ipsilateral volume minus contralateral volume. Swelling was determined as volume gain divided by contralateral volume. Volume of infarction corrected for hemispheric swelling was calculated as volume of infarction divided by swelling plus 1. Due to varying total volumes of infarction, swelling was additionally calculated with reference to 100 cm^3 of infarction.

Outcome Measures

The primary outcome measure was in-hospital mortality due to transtentorial herniation. Secondary clinical outcome measures included all other forms of in-hospital mortality, time from symptom onset to treatment, estimated blood loss, postoperative ICP crisis, postoperative ICP treatment, postoperative surgical complications, postoperative rate of systemic infections, length of intubation and time from stroke onset to rehabilitation.

Secondary infarct-related neuroimaging outcome measures included the corrected and uncorrected volumes of infarction, volume gain, swelling and midline shift. Secondary bone-flap related neuroimaging outcome measures included the volume of the bone flap, length/width/height of craniectomy, as well as the spherical diameter of the craniotomy.

Statistical Analysis

Descriptive summary statistics were calculated for all variables. Statistical significance was set at $p < 0.05$. The χ^2 test, Mann–Whitney U test or Student's t test was used as appropriate. Univariate analysis was performed for all variables to identify differences be-

tween treatment groups and variables associated with transtentorial herniation and overall in-hospital mortality. All tests were 2-tailed. Statistics were performed using the SPSS 21.0 software package (SPSS Inc., Chicago, Ill., USA).

Results

Of the 97 patients included in the present analysis, 40 were treated by eDHC and 57 by sDHC. Clinical and demographical patient characteristics are given in table 1.

Importantly, baseline demographic and clinical data such as the preoperative National Institute of Health Stroke Scale, size of the infarction, affected vascular territories, time to treatment, blood loss during surgery, rates of surgical and non-surgical complications as well as ICP lowering treatment, duration of intubation and hospital stay did not differ between groups (table 1). Neuroimaging characteristics are shown in table 2.

In-hospital mortality due to transtentorial herniation was observed in 6 patients who underwent sDHC compared to 0 patients who received eDHC (sDHC 11% vs. eDHC 0%; OR 0.56 in favor of extended hemicraniectomy; 95% CI 0.47–0.67; $p = 0.04$), which was paralleled by a significantly larger volume of the craniectomy following eDHC (eDHC 132 ± 33 cm^3 vs. sDHC 96 ± 25 cm^3; $p < 0.001$; tables 1 and 2). Clinical variables that were significantly related to herniation were the number of ICP crisis events ($p = 0.002$) and postoperative osmotic ICP therapy ($p = 0.02$). There was no significant association between the time intervals from symptom onset to surgery or transtentorial herniation ($p = 0.90$).

Although other forms of in-hospital mortality were also more frequent following standard decompression (sDHC 18% vs. eDHC 13%), this did not reach statistical significance. Although these other forms of in-hospital mortality were significantly associated with higher rates of systemic infections ($p = 0.02$); importantly, this association was not found for the number of ICP crisis events ($p = 0.10$). Causes of death other than herniation were sepsis (2 patients), cardiogenic shock (1 patient) and withdrawal of care (1 patient) in the sDHC group, next to cardiogenic shock (1 patient) and withdrawal of care (4 patients) in the eDHC group.

Regarding infarct-related secondary outcome measures, patients who underwent eDHC also suffered significantly less cerebral swelling (eDHC 21 ± 8% vs. sDHC 25 ± 9%; $p = 0.03$).

Mean time from DHC to cranioplasty (CP) were 191 ± 122 days in the eDHC group compared to 156 ± 162 days in the sDHC group ($p = 0.36$). Complications that were recorded around the time of CP appeared to be comparable in both treatment groups: subdural hematoma: 3 (eDHC) versus 2 (sDHC), epidural hematoma: 3 (eDHC) versus 1 (sDHC), subgaleal hematoma: 2 (eDHC) versus 1 (sDHC), intracranial hematoma: 1 (eDHC) versus 0 (sDHC), ischemic stroke: 1 (eDHC) versus 0 (sDHC), hydrocephalus/shunt: 4 (eDHC) versus 3 (sDHC), wound healing issues: 3 (eDHC) versus 8 (sDHC). The total number of patients suffering at least one complication was 10 (29.4%) after eDHC versus 13 (31.7%) after sDHC ($p = 0.83$).

Discussion

With this retrospective cohort study, we were able to provide first evidence that an eDHC with removal of the entire bone of the affected hemisphere significantly improves early mortality due to herniation in patients suffering from MMI without increasing the risk of severe surgery-related complications in our setting.

At present, 22–33% of all MMI patients die within the first few days after DHC, which may be partially attributed to an insufficient decompression in these patients [6, 9, 18]. Although the optimal size of decompression remains unknown, previous studies have argued for a diameter of at least 12 cm to provide sufficient volume for the swollen brain to occupy [1, 15, 16], since the beneficial effect of an eDHC is most probably due to a larger volume created by the craniectomy. This hypothesis appears in line with the present analysis, showing that the volume occupied by swollen tissue in patients who received eDHC (110.7 ml) was compensated by the volume created by the extended craniectomy (131.8 ml). Moreover, the beneficial effect of eDHC was not associated with differences between other relevant infarct or treatment characteristics, and eDHC was not only associated with a lower rate of transtentorial herniation but also with a significant reduction of tissue swelling despite equal volumes of infarction, which argues against the assumption that decompressing brain tissue with cerebral edema may give rise to an exaggerated swelling [22–24]. The observation that there was no statistical difference in ICP crisis may seem counter-intuitive at first sight but is in line with a case-series including 19 patients with mean ischemic tissue volume of 241.3 ± 83 cm^3 and mean midline shift of 6.7 ± 2 mm. Interestingly, ICP values were always <20 mm Hg in 12 patients (73.2%) and even in 2 patients with anisocoria [25]. Despite the known limita-

Table 1. Demographical and clinical characteristics of the patients

Characteristics	Extended hemicraniectomy (n = 40)	Standard hemicraniectomy (n = 57)	p value
Age, years, median (IQR)	57 (47–64)	54 (48–62)	0.77
Age group, years, n (%)			0.84
<55	19 (47.5)	29 (50.9)	
≥55	21 (52.5)	28 (49.1)	
Gender, n (%)			0.53
Female	14 (35.0)	24 (42.1)	
Male	26 (65.0)	33 (57.9)	
NIHSS total score			0.39
Assessable, n (%)	21 (53)	7 (12)	
Median (IQR)	18 (14–21)	20 (17–20)	
Site of infarction, n (%)			0.62
MCA	19 (57.6)	32 (60.4)	
MCA and anterior cerebral artery	10 (30.3)	15 (28.3)	
MCA and posterior cerebral artery	1 (3.0)	4 (7.5)	
Middle anterior and posterior cerebral artery	3 (9.1)	2 (3.8)	
Stroke in dominant hemisphere, n (%)	17 (42.5)	16 (28.1)	0.19
Time to treatment, h, n (%)			0.71
<49	25 (83.3)	23 (88.5)	
≥49	5 (16.7)	3 (11.5)	
Time to treatment, h, mean ± SD	45.3±37.0	31.0±16.8	0.08
Estimated blood loss, liters, mean ± SD	0.84±0.62	0.65±0.77	0.21
Postoperative ICP crises, n (%)			0.30
None	24 (63.2)	18 (58.1)	
1–10	9 (23.7)	5 (16.1)	
11–20	1 (2.6)	0 (0.0)	
>20	4 (10.5)	8 (25.8)	
ICP lowering therapies, n (%)			0.55
None	14 (35.9)	16 (39.0)	
1	14 (35.9)	8 (19.5)	
2	4 (10.3)	7 (17.1)	
3	5 (12.8)	7 (17.1)	
4	2 (5.1)	3 (7.3)	
Postoperative local/CNS infections, n (%)			0.43
None	37 (94.9)	39 (88.6)	
Wound healing deficit	0 (0.0)	3 (6.8)	
Meningitis	1 (2.6)	1 (2.3)	
Both	1 (2.6)	1 (2.3)	
Postoperative systemic infections, n (%)			0.10
None	12 (30.8)	5 (12.5)	
Pneumonia	17 (43.6)	28 (70.0)	
Urinary tract infection	4 (10.3)	2 (5.0)	
Other	6 (15.4)	5 (12.5)	
Time of intubation, h, mean ± SD	182.3±159.2	215.1±207.9	0.44
Time stroke to rehabilitation, days, mean ± SD	17.6±9.6	18.4±15.0	0.78
In hospital mortality, overall, n (%)	5 (12.5)	10 (17.5)	0.58
In hospital mortality, d/t herniation, n (%)	0 (0.0)	6 (10.5)	0.04*

Differences in corresponding total numbers to 40 respectively 57 result from missing specifications. Chi-square test, except * $p < 0.05$.

IQR = Interquartile range; CNS = central nervous system; mRS = modified Rankin Scale; NIHSS = National Institute of Health Stroke Scale.

Table 2. Imaging characteristics of the patients

Characteristics	Extended hemicraniectomy (n = 40)	Standard hemicraniectomy (n = 57)	p value
Infarct-associated volumetric analysis			
Vol. hemisphere ipsilateral (n = 90), ml	643.7±86.4	661.2±83.0	0.33
Vol. hemisphere contralateral (n = 90), ml	536.6±58.7	531.3±64.8	0.69
Vol. gain (n = 89), ml	110.7±47.3	130.0±46.3	0.06
Swelling (n = 89), %	20.6±8.2	24.7±9.2	0.03*
Swelling/100 ml infarction (n = 89)	7.4±2.5	11.0±6.4	0.001*
Vol. infarction (n = 90), ml	346.7±115.4	323.3±113.4	0.34
Vol. infarction corrected (n = 89), ml	287.8±80.8	260.0±93.4	0.14
Midline shift (n = 80), mm	3.4±3.4	3.6±2.8	0.75
Bone-flap associated volumetric analysis			
Vol. craniectomy bone (n = 90), ml	131.8±32.9	95.5±24.8	<0.001*
Craniotomy length (n = 84), mm	152.7±9.4	121.0±13.8	<0.001*
Craniotomy height (n = 84), mm	90.3±8.5	86.1±9.3	0.04*
Craniotomy width (n = 84), mm	44.0±11.3	20.8±9.0	<0.001*
Spherical length (n = 82), mm	262.3±17.1	131.5±19.2	<0.001*

Differences in corresponding total numbers to 40 respectively 57 result from missing specifications. Chi-square test, except * $p < 0.05$.

IQR = Interquartile range; CNS = central nervous system; mRS = modified Rankin Scale. Vol. = volume; Vol. infarction = ischemic brain tissue and edema; Vol. infarction corrected = ischemic brain tissue only; Vol. gain = volume of the ipsilateral hemisphere minus volume of the contralateral hemisphere corresponding to volume of swelling; swelling/100 ml = volume of tissue swelling corrected for volume of infarction.

tions of retrospective study protocols, the observed beneficial effects could be explained by the following main factors. First, small craniectomies bear a high risk for complications such as increased tissue swelling secondary to shear forces and venous congestion at the edge of the craniectomy [12]. Second, observational studies in animals and humans have shown that DHC improves cerebral blood flow, brain tissue oxygenation and perfusion of leptomeningeal collaterals, which together could prevent further infarct propagation and reduce tissue swelling [26, 27].

Most importantly, eDHC did not seem to bear a higher surgical risk than sDHC in our institution and intraoperative complications such as bleeding from the sinus and arachnoid granules were successfully managed without significant blood loss or air embolism. Furthermore, perioperative blood loss, postoperative infections, duration of intubation and time to rehabilitation did not differ between groups, which is in line with a previous report on 60 patients who were treated with sDHC in 2001 and a recent publication from 2011 on 25 patients with large craniectomies, where surgical revision was necessary in only 1 patient because of an epidural hematoma [12, 28]. In contrast to our protocol, however, in both these studies, DHC was performed as a rescue treatment at a time when signs of herniation were already present. Therefore, the preventive nature of the early decompression in the present analysis may have had a secondary positive effect on surgery-associated complications. Nevertheless, it should be noted that in-hospital mortality was not significantly reduced by eDHC, which is most likely due to the high risk of secondary complications in MMI, such as prolonged intensive care treatment, sepsis or cardiopulmonary insufficiency, among others.

Naturally, the retrospective and single-center design of our study bears well-known limitations. There may be selection bias as the decision to perform sDHC or eDHC was left at the discretion of the treating surgeon. There may also be information bias because of missing data as outlined in the tables, which may underestimate potential confounders. With respect to the safety of eDHC it is very important to emphasize that intraoperative complications, especially bleedings from the sinus in 2 patients, are life-threatening events in inexperienced surgeons. However, we had a positive experience with performing the procedure cautiously following the above-mentioned protocol. Furthermore, although we did not observe an increase in complications after ex-

tended craniectomy, the procedure can still be associated with a higher morbidity, which may have escaped our observation by coincidence or due to other reasons like systematic biases that none of the authors thought of. In particular, we did not obtain data on long-term outcome in a standardized fashion and are thus not able to report reliable information on delayed complications of eDHC, such as postoperative hydrocephalus or problems with wound healing following CP. Finally, explanations for reduced brain swelling in eDHC remain speculative, as we did not obtain measurements of cerebral hemodynamics, cerebral microvascular reactivity or cerebral metabolic activity.

In conclusion, our study suggests that eDHC may be used to effectively reduce early mortality due to transtentorial herniation in patients with MMI. The beneficial effect is most likely related to the larger additional volume created by the extended craniectomy and seems to be associated with reduced cerebral swelling. Although the technique appears to be feasible and safe, these results need to be validated in a prospective setting before general recommendations can be made.

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