Intracranial pressure in patients undergoing decompressive craniectomy: new perspective on thresholds

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OBJECTIVE Decompressive craniectomy (DC) is an established part of treatment in patients suffering from malignant infarction of the middle cerebral artery (MCA) or traumatic brain injury (TBI). However, no clear evidence for intracranial pressure (ICP)-guided therapy after DC exists. The lack of this evidence might be due to the frequently used, but simplified threshold for ICP of 20 mm Hg, which determines further therapy. Therefore, the objective of this study was to evaluate this threshold's accuracy and to investigate the course of ICP values with respect to neurological outcome.

METHODS Data on clinical characteristics and parameters of the ICP course on the intensive care unit were collected retrospectively in 102 patients who underwent DC between December 2007 and April 2014 at the authors' institution. The postoperative ICP course in the first 168 hours was recorded and analyzed. From these findings, ICP thresholds discriminating favorable from unfavorable outcome were calculated using conditional inference tree analysis. Additionally, survival analysis was performed using the Kaplan-Meier method. Prognostic factors were assessed via univariate analysis and multivariate logistic regression. Favorable outcome was defined as a score of 0–4 on the modified Rankin Scale.

RESULTS Multivariate logistic regression revealed that anisocoria, diagnosis, and ICP values differed significantly between the outcome groups. ICP values in the favorable and unfavorable outcome groups differed significantly ($p < 0.001$), while the mean ICP of both groups lay below the limit of 20 mm Hg (17.5 and 11.5 mm Hg, respectively). These findings were reproduced when analyzing the underlying pathologies of TBI and MCA infarction separately. Based on these findings, optimized time-dependent threshold values were calculated and found to be between 10 and 17 mm Hg. These values significantly distinguished favorable from unfavorable outcome and predicted 30-day mortality ($p < 0.001$).

CONCLUSIONS This study systematically evaluated ICP levels in a long-term analysis after DC and provides new, surprisingly low, time-dependent ICP thresholds for these patients. Future trials investigating the benefit of ICP-guided therapy should take these thresholds into consideration and validate them in further patient cohorts.

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KEY WORDS intracranial pressure; decompressive craniectomy; stroke; traumatic brain injury; neurocritical care; diagnostic technique

DECOMPRESSIVE craniectomy (DC) has been a well-established neurosurgical intervention for more than 100 years in patients suffering from space-occupying cerebral infarctions of the middle cerebral artery (MCA) and leads to reduced intracranial pressure (ICP).²⁴ DC verifiably prevents secondary brain injury,

optimizes perfusion of the penumbra, and results in an overall reduction in mortality and an improvement in functional recovery, especially in younger patients.^{23,41} The lifesaving benefit and outcome improvement of the DC has been proven by several randomized controlled studies in the past.^{16,22,23,41} DC is also a common treatment in patients

ABBREVIATIONS AUC = area under the curve; BEST-TRIP = Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure; CPP = cerebral perfusion pressure; DC = decompressive craniectomy; EVD = external ventricular drain; GCS = Glasgow Coma Scale; ICM = Integrated Care Manager; ICP = intracranial pressure; ICU = intensive care unit; MCA = middle cerebral artery; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; RASS = Richmond Agitation Sedation Scale; SAPS = Simplified Acute Physiology Score; SDH = subdural hematoma; TBI = traumatic brain injury.

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with traumatic brain injury (TBI), although clear evidence from prospective clinical trials is subject to ongoing clinical and ethical discussions.^{10,19,35}

Regardless of the underlying diagnosis, brain ischemia and injury may lead to an increased ICP caused by cerebral edema.⁸ ICP monitoring is generally recommended for patients with severe TBI.^{2,39} There are no guidelines for ICP monitoring in patients suffering from malignant MCA infarction, but ICP monitoring after DC is often part of further therapy in the intensive care unit (ICU).²¹

Although ICP monitoring is a common practice, there is no Level I evidence for the benefit of ICP monitoring and ICP-guided therapy. A recently published prospective controlled trial failed to fill this void.⁹ The Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure (BEST:TRIP) trial showed that ICP-guided treatment does not lead to increased therapeutic success compared with a CT-based clinical assessment.⁹ The authors of this study expressed concern that these findings may lead to a premature end of ICP monitoring in ICUs and noted that the failure of ICP-guided therapy may be due to simplified strategies and the lack of evidence for 20 mm Hg as the threshold, although this determines further therapy.^{6,7}

This lack of evidence and the simplified threshold of 20 mm Hg should be questioned even more in patients after DC, because the integrity of the skull is compromised and the physical preconditions are completely different. Factors associated with favorable outcome remain a matter of debate and ICP recordings did not sufficiently correlate with neurological outcome.^{32,38} It is undisputed that ICP decreases rapidly after DC in patients with TBI or MCA infarction,³⁰ but little data are available on the ICP course following DC, because most studies evaluated only a small number of patients with a limited recording of ICP values.^{25,29,31,32,38} In particular, the validity of the ICP threshold has not been addressed thoroughly. The present recommendations regarding ICP thresholds do not take surgical interventions into consideration or the lack of clear evidence.^{3,21}

The aim of this single-center study was to analyze the ICP level and course after DC in patients with cerebral infarction and TBI and to correlate these parameters with the neurological outcome. Particular emphasis was placed on the evaluation of the commonly accepted ICP threshold of 20 mm Hg.

Methods

This single-center study retrospectively analyzed patients who underwent unilateral decompressive craniectomy from December 2007 through April 2014. To increase comparability, only TBI patients with an acute subdural hematoma (SDH) causing a critical mass effect on the brain were enrolled in this study. Procedures that were not comparable due to the use of a different surgical technique (such as bifrontal decompressive craniectomy) or patient criteria (age < 14 years, death before arriving at the ICU) were excluded. The patients' postsurgical ICP values for the next 168 hours following DC, as well as their functional outcome assessed via the modified Rankin Scale (mRS)

at the end of rehabilitation, were analyzed. Favorable outcome was defined as a score of 0–4 on the mRS according to Vahedi et al.⁴¹ This study was conducted according to the Declaration of Helsinki, local and institutional laws, and was reported to the local ethics committee.

Clinical Data

Demographic and clinical data were collected, including sex, age, primary diagnosis, side and size of DC, pupillary status, duration of sedation, Glasgow Coma Scale (GCS) score, and National Institutes of Health Stroke Scale (NIHSS) score. The patients' level of sedation was measured using the Richmond Agitation Sedation Scale (RASS) and logged initially after DC and subsequently once every 24 hours.³⁷ The presence of postoperative anisocoria was recorded.

To determine the patients' morbidity, the Simplified Acute Physiology Score (SAPS) II on the day of surgery was analyzed.²⁶ The SAPS II was calculated semiautomatically via the clinical information system (Integrated Care Manager [ICM], Dräger), which filters all relevant data in a given 24-hour period for the worst value. The size of the trepanation (A) was calculated by the formula: $A = \pi/4 \times b \times c$, in which b is the maximal frontooccipital and c is the maximal parietotemporal extent of the defect.¹¹ These data were collected on postoperative CT scans.

Treatment

Indication for surgical decompression in patients with TBI and acute SDH followed the recommendations of Bullock et al. and/or the German TBI Guidelines (The Association of the Scientific Medical Societies in Germany, 2015) based on the clinical status (age, GCS score, anisocoria) and CT scan (thickness of SDH, midline shift) in an interdisciplinary case-by-case discussion.^{4,14} If a DC was indicated, surgery began as soon as possible. Concurrently, conservative treatment was started using a standardized protocol. Blood gases were analyzed frequently (at least every 4 hours). Continuous monitoring of electrocardiography, oxygen saturation, arterial blood pressure, and respiratory minute volume and tidal volume was performed.

In patients suffering from MCA infarction at risk for a malignant clinical course, the indication for early DC was verified by the senior neurosurgeon and the senior neurologist in charge. The decision was based on the patient's characteristics (age, medical history, laboratory findings), neurological condition (clinical examination, NIHSS score, GCS score), imaging, exhausted conservative treatment, time since onset of the neurological symptoms, and clinical deterioration according to treatment recommendations.¹⁹

Postsurgical treatment on the ICU included ICP-guided therapy according to current guidelines.²¹ This treatment included elevation of the head by 20°–30°, hemodynamic stabilization to avoid hypotension (systolic blood pressure < 90 mm Hg) and hypoxia (PaO_2 < 60 mm Hg), sedation, and hyperosmolar therapy. Patients were ventilated in biphasic positive airway pressure mode (Evita Infinity V500 Ventilator, Dräger) with the aim of maintaining physiological pH and lower normal PaCO_2 (35–38 mm Hg).

DC and ICP Monitoring

A question mark-shaped skin incision was made frontoparietotemporally, ending approximately 10 mm anterior to the tragus, followed by retraction of the musculocutaneous flap, removal of the bone flap, and dural opening.^{20,35} Before readapting the temporalis muscle and scalp flap, an intraparenchymal ICP monitor (Codman MicroSensor, Johnson & Johnson Professional Inc.) was placed ipsilaterally at the end of surgery according to the recommendations of the Milan consensus conference on ICP monitoring and current guidelines.^{21,39}

ICP values and mean arterial pressure were measured continuously. Based on these measurements, cerebral perfusion pressure (CPP) values were calculated. These measurements were performed automatically and stored in the clinical information system (ICM) beginning at arrival in the ICU. Hourly ICP and CPP values were extracted for the first 168 hours following DC and used to perform further statistical analyses. A total of more than 22,000 ICP and CPP values were analyzed in this study.

Statistical Analysis

Continuous data are presented as means and ranges. The Wilcoxon rank-sum test was used to compare non-parametric values. Comparisons including multiple ICP values were corrected for repeated measures. Categorical data are presented as counts and percentages and were compared using chi-square and Fisher's exact tests. The prognostic significance of the models was analyzed via multivariate logistic regression. ICP thresholds were assessed using conditional inference tree analysis.¹⁷ Survival analysis was performed using the Kaplan-Meier method and log-rank test. Statistical analyses were performed using IBM SPSS (version 19, IBM Corp.) and MATLAB R2014b (The MathWorks, Inc.). Probability values < 0.05 were considered statistically significant.

Results

A total of 102 patients (38 females, 37.3%) were included in this study. The mean age of the cohort was 53.2 years (range 14–79 years). Fifty-seven patients underwent DC due to a space-occupying MCA infarction and 45 patients suffered from an acute SDH due to severe TBI. In detail, 33 patients (73.3%) suffered from an acute SDH with a thickness of more than 10 mm and/or a midline shift of more than 5 mm, regardless of the GCS score, while 8 comatose patients (17.8%) presented with an SDH of less than 10-mm thickness and a midline shift of less than 5 mm, but presented with either a drop in the GCS score of more than 2 points or asymmetrical or fixed and dilated pupils. In 4 patients the decision was based on a clinical decision according to the German TBI guidelines.

Forty-two patients (41%) showed a favorable outcome at the end of rehabilitation (mean follow-up of 129 days after DC). No statistically significant differences between the outcome groups were detected regarding sex, age, side of DC, size of trepanation, GCS score, NIHSS score, RASS score, SAPS II, or presence of an external ventricular drain (EVD; Tables 1 and 2). EVDs were only present in 4 patients in the unfavorable outcome group (2 patients

TABLE 1. Demographic and clinical parameters separated by outcome

Characteristic	mRS Score 0–4 (favorable)	mRS Score 5–6 (unfavorable)	p Value
No. of patients	42	60	
Sex (%)			NS
Males	23 (54.8)	41 (68.3)	
Females	19 (45.2)	19 (31.7)	
Diagnosis (%)			0.003*
TBI	11 (26.2)	34 (56.7)	
MCA infarction	31 (73.8)	26 (43.3)	
Mean age in yrs (range)	52.2 (23–72)	53.9 (14–79)	NS
Side (%)			NS
Rt	23 (54.8)	37 (61.7)	
Lt	19 (45.2)	23 (38.3)	
GCS score			NS
No. completed (% valid)	36 (85.7)	57 (95.1)	
Mean score (range)	9.5 (3–15)	8.8 (3–15)	
Anisocoria (%)	20 (47.6)	42 (70.0)	0.026†
Mean size of trepanation in cm ² (range)	128.8 (82.5–168.0)	122.7 (64.0–165.7)	NS
Mean RASS score (range)	–3.7 (–5 to 0)	–3.9 (–5 to 3)	NS
Mean SAPS II (range)	40.3 (17–68)	45 (21–91)	NS
EVD (%)	0 (0)	4 (6.7)	NS
Mean ICP ± SD of the first 168 hrs (mm Hg)	11.5 ± 1.4	17.5 ± 3.4	<0.001‡

NS = not significant.

* Significant in multivariate analysis ($p < 0.01$).

† Significant in multivariate analysis ($p < 0.05$).

‡ Assessed with the Wilcoxon rank-sum test.

with mRS scores of 6). Univariate analysis revealed that anisocoria and diagnosis differed between the outcome groups.

In 91.2% of the patients with MCA infarction, DC was performed within the first 72 hours after onset of neurological symptoms and 75.4% within the first 48 hours.¹⁹ We performed a subgroup analysis and compared clinical characteristics and outcomes in patients with DC less than 48 hours versus patients in whom DC was performed more than 48 hours after stroke onset. We found no significant differences regarding age ($p = 0.977$), NIHSS score ($p = 0.231$), anisocoria ($p = 0.708$), mean ICP ($p = 0.330$), SAPS II ($p = 0.992$), and mRS score ($p = 0.303$).

ICP Analysis of the First 168 Hours

The mean ICP values in both outcome groups were analyzed. Figure 1 shows an ICP-versus-time plot of the first 168 hours after DC. The ICP values of the favorable outcome group (mRS score 0–4) started and remained at

TABLE 2. Demographic and clinical parameters separated by outcome and diagnosis

Characteristic	mRS Score 0–4		mRS Score 5 or 6		p Value
	TBI	MCA Infarction	TBI	MCA Infarction	
No. of patients	11	31	34	26	
Sex (%)					NS
Males	5 (45.5)	18 (58.1)	26 (76.5)	15 (57.7)	
Females	6 (54.5)	13 (41.9)	8 (23.5)	11 (42.3)	
Mean age $\pm$ SD (yrs)	50.7 $\pm$ 16.6	52.7 $\pm$ 9.7	54.4 $\pm$ 19.6	53.3 $\pm$ 12.0	NS
Side (%)					NS
Rt	7 (63.6)	16 (51.6)	21 (61.8)	16 (61.5)	
Lt	4 (36.4)	15 (48.4)	13 (38.2)	10 (38.5)	
Mean GCS score $\pm$ SD	5.8 $\pm$ 4.3	10.9 $\pm$ 4.2	7.7 $\pm$ 4.7	10.4 $\pm$ 4.3	NS/<0.001*
Mean NIHSS score $\pm$ SD		16.2 $\pm$ 6.6		15.7 $\pm$ 4.1	NS
Anisocoria (%)	4 (36.4)	16 (51.6)	23 (67.6)	19 (73.1)	NS
Mean size of trepanation $\pm$ SD (cm ²)	129.8 $\pm$ 27.7	128.5 $\pm$ 20.0	116.8 $\pm$ 25.5	130.6 $\pm$ 16.3	NS
Mean RASS score $\pm$ SD	-2.8 $\pm$ 2.6	-3.7 $\pm$ 0.7	-4.2 $\pm$ 0.9	-3.3 $\pm$ 1.5	NS
Mean SAPS II $\pm$ SD	47.6 $\pm$ 12.0	37.5 $\pm$ 13.5	48.4 $\pm$ 14.8	40.0 $\pm$ 14.5	NS/0.008*
EVD (%)	0 (0)	0 (0)	3 (9)	1 (4)	NS

* Nonsignificant p values between the outcome groups, but significant differences between the diagnoses.

lower levels than those of the unfavorable group (mRS score 5 or 6). Values did not exceed 14 mm Hg (mean 11.5 mm Hg, maximum 13.4 mm Hg) at any point in the favorable group.

The ICP values in the unfavorable group were higher but rarely exceeded 20 mm Hg (mean 17.5 mm Hg [168 hours], range 10.7–25.0 mm Hg). In the first 72 hours, the ICP values of the unfavorable group were below 20 mm

FIG. 1. Graph of the mean ICP in the first 168 hours after DC. **A:** In the favorable outcome group (blue curve) the mean ICP was 11.5 mm Hg compared with 17.5 mm Hg in the unfavorable group (red curve; $p < 0.001$). The blue curve does not exceed 14 mm Hg, and even the red curve stays predominantly below the limit of 20 mm Hg. In the first 72 hours the red curve barely exceeds 20 mm Hg. Error bars indicate the standard error of the mean. **B:** Distributions of the scores on the mRS in the entire cohort. Figure is available in color online only.

FIG. 2. Graphs of mean ICP separated by diagnosis. **A:** Mean ICP in the first 168 hours after DC in patients with malignant MCA infarction. The mean ICP was 11.7 mm Hg in the favorable group (blue curve) and 19.7 mm Hg in the unfavorable group (red curve; $p < 0.001$). No crossing of the 20 mm Hg threshold occurred during the first 57 hours. **B:** Mean ICP in the first 168 hours after DC in patients with TBI. Mean ICP was 10.9 mm Hg in the favorable group (blue curve) compared with 15.8 mm Hg in the unfavorable outcome group (red curve; $p < 0.001$). The mean ICP did not exceed 20 mm Hg in the first 31 hours after DC. Figure is available in color online only.

Hg (mean 17.2 mm Hg). The mean ICP values crossed the 20 mm Hg threshold on only 11 occasions (15.1%). In 31 patients (51.7%) with an unfavorable outcome, the ICP values did not exceed 20 mm Hg at any point during the first 3 days. When corrected for repeated measures, statistical analysis revealed a significant difference ($p < 0.001$) between the 2 groups. In the last few hours of ICP measurement, the curves began to approximate each other. The mean ICP curves were also analyzed separated by diagnosis. In both subgroups the mean ICP in the first 168 hours was below 20 mm Hg in the favorable and unfavorable outcome groups. More precisely, the ICP values of the favorable outcome group remained below 15 mm Hg regardless of the underlying diagnosis (Fig. 2).

In the following sections, only the results of analyses of ICP values are presented because the analysis of CPP val-

ues did not provide additional information in our cohort (for an overview of the CPP course, see Supplementary Fig. 1).

Predictive Power Analysis (receiver operating characteristic)

Based on the results of the univariate analysis, diagnosis, anisocoria, and the mean ICP in the first 12 hours were tested further regarding their prognostic value using multivariate logistic regression. Figure 3 shows the predictive power of diagnosis, ICP, and anisocoria compared with diagnosis and SAPS II as a validated score to assess hospital mortality, regardless of the underlying diagnosis.^{15,26,34} Combining diagnoses, ICP and anisocoria resulted in a significantly larger area under the curve (AUC; 0.837 vs

FIG. 3. Significance of mean ICP (12 hours) in outcome prediction. In this receiver operating characteristic curve, the models for outcome prediction detected via multivariate logistic regression are displayed. Models were tested for correct outcome prediction against the null hypothesis. Diagnosis and SAPS II showed an AUC of 0.707. Including diagnosis, ICP, and anisocoria resulted in a significantly higher AUC of 0.837 ($p < 0.001$, DeLong test). CI = confidence interval.

0.707, $p < 0.001$), while adding SAPS II to the calculation did not further improve its significance (data not shown).

Threshold Analysis

Because the mean ICP values of both outcome groups clearly lay below 20 mm Hg and their predictive power

could be demonstrated, new threshold values discriminating the outcome groups were calculated. These optimized threshold values were determined by conditional interference tree analysis in several time periods (Fig. 4). Twelve-hour time frames were used for the calculation. Due to the dynamics of the ICP values, 6-hour intervals were chosen to achieve better resolution during the first 48 hours. These new thresholds were between 9.8 mm Hg and 16.9 mm Hg and were able to significantly distinguish favorable from unfavorable outcome. Between hours 12 and 24 the calculated values were not quite significant. After 120 hours, no significant threshold values could be calculated.

Kaplan-Meier Survival Estimates

With the aim of detecting an early predictive parameter regarding survival, an ICP threshold was calculated via conditional inference tree analysis based on the ICP values of the first 12 hours. As a result, 15 mm Hg was determined as the cutoff value between a low and a high ICP group. The Kaplan-Meier method was used to analyze the 30-day survival rate in both groups, showing a significantly higher survival rate in the low ICP group ($p < 0.001$; Fig. 5). The survival probability of the low ICP group was above 75%. In the high ICP group, survival probability fell below 40% in the first 10 days following DC.

Discussion

Our study demonstrates that in a selected study population, postsurgical ICP values differed between the favorable and unfavorable outcome groups. Surprisingly, the mean ICP values were generally below 20 mm Hg in both outcome groups. As expected from pathophysiological mechanisms, the ICP values of the unfavorable outcome group were consistently higher than those of the favorable group.²⁷ This difference was observed regardless of the

FIG. 4. Calculated ICP thresholds in the first 168 hours after DC. * $p < 0.05$, ** $p < 0.01$, ns = not significant, for the conditional inference tree analysis. Figure is available in color online only.

FIG. 5. Kaplan-Meier survival curves for the first 30 days after DC. Comparison of the 30-day survival probability of patients with low ICP (mean ICP ≤ 14.9 mm Hg; blue curve) with that for patients with high ICP (mean ICP ≥ 15.0 mm Hg; red curve) showed significantly higher survival in the low ICP group ($p < 0.001$, log-rank test, merged diagnoses). Figure is available in color online only.

underlying diagnosis. In the last few hours of ICP measurement the curves began to approximate each other due to the dropout of patients who had died.

The type of ICP monitoring was standardized in our study, because only ipsilateral intraparenchymal probes were used. The accuracy and comparability of this technique has recently been proven.⁴² Prospective analyses conducted with the ICP sensor used have demonstrated an overall small zero drift of 2.0 mm Hg over more than 100 hours.¹ Thus, relevant drifts occurred in a small number of cases. Because zero drift increases over time, it is unlikely to confound the results presented here, because the further analysis of the ICP thresholds was based on the initial period after DC (Figs. 3–5).

To assess the extent of sedation as a possible confounder of the ICP level, the RASS score was used as an established reliable parameter of sedation status.¹³ Because all patients in this study were deeply sedated postoperatively, the RASS score did not differ between the 2 outcome groups. The level of sedation was therefore unlikely to be a confounder regarding patient ICP.

In the next step, the early postsurgical ICP values combined with diagnosis and anisocoria showed a highly predictive power in determining the neurological outcome after rehabilitation. This finding demonstrates the value of the ICP level as an independent predictor, whereas SAPS II did not show any additional predictive power. This finding may be a result of the highly selected subgroup of surgically treated neurointensive care patients. SAPS II primarily focuses on nonneurological parameters and therefore might not be suitable for assessing functional outcome in our cohort.^{36,40} GCS score alone did not differ in the outcome groups either, reflecting its vague significance in outcome prediction.³³ Anisocoria was associated with an unfavorable outcome as previously demonstrated.²⁸ In the TBI group, we focused on patients with acute SDH as the leading radiological finding, because the indication for surgery is well defined in these cases.^{4,14} However, DC is

often performed in diffuse TBI as well, and this remains to be studied.

The mean ICP values of both outcome groups lay well below 20 mm Hg. Moreover, the analysis of the ICP course revealed a surprisingly low range of values in the unfavorable outcome group, predominantly staying below the threshold of 20 mm Hg, especially in the first 72 hours after intervention. Therefore, the 20 mm Hg threshold was unable to distinguish between the outcome groups. In general, 20–25 mm Hg is recommended as the threshold above which additional therapy should be strongly considered, yet Level I evidence is missing due to insufficient studies.^{3,27} As a consequence, we calculated new time-dependent threshold values and investigated their correlation with neurological outcome (Figs. 4 and 5). These calculations revealed that a mean ICP value below 15 mm Hg in the first 12 hours was associated with lower mortality. Moreover, our findings suggest a higher probability of favorable neurological outcome in a time-dependent corridor between 10 and 17 mm Hg in patients after DC.

Courses of CPP were also evaluated analogously (see Supplementary Fig. 1). Because CPP values differed significantly in both outcome groups, a confounding effect of lower mean arterial pressure in patients with unfavorable outcome appears unlikely.

The surprisingly low calculated threshold values may be due to the previously performed DC. This may lead to the missing evidence of the benefit of ICP monitoring and ICP-guided therapy.^{5,6} Studies evaluating the use of ICP-guided therapy in patients suffering from TBI or malignant MCA infarction may have failed due to a higher and fixed threshold that served as the crucial parameter for further therapeutic interventions or clinical assessment.^{6,9,32} In the BEST:TRIP trial, almost one-third of the patients in the pressure-monitoring group and in the imaging-clinical examination group received a craniectomy.⁹ This may have influenced the overall findings, because 20 mm Hg was the treatment threshold, regardless of neurosurgical procedures.

Although lower ICP thresholds guiding therapeutic strategies in patients after craniectomy have been discussed previously, this has not had an effect on current guidelines and further studies.^{3,12} Our study offers a new perspective on the current nonspecific threshold concept.

However, the question remains whether ICP-guided treatment has a positive impact on clinical outcome. This is beyond the scope of this analysis and will have to be assessed via prospective randomized controlled trials. Our study does not prove the benefit of ICP monitoring but it does provide, for the first time, a systematic analysis of ICP thresholds in patients undergoing DC. Because we found remarkably low ICP values in both outcome groups following DC, it will be necessary to reassess the ICP thresholds used to guide therapy in future studies. Furthermore, there might be a need to review ICP thresholds at an individual level in all subgroups of neurological patients in which ICP-guided therapy is applied, because ICP values are likely to differ significantly in patients with an intact cranium. New individualized, multimodal ICP threshold strategies need to be established based on an improved evidence level. This may prevent the unjustified abandon-

ing of ICP measurement as an easily accessible real-time tool in the ICU.

Surprisingly, the ICP courses were quite similar for both diagnoses, although they reflect completely different mechanisms of brain injury. The different pathological mechanisms of TBI and MCA infarction are, of course, beyond question. Yet, our findings regarding ICP thresholds after DC appear to be valid for both diagnoses as shown by our analyses.

The major limitations of our study are its retrospective design and single-center character. Patients who died on emergency department arrival or directly after surgery did not receive an ICP sensor or no ICP recordings could be performed. This might be a potential bias in the study results. However, our patient cohort contained those patients in whom ICP recording after DC might have been in any way relevant and reflects the reality of a specialized neuro-intensive care unit. We also excluded patients operated on using different surgical techniques (for example, bifrontal decompression) and patients with insufficient ICP recordings or clinical data. The goal of the study was to investigate ICP thresholds over a period of 7 days in an ICU after DC and therefore it cannot prove the effectiveness of ICP-guided therapeutic concepts at all. We demonstrated that the ICP level in almost all patients, regardless of the pre-existing brain damage, rarely exceeded 20 mm Hg, which does not prove that lowering ICP levels is clinically useful. Furthermore, our analysis was not designed to determine ICP cutoffs as an indication for surgery. Nevertheless, we are convinced that our study produced valid and detailed data on ICP values after DC and will provide an impetus for further investigation of this topic.

Conclusions

Our study suggests a new time-dependent threshold based on the ICP analysis of the first 168 hours after DC. This paper cannot provide therapeutic evidence but does give a new perspective on ICP monitoring. As a consequence, therapeutic concepts based on 20 mm Hg as an established but unproven cutoff should be reconsidered and evidence-based thresholds are needed for future trials. Individual thresholds would ensure that the therapeutic concept is more than a paradigm of keeping the pressure below a fixed threshold.

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Disclosures

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Author Contributions

Conception and design: Sauvigny, Götsche. Acquisition of data: Sauvigny, Götsche. Analysis and interpretation of data: Sauvigny, Götsche, Czorlich, Vettorazzi. Drafting the article: Sauvigny, Götsche, Czorlich. Critically revising the article: Sauvigny, Götsche, Westphal, Regelsberger. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Sauvigny. Statistical analysis: Sauvigny, Vettorazzi. Administrative/technical/material support: Götsche. Study supervision: Westphal, Regelsberger.

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