Child's Nervous System (2019) 35:1517–1524
https://doi.org/10.1007/s00381-019-04303-z

ORIGINAL ARTICLE

From decompressive craniectomy to cranioplasty and beyond—a pediatric neurosurgery perspective

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Received: 23 May 2019 / Accepted: 8 July 2019 / Published online: 20 July 2019

Abstract

Purpose Decompressive craniectomy (DC) is an established neurosurgical emergency technique. Patient selection, optimal timing, and technical aspects related to DC and subsequent cranioplasty remain subjects of debate. For children, the overall degree of evidence is low, compared with randomized controlled trials (RCTs) in adults.

Methods Here, we present a detailed retrospective analysis of pediatric DC, covering the primary procedure and cranioplasty. Results are analyzed and discussed in the light of modern scientific evidence, and conclusions are drawn to stimulate future research.

Results The main indication for DC in children is traumatic brain injury (TBI). Primary and secondary DC is performed with similar frequency. Outcome appears to be better than that in adults, although long-term complications (especially bone flap resorption after autologous cranioplasty) are more common in children. Overt clinical signs of cerebral herniation prior to DC are predictors of poor outcome.

Conclusions We conclude that DC is an important option in the armamentarium to treat life-threatening intracranial hypertension, but further research is warranted, preferentially in a multicenter prospective registry.

Keywords Intracranial hypertension · Cranial reconstruction · Bone flap resorption

Background

The appeal of decompressive craniectomy (DC) as a universal treatment of severely raised intracranial pressure (ICP) is considerable, as it is a technically simple operation with logical pathophysiological benefit: DC is providing an additional space for a swollen brain by opening the "closed container" represented by the skull [1]. However, the impacts of primary and secondary brain injury have to be taken into account, as well as complications and limitations of DC itself and of subsequent cranioplasty [2, 3].

In adults, the RESCUEicp trial of delayed or secondary DC in patients with refractory intracranial hypertension (> 25 mmHg) after severe TBI indicated lower mortality compared with conservative management [4]. Another RCT (DECRA) had a lower ICP threshold (> 20 mmHg) and demonstrated lower mortality but more unfavorable outcomes after DC [5]. Uncertainty has also been demonstrated in clinical reality concerning primary DC for acute subdural hematoma [6]. This has led to a RCT investigating the role of primary DC (RESCUE-ASDH), but final results are pending [7].

For space-occupying (malignant) ischemic supratentorial stroke, several RCTs in adults (e.g., HAMLET, DECIMAL, and DESTINY I and II) demonstrated significant reduction of mortality, although DC renders a relevant proportion of patients with moderately severe disability [8–11].

In contrast, high-level evidence is unavailable for children. The only RCT in pediatric TBI suggested benefit of surgery without reaching statistical significance, and the surgical technique differed from what pediatric neurosurgeons would nowadays consider a standard DC [12]. Data for DC in pediatric stroke is limited to case series and anecdotal case reports [13–15]. To fill these evidence gaps, study results obtained from adult patients can only be extrapolated to children under a caveat: there are relevant differences in anatomy and physiology between adults and children, as well as within the pediatric age

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spectrum [16]. Additionally, a fixed point of outcome assessment as used in adults (e.g., after 12 months) might not adequately reflect impact of injuries or treatments on the developing brain, which would require longitudinal observation.

Current knowledge with regard to cranioplasty is based on low-level evidence in all age groups [17, 18]. Both autologous and alloplastic cranioplasties are associated with relevant complications. Outcome of autologous cranioplasty appears to be worse in children due to high rates of aseptic bone flap resorption. In the absence of reliable data on risk factors for failure of autologous implants, institutional protocols with regard to bone flap storage and timing of reimplantation vary significantly and no consensus exists.

Pooling of published data is hampered by heterogeneous data elements and missing information. A recent systematic review on pediatric cranioplasty reported resorption rates between 20 and 80%, but almost 50% of publications do not explicitly state resorption rates [18]. Few studies provide long-term information reaching from craniectomy to cranioplasty, although both operations are closely related and relevant to overall morbidity and outcome. We therefore provide a detailed analysis of a well-documented single-center cohort of children undergoing DC and subsequent cranioplasty.

Methods

This retrospective study covering the years 2010–2018 was approved by the ethics committee (study no. 2019-415-RetroDEuA). We included patients aged less than 18 years at the time of DC.

Radiological studies were retrieved and the following parameters measured as presented in Fig. 1: maximum fronto-occipital skull length was determined as an indicator of age-dependent skull size. Maximum anterior-posterior (A) and cranio-caudal (B) diameters of hemicraniectomies were used to calculate approximate decompression areas ($A \times B$). Maximum horizontal brain diameters were measured before (C) and after (D) hemicraniectomy as surrogate parameters of volume gain ($D - C$). If bone flap resorption occurred, it was classified according to the Oulu resorption score [19]. In the TBI subgroup, computed tomography (CT) characteristics were classified according to Rotterdam CT score [20].

Outcome was categorized according to King's Outcome Scale for Childhood Head Injury (KOSCHI) and trichotomized into good outcome (KOSCHI 4 and 5), poor outcome (KOSCHI 2 and 3), and death (KOSCHI 1) [21].

Statistical analysis was performed with GraphPad Prism (GraphPad Software, USA). Statistical significance was assessed using two-sided Student's t test and bivariate correlation with Pearson correlation coefficient.

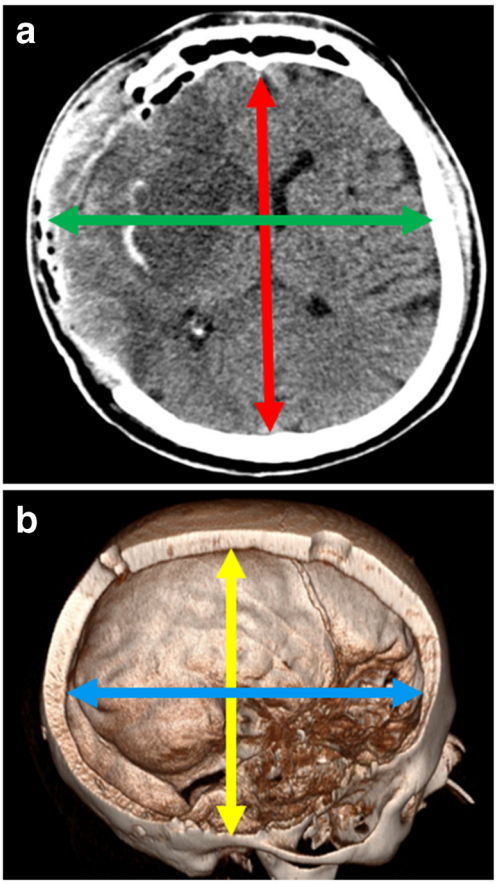

Fig. 1 Morphometric measurements obtained in this study. **a** Maximum fronto-occipital skull length was determined as an indicator of age-dependent skull size (red line). Maximum horizontal brain diameters were measured before (not shown) and after hemicraniectomy (green line) as a surrogate parameter of volume gain. **b** Maximum anterior-posterior (blue line) and cranio-caudal (yellow line) diameters of hemicraniectomies were used to calculate the approximate decompression area

Results

Decompressive craniectomy

Fifteen children (mean age 12 years, range 1–17) underwent DC for TBI ($N = 12$), hemorrhage ($N = 2$), or ischemic stroke ($N = 1$) within the study period (Table 1). We performed 9 unilateral hemicraniectomies, 3 bilateral hemicraniectomies, and 3 bifrontal craniectomies. Therapeutic pathways are summarized in Fig. 2. The surgical aim was a large craniectomy with wide dural opening and expansion duroplasty, using a xenogenic dural substitute (Tutopatch, Tutogen Medical GmbH, Germany). The standard procedure at our institution for a lateralized lesion is hemicraniectomy. Bilateral hemicraniectomy was performed for either significant bilateral lesions (such as temporal contusions) or patients who develop raised ICP or a new contralateral lesion after hemicraniectomy. Bifrontal DC was mainly performed for global cerebral edema without lateralization, as reflected by

the delayed timing of DC and absent midline shift in these patients (Table 1). Autologous bone flaps were cryoconserved at − 80 °C.

The TBI subgroup comprised 12 children (7 boys, 5 girls, mean age 12 years) with mean initial GCS of 4 (range 3–7) and mydriasis prior to DC in 6 cases. Trauma mechanisms were road traffic accidents (RTA) as a pedestrian/cyclist ($N = 6$), falls from large height ($N = 3$), RTA as a passenger ($N = 2$), and violence ($N = 1$). Median distance from the trauma scene to the tertiary care hospital was 19 km (range 4–56 km). Nine patients were transported directly, and 3 patients were first admitted to secondary care hospitals and referred after initial survey and imaging. No invasive measures were performed at these hospitals. Additional injuries were present in 11 children, mainly thoracic trauma. Initial CT findings were acute subdural hematoma ($N = 9$), traumatic SAH ($N = 8$), cerebral contusions ($N = 6$), skull fractures ($N = 7$), cerebral edema ($N = 5$), and signs of diffuse axonal injury ($N = 3$). Mean midline shift was 6 mm (range 0–16) and basal cisterns were compressed in 10 cases. The mean Rotterdam CT score for this subgroup was 5 (range 3–6). Immediate DC with evacuation of space-occupying traumatic lesions was performed in 7 children. The remaining children ($N = 5$) received ICP- and cerebral perfusion pressure (CPP)-guided therapy and underwent delayed DC for refractory intracranial hypertension and clinical/radiological signs of (impending) herniation at mean day 4 (range 1–6). Monitoring data from an exemplary case, including the immediate effect of DC on ICP and CPP, is presented in Fig. 3.

Intraoperative complications occurred in two children, who both died in the later course: a one-year-old girl with severe additional injuries (thoracic trauma, pelvic fractures, retroperitoneal hematoma) suffered hemorrhagic shock despite blood transfusions and a 10-year-old boy had massive external brain herniation despite large DC. Complications of DC requiring surgical revision within 30 days occurred in 3 cases (contralateral epidural hematoma ($N = 2$) and hygroma ($N = 1$)). Complications not requiring revision were observed in 4 children (hygroma ($N = 3$), posttraumatic generalized seizures ($N = 1$)). Only one child had posttraumatic hydrocephalus and received a ventriculoperitoneal shunt. At a mean follow-up in this subgroup of 26 months (range 2–84), 42% of children reached good outcome ($N = 5$), 25% reached poor outcome ($N = 3$), and 33% died ($N = 4$). Statistical analysis revealed a correlation between mydriasis and outcome (Pearson correlation coefficient $R = -0.642$, $P = 0.0098$), but no role of transportation distance or referral pattern and no difference in outcomes between patients receiving immediate versus delayed DC. Rotterdam CT score category 6 was the most common ($N = 6$), and mortality in this group was 33% ($N = 2$).

The non-TBI subgroup comprised 3 children (2 boys, 1 girl, mean age 13 years), who suffered malignant right-sided

Table 1 Overview of demographic, radiological, surgical, and outcome data of patients

Age (years)	Primary insult	Initial GCS	Type of DC	Time insult to DC (days)	Mydriasis	Midline shift (mm)	Basal cisterns	KOSCHI at initial discharge	Last recorded KOSCHI at follow-up (months)
1	TBI	4	Hemi (unilateral)	0	Bilateral	2	Obliterated	1 (hemorrhagic shock)	NA
5	Stroke	NA	Hemi (unilateral)	2	No	6	Obliterated	3a	4b (96)
6	TBI	3	Hemi (unilateral)	0	Bilateral	14	Obliterated	2	5a (60)
10	TBI	3	Hemi (unilateral)	0	Unilateral	8	Obliterated	1 (brain death)	NA
11	TBI	3	Hemi (unilateral)	0	Unilateral	8	Obliterated	1 (brain death)	NA
11	TBI	3	Bifrontal	1	Bilateral	0	Patent	1 (brain death)	NA
11	TBI	3	Hemi (bilateral)	6	Unilateral	2	Patent	2	5a (84)
13	TBI	3	Hemi (unilateral)	2	No	2	Obliterated	3a	3a (2)
14	TBI	4	Hemi (bilateral)	0	No	6	Obliterated	2	5a (18)
16	ICH	7	Hemi (unilateral)	4	Unilateral	8	Obliterated	3a	4b (120)
17	TBI	3	Hemi (bilateral)	0	No	16	Obliterated	2	2 (21)
17	TBI	4	Hemi (unilateral)	0	Unilateral	8	Obliterated	3a	4b (18)
17	TBI	7	Bifrontal	6	No	0	Obliterated	3a	3a (2)
17	TBI	7	Bifrontal	6	No	0	Obliterated	2	5a (14)
17	ICH	7	Hemi (unilateral)	0	Bilateral	5	Obliterated	3a	3a (8)

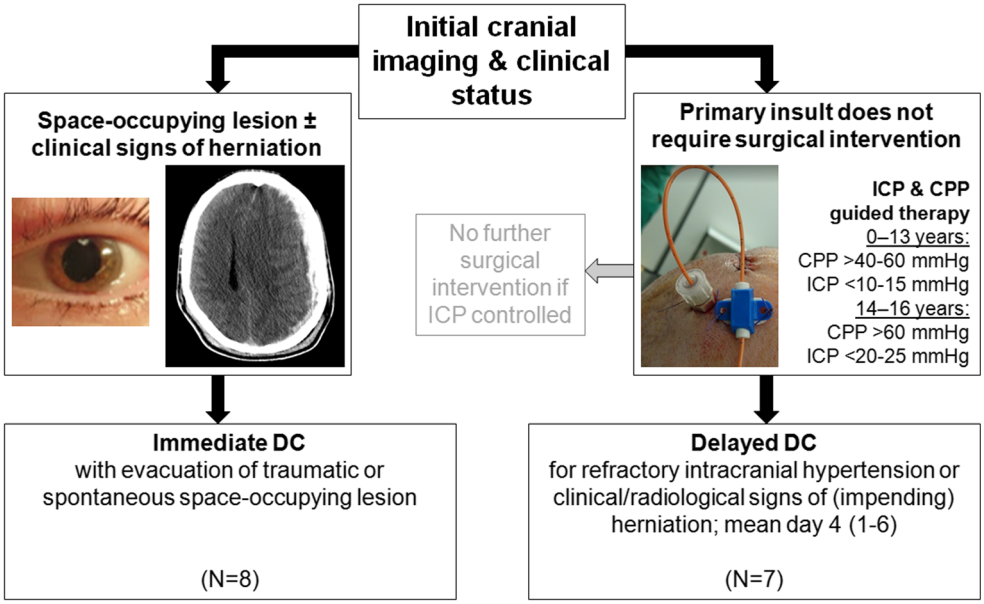

Fig. 2 Illustration of the therapeutic pathways for primary (immediate) and secondary (delayed) DC according to our institutional protocol

middle cerebral artery infarction associated with sickle cell anemia, intracerebral hemorrhage due to Moyamoya disease, and intracerebral hemorrhage secondary to vasculitis, respectively. Mean midline shift was 6 mm (range 5–8), and basal cisterns were compressed in all cases. Mydriasis was present in two cases prior to DC. Immediate DC with evacuation of a space-occupying hemorrhage was performed in one child. The remaining two children were treated with delayed DC upon clinical deterioration at days 2 and 4 after initial insult. Of note, the boy with malignant MCA infarction was decompressed at day 2 when cranial imaging showed progressive midline shift, but before clinical signs of herniation developed. Complications of initial surgery requiring revision within 30 days occurred in one case (recurrent intracerebral hemorrhage in a boy with vasculitis). At a mean follow-up in this subgroup of 75 months (range 8–120), 67% of children reached good outcome ($N = 2$) and 33% poor outcome ($N = 1$).

Morphometric analysis

For reasons of comparability, the morphometric analysis comprises a subgroup of 13 hemicraniectomies in 10 patients (6

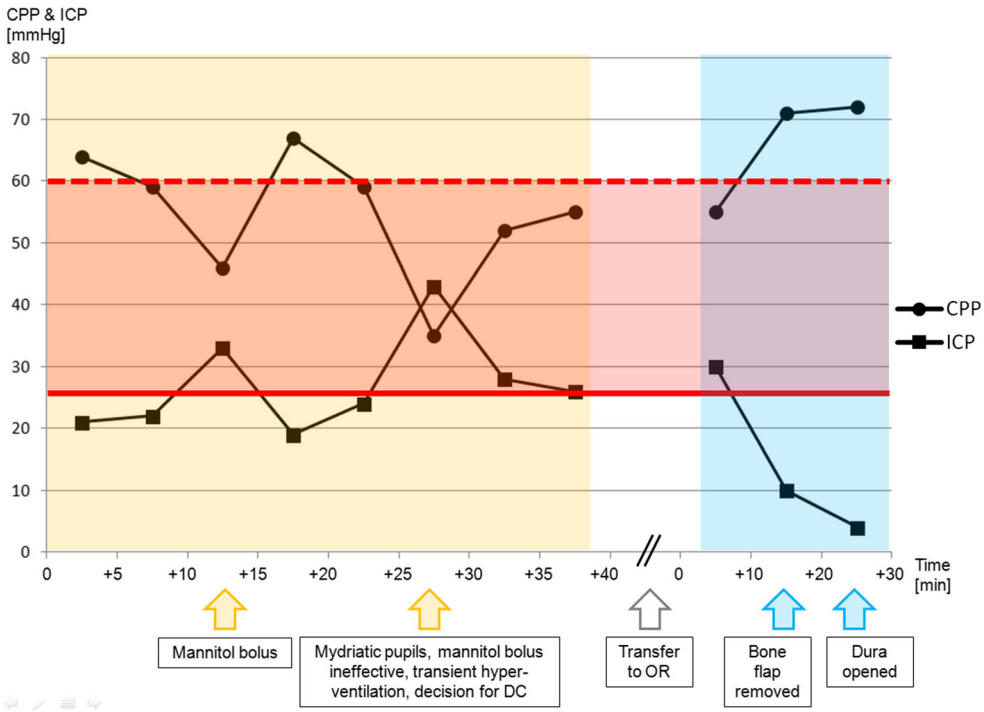

Fig. 3 Exemplary excerpt from the monitoring of a 13-year-old boy after severe TBI. The red area indicates the critical range of ICP and CPP, respectively. The yellow area indicates monitoring at the intensive care unit along with clinical and therapeutic information. Decision for DC is made due to refractory intracranial hypertension. The blue area indicates monitoring obtained in the OR, demonstrating the stepwise improvement of ICP during DC

boys, 4 girls) with a mean age of 13 years (range 5–17 years). The fronto-occipital skull length demonstrated an almost linear correlation with age, although the range was narrow between 14.2 and 17.5 cm (Pearson correlation coefficient $R = 0.8044$). The mean maximum anterior-posterior craniectomy diameter was 11.7 cm (range 9.4–14.1 cm), independent of age (Pearson correlation coefficient $R = -0.02$). The mean craniectomy area was 12,166 mm^2 (range 7520–15,933 mm^2). The mean postoperative gain in a horizontal brain diameter was 1.3 cm (range 0.3–2.4 cm), with larger measures in the subgroup with poor outcome or death (1.28 ± 0.29 cm versus 0.70 ± 0.07 cm, two-sided *t* test $P = 0.0372$).

Cranioplasty

Eleven children survived and received cranioplasty after a mean latency of 1.5 months after DC (range 1–4 months), as summarized in Fig. 4. Autologous cranioplasty was performed in 10 children with 13 bone flaps. One child received a primary computer-aided design and computer-aided manufacturing (CAD-CAM) implant due to multiple fractures of bifrontal bone flap. Early complications within 30 days requiring surgical revision occurred in one case (cerebrospinal fluid leak). Complications not requiring revision were observed in 4 children (hygroma ($N = 2$), cerebrospinal fluid leak ($N = 1$), subdural hematoma ($N = 1$)). One bone flap infection was observed 5 months after cranioplasty and treated with implant removal and intravenous antibiotics, followed by alloplastic cranioplasty.

Bone flap resorption was observed in 8 patients (10 bone flaps) within a mean period of 19 months after reimplantation (range 4–54 months). The degree of bone flap resorption according to the Oulu resorption score was grades II ($N = 4$) and III ($N = 1$), with a mean score of 7 (range 5–9). Implantation of 6 secondary CAD-CAM implants was performed in 4 patients affected by osteolysis using alloplastic materials: polymethylmethacrylat ($N = 3$), fiber-reinforced composite with bioactive glass ($N = 2$), and polyetheretherketon ($N = 1$). Early complications within 30 days were observed in two cases (cerebrospinal fluid leak ($N = 1$), subdural hematoma ($N = 1$)), with the cerebrospinal fluid leak necessitating revision surgery.

Discussion

This study demonstrates that the main indication for DC in children is TBI and that almost equal numbers of patients require immediate and delayed DC. Outcome appears comparable to that of adult TBI patients, although there is a tendency towards higher proportion of good outcome in children. Figure 5 shows a comparison of our cohort with the surgical arm of the RescueICP trial to give an impression of outcomes

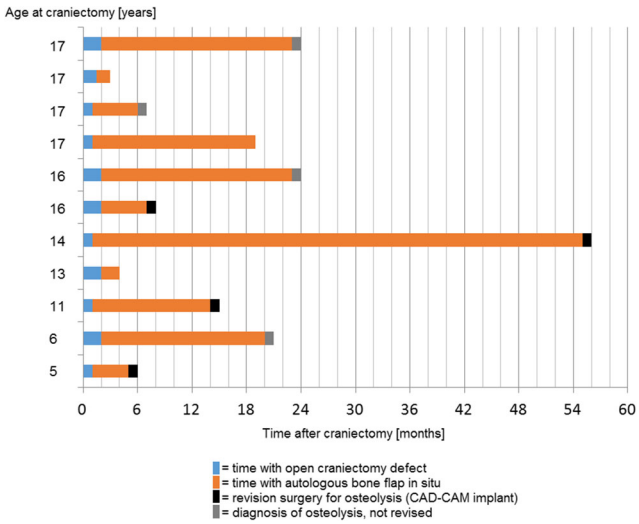

Fig. 4 Overview of cranioplasty timing after DC and further clinical course in our cohort

in adult and pediatric TBI patients [4]. However, this has to be interpreted with caution, as RescueICP investigated delayed DC and our pediatric cohort (for reasons of small numbers) comprises both immediate and delayed DC. The most common Rotterdam CT score in this cohort was 6 and the corresponding mortality was 33%, which compares favorably with previously published mortality for adults in this category of 61% [20]. In our series, preoperative mydriasis is associated with poor outcome and death, indicating that (similar to adults) optimal timing of DC to avoid cerebral herniation is crucial. Of those children initially admitted to secondary care hospitals and then referred to our institution after initial survey, none received any invasive measures at these hospitals. Taking into account the considerable number of children requiring immediate DC, we assume that suspicion of severe TBI should guide pre-hospital triage to designated pediatric trauma centers with neurosurgical service. Although the present study only analyzed children undergoing DC and excluded patients undergoing other or non-surgical interventions, we consider our cohort representative for the subgroup of most severely head injured patients. In contrast, pediatric patient numbers for non-traumatic indications of DC are too small to draw relevant conclusion from a single-center series. As TBI was the main indication for DC in this study, the age distribution of this cohort within the pediatric age spectrum reflects the demographic profile of TBI in Germany. Recently published data from the national registry of the German Trauma Society confirms that the incidence of moderate and severe TBI has a peak during puberty [22].

From a technical point of view, our data suggest that within the pediatric age group represented in this study, the surgical aim should be an anterior-to-posterior craniectomy diameter of at least 12 cm, similar to adults. An increase in skull size across this age group was small, as head growth is accelerated

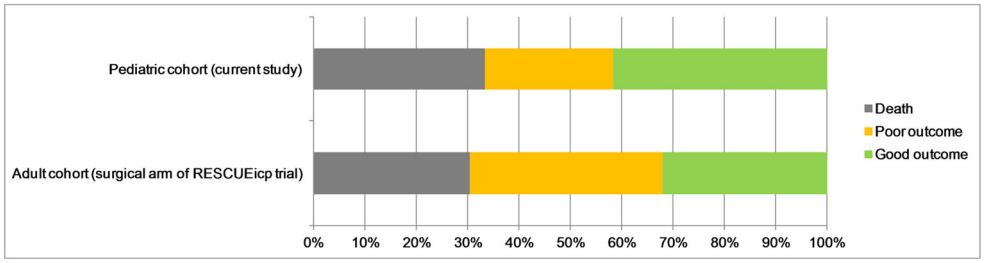

Fig. 5 Comparison of our cohort with the surgical arm of the RescueICP trial to give an impression of outcomes in adult and pediatric TBI patients

mainly in the first year of life. Adapting craniectomy size to age seems to play a minor role beyond infancy. When a large hemicraniectomy is achieved, a gain in a horizontal brain diameter of more than 1 cm might indicate severe brain herniation through the craniectomy defect, correlating with unfavorable outcome. An insufficiently sized DC has to be avoided, as this leads to suboptimal volume gain as well as exacerbated external brain herniation with shear forces along bone edges, subsequent kinking of cerebral veins, and secondary intraparenchymal hemorrhage [23].

Comparing our results with the published literature, the general findings are confirmed: DC is effective in controlling intracranial pressure and appears to be associated with reduced mortality and improved outcome in a variety of conditions associated with raised intracranial pressure, predominantly TBI. However, even for TBI as the most common indication for pediatric DC, this assumption is mainly based on retrospective single-center studies including mean cohorts of 22 children (range 5–53) [24]. To our knowledge, the only prospective randomized trial of DC for pediatric TBI enrolled 27 patients over 7 years, with 13 children randomized into the surgical arm [12]. These children received small bitemporal craniectomies (diameter 3–4 cm, dura not opened). This study indicated that ICP control and outcome might be improved, but failed to reach a statistical significance. A recent systematic review article comes to a similar conclusion; although all published studies indicate benefit of DC in children, the current quality of evidence is low and future high-quality studies with larger patient numbers are required [24]. In our opinion, the most important aspect to be clarified would be optimal timing of delayed or secondary DC for refractory intracranial hypertension in different age groups. Although this aspect has been investigated with high-quality methodology in adults, clinical routine practice deviates from study scenarios [25–27].

Autologous cranioplasty was associated with a 50% overall complication rate and a 15% surgical revision rate. In comparison, we observed a 33% overall complication rate and a 16% surgical revision rate after CAD-CAM cranioplasty. The bone flap resorption rate was 70% after 19 months, which indicates that revision cranioplasty should be expected in most children after DC if autologous bone flaps are used. In a recent systematic review of pediatric cranioplasty, the complication rate was 30%, with bone flap resorption, cerebrospinal fluid disorders, and infection being the most common problems [18]. Unfortunately, 50% of publications did not explicitly state resorption rates. Comparing publications reporting resorption rate after autologous cranioplasty, a wide spectrum from 20 to 80% becomes evident. This finding could theoretically be explained by different age groups, latency of cranioplasty after DC, and types of bone flap preservation, which were implicated before as predictors of resorption risk [28]. However, confounders (e.g., dura opening, duroplasty material, or presence of cerebrospinal fluid shunt) might influence bone viability and are not consistently reported [29].

CAD-CAM cranioplasty is often used as second-tier treatment [30–33]. A variety of alloplastic materials are available, including metals, polymers, and mineral-based and composite materials. Although the literature suggests certain advantages and disadvantages, including different degrees of osteointegration, no evidence-based recommendations can be made [34]. In younger children, impact of cranial growth has to be taken into account. Therefore, a successful autologous cranioplasty, not hit by bone flap resorption, is the most physiological way of cranial reconstruction.

The main limitation of this study is the small cohort and the inability to perform further statistical analyses, such as multivariate regression analysis. An exploratory look into previous publications confirms that most centers operate less than five cases a year on average. Therefore, small patient numbers can only be overcome by either extending the retrospective study period or by pooling data from multiple centers. In our experience, the first solution would lead to "historical" cohorts with incomplete data and different treatment approaches (also regarding intensive care protocols). The latter option is the preferred way of collecting data: A multicenter, prospective, non-interventional registry enrolling children undergoing DC and subsequent cranioplasty with long follow-up of at least 2 years (preferably until adolescence) and meaningful parameters (including common data elements, patient-reported outcomes, and quality of life) would be a valuable contribution to evidence-based treatment of children. In contrast, a randomized controlled trial in children would require more efforts, face higher obstacles, and might be unethical due to lack of equipoise.

Conclusions

DC is a valid treatment option in children, as better ICP control and reduced mortality are reproducible findings across studies. Impact on functional outcome, quality of life, and role of specific aspects (such as optimal timing of delayed DC) remain unclear. Autologous cranioplasty, if successful, is the best modality of cranial reconstruction in children with regard to osteointegration and long-term outcome as well as cost-effectiveness. However, autologous cranioplasty is often complicated by bone flap resorption. Variation in resorption rates across studies might be explained by differences in cranioplasty timing and bone flap storage, among other factors. Prospective multicenter studies, such as specific registries, are the most promising means to generate high-quality, comparable, longitudinal datasets and overcome the typically low single-center annual numbers of pediatric DC and cranioplasty.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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