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FOCUS SESSION

Cranioplasties following craniectomies in children—a multicenter, retrospective cohort study

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Abstract

Objective Complications following pediatric cranioplasty after craniectomy with either autologous bone flaps or cranial implants are reported to be common, particularly bone flap resorption. However, only sparse data are available regarding cranioplasty strategies, complications, and outcomes. This manuscript describes a Canadian-Dutch multicenter pediatric cohort study with autografts and cranial implant cranioplasties following craniectomies for a variety of indications.

Methods The study included all children (< 18 years) who underwent craniectomy and subsequent cranioplasty surgeries from 2008 to 2014 (with a minimum of 1-year follow-up) at four academic hospitals with a dedicated pediatric neurosurgical service. Data were collected regarding initial diagnosis, age, time interval between craniectomy and cranioplasty, bone flap storage method, type of cranioplasty for initial procedure (and redo if applicable), and the postoperative outcome including surgical site infection, wound breakdowns, bone flap resorption, and inadequate fit/disfigurement.

Results Sixty-four patients (46 males, average age 9.7 ± 5.5 years) were eligible for inclusion, with mean follow-up of 82.3 ± 31.2 months after craniectomy. Forty cranioplasties (62.5%) used autologous bone re-implant, 23 (57.5%) of which showed resorption. On average, resorption was documented at 434 days (range 62–2796 days) after reimplantation. In 20 cases, a revision cranioplasty was needed. In 24 of the post-craniectomy cases (37.5%), a cranial implant was used with one of ten different implant types. Implant loosening prompted a complete revision cranioplasty in 2 cases (8.3%). Cranial implants were associated with low morbidity and lower reoperation dates compared to the autologous cranioplasties.

Conclusion The most prominent finding in this multicenter cohort study was that bone flap resorption in children remains a common and widespread problem following craniectomy. Cranioplasty strategies varied between centers and evolved over time within centers. Cranial implants were associated with low morbidity and low reoperation rates. Still, longer term and prospective multicenter cohort studies are needed to optimize cranioplasty strategies in children after craniectomies.

Keywords Cranial reconstruction · Long-term · Complications · Pediatric neurosurgery

Introduction

Craniectomies are common procedures for adult and pediatric patients, done mostly because of elevated intracranial pressure caused primarily by traumatic brain injury or stroke [2, 23]. Advances in medical and surgical care have led to increased survival for patients who undergo craniectomy. Therefore, a larger number of patients are living with a cranial defect that require subsequent cranioplasty to protect the underlying brain and improve cosmesis.

In children, complications following cranioplasty with either autologous bone flaps or cranial implants are reported to be common. Bone flap resorption and surgical site infections occur frequently after cranial bone repair, with documented rates of 21–

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80% and 10–12% respectively [2, 10, 11, 16, 17, 19, 22]. Other post-cranioplasty complications include the occurrence of hydrocephalus [2, 21], poor cosmesis [15], and mechanical problems such as migration, fracturing, or loosening [10].

Despite the well-documented complications in the setting of a frequently performed procedure, there remains a scarcity of data available regarding operative strategy and long-term outcome.

This study addresses this by examining a pediatric cranioplasty patient cohort at four pediatric hospitals in Canada and the Netherlands.

Methods

Patient sample

Four academic hospitals (University Medical Center Utrecht, British Columbia Children's Hospital, University Hospital Center Sainte Justine, Children's Hospital of Eastern Ontario) with a dedicated pediatric neurosurgical service joined this study after independent approval from each of their ethical review boards. All consecutive children (under 18 years) who underwent a first-time cranioplasty following craniectomy between 2008 and 2014 were included.

Clinical variables

Each variable was clearly defined before chart review to minimize measurement bias. Prior examination of the literature as well as expert opinion guided the selection of variables to be collected from medical records. These included the following: indication for craniectomy, age at the time of craniectomy, time interval between craniectomy and cranioplasty, type of cranioplasty, bone flap storage method, revision cranioplasties, and postoperative complications including surgical site infection, bone flap resorption, wound breakdowns, hydrocephalus, and loosening of the cranial implant.

Surgical site infection was defined as the occurrence of an infectious complication that necessitated surgical removal of the implant as well as antibiotic therapy. A patient who only received antibiotic therapy and did not undergo surgical removal of the implant would not be considered to have had a surgical site infection. Bone flap resorption could vary from thinning of the (rim of the) autologous bone flap to bone lysis through the tabula externa and tabula interna, measured by palpation and/or CT scans. The follow-up period after cranioplasty needed to be at least 1 year to be included in the study.

Statistical analysis

Deidentified patient data were analyzed at the UMC Utrecht, the Netherlands, in close collaboration with the partnering hospitals. Statistical analysis was performed using IBM SPSS Statistics, version 25 (IBM Corp., Armonk, NY, USA).

Results

Participating hospitals identified a total of 64 patients (46 boys, mean age 9.7 ± 5.5 years) who had undergone cranioplasty after craniectomy within the study timeframe. The main indications for craniectomies performed were brain swelling following traumatic brain injury, skull tumors, vascular diseases, intracerebral infectious diseases, and epilepsy surgery. The number of included patients per center ranged from 6 to 28. The mean follow-up period after craniectomy was 82.3 ± 31.2 months and the mean follow-up after patients received their last cranioplasty was 66.5 ± 33.6 months. All patient demographics are reported in Table 1.

The mean time interval between craniectomy and cranioplasty was 6.7 ± 9.7 months. Further post-craniectomy

Table 1 Patient demographics (all data given as number of patients (%) unless otherwise indicated)

Variable	Value
Patients	64
Mean age at craniectomy ± SD (years)	9.7 ± 5.5
Males	46 (71.9)
Indications for craniectomy	
Trauma	33 (51.6)
Tumor	11 (17.2)
Vascular disease	8 (12.5)
Infection	5 (7.8)
Epilepsy surgery	3 (4.7)
Other	4 (6.3)
GCS ≤ 8 at diagnosis■	29 (50.9)
Pre-incision antibiotics▲	
Yes	52 (96.3)
No	2 (3.7)
Laterality	
Unilateral	59 (92.2)
Bilateral	5 (7.8)
Mean defect size ± SD (cm^2)●	68.4 ± 34.7
Presence of CSF drain/LP◆	7 (11.3)
VP shunt dependency	1 (1.6)
Mean follow-up after craniectomy ± SD (months)	82.3 ± 31.2
Mean follow-up after last cranioplasty ± SD (months)	66.5 ± 33.6

■ 7 missings

▲ 10 missings

● 19 missings

◆ 2 missings

Calculated mean defect size: $\pi \cdot \left(\frac{\text{maximumlength axis}}{2}\right) \cdot \left(\frac{\text{maximumwidth axis}}{2}\right)$

characteristics are depicted in Table 2. Table 3 shows the various implant materials that have been used.

Autologous cranioplasty

Most of the first cranioplasties after craniectomy were autologous bone flap reimplants ($n = 40$, 62.5%) that were sterilized between surgeries using cryosterilization or cryosterilization plus radiation. The majority of bone flaps were stored frozen. On average, the time interval between craniectomy and autologous cranioplasties was 4.5 ± 4.8 months.

Resorption of the autologous bone graft occurred in the majority of cases (23/40–57.5%, Table 4). The mean time interval between cranioplasty and documentation of bone graft resorption was 14.8 ± 18.7 months. Young age (under 6 years) was not found to be a significant predictor of bone resorption (OR 2.11, 95% CI 0.56–8.67). Figure 1 shows the risk of resorption with time interval to autologous cranioplasty and age at craniectomy, especially when the time interval exceeds 7 months.

Out of the 23 bone resorption cases, 16 cases underwent revision surgery using PEEK in 5 cases, methyl methacrylate in 3 cases, polyethylene and titanium mesh in 3 cases, bioceramic custom bone in 2 cases, and titanium, polyethylene, and split cranial autograft each in 1 case. In no cases, a second revision cranioplasty was needed.

Table 2 Post-craniectomy characteristics (all data given as number of patients (%) unless otherwise indicated)

Variable	Value
Bone flap sterilization ($N = 40$)	
Cryosterilization	32 (80.0)
Cryosterilization + radiation	4 (10.0)
Unspecified	4 (10.0)
Bone flap storage ($N = 40$)	
Subcutaneous	3 (7.5)
Room temperature	13 (32.5)
Frozen	23 (57.5)
Unspecified	1 (2.5)
Wound healing problem after craniectomy ($N = 64$)	4 (6.3)
Mean hospital stay after craniectomy ± SD (days)▪	29.4 ± 34.1
Secondary outcome after craniectomy ($N = 64$)	
Intracranial hematoma	1 (1.6)
Hydrocephalus	1 (1.6)
Infection	5 (7.8)
Growing skull defect	1 (1.6)
Pseudomeningocele	1 (1.6)
Mean time interval between craniectomy and cranioplasty ± SD (months)	6.7 ± 9.7

▪ 4 missings

Table 3 Cranioplasty materials (all data given as number of patients (%) unless otherwise indicated)

Variable	Value
Autologous graft type	40 (62.5)
Cranial implants	24 (37.5)
Bioceramic custom bone	1 (1.6)
Calcium phosphate	1 (1.6)
Calcium phosphate + autograft	1 (1.6)
Glass fiber–reinforced composite	1 (1.6)
Hydroxyapatite	4 (6.3)
Methylmethacrylate	12 (18.8)
Methylmethacrylate + titanium mesh	1 (1.6)
PEEK	1 (1.6)
Polyethylene	1 (1.6)
Titanium mesh + autograft	1 (1.6)

In the autologous group, infection occurred in 4 cases (10.0%). The infected bone flaps were then removed and replaced by either a split cranial autograft or a cranial implant (methyl methacrylate or glass fiber–reinforced composite).

A total of 20 patients underwent revision surgery using mostly a cranial implant. In no cases, a second revision was necessary.

Cranial implants

In 24 (37.5%) of post-craniectomy cases, a cranial implant was used. The mean time interval between craniectomy and cranioplasty was 10.5 ± 13.9 months. Methyl methacrylate was the most frequently used material ($n = 12$, 18.8%).

The most common complication of the cranial implants was implant loosening, which occurred in 3 of the 5 calcium phosphate and hydroxyapatite implants (and none of the other cranial implants). In two of these cases, revision surgery was done using another type of cranial implant (methyl methacrylate or titanium mesh). One patient received a cranial implant made of autologous bone in combination with a titanium mesh, and, in this case, resorption of the autologous material occurred.

A total of two patients underwent revision surgery using a cranial implant, and there were no second revisions necessary. This number was significantly lower ($p < 0.001$) than the amount of revision cranioplasties in the autologous group (Table 4). Other differences in cranioplasty strategies and post-cranioplasty outcomes between autografts and cranial implants are shown in Fig. 2. Figure 3 shows the differences between strategies and outcomes within the various medical centers included in this study.

Discussion

This Canadian-Dutch multicenter retrospective cohort study was a collaborative effort, with a relatively long follow-up period, involving four different pediatric neurosurgical hospitals (University Medical Center Utrecht, British Columbia Children's Hospital, University Hospital Center Sainte Justine, Children's Hospital of Eastern Ontario), to obtain a better understanding of cranioplasty strategies, complications, and long-term outcomes in children.

Autologous cranioplasty

Of the cases where autologous bone grafts were used, most (57.5%) suffered from resorption, typically requiring revision surgery using a cranial implant. Previously identified risk factors for *resorption* include an underlying contusion, comminuted skull fractures, young age (≤ 2.5 years), posttraumatic hydrocephalus, increased area of the cranial defect (≥ 75 cm^2), late bone flap replacement (≥ 6 weeks), and the presence of EVD's and lumbar shunts [2, 16, 21, 22]. Furthermore, using cryopreserved bone flaps during cranioplasty may lead to a higher rate of bone resorption than using bone flaps stored at room temperature [23].

In our cohort, the relatively large area of cranial defect, long time interval between craniectomy and cranioplasty, and cryopreserved bone flap storage could have contributed to the high resorption rate.

As shown, when the time interval to autologous cranioplasty exceeded 7 months and the patient was of young age, almost all autologous bone flaps resorbed. This is in accordance with earlier published studies which have shown that young age can be a risk factor for bone flap resorption [2, 10, 11, 19, 21, 22].

Other previously published studies on cranioplasty in pediatric patients reported that there is no appreciable effect of defect size or freezer time on the occurrence of resorption [2, 23]. An alternative storage method to cryopreservation or storing at room temperature is subcutaneous abdominal storage. Nevertheless, subcutaneous storing of bone flap has not been proven to prevent later bone resorption, and it must be taken into account that such storage has the disadvantage of the need for a second surgical site and procedure [10, 23].

Our resorption rate is similar to rates in previously published studies [2, 16, 19, 21]. Bowers et al. reported a resorption rate of 50% in 54 patients [2], Grant et al. found a 50% resorption rate in 40 patients [16], Martin et al. reported on 27 patients with an 81.8% resorption rate [19], and Piedra et al. described 61 patients with a 29.5% resorption rate [21].

A recent multicenter cohort study by Rocque et al. reported a resorption rate of 21.7%, a rate fairly lower than ours [22]. The patients included in this cohort were similar in age, but might have had a smaller cranial defect size, a shorter time interval between craniectomy and cranioplasty, and/or a different storage method.

In patients who underwent bone flap resorption, revision cranioplasty was very successful as the final definitive surgery (16 of 16, 100%).

In our autologous group, *infection* occurred in 9.5%. The presence of a VP shunt, gastrostomy, and ventilator dependence have been identified as significant risk factors for cranioplasty infection, when either an autologous bone flap or cranial implant has been used [22]. The use of cryopreserved bone flaps may lead to a lower rate of infection, in contrast to the higher rate of resorption [23]. None of our patients were dependent on gastrostomy and none required mechanical ventilation. Only one of our patients was dependent on a VP shunt. Our infection rate is similar to previously published infection rates from various studies examining pediatric cohorts [2, 17, 21, 22]. Bowers et al. reported an infection rate of 16.7% in 54 patients [2], Josan et al. found a 12.5% (3/24) infection rate in 24 autologous cranioplasties [17], Piedra et al. reported on 61 patients with a 6.6% infection rate [21], and Rocque et al. reported an infection rate of 10.5% in 359 patients [22].

In our cohort, revision cranioplasty was successful (without infection or need for reoperation) in all 4 patients whose bone flap implant became infected.

Cranial implants

In the 24 allograft cranioplasties, using different types of synthetic materials, low morbidity was found. Loosening of the cranial implant was the most common complication, seen in 3 of the patients, all of whom had carbonated calcium phosphate or hydroxyapatite grafts. Even though these materials are osteoconductive (since they promote bony ingrowth into the material), represent the principal component of the bone, and can thus be considered as an almost ideal bone substitute, their structural integrity can be lost when exposed to cerebrospinal fluid or blood, and when moved by CSF or blood pulsations. This can lead to inadequate setting and loosening of the bone flap [6–8, 14, 16]. These complications have mainly been reported when hand-made bone cements were used in surgeries [25]. Custom-made porous hydroxyapatite implants showed few complications and appeared to be an effective cranial implant material [12–14].

In our study, no *infections* occurred after inserting a cranial implant. Earlier published studies that specifically reported on the occurrence of infection after cranial reconstruction with synthetic materials also showed very low infection rates [15, 17]. Furthermore, multiple studies have demonstrated that there is no significant association between the use of any cranioplasty material and the incidence of infection [17, 22, 23, 25].

Table 4 Complications and revisions following cranioplasty

Variable	Autografts ($N = 40$)*	Cranial implants ($N = 24$)*	p value
Resorption of autologous bone graft	23 (57.5)	N/A	
Infection	4 (10.0)	0 (0.0)	NS
Cranioplasty loosening	0 (0.0)	3 (12.5)	NS
Hematoma	2 (5.0)	0 (0.0)	NS
Extra bone formation, disfiguring	N/A	1 (4.2)	
Need for redo cranioplasty	20 (50.0)	2 (8.3)	$p < 0.001$

*All data given as number of patients (%) unless otherwise indicated

N/A, not applicable; *NS*, not significant

Despite the generally positive results, synthetic materials are currently still not often used for reconstruction of the pediatric calvarium, primarily because of apprehension regarding the fit of a static, non-expansible, graft shape within a growing skull, and the effect of fixation to the graft on the growth of the surrounding cranial vault [15, 24].

Fu et al. examined 30 patients with a mean age of 4.37 ± 5.57 years who received a cranial implant and no skull growth restriction was seen in the mean follow-up period of 2.33 ± 2.76 years [15]. Other authors did not specifically report on whether or not skull growth had been restricted by the use of allografts during their follow-up period [17, 22, 25].

In our cohort, no disfigurement problems were seen in the patients receiving a synthetic cranial implant in a follow-up period of 82.3 months, which is the longest follow-up time of cranial implants thus far [1, 3–5, 9, 12, 13, 15, 18, 20, 26].

Cranioplasty strategies appeared to vary over time within and among centers. In almost every center, autologous cranioplasty was the most used primary cranioplasty. Notable is that one center only used autologous bone grafts, all of them which showed resorption. All centers used different implant materials for revision surgery after resorption of the autologous bone flap, probably reflecting availability and experience with different kinds of implants.

It is important to obtain a clear understanding of long-term outcomes following cranioplasty in the pediatric population. Potential complications like a lack of osteointegration or an insufficient growth capacity and implant instability could occur after a long period of time, which puts children at risk for undergoing multiple surgeries later on in life.

Most studies that currently exist on pediatric cranioplasty lack an adequate duration of follow-up and are mostly retrospective. Based on these retrospective short-term follow-up studies alone, one cannot reach consensus regarding the optimal material to use in pediatric cranioplasty.

Large-scale prospective multicenter cohort studies with uniform well-defined outcome parameters followed over a long period of time are necessary to eventually reach this consensus and help guide clinical practice.

Limitations

This study is one of the only multicenter retrospective studies [12, 13, 18] on pediatric cranioplasty, which allows for analysis of a varied population of patients. The primary limitations

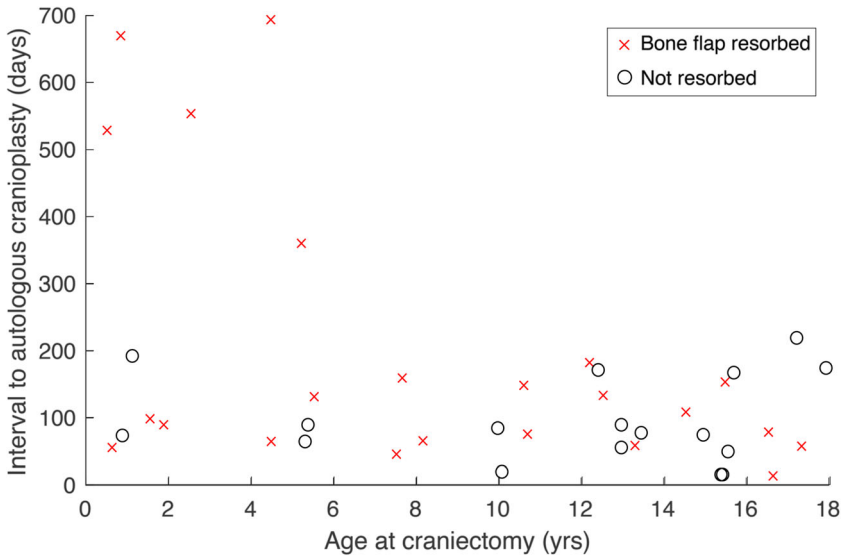

Fig. 1 Risk of resorption with time interval to autologous cranioplasty and age at craniectomy

	Autologous cranioplasty N = 40 (62.5%)												
Complication	Resorption N = 23 (57.5%)								Infection N = 4 (10.0%)			Loosening N = 0	Hematoma N = 2 (5.0%)
Re-do cranioplasty	No re-do N = 7 (30.4%)	PEEK N = 5 (21.7%)	MMA N = 3 (13.0%)	Polyethylene/ titanium mesh N = 3 (13.0%)	Bio-ceramic custom bone N = 2 (8.7%)	Titanium N = 1 (4.3%)	Polyethylene N = 1 (4.3%)	Split cranial autograft N = 1 (4.3%)	Glass fiber-reinforced composite N = 1 (25%)	MMA N = 1 (25%)	Split cranial autograft N = 2 (50%)		No re-do N = 2 (100%)
Complication		None	None	None	None	None	None	None	None	None	None		

	Cranial implants N = 24 (37.5%)										
Implant material	Bio-ceramic custom bone N = 1 (1.6%)	Calcium phosphate N = 1 (1.6%)	Calcium phosphate + autograft N = 1 (1.6%)	Glass fiber-reinforced composite N = 1 (1.6%)	Hydroxyapatite N = 4 (6.3%)		MMA N = 12 (18.8%)	MMA + titanium mesh N = 1 (1.6%)	PEEK N = 1 (1.6%)	Polyethylene N = 1 (1.6%)	Titanium mesh + autograft N = 1 (1.6%)
Complication	None	Loosening N = 1 (100%)	None	None	None N = 2 (50%)	Loosening N = 2 (50%)	None	Extra bone formation/ Disfigurement N = 1 (100%)	None	None	Resorption of autograft N = 1 (100%)
Re-do cranioplasty		No re-do N = 1 (100%)				MMA N = 1 (50%) Titanium mesh N = 1 (50%)		Extra bone shaving N = 1 (100%)			No re-do N = 1 (100%)
Complication						None None		None			

Fig. 2 Differences between autografts and cranial implants

	UMC Utrecht N = 28 (43.8%)													
Implant material	Autologous cranioplasty N = 16 (57.1%)								MMA N = 7 (25%)	Hydroxyapatite N = 3 (10.7%)			Bio-ceramic custom bone N = 1 (3.6%)	Glass fiber-reinforced composite N = 1 (3.6%)
Complication	Resorption N = 7 (43.8%)				Loosening N = 0	Hematoma N = 1 (6.3%)	Infection N = 2 (12.5%)		None	None N = 1 (33.3%)	Loosening N = 2 (66.7%)		None	None
Re-do cranioplasty	No re-do N = 1 (14.3%)	MMA N = 3 (42.9%)	Bio-ceramic custom bone N = 2 (28.6%)	Titanium N = 1 (14.3%)		No re-do N = 1 (100%)	MMA N = 1 (50%)	Glace N =1 (50%)			MMA N = 1 (50%)	Titanium mesh N = 1 (50%)		
Complication		None	None	None			None	None			None	None		

	BC Children's Hospital N = 20 (31.3%)											
Implant material	Autologous cranioplasty N = 10 (50%)						MMA N = 5 (25%)	MMA + titanium mesh N = 1 (5%)	Hydroxy-apatite N = 1 (5%)	Calcium phospha te N = 1 (5%)	Calcium phosphate + autograft N = 1 (5%)	Poly-ethylene N = 1 (5%)
Complication	Resorption N = 5 (50%)			Loosening N = 0	Hematoma N = 1 (10%)	Infection N = 0	None	Disfigure-ment N = 1 (100%)	None	Looseni ng N = 1 (100%)	None	None
Re-do cranioplasty	No re-do N = 1 (20%)	Poly-ethylene/ Titanium mesh N = 3 (60%)	Poly-ethylene N = 1 (20%)		No re-do N = 1 (100%)			Extra bone shaving N = 1 (100%)		No re-do N = 1 (100%)		
Complication		None	None					None				

Fig. 3 Differences between various medical centers

	Sainte Justine Hospital Montreal N = 10 (15.6%)						
Implant material	Autologous cranioplasty N = 8 (80%)					PEEK N = 1 (10%)	Titanium mesh + autograft N = 1 (10%)
Complication	Resorption N = 5 (62.5%)		Loosening N = 0	Hematoma N = 0	Infection N = 2 (25%)	None	Resorption of autograft N = 1 (100%)
Re-do cranioplasty	No re-do N = 4 (80%)	Split cranial autograft N = 1 (20%)			Split cranial autograft N = 2 (100%)		No re-do N = 1 (100%)
Complication		None			None		

	Children's Hospital of Eastern Ontario N = 6 (9.4%)				
Implant material	Autologous cranioplasty N = 6 (100%)				
Complication	Resorption N = 6 (100%)		Loosening N = 0	Hematoma N = 0	Infection N = 0
Re-do cranioplasty	No re-do N = 1 (16.7%)	PEEK N = 5 (83.3%)			
Complication		None			

Fig. 3 (continued)

of our study are the retrospective, nonrandomized nature and the small sample size. Although our patients have been followed for a relatively long period of time, it would be even better to structurally follow them up into adulthood.

Conclusion

This multicenter cohort study, with a relatively long duration of follow-up, has shown that bone flap resorption remains a common and widespread problem after autologous cranioplasty in children. Cranial implants revealed low morbidity and lower rates of revision surgeries when compared to autologous cranioplasties. Cranioplasty strategies appeared to vary over time within and among centers. Therefore, longer term and prospective multicenter cohort studies are necessary to improve strategies in pediatric patients in need for cranioplasties.

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Compliance with ethical standards

Conflict of interest With the submission of this manuscript, I would like to state that the authors report no conflict of interest concerning the materials and methods used or the findings specified in this paper. Furthermore, the authors declare that this study was performed in accordance to the research ethical guidelines.

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