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Failure of autologous bone–assisted cranioplasty following decompressive craniectomy in children and adolescents

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Object. The authors have routinely performed primary autologous cranioplasty to repair skull defects after decompressive craniectomy. The high rates of subsequent bone resorption occurring in children prompted this study.

Methods. In an institutional review, the authors identified 40 (32 male and eight female) children and adolescents ranging from 4 months to 19 years of age in whom autologous cranioplasty was performed after decompressive craniectomy. The defect surface area ranged from 14 to 147 cm^2. In all cases, the bone was fresh frozen at the time of the decompression. Symptomatic bone resorption subsequently occurred in 20 children (50%) in all of whom reoperation was required. The incidence of bone resorption significantly correlated with an increased skull defect area ($p < 0.025$). No significant correlation was found with age, sex, or anatomical location of the skull defect, number of fractured bone fragments, presence of a shunt, cause for decompressive craniectomy, method of duraplasty, or interval between the craniectomy and the cranioplasty. Reoperation to repair the resorbed autologous bone was performed 2 to 76 months after the initial procedure.

Conclusions. The use of autologous bone to reconstruct skull defects in pediatric patients after decompressive craniectomy is associated with a high incidence of bone resorption. The use of autologous bone should be reevaluated in light of the high rate of reoperation in this pediatric population.

KEY WORDS • autologous cranioplasty • craniectomy • decompression surgery • pediatric neurosurgery • children

In many neurosurgical trauma centers, decompressive craniectomy is undertaken as a last resort for treating intracranial hypertension refractory to medical therapy. Because emergency therapy in patients with severe head injury has improved, an increasing number of children survive and are left with a skull defect.[13,15,28,32] Cranioplasty is then performed to fill the defect after the cerebral swelling has resolved. Replacing the cranium is not only a cosmetic and protective measure, but may also reverse the altered physiological state that occurs following craniectomy. Cranioplasty can improve electroencephalographically documented abnormalities, aberrations of cerebral blood flow, cerebrospinal fluid dynamics, and clinically apparent neurological abnormalities.[12,16,37,40]

Historically the skull has been one of the most difficult regions in which to use autograft because of the cranium's propensity for resorption.[3,17,19,31,34] Numerous cranioplasty techniques have involved a spectrum of alloplastic or autologous sources of reconstructive material.[1,3,6,17,19,31,34] Placement of the original bone removed in the craniectomy is ideal because no other graft or foreign materials are then introduced. In pediatric patients, this method is also preferred because the child's original skull material will become reintegrated as he or she matures. Unfortunately, the replaced bone flap often undergoes bone resorption, which results in structural breakdown necessitating reoperation and replacement with plastic, metal, or other materials.[17,31,34] Researchers have shown that cryopreservation of the bone flap may compromise its function to serve as an osteoconductive template for remodeling.[29,33,34] Furthermore, traumatic injuries requiring a decompressive craniotomy often involve multiple skull fractures, which increase the surface area of the defect.

Although trephination is the oldest known surgical procedure, long-term objective data regarding autologous cranioplasty after decompressive craniectomy, and similar cases requiring delayed closure, are lacking in the pediatric population. In the contemporary pediatric neurosurgery literature, it is recommended that cranioplasty in children in whom delayed closure is required should be performed using the child's own skull flap whenever possible. Data in the literature support the placement of foreign materials after at least 1 year to allow for the possibility of spontaneous ossification and to be used only when the brain is unprotected or cosmesis is unsatisfactory.[17,31] Because of the difficulties inherent in autologous cranioplasty, several other methods have been recom-

Abbreviations used in this paper: CT = computerized tomography; HA = hydroxyapatite; MMA = methylmethacrylate.

mended including placement of MMA, HA cement, titanium mesh, and metal plates.[3,6,17,23,24,31,34,38,39,41]

This study was prompted in response to the high rates of reoperation secondary to centripetal bone resorption after autogenous cranioplasty in the pediatric population. We sought to determine failure rates following decompressive craniotomy and analyze factors that might be associated with failure.

Clinical Material and Methods

Between October 1987 and March 2001, 40 children and adolescents younger than age 20 years (mean 9.3 years; range 6 weeks–19 years) at time of initial injury underwent autologous bone–assisted cranioplasty after a decompressive craniectomy or a procedure requiring delayed replacement of bone flap. Serial CT scans were obtained and systematically evaluated, as were demographic, operative, and clinic data. The mean follow-up interval was 4.8 years (range 6 months–6 years). Data derived from the CT scans were used to calculate an approximate surface area of the cranial defect. In all cases, the bone was fresh frozen using standard techniques at the time of craniotomy and replaced at the time of cranioplasty. The bone was secured using titanium miniplates and screws, and the scalp was closed uniformly using absorbable vicryl galeal sutures and running prolene skin sutures. At the time of the cranioplasty revision, the easily accessible and loose bone pieces were removed, and the defect was reinforced using a combination of titanium mesh and/or MMA or HA. Statistical analyses were conducted using commercially avaliable software (S+2000; MathSoft, Seattle, WA). The two-tailed Pearson correlation coefficient was used and a probability value of less than 0.05 was considered significant.

Results

Twenty (50%) of 40 patients suffered symptomatic bone resorption (Figs. 1 and 2). Reoperation was necessary in all 20 cases. The mean size of the original defect was 99.4 cm^2 (range 14–147 cm^2). Symptomatic bone resorption is defined as a defect large enough to cause concern about the risk of damage to the brain or result in a cosmetic defect unacceptable to the family or treating physicians. The incidence of bone graft failure due to resorption correlated with a larger skull defect area (Pearson correlation coefficient 0.36, $p < 0.024$). The correlation between failure of the autograft and increase in defect size was more pronounced when the skull defect area was stratified into six subgroups based on defect size (Table 1; Pearson correlation coefficient 0.41, $p < 0.008$). There was no significant correlation between the multiple-piece bone flap at the time of cranioplasty and increased bone resorption. In addition, there was no correlation of bone resorption and the method of duraplasty (that is, pericranium compared with bovine pericardium or dura).

The cause (Table 2) and location (Table 3) of the injury did not correlate with the rate of resorption. Patient age and sex also did not correlate with failure of autograft. The mean interval between the initial craniectomy and subsequent cranioplasty was 4.8 months (Fig. 3). A longer time interval of cryopreservation did not correlate with subsequent onset of bone resorption. Nine of 40 patients developed some form of hydrocephalus requiring placement of a subdural or an intraventricular shunt. Shunt therapy also did not correlate with an increased rate of resorption.

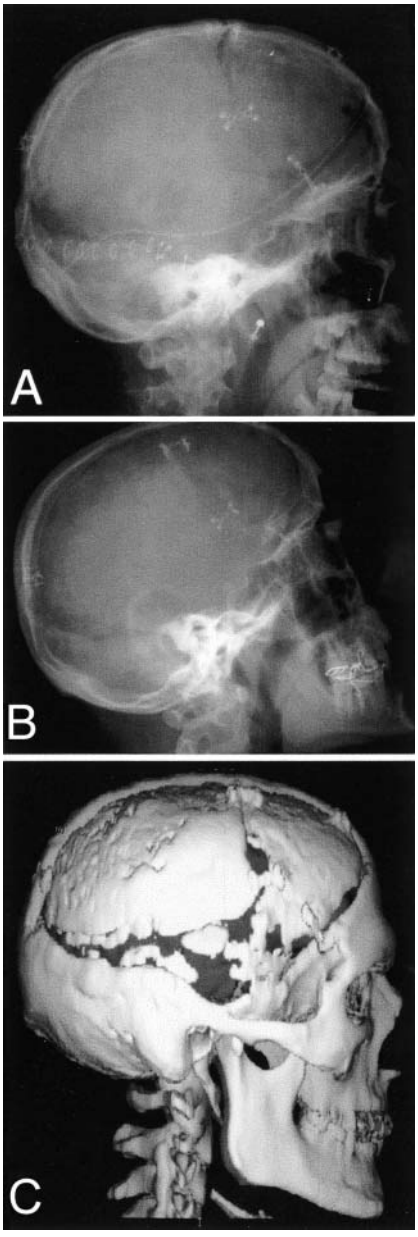

FIG. 1. Imaging studies obtained in a 14-year-old boy. A: Radiograph obtained after autologous bone cranioplasty. B: Radiograph obtained 15 months later after development of progressive bone resorption. C: Three-dimensional CT reconstructions acquired 2 years later.

Twenty patients underwent reoperation for symptomatic bone resorption. Reoperation was required in 20 of the 20 patients in whom symptomatic resorption occurred. This was performed between 2 and 76 months (mean 13.3 months) after the original cranioplasty. Repair was performed using various materials including HA, MMA, dynamic titanium mesh, stainless steel interosseous wire, and/or miniplates and microplates (Fig. 4). No infections

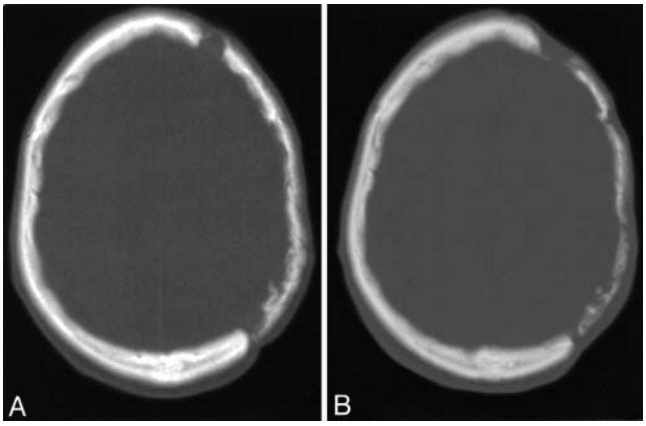

FIG. 2. Axial CT scans revealing progressive bone resorption over a 5-month period.

were identified at the time of the cranioplasty revision that could primarily account for the bone resorption. In one of 20 patients, however, a bone flap infection developed 2 months after revision, and another patient developed a superficial wound infection and dehiscence requiring irrigation, debridement, and wound reclosure. Therefore, the overall infection rate was 10% (two of 20 patients).

Discussion

Published data concerning the results of cranioplasty in children are limited, but analysis of those that exist suggest that using an autologous skull flap for immediate closure of a large craniectomy is not problematic.[17] In contrast, patients in whom delayed closure was performed present a dilemma: should the surgeon use autologous bone or one of various other materials?[1,3,17,19,38,39] In this study, we sought to revisit the problem of resorption and analyze possible risk factors that might contribute to a higher failure rate. In children who underwent decompressive craniectomy followed by autologous bone–assisted cranioplasty, symptomatic resorption of the grafts occurred in 50% of patients, all of whom required reoperation and revision involving other materials. Failure of the graft strongly correlated with the size of the original skull defect. Defects greater than 75 cm^2 had a failure rate greater than 60%, whereas those smaller than 75 cm^2 were associated with no failures. Unfortunately, the mean size of the skull defect in this population was 99 cm^2, and in 82% the defects were greater than 75 cm^2. Although the size of the defect is useful information in predicting failure, clinical circumstances dictate the size of the cranioplasty. Because intracranial hypertension at the time of reimplantation may lead to a higher rate of failure, the primary cranioplasty was often delayed for 3 to 6 months (mean 4.8 months) after the decompressive craniectomy.

The duration (between failure and replacement) and method of bone flap preservation have previously been suggested to lead to breakdown of the bone flap, possibly predisposing it to resorption.[29,33,34] Autoclaving the bone flap has been shown to denature bone protein and impair vascularization and resorption and therefore is not routinely performed.[20] In a recent study, investigators reevaluated the use of fresh-frozen autologous bone flaps in patients undergoing delayed cranioplasty; they reported bone resorption in only one (4%) of 49 cases 15 months following cranioplasty. Interestingly, the resorption occurred in a 12-year-old boy.[21] It has also been shown that the structural proteins necessary for revitalization of the bone flap remained intact regardless of the duration of cryopreservation.[21,33] In the present study, no significant correlation was found between time to replacement of the autologous bone and failure of the autogenous cranioplasty, even though the duration between replacement ranged from 1 to 17 months (mean 4.8 months). Similarly, no significant correlation was found between failure and the following variables: age, sex, cause of injury, number of bone flap pieces, presence of duraplasty, or presence of shunt. Although the number of pieces in the cranioplasty after trauma seemed a likely predictor because a greater area of bone would require healing, no such relationship was found. Other authors have suggested that patients retain an increased propensity for skull healing when cranioplasty is performed prior to puberty.[17] All but five of our patients were younger than 15 years; thus, sufficient power to analyze such a relationship is lacking in this study. Nevertheless, the high failure rates in general would suggest that pediatric patients also suffer from resorption in this clinical setting. We hypothesize that the high rates of resorption may predominate in children solely due to the thinness of the calvaria.

TABLE 1

Summary of resorption rates stratified by distribution of defect area

Skull Defect Area (cm^2)	No. of Cases	Resorption Rate (%)
0–24	3	0
25–49	3	0
50–74	1	0
75–99	9	62.5
100–124	16	56.3
≥125	8	66.6

Of the 20 patients who underwent reoperation for resorption, one patient suffered a purulent wound infection requiring removal of the autologous bone graft and later replacement with titanium mesh and MMA without further sequelae. There was no obvious infection at the time of the resorption-based surgery for failure, although cultures were not routinely taken at the time of the operation.

The merits of using autologous bone include a return of the former cranial contour, and no need to introduce foreign materials. Although autologous bone graft has been the preferred material, the associated rate of failure and high rates of reoperation in patients with large defects suggest that alternative methods might be considered at the time of initial cranioplasty. At the time of cranioplasty involving autologous bone, we now drill down the edges of both the donor and recipient bones and overlap the edges as much as possible using a tongue-and-groove technique to maximize bone–bone contact and promote osteoblastic ingrowth. Studies involving nonvascularized autologous bone grafts have shown that rigid fixation of the graft is critical to minimize graft resorption and facilitate osteoconduction.[7,9,30] The potential added advantage of this

TABLE 2

*Summary of resorption rates stratified by injury types**

Cause	No. of Cases	Resorption Rate (%)
MVA	19	42
fall	7	42
spontaneous ICH	5	60
blunt trauma	4	50
pedestrian/MVA	3	100
infection	1	0
tumor	1	100

* ICH = intracerebral hemorrhage; MVA = motor vehicle accident.

technique, however, has not been proven. Many other materials have also been used including metal plates (titanium, tantalum, stainless steel), HA cement, and MMA. Although metal plates are strong, they are difficult to contour to a child's natural skull shape, they do not always fit well, and they impede CT scanning.[1] Hydroxyapatite represents the principal component of bone and is unique compared with the other materials in that it can facilitate bone ingrowth. Difficulties have been reported in association with the prolonged water solubility of HA, which results in inadequate setting and loss of structural integrity when exposed to cerebrospinal fluid or blood.[8] Prefabrication of HA ceramics may alleviate some of these problems, as might new formulations that harden more quickly,[8,26,39] but further clinical trials in children should be pursued. Alloplastic grafts (for example, MMA, HA, titanium, polyethylene, or polypropylene polyester) are attractive alternatives to autologous bone grafts (calvaria, rib, or ilium), because postoperative resorption is nonexistent; however, infection rates may be higher.

Of the foreign materials used, MMA has been most extensively studied in children. Gruber, et al.,[17] found that of 33 children who underwent decompressive craniectomies, all 14 patients in whom immediate closure was performed using either autologous bone or MMA experienced satisfactory results. In contrast, in nine patients in whom closure was delayed a mean of 3.5 months, macular resorption of some extent (not requiring intervention) occurred in six and MMA-based repair was needed in three. Based on the results observed in the nine cases involving delayed closure, they recommended using the patient's bone flap whenever possible, reserving foreign materials only in cases in which the autologous material had failed. In a larger study, Pochon and Kloti[31] examined 36 children with skull defects. Three of eight autologous skull flaps underwent resorption and required further MMA-augmented cranioplasty. In contrast, the 21 patients in whom MMA-augmented cranioplasties had been performed were all satisfactory, with no clinical evidence of

TABLE 3

Summary of resorption rates stratified by lobular location

Location	No. of Cases	Resorption Rate (%)
frontal	22	45.0
temporal	17	47.1
parietal	19	42.1
occipital	5	40.0

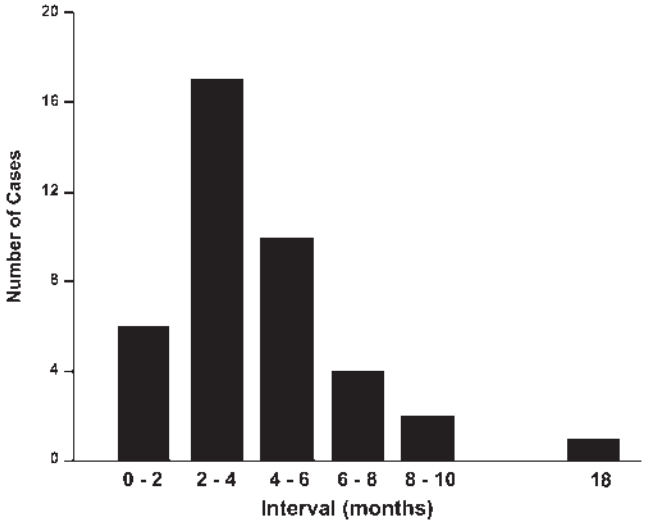

FIG. 3. Bar graph showing time interval between decompressive craniectomy and cranioplasty.

resorption and one instance of infection. They concluded that MMA implants are a viable material for closure and recommended broad utilization.

The aforementioned studies are encouraging, but the long-term results of MMA have recently been called into question. Blum, et al.,[6] investigated the long-term outcome of 42 children who underwent MMA-augmented cranioplasty for postraumatic skull fractures and 33 for nontraumatic causes over a 15-year period. Within 8 years of the initial cranioplasty, 17 complications (23%) occurred. Infection accounted for the majority of late complications and was associated with radiotherapy in the treated area and frontal sinus involvement. Furthermore, the mean area of the defect was 36 cm^2, and larger-sized MMA cranioplasties proved more prone to failure. All fractures of the cement occurred in defects larger than 42 cm^2. In our study the mean size of the defect was 99 cm^2, and based on the study by Blum, et al.,[6] MMA alone does not appear suitable for primary closure after decompressive craniectomy. Titanium mesh implants can be used in conjunction with MMA, and they likely produce a stronger prosthesis; however, this hypothesis was not tested in the study. Although MMA is the most widely applied alloplastic material in use today because of its excellent tensile strength, its lack of donor site incorporation and its fracture rate continue to be problematic.

Hydroxyapatite has also been used to provide smooth contour of the skull and is biocompatible and osteoconductive. It allows for osseous ingrowth over time and has been used often in combination with titanium mesh and miniplates for the repair of large cranial defects.[10,11] Its puttylike consistency is ideal for repair of small cranial defects and can be contoured for excellent cosmetic results. The repair of large defects, however, can be problematic because of the significant settling that can occur as the cement hardens and becomes brittle and also because of the high rates of infection.[11] Customized ceramic prostheses for cranioplasty have also been used with aesthetically acceptable results, although they are quite expensive.[30]

In light of the aforedescribed studies, an ideal means of

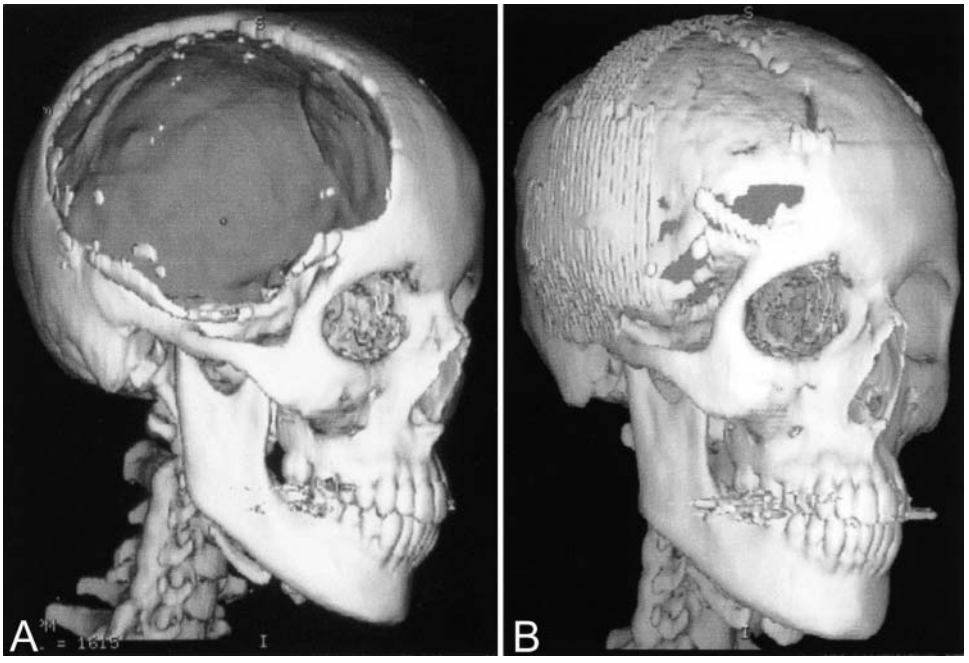

FIG. 4. Three-dimensional reconstructions obtained before (A) and after (B) cranioplasty.

performing cranioplasty after decompressive craniectomy, or in other cases necessitating delayed closure, remains to be determined. Bone graft healing is complex and involves processes of revascularization, osteoconduction, osteoinduction, and osteogenesis. Osteogenesis involves new bone formation by surviving preosteoblasts within the graft. The bone graft functions as a nonviable scaffold for the gradual ingrowth of blood vessels and osteoprogenitor cells from the recipient site, with gradual bone resorption and deposition of new bone. As the healing progresses, the bone graft is remodeled through bone resorption and new bone formation. The calvaria is a membranous bone, demonstrated to undergo less resorption because of its structural integrity.[27] The normal microenvironment of the cranium, however, is not sufficient to promote osteogenesis and may require the addition of growth factors to recruit cells and stimulate bone repair. Researchers have studied the use of bone growth factors including insulin-like growth factor–I, transforming growth factor–β_1, and other growth factors.[1,2,4,5,14,22,25,35,36] Insulin-like growth factor–1 stimulates the replication of osteoblasts and the synthesis of bone matrix.[18] Transforming growth factor–β_1 regulates cell types directly involved in bone remodeling and fracture healing, including chondrocytes, osteoblasts, and osteoclasts.[5] These bone growth factors have been integrated into extended-release biodegradable polymers and maintain their ability to stimulate cellular responses to encourage bone regeneration. Recombinant growth factor technology involving recombinant human bone morphogenetic protein–2 or transforming growth factor–β_1 has also shown promise in the closure of calvarial defects in animal models.[25,29,33,39] Another means of closing large cranial defects that has been explored in preclinical models involved solid template ($CaCO_3$ from natural coral), osteoinductive factors derived from bone protein extracts, and autologous bone marrow cells.[1,2]

Conclusions

In summary, it appears that current failure rates of autografts after decompressive craniectomy in the pediatric population are unacceptably high; however, an ideal means of delayed closure has yet to be found. Use of biodegradable templates in combination with extended-release recombinant human bone growth factors holds promise for resolving the long difficult history associated with autologous cranioplasty. Further basic science inquiry and clinical application remain essential in determining the feasibility and safety of such therapy in the future.

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