Decompressive craniectomy is the standard surgical treatment for malignant cerebral edema and brain herniation resulting from cerebral infarction, intracranial hemorrhage, or severe traumatic brain injury. After resolution of the brain edema or reduction of the intracranial pressure, cranioplasty is often required to achieve cosmetic recovery and protect against the development of sinking–skin flap syndrome.

Various kinds of grafts, including porous polyethylene, methyl methacrylate, titanium, silicone, celluloid, gold, vitallium, tantalum, stainless steel, acrylic resins, hydroxyapatite, ceramics, and osteoconductive bioresorbable ma-

### Cranioplasty with autogenous bone flaps cryopreserved in povidone iodine: a long-term follow-up study

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**OBJECTIVE** The aim of this study was to investigate the long-term therapeutic efficacy of cranioplasty with autogenous bone flaps cryopreserved in povidone-iodine and explore the risk factors for bone resorption.

**METHODS** Clinical data and follow-up results of 188 patients (with 211 bone flaps) who underwent cranioplasty with autogenous bone flaps cryopreserved in povidone-iodine were retrospectively analyzed. Bone flap resorption was classified into 3 types according to CT features, including bone flap thinning (Type I), reduced bone density (Type II), and osteolysis within the flaps (Type III). The extent of bone flap resorption was graded as mild, moderate, or severe.

**RESULTS** Short-term postoperative complications included subcutaneous or extradural seroma collection in 19 flaps (9.0%), epidural hematoma in 16 flaps (7.6%), and infection in 8 flaps (3.8%). Eight patients whose flaps became infected and had to be removed and 2 patients who died within 2 years were excluded from the follow-up analysis. For the remaining 178 patients and 201 flaps, the follow-up duration was 24–122 months (mean 63.1 months). In 93 (46.3%) of these 201 flaps, CT demonstrated bone resorption, which was classified as Type I in 55 flaps (59.1%), Type II in 11 (11.8%), and Type III in 27 (29.0%). The severity of bone resorption was graded as follows: no bone resorption in 108 (53.7%) of 201 flaps, mild resorption in 66 (32.8%), moderate resorption in 15 (7.5%), and severe resorption in 12 (6.0%). The incidence of moderate or severe resorption was higher in Type III than in Type I (p = 0.0008). The grading of bone flap resorption was associated with the locations of bone flaps (p = 0.0210) and fragmentation (flaps broken into 2 or 3 fragments) (p = 0.0009). The incidence of bone flap collapse due to bone resorption was higher in patients who underwent ventriculoperitoneal (VP) shunt implantation than in those who did not (p = 0.0091).

**CONCLUSIONS** Because of the low incidence rates of infection and severe bone resorption, the authors conclude that cranioplasty with autogenous bone flaps cryopreserved in povidone-iodine solution is safe and effective. The changes characteristic of bone flap resorption became visible on CT scans about 2 months after cranioplasty and tended to stabilize at about 18 months postoperatively. The bone resorption of autogenous bone flap may be classified into 3 types. The rates of moderate and severe resorption were much higher in Type III than in Type I. The grade of bone flap resorption was associated with bone flap locations. Fragmented bone flaps or those implanted in patients treated with VP shunts may have a higher incidence of bone flap collapse due to bone resorption.

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terials, have been used to reconstruct calvarial defects.\(^1,6,9,10,23,25,36,37,39,41\) Since the autogenous bone flaps obtained during the initial operation have the advantages of perfect shape, weak rejection reaction, low cost, and high patient acceptance,\(^2\) they are currently considered the ideal material for skull defect reconstruction.\(^2,14,15,35,38,41\)

The autogenous bone flap that is obtained during decompressive hemicraniectomy may be preserved in vivo or in vitro.\(^4,17,18,36\) For in vivo preservation, the bone flaps may be placed between the inner abdominal fat and the abdominal muscles, in a subcutaneous pocket in the thigh or abdomen, or in a subgaleal pocket. This method involves increased surgical pain due to embedding and extraction and results in localized pain and discomfort as well as varying degrees of absorption.\(^19\) Therefore, in vivo preservation is now rarely used. In vitro preservation includes room temperature preservation and cryopreservation. Room temperature preservation refers to storing the bone flaps in solutions such as 80% alcohol\(^27\) or 10% formalin (formaldehyde).\(^42\) Cryopreservation, the most common means of preservation, includes 2 methods: pure cryopreservation, in which after drying and aseptic packaging, the bone flaps are stored at \(-17\) to \(-83\)\(^1\)\(^2\)°C; and cryopreservation in antibacterial or antiseptic solutions such as bacitracin or povidone-iodine solution.\(^5,33\)

Infection and bone resorption are the main postoperative complications of cranioplasty, with autogenous bone flaps often leading to surgical failure.\(^8,40\) Cryopreservation of bone flaps in antibacterial or antiseptic solutions is considered to be a method for reducing the risk of infection, although studies of this method are sparse.\(^5,33\) The incidence of postoperative bone flap resorption reported in the literature varies widely. Moreover, there are no widely accepted uniform diagnostic criteria for bone resorption.

In this study, we propose a new clinical classification and grading system for bone flap resorption and discuss risk factors for postoperative bone resorption.

Methods

General Information

This retrospective study was approved by the ethics committee of Linyi People’s Hospital. A total of 188 patients underwent cranioplasty with 212 autogenous bone flaps cryopreserved in povidone iodine at our institution between January 2001 and December 2012. The clinical data pertaining to these cases were reviewed and analyzed. The reasons for hemicraniectomy included craniocerebral trauma in 154 cases, subarachnoid hemorrhage in 13 cases, cerebral hemorrhage due to hypertension in 12 cases, intracranial tumor in 6 cases, and cerebral arteriovenous malformation in 3 cases.

Bone Flap Preservation

Bone flaps obtained during decompressive craniectomy were rinsed with physiological saline, placed in sterile gloves, and immersed in a 0.5% povidone-iodine solution. After the air was eliminated and the glove was tied tightly and sealed, the glove was placed into another sterile glove, which was then also tightly sealed. The glove was then labeled with the patient’s name, sex, age, case number, date of surgery, and the number of bone flaps contained and placed into a storage bag for cryopreservation at \(-20\)°C.

Cranio­plasty

Patients underwent cranioplasty at 2–6 months after the index craniotomy. An incision was made along the original incision line and the epidural musculocutaneous flap was stripped. The cryopreserved bone flap was thawed with warm sterilized saline solution and then re-implanted and fixed in place with silk sutures or titanium plates. A catheter was placed under the bone flap for drainage and was removed 24–48 hours after the surgery. Patients who had hydrocephalus previously or at the time of the procedure received a ventriculoperitoneal (VP) shunt. Antibiotics were administered intravenously for 4 to 7 days after the operation.

Classification and Grading of Bone Flap Resorption

CT examinations were performed to evaluate resorption after bone flap reimplantation. Bone flap resorption was classified into 3 types according to CT features. In Type I, the bone resorption occurs mainly at the surface and the rim of the bone flap. This type of resorption is characterized by bone flap thinning and bone gap widening (Fig. 1). In Type II, the bone resorption mainly shows a homogeneous decrease of density, with or without bone flap thinning (Fig. 2). In Type III, the bone flap displays...
limited or extensive osteolysis, characterized by a “moth-eaten” appearance (Fig. 3).

In patients with bone flap resorption, the extent of resorption was graded as mild, moderate, or severe. In mild resorption, the bone flap shows thinning, but the thickness remains greater than two-thirds the thickness of the bone plate (Fig. 1A), or the density is slightly reduced (Fig. 2A and B), or the bone flap shows a mildly moth-eaten appearance (Fig. 3A and B). In moderate resorption, the thickness of the bone flap is less than two-thirds the thickness of the bone plate (Fig. 1B) or its density reduced greatly (Fig. 2C) or it shows a significantly moth-eaten appearance (Fig. 3C and D), while the functions of support and protection are maintained. In severe resorption, the bone flap collapses due to resorption and loses its support function, necessitating reconstruction with artificial materials (Fig. 1C and D, Fig. 3E and F).

Follow-Up
Follow-up was scheduled at 1, 3, 6, and 12 months after cranioplasty and annually thereafter with clinical and CT examinations in our outpatient department. If there were no radiological signs of bone flap resorption, the time to the next scheduled CT examination might be extended.

Statistical Analysis
SAS (version 9.1, SAS Institute) was used for statisti-
Results

After the surgery, subcutaneous or extradural seroma collections were seen in association with 19 of the 211 flaps and were successfully treated by puncture suction and compression bandage in all 19 cases. Epidural hematomas occurred in association with 16 of 211 flaps; in 2 of these 16 cases, the hematomas were treated with secondary surgical procedures (1 of these patients died within the period of hospital stay). Eight of 188 patients developed infection. In 6 of these 8 cases, the infection was identified within 2 weeks after cranioplasty, in 1 case within 1 month, and in 1 case within 3 months. All of the cases of infection necessitated removal of the bone flap and a second cranioplasty 6 months later.

Excluding the 8 patients with infection and 2 patients who died within 2 years, the mean duration of follow-up for the remaining 178 patients (with 201 flaps) was 63.1 months (range 24–122 months).

Classification and Grading of Bone Flap Resorption

The changes of bone flap resorption became visible on CT scans about 2 months after cranioplasty and tended to stabilize at about 18 months postoperatively. According to CT examinations, 93 (46.3%) of 201 flaps displayed visible bone resorption, classified as Type I in 55 cases (29.0%) (Fig. 1), Type II in 11 (11.8%) (Fig. 2), and Type III in 27 (29.0%) (Fig. 3). In most of the Type II (9/11) and Type III (23/27) cases, the resorption was accompanied by bone flap thinning and/or bone gap widening. Most of the Type III cases displayed a limited or heterogeneous decrease of density at the early stages, with moth-eaten changes appearing later.

Among the 201 bone flaps, 108 (53.7%) displayed no bone resorption; in the 93 flaps that showed bone resorption, it was mild in 66 (32.8% of the total), moderate in 15 (7.5%), and severe in 12 (6.0%). In all the cases of severe resorption, reconstruction was performed using artificial materials.

The grading of Type I, II, and III resorption is demonstrated in Table 1. The bone resorption of Type I and Type II was predominantly mild. In Type I, moderate and severe resorption accounted for 9.1% and 7.3% of cases, respectively. However, in Type III, moderate and severe resorption accounted for 25.9% and 29.6% of cases, respectively. The difference in extent of bone resorption between Type I and Type III was statistically significant (Ridit analysis by SAS, F = 7.87, p = 0.0008) (Table 1).

Factors Potentially Associated With Bone Resorption

Factors potentially associated with bone resorption in the 178 patients included in the analysis are presented in Table 2. This group included 131 male and 47 female patients, with ages ranging from 15 to 67 years. There were no significant differences in the grading of bone flap resorption between men and women (F = 0.13, p = 0.9427, Ridit analysis by SAS). The mean age of the 92 patients without bone resorption was 41.3 ± 15.35 years, while that of those with mild, moderate, and severe bone resorption were 38.7 ± 12.50, 38.5 ± 11.51, and 35.5 ± 14.63, respectively. There seems to be a trend toward association of increasing resorption grade and decreasing mean age, but there was no statistically significant difference in mean age between the groups of patients with the 3 different grades of flap resorption severity (F = 0.99, p = 0.399, GLM [general linear models] procedure by SAS).

The autogenous bone flaps were re-implanted at 60–179 days after the first craniotomy. The mean bone flap size was 78.7 ± 25.36 cm² (range 42.0–120.0 cm²). There was no statistically significant difference between the resorption severity groups with respect to either mean time to replacement or mean flap size (F = 0.15, p = 0.9268, and F = 0.42, p = 0.7409, respectively, GLM procedure by SAS).

The hemicraniectomy locations for the 201 bone flaps were as follows: 127 flaps, frontotemporal; 35 flaps, frontal; 31 flaps, temporal; and 5 flaps, occipital. Severe resorption occurred in the temporal and frontotemporal flaps, and the resorption seemed to be more significant at the temporoparietal attachment sites. Ridit analysis of the ranked data of multiple samples revealed that the difference among the 4 groups was statistically significant (F = 3.32, p = 0.0210, Ridit analysis by SAS).

In our study, 16 re-implanted bone flaps were fragmented into 2 or 3 fragments, while the other 185 flaps were intact. The fragmented bone flaps were associated with a higher incidence of moderate and severe bone resorption than the intact flaps (F = 5.76, p = 0.0009, Ridit analysis by SAS).

In the 16 flaps that were implanted in patients who underwent VP shunt implantation for management of hydrocephalus, 4 flaps (25.0%) collapsed due to bone resorption. Among the 185 flaps implanted in patients who did not undergo VP shunt implantation, 8 (4.3%) flaps collapsed due to bone resorption. The difference between the 2 groups was statistically significant (p = 0.0091, Fisher’s exact test). Of the 4 flaps that collapsed in patients with VP shunts, 3 mainly showed bone gap widening, while the flap thinning was relatively mild (Fig. 4). In one particularly interesting case, the bone flap was fine when the VP shunt was implanted 6 months after cranioplasty. However, the bone flap began to collapse 1 month later, and 9 months later the bone gap had widened to a significant extent, while the bone flap thinning was still relatively mild.
Discussion

Infection is a severe postoperative complication of autologous bone flap cranioplasty that must be removed surgically once found. Bhaskar et al.4 reported on 179 cases of cranioplasty with cryopreserved autogenous bone flaps and found that 17 (9.5%) had postoperative severe infection. Kim et al.22 analyzed factors affecting infection after cranioplasty and found that it was associated with previous resection of the temporalis muscle, preoperative presence of subgaleal fluid collection, surgical time greater than 120 minutes, and postoperative “wound disruptions.” The infection rate in our group was relatively low (4.3%), suggesting a possible benefit of the bactericidal action of povidone iodine.

Bone resorption is the other main postoperative complication of autologous bone flap cranioplasty. The timing of bone resorption after cranioplasty with autogenous bone flaps is not yet fully understood. In our series of cases, the changes associated with bone flap resorption typically became visible on CT scans about 2 months after cranioplasty and tended to stabilize at about 18 months after cranioplasty. Moreover, in all 12 cases of bone flap collapse due to severe resorption, the bone flap collapsed within 18 months after cranioplasty. Therefore, the follow-up period after cranioplasty should be at least 18 months.

The reported incidence of bone resorption after cranioplasty with autologous bone flaps ranges from 1.4% to 50%,8,17,52,36,38,45 and the incidence of severe bone resorption has been reported as 0.8%–20%.14,18,25,40 There are no accepted diagnostic criteria for bone resorption, which may mainly account for the great difference in the reported incidence. Consequently, we developed classification and grading methods for bone resorption. According to our criteria, 46.3% of the bone flaps re-implanted displayed visible bone resorption, and in most of these cases the resorption was mild and did not require reconstruction with artificial materials. Only 12 bone flaps (6.0%) had to be replaced with artificial materials due to severe resorption, which suggests that cranioplasty with autogenous bone flaps had good security and reliability.

There are few reports on the classification of bone resorption in autogenous bone flaps. Dünisch et al.11 defined 2 different types of necrosis according to the CT features: a thinning of the bone flap and/or the beginning of resorption along the rims of the flap was classified as Type I necrosis, whereas a Type II bone flap necrosis was characterized by a circumscribed, complete lysis of the bone within the flap, with loss of bony protection of the brain. According to what we have observed in this study, 3 kinds of bone resorption forms may be identified on CT scans: bone flap thinned, bone density decreased, and bone dissolved (osteolysis). Although in some cases, 2 or 3 forms of bone resorption might be seen in the same flap, one form often was dominant in most cases. Thus we classified bone resorption of autogenous bone flaps into 3 types: in Type I, the bone resorption mainly occurred at the border of the flap characterized by bone flap thinned and bone gap widened; in Type II, bone density decreased; and in Type III, limited or extensive osteolysis.

Type I was the most common form of bone flap resorption, accounting for 59.1% cases of visible bone resorption. Most of Type II (9/11) and Type III (23/27) cases were accompanied by bone flap thinned or bone gap widened (features of Type I). The bone resorption of Type I and Type II was predominantly mild. The rate of moderate and severe resorption in Type I was low (9.1% and 7.3%). Type II displayed a homogeneous decrease in density, while Type III usually showed a limited or heterogeneous decrease in density at the early stage with development of moth-eaten changes over time. The rate of moderate
or severe resorption in Type III was much higher than in Type I. Consequently, patients who show a limited or heterogeneous decrease of bone flap density should be closely followed up. Because Type III is closely related to severe bone resorption, the mechanism of this type should be the focus of further study.

The reason for bone resorption after cranioplasty with autogenous bone flaps remains unclear. Some reports have stated that autogenous bone flap resorption was associated with preoperative high-pressure steam sterilization of the bone flap, multiple fracture lines, patient age, skull defect size, cryopreservation time, extent of opening of the dura mater, or VP shunt implantation. This study revealed that moderate and severe resorption mostly occurred in temporal bone flaps, whereas most of the cases of resorption in the frontal and occipital bone flaps were mild. We suspected that this occurred for the following reasons. 1) In the first operation, to ensure full decompression, excessive bone was removed, resulting in bone defects, especially in the temporal area adjacent to the skull base. 2) Temporal bone is thinner than other skull bones, which results in better performance with the same degree of resorption. 3) The temporal area is covered by the temporalis muscle, which has an abundant blood supply.

Resorption was common after the reimplantation of bone flaps with fractures. In this study, the flaps with fragmentation had a higher incidence of moderate or severe resorption after reimplantation than those without fragmentation. We believe that after reimplantation, the bone flaps with fractures may have local fine motion that promotes resorption. Thus, we recommend the reconstruction of skull defects using artificial materials when bone flaps are fragmented.

The rate of autogenous bone resorption in patients who underwent VP shunt implantation was higher than the rate in patients without VP shunts. Most of the cases of flap collapse due to bone resorption among the patients with VP shunts manifested primarily as bone gap widening with only relatively mild flap thinning. As noted in Results, in one of our patients, the bone flap was fine when a VP shunt was implanted 6 months after cranioplasty, but it began to collapse 1 month later, with the significant bone gap widening evident 9 months later, while the bone flap thinning was still relatively mild. We hypothesized that the dramatic changes of intracranial pressure due to the siphon action of the VP shunt led to fine motion of the bone flap and increased bone resorption, particularly at the edge of the bone flap. Moreover, fine motion of the bone flap might cause titanium screw loosening and fixation failure. Therefore, in patients who require cranioplasty and a VP shunt, we recommend that the skull defects be reconstructed with artificial materials.

Conclusions

Because of the low incidence of infection and severe bone resorption, our results suggest that cranioplasty with autogenous bone flaps cryopreserved in povidone iodine...
is safe and effective. In patients with bone flap resorption, characteristic changes became visible on CT scans about 2 months after cranioplasty and tended to stabilize at about 18 months postoperatively. The bone resorption of autogenous bone flaps may be classified into 3 types, as described in Results. The rate of moderate or severe resorption in Type III was much higher than in Type I. The grade of bone flap resorption was associated with the locations of bone flaps. Fragmentation of bone flaps and VP shunt implantation may each result in a higher incidence of bone flap collapse due to bone resorption.

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