Time Interval Reduction for Delayed Implant-Based Cranioplasty Reconstruction in the Setting of Previous Bone Flap Osteomyelitis

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Background: Reinfections following implant-based cranioplasty, in the setting of previous bone flap osteomyelitis, are common and associated with significant morbidity. The timing of reconstruction following initial osteomyelitic bone flap removal remains controversial; most advocate for prolonged time intervals of approximately 6 to 12 months. Thus, the authors investigated their delayed cranioplasty outcomes following both early (between 90 and 179 days) and late (≥180 days) time intervals with custom craniofacial implants to determine whether timing affected outcomes and rates of reinfection.

Methods: An institutional review board–approved retrospective cohort review of 25 consecutive cranioplasties, from 2012 to 2014, was conducted. A nonparametric bivariate analysis compared variables and complications between the two different time interval groups, defined as early cranioplasty (between 90 and 179 days) and cranioplasty (≥180 days).

Results: No significant differences were found in primary and secondary outcomes in patients who underwent early versus late cranioplasty ($p > 0.29$). The overall reinfection rate was only 4 percent (one of 25), with the single reinfection occurring in the late group. Overall, the major complication rate was 8 percent (two of 25). Complete and subgroup analyses of specific complications yielded no significant differences between the early and late time intervals ($p > 0.44$).

Conclusions: The results suggest that early cranioplasty is a viable treatment option for patients with previous bone flap osteomyelitis and subsequent removal. As such, a reduced time interval of 3 months—with equivalent outcomes and reinfection rates—represents a promising area for future study aiming to reduce the morbidity surrounding prolonged time intervals. (*Plast. Reconstr. Surg.* 137: 394e, 2016.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Irrespective of neurosurgical technique, the risk of bone flap osteomyelitis following craniotomy exists forever because of peripheral resorption and primary/secondary infection.[1–3] As such, a wide spectrum of treatment algorithms are described for managing bone flap osteomyelitis. These include bone flap removal and cranial reconstruction with various autologous or alloplastic materials. However, the timing of these definitive reconstructions remains in question—and is currently performed at various time intervals ranging from immediately to 1 year after osteomyelitic bone flap removal (Fig. 1).[1,3–8] One of the most common approaches involves osteomyelitic bone flap removal, scalp débridement, intravenous antibiotics, and delayed secondary reconstruction with custom cranial implant.[1,3,4] Although the association between implant material and infection has been well documented, the optimal time interval from infected bone flap removal to delayed implant-based cranioplasty has yet to be defined and remains controversial.[1] In fact, the literature offers no definitive recommendation or treatment algorithm for using

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alloplastic cranial implants in patients after osteomyelitic bone flap removal.[1]

To date, several studies have documented high reinfection rates and complication profiles approaching 40 percent with the use of custom cranial implants in this type of clinical setting.[4] Therefore, the purpose of this study was to answer the following question: Does early (between 90 and 179 days) versus late (≥180 days) delayed implant-based cranioplasty reconstruction following bone flap osteomyelitis result in higher reinfection and complication rates? Our group's hypothesis was that an early delayed implant-based cranioplasty has outcomes equivalent to late delayed cases, using a standard treatment algorithm. As such, the specific aims of this study were to (1) identify all patients with implant-based cranioplasty reconstruction following osteomyelitic bone flap removal, (2) investigate reinfection and major complication rates in early- versus late-stage cranioplasties, and (3) propose a reconstructive treatment algorithm.

PATIENTS AND METHODS

Study Design/Sample

This study included a retrospective cohort of all adult patients undergoing delayed implant-based cranioplasty reconstruction over a 3-year period at a multidisciplinary adult cranioplasty center within a university hospital (January of 2012 to December of 2014). All patients were selected based on the following inclusion criteria: (1) age 18 years or older, (2) history of bone flap osteomyelitis requiring removal, (3) completion of at least a 6-week course of tailored antibiotic therapy, and (4) delayed reconstruction with customized cranial implant. Exclusion criteria included (1) history of failed cranioplasty with previously placed alloplastic materials transferred for care from an outside institution, (2) failure to complete mandatory antibiotic therapy as prescribed, and (3) pediatric patients younger than 18 years. The study was approved by the Institutional Review Board of the Committee on Clinical Investigation at The Johns Hopkins University School of Medicine.

Primary Predictor Variable: Elapsed Time Interval from Bone Flap Removal/Débridement to Definitive Cranioplasty

The two groups, labeled early and late, were categorized on the total amount of elapsed time from their first-stage operation (i.e., osteomyelitic bone flap removal) to their second-stage operation (i.e., implant-based cranioplasty reconstruction).

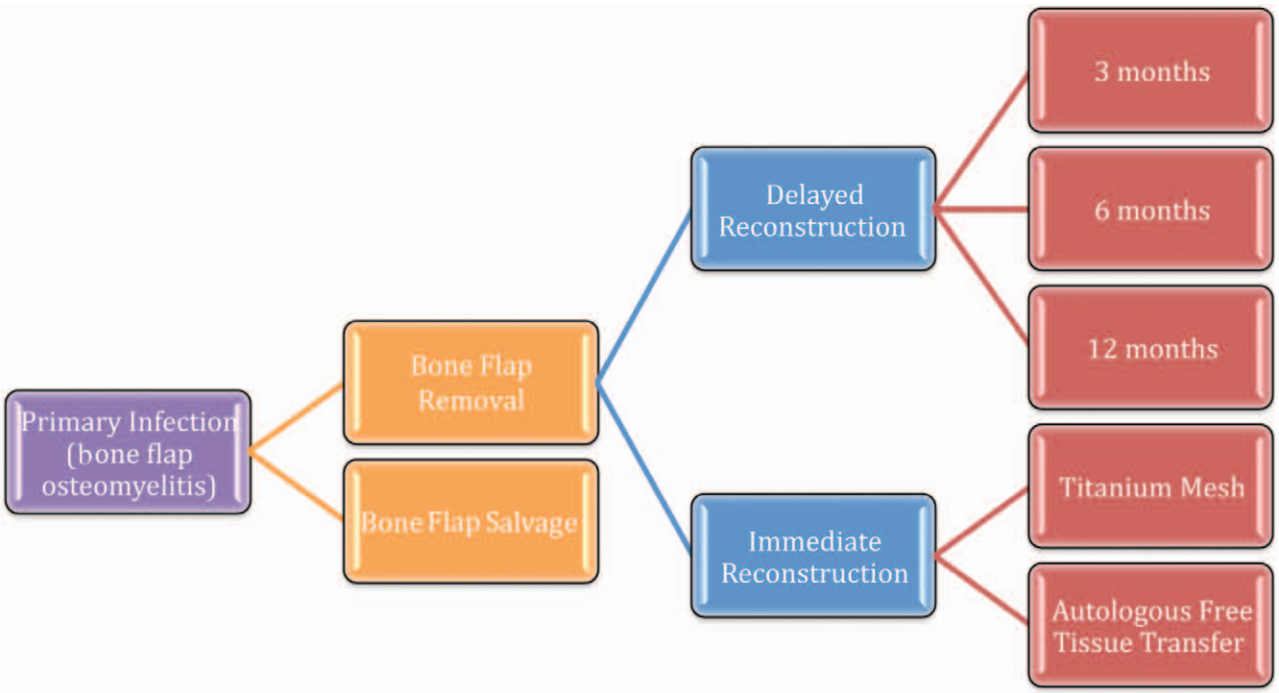

Fig. 1. Bone flap osteomyelitis treatment options, representing the choice between removal and reimplantation (bone flap salvage) of the original bone flap followed by differences in timing of definitive reconstruction. Immediate secondary cranioplasty occurs at the time of bone flap removal using either titanium mesh or autologous free tissue transfer versus delayed cranioplasty involving an elapsed time interval ranging from 3 (early) to 6 to 12 months (late).

Exact time intervals were measured from day 0 (date of bone flap removal) to day *x* (date of implant-based cranioplasty reconstruction). Once all the data were captured, the early group was selected, and encompassed all patients undergoing delayed reconstruction within 90 to 179 days from date of bone flap removal. The late group was defined as those who had undergone cranioplasty reconstruction at exactly 180 days or greater.

Secondary Predictor Variables

The following demographic and patient-specific variables were collected: age, sex, race, smoking status, comorbidities, history of chemotherapy, history of radiation therapy, anticoagulation therapy status, indication for initial craniotomy, location of craniotomy, elapsed time interval from craniotomy to bone flap osteomyelitis presentation, duration of follow-up, and custom cranial implant material. Smoking status was defined as those actively smoking through the period of cranioplasty surgery. All patients on necessary perioperative anticoagulation were managed by our hematology team members. All custom cranial implants used in this study were made of either polyetheretherketone or polymethylmethacrylate (Stryker CMF, Kalamazoo, Mich.).

Management Technique

The sections of craniofacial plastic surgery, neurosurgery, infectious disease, and hematology work in close collaboration by means of a multidisciplinary center dedicated solely to cranioplasty reconstruction, and therefore all patients with bone flap osteomyelitis are managed jointly (Fig. 2). Appropriate imaging (head computed tomography and/or magnetic resonance imaging) was obtained preoperatively for all patients to determine the overall extent of infection and to guide treatment. In cases where bone flap osteomyelitis was suspected, the patient was taken to the operating room for bone flap/hardware removal,

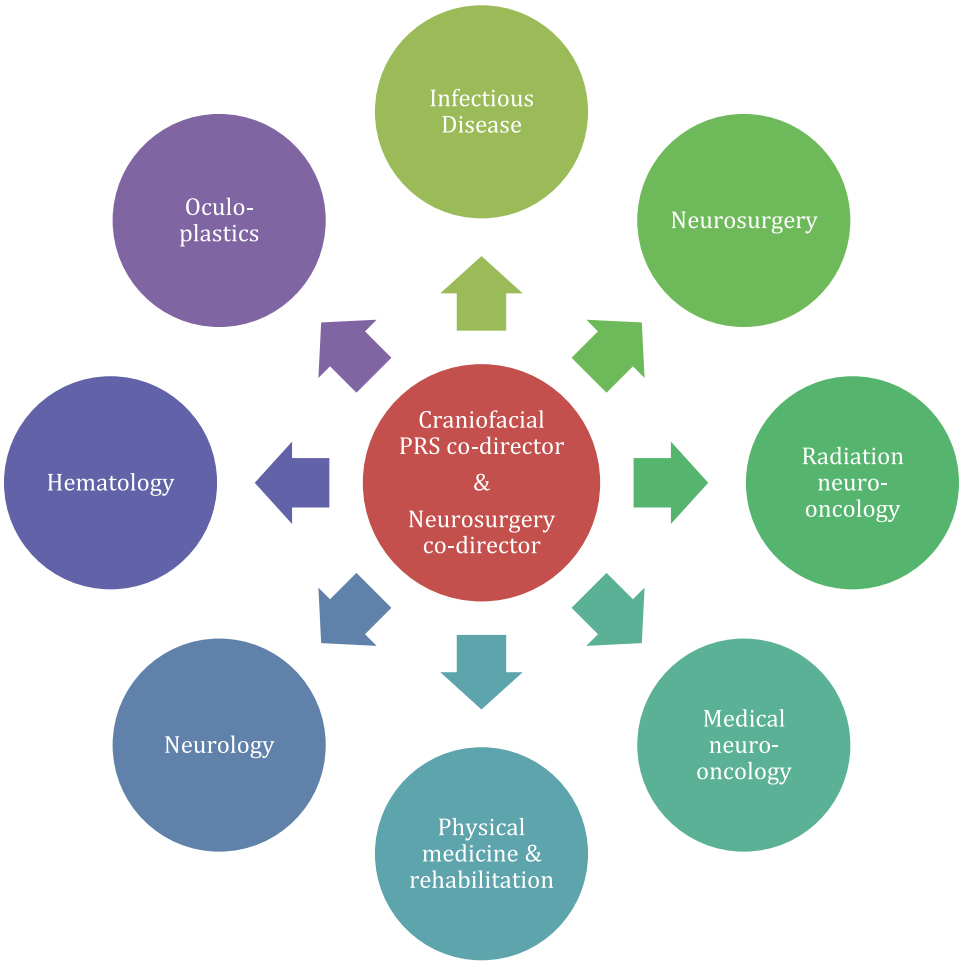

Fig. 2. Diagram illustrating the multiple specialties collaborating within the multidisciplinary adult cranioplasty center in an effort to improve patient outcomes. *PRS*, plastic and reconstructive surgery.

scalp débridement/closure, collection of swab/tissue cultures, and copious irrigation with antibiotic solution (Fig. 3). In conjunction with neurosurgery, the craniofacial surgeon determined the timing and materials used for subsequent reconstruction based on each patient's wound healing progress by means of clinical examination. In addition, a 6-week course of intravenous antibiotic therapy was selected by our infectious disease team members and tailored specifically to the cultures obtained during the first-stage operation. Resolution of infection (absent drainage/erythema with complete wound healing) was considered necessary before proceeding with second-stage, implant-based cranial reconstruction (Fig. 3).

Surgical Technique

We used the technique of pericranial-onlay cranioplasty, which has been described previously.[9] Briefly, all custom cranial implants were implanted within a new tissue plane—sandwiched *underneath* a transposed, skeletonized fasciocutaneous scalp flap (containing only skin/galea aponeurosis), and *above* an inferiorly based pericranial-onlay flap covering the epidural space/dural substitute. Both vascularized flaps remain perfused by the superficial temporal system. This technique allows the implants to remain separate from the previously infected epidural space.

Outcomes

The primary outcome of interest in this study was reinfection of the alloplastic implant following delayed cranioplasty reconstruction. This complication was defined based on the following clinical signs/symptoms as evidence of reinfection: wound drainage, persistent erythema/cellulitis, pain/tenderness along the implant, scalp dehiscence, and/or implant extrusion. Secondary outcomes included several major and minor complications. Major complications were defined as adverse outcomes that required readmission and/or reoperation for treatment, including reinfection requiring implant removal, epidural collection requiring evacuation (hematoma/seroma), stroke, cerebrospinal fluid leak, and/or death. Minor complications were defined as adverse outcomes that did not require readmission and/or reoperation and

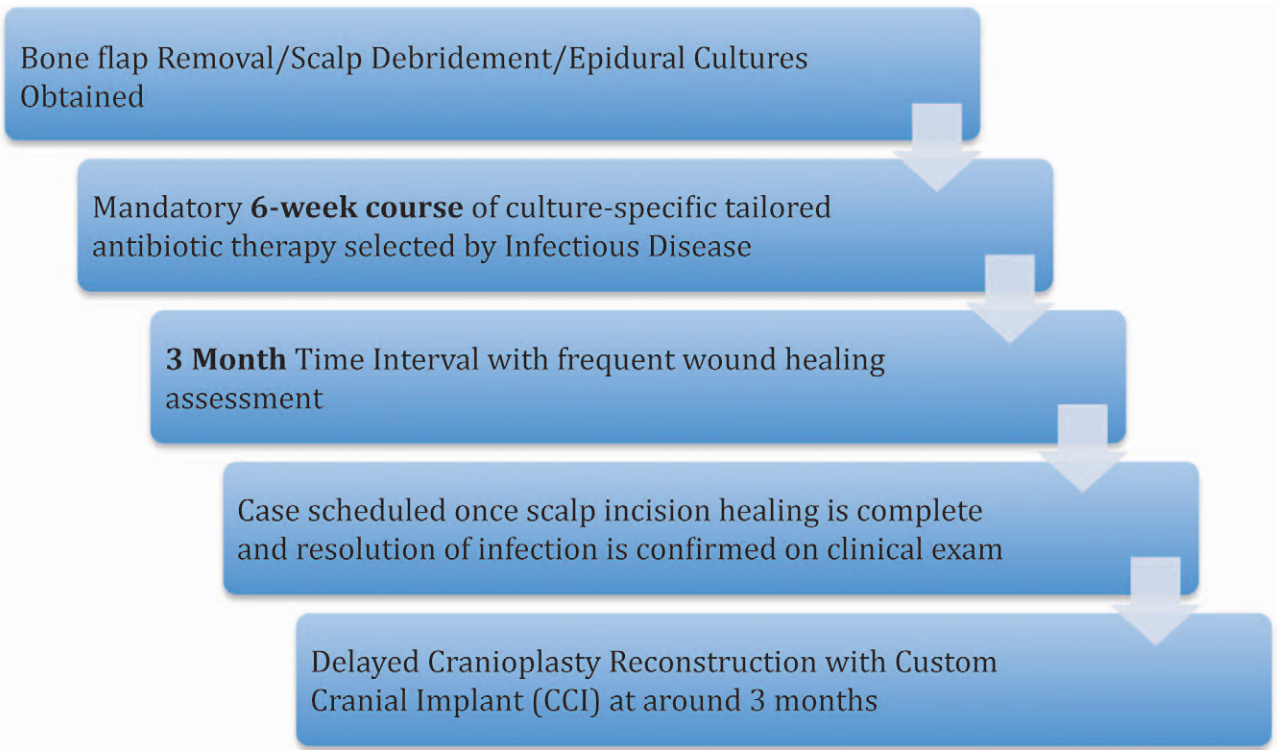

Fig. 3. Proposed algorithm for bone flap osteomyelitis management: Time from bone-flap removal to definitive cranioplasty in 3 months. In the first stage, the bone flap is removed, the site is radically débrided, and microbiological epidural cultures are obtained for targeted antibiotic therapy. Monthly visits to the craniofacial plastic surgeon for wound checks ensure absence of clinical signs of persistent infection. If scalp wound is fully healed and without erythema, drainage, and/or signs of infection, secondary cranioplasty with a custom cranial implant is performed at approximately 3 months.

included superficial wound dehiscence, partial scalp necrosis, and self-limiting fluid collections found incidentally on follow-up radiographic examination.

Statistical Analysis

All deidentified data were iteratively entered into a statistical database (IBM SPSS, Version 20.0; IBM Corp., Armonk, N.Y.) over the course of the study. Descriptive statistics were computed for the study population to provide an overall assessment of the sample. Given the lack of confirmed normality within the sample, nonparametric bivariate analyses (i.e., Fisher's exact test for categorical measures and Mann-Whitney *U* test for continuous measures) were used to identify associations between the predictor variables and complications. A value of $p < 0.05$ was considered statistically significant.

RESULTS

From 2012 to 2014, a total of 25 of 108 (23 percent) consecutive, implant-based cranioplasties were performed in the setting of previous bone flap osteomyelitis by the senior author (C.R.G.). The cohort consisted of 12 women and 13 men with a mean age of 50 years (range, 22 to 82 years) (Table 1). Fourteen patients (56 percent) were included in the early group (between 90 and 179 days) and 11 patients (44 percent) were included in the late group (≥180 days). Mean duration of follow-up for the entire cohort was 18 ± 9.6 months (range, 7 to 43 months). Intraoperative cultures from bone flaps removed at presentation included *Propionibacterium acnes* [eight of 25 (32 percent)], methicillin-resistant *Staphylococcus aureus* [five of 25 (20 percent)], methicillin-sensitive *Staphylococcus aureus* [three of 25 (12 percent)], *Pseudomonas aeruginosa* [one of 25 (4 percent)], *Staphylococcus epidermidis* [one of 25 (4 percent)], and *Enterobacter cloacae* [one of 25 (4 percent)]. The remaining cases involved mixed flora [three of 25 (12 percent)] or exhibited no growth [three of 25 (12 percent)].

Primary Outcome

The overall reinfection rate in our cohort for delayed cranioplasty reconstruction following osteomyelitic bone flap removal was 4 percent using custom alloplastic implants (one of 25). For the early group, the reinfection rate was 0 percent (zero of 14). For the late group, the reinfection rate was 7 percent (one of 11) (Table 2). Of note, the single patient from the late group with reinfection had *Propionibacterium acnes*–positive cultures and was a heavy, active chronic cigarette smoker. These outcome differences, between the early and late groups, were *not* found to be statistically significant ($p = 0.44$).

Secondary Outcome

The overall complication rate, including both groups undergoing delayed cranioplasty reconstruction with custom cranial implants, was 12 percent (three of 25) (Table 2). Overall complication rates and subgroup analyses of specific complications yielded no significant differences between the early and late time points ($p > 0.44$). For the early delayed group, the overall complication rate was 7 percent (one of 14). The single early group complication involved a large postoperative epidural hematoma on postoperative day 2 requiring decompression. In the late group, the overall major complication rate was 9 percent (one of 11). This involved a heavy, active smoking patient who required reoperation and implant removal after presenting with a nonhealing, infected wound at 1 month. The single minor complication (9 percent) in the late group involved a small epidural fluid collection that was managed nonoperatively and found incidentally on postoperative imaging. In summary, the time interval spanning osteomyelitic bone flap removal and delayed, implant-based cranioplasty reconstruction was not associated with significant differences in complication rates when comparing both early and late groups.

DISCUSSION

Delayed reconstruction with prolonged time intervals following osteomyelitic bone flap removal accompanies significant perioperative morbidity. This is related to both the required helmet therapy for cerebral protection and the subsequent deformities acquired along the temporal region secondary to temporalis malposition/foreshortening and temporal fat pad atrophy (i.e., known as temporal hollowing or wasting).[10] Therefore, patients with prolonged time intervals approaching 6 to 12 months face several major quality-of-life issues such as increased time away from work (social stigmata), loss of potential earning potential (job restrictions), the unfortunate agony related to social withdrawal from wearing a padded helmet in public, and an altered visual appearance related to unavoidable craniofacial deformity (Figs. 4, *above* and 5, *above*).[10] As such, clinical algorithms aiming to decrease the time to

Table 1. Patient Demographics of the Cohort Spanning 25 Consecutive Early (90 to 179 days) and Late (≥180 days) Implant-Based Cranioplasty Reconstruction Cases

Characteristic	Early Cranioplasty (%)	Late Cranioplasty (%)	All Cases Combined (%)	*p*
No. of patients	14	11	25	
Age, yr				0.4594
Mean	53	45	50	
Range	33–82	22–75	22–82	
Male-to-female ratio	5:9	8:3	13:12	0.1107
Race				0.3604
White	9 (64)	9 (82)		
African American	2 (14)	2 (18)		
Other	2 (21)	0		
Time from bone-flap removal to cranioplasty, mo				0.0000223
Mean	3.77	8		
Range	3–5	6–19		
Follow up time, mo				
Mean ± SD			5.5 ±4.6	
Range			0.6–21	
Operative time, min				
Mean			201	
Range			77–809	
Length hospital stay, days				
Mean			4	
Range			2–14	
Indication for craniectomy/craniotomy				0.7161
Trauma	1 (7)	2 (18)	3 (12)	
Vascular	4 (4)	2 (18)	6 (24)	
Tumor	9 (64)	7 (64)	16 (64)	
Location of secondary cranioplasty				0.8672
Frontal	3 (21)	1 (9)		
Frontoparietal	2 (14)	2 (18)		
Frontotemporal	0 (0)	1 (9)		
Pterional	8 (57)	7 (64)		
Temporal	1 (7)	0 (0)		
Surgical side				1
Bilateral	1 (7)	1 (9)		
Left	6 (43)	4 (36)		
Right	7 (50)	6 (55)		
Cranioplasty material				0.5648
PMMA	14 (100)	7 (63)	21 (84)	
PEEK	0 (0)	4 (36)	4 (16)	
Operative time, min				
Average			201	
Range			77–809	
Follow-up time				
Average			4.8	
Range			0.1–21.7	
Comorbidities				
Smoking history	4 (28)	9 (82)	13 (52)	0.01542
Active smoking	2 (14)	6 (55)	8 (32)	0.08098
Obesity	0 (0)	1 (9)	1 (4)	0.44
Hypertension	5 (36)	3 (27)	6 (24)	1
Cardiovascular disease	2 (14)	0 (0)	2 (8)	0.4867
Hyperlipidemia	1 (7)	0 (0)	1 (4)	1
Diabetes mellitus	2 (14)	0 (0)	2 (8)	0.4867
Insulin dependence	1 (7)	0 (0)		1
Coagulopathy	0 (0)	2 (18)	2 (8)	0.1833
Preoperative anticoagulation therapy	1 (7)	1 (9)		1
Any coagulopathy	1 (7)	2 (18)		0.5648
Hypothyroidism	1 (7)	0 (0)		1
Cancer	9 (64)	7 (64)	16 (64)	0.8813
Other comorbidity	8 (57)	8 (73)	16 (64)	0.6766
Prior chemotherapy/radiation therapy near/at site of surgery	3 (21)	2 (18)	5 (16)	1
Discharged with drains	3 (21)	4 (36)		0.6564

PMMA, polymethylmethacrylate; PEEK, polyetheretherketone.

Table 2. Description of Major and Minor Complications in the Early and Late Secondary Cranioplasty Groups

Complication	Early Cranioplasty (%)	Late Cranioplasty (%)	All Patients (%)	*p*
No. of patients	14	11	25	
Postoperative wound infection	0 (0)	1 (9)	1 (4)	0.44
Major complication	1 (7)	1 (9)	2 (8)	1.00
Epidural/hematoma fluid collection	1 (7)	0 (0)	1 (4)	1.00
Postoperative infection	0 (0)	1 (9)	1 (4)	0.44
Minor complication	0 (0)	1 (9)	1 (4)	0.44
Epidural/hematoma fluid collection	0 (0)	1 (9)	1 (4)	0.44
Total complication	1 (7)	2 (18)	3 (12)	0.56

definitive reconstruction with implants, in the setting of previous bone flap osteomyelitis, are undeniably warranted—especially because any form of time interval reduction may have a dramatic effect on one's quality of life. Considered together, we propose a safe time interval reduction of approximately 50 to 75 percent—by reducing the average interval between infected bone flap removal and reconstructive cranioplasty from 6 to 12 months to approximately 3 months.

Unfortunately, previous attempts at time interval reduction using similar study cohorts with alloplastic implants were tempered because of high rates of reinfection. In fact, it is well established in the literature that a previous cranial infection (i.e., bone flap osteomyelitis) is an independent risk factor for complications following cranioplasty reconstruction using alloplastic implants.[1,4,9,11,12] In 1986, Manson and colleagues reported a significant reinfection rate of 16 percent (four of 25).[3] Similarly, Frederick et al. reported a 40 percent (19 of 48) reinfection rate with a larger series of patients—which is a 10-fold increase in reinfections compared with our experience presented here.[4] Similarly, Tokoro et al. reported a 23 percent (three of 13) reinfection rate when using a time interval of 4 to 9 months (Table 3).[3–8,12,13] Overall, the literature suggests that surgical outcome for delayed, implant-based cranioplasty reconstruction in patients with previous bone flap osteomyelitis is poor and portends significant risk for reinfection (range, 16 to 40 percent).[1,3,4,13–17]

As a result, the surgical management of these patients with osteomyelitis continues to be challenging for craniofacial surgeons, infectious disease specialists, and neurosurgeons alike.[1,14,18] To mitigate the risk of reinfection, most surgeons opt for a conservative time interval of at least 6 to 12 months before pursuing definitive reconstruction.[1,3,11,15,19,20] However, more recently, some authors have focused on defining a shorter, safe interval. For example, Yoshioka believes that delayed cranial reconstructions can be performed as early as 3 to 4 months after bone flap removal.[16] Some investigators have even gone a step further and now question the need to delay definitive reconstruction (Table 3). Kshettry et al. recently reported a 17 percent reinfection rate (two of 12) after performing immediate cranioplasty reconstruction with titanium mesh—at the same time of infected bone flap removal.[13] Similarly, Lee et al. recently published their experience using single-stage, autologous free tissue transfer at the time of osteomyelitic bone flap removal and reported no reinfections in a small cohort of patients (zero of 14).[7] A different study, by Lee et al. reported favorable results using autologous split calvarial grafts [15 of 25 (60 percent)], which had a 13 percent (two of 15) reinfection rate compared with the 43 percent (three of seven) reinfection rate when using a mixture of alloplastic materials [seven of 25 (28 percent)].[8] Unfortunately, Lee et al. did not report timing of secondary cranioplasty, and the cohort was heterogeneous, making a true comparison difficult.[8]

Although the use of vascularized composite flap reconstruction and autologous split calvarial grafts sounds promising, these methods are limited by several negative factors, including significant donor-site morbidity (irrespective of whether autologous bone elements are included), suboptimal cerebral protection from trauma, questionable long-term stability related to nonnative bone remodeling/resorption, and suboptimal symmetry on appearance secondary to the mismatch of flap thickness compared to the surrounding native scalp.[7,8] Lastly, several authors have examined the efficacy of antibiotic irrigation systems[5] and/or radical débridement[6]—in an attempt to salvage all infected bone flaps. Unfortunately, the usefulness of these systems has come into question given their variable effectiveness, with reinfection rates ranging from 8 percent (one of 12) to 61 percent (eight of 13).[5,6]

To maximize the benefits of early-stage reconstruction and to minimize the potential morbidity

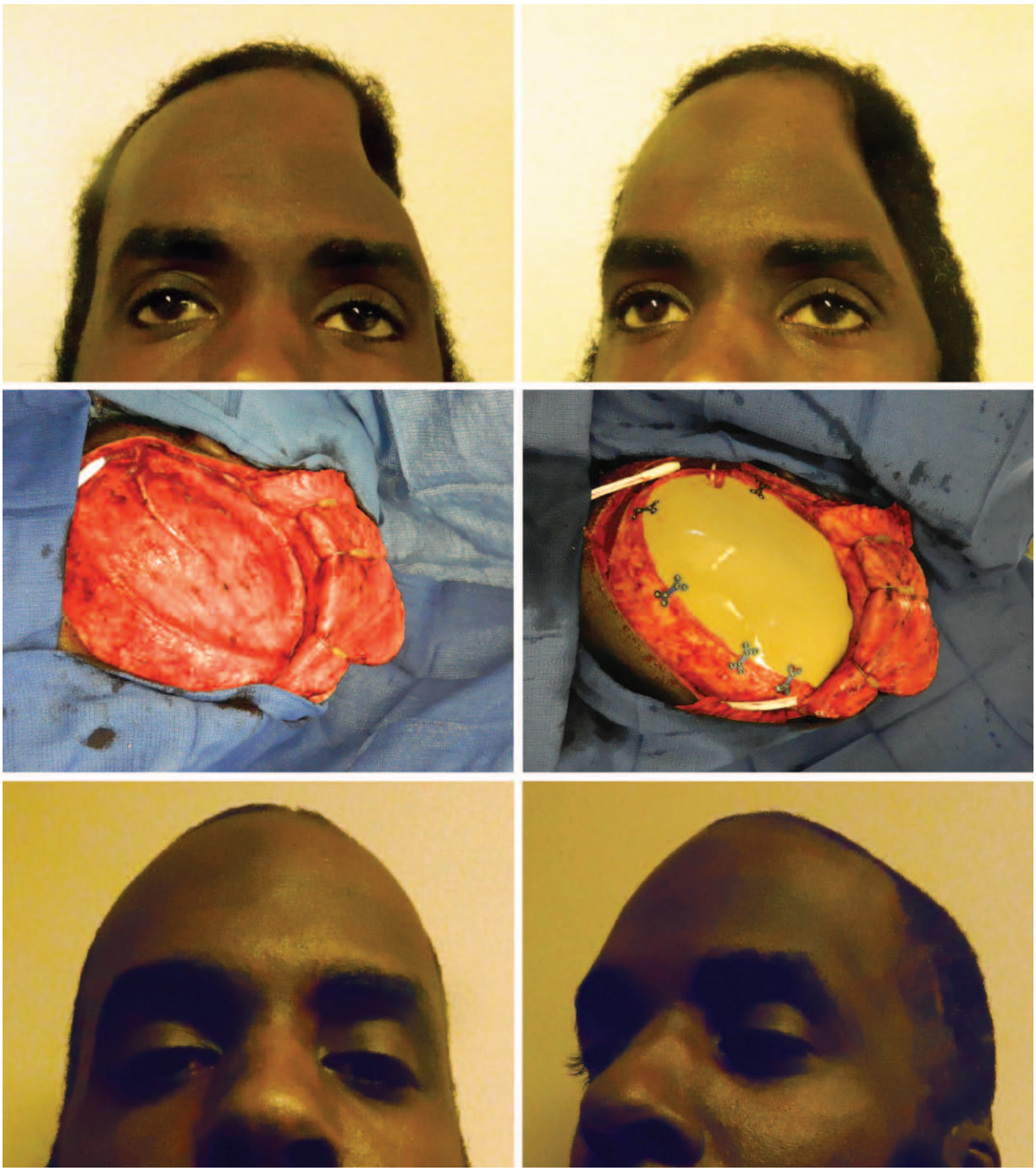

Fig. 4. Preoperative photographs of male subject following removal of infected bone flap: frontal (*above*, *left*) and oblique views (*above*, *right*). (*Center*) Intraoperative photographs showing the dissection separating the inferiorly based pericranial-onlay and the transposed fasciocutaneous scalp flap, thereby creating a vascularized pocket (*center*, *left*) into which the implant is rigidly fixated (*center*, *right*). Three-month postoperative frontal (*below*, *left*) and oblique (*below*, *right*) photographs demonstrating restoration of symmetrical craniofacial contour. [Intraoperative photography assistance was provided by Brad Rabinovitz.]

of performing surgery too early, we chose to investigate our long-term outcomes in a select cohort of patients who had undergone an early cranioplasty with a reduced time interval of 90 to 179 days after bone flap removal. Furthermore, based on our experience with variable time intervals before definitive cranioplasty that resulted from secondary factors such as chemotherapy, radiation therapy, and geographic travel constraints (i.e., international patients), we hypothesized that

Table 3. Summary and Comparison of Published Reinfection Rates after Delayed, Implant-Based Cranioplasty Reconstruction following Previous Osteomyelitic Bone Flap Removal

Reference	No.*	Reinfection Rate (%)	Reconstruction Timing	Reconstruction Material Used
Manson et al.,1986[3]	25	16	Delayed (>6 mo)	Various materials
Frederick et al., 2011[4]	48	40	Delayed (not specified)	Alloplastic
Tokoro et al., 1989[12]	13	23	Delayed (>6 mo)	Alloplastic
Kshettry et al., 2011[13]	12	17	Immediate	Titanium mesh
Lee et al., 2013[7]	14	0	Immediate	Autologous vascularized flaps
Lee et al., 2014[8]	25	20	Not specified	Split calvarial bone grafts and alloplastic materials
Bruce and Bruce, 2003[6]	13	61	Immediate	Bone flap salvage
Auguste and McDermott, 2006[5]	12	8	Immediate	Bone flap salvage
Lopez et al., 2015	25	4	Early (90–179 days) and delayed (≥180 days)	Alloplastic

*Sample size the authors used to calculate reinfection rates.

complication rates following early cranioplasty (between 90 and 179 days) could be equivalent to those of the standard accepted practice of waiting 6 to 12 months.

For the sake of true comparison, we reduced the number of predictor variables and limited our outcome analysis to only those patients who underwent reconstruction with alloplastic implants following osteomyelitic bone flap removal (n = 25 patients). Surprisingly, our cohort was found to have only a 4 percent reinfection rate (one of 25) and a low overall major complication rate of 8 percent (two of 25) (Table 2). In fact, the only reported complication in the early group [one of 25 (4 percent)] was an epidural hematoma requiring evacuation on postoperative day 2. Of the 25 patients, only one patient (4 percent) required implant removal because of reinfection, and this involved a heavy active smoker.

Although our cohort was composed of a challenging diverse patient population with significant risk factors for complication and reinfection—including those with malignant brain tumors requiring adjuvant chemotherapy/radiation therapy and those with frontal sinus invasion at the time of extirpation requiring sinus obliteration/cranialization—we hypothesize that our low incidence of postoperative complications may be attributable to our previously described, pericranial-onlay cranioplasty technique.[1,21] For this type of approach, the dissection plane is pristine, which in turn avoids undesirable contact of the alloplastic implant with the previously infected epidural space (Figs. 4, *center* and 5, *center*). In addition, the vascularized pericranial onlay provides a well-perfused barrier against infection by enhancing the delivery of systemic antibiotics to the area (Figs. 4, *center*, *left* and 5, *center*, *left*). In addition to a putative role in reducing infections, this technique also provides a tension-free scalp closure through simultaneous "component release" of the fibrous attachments found between the galea aponeurosis, and deep back-cuts along the undersurface. In turn, this eliminates the need for preemptive tissue expansion devices, which are suboptimal in the setting of previous bone flap osteomyelitis.[21] Lastly, this new technique becomes increasingly important when there is significant scalp contracture between staged surgery (i.e., sunken flap), which is often the case following a delay of 3 to 12 months.[1,17]

Given the encouraging results of this preliminary study, we propose here a new reconstructive treatment algorithm to allow a time interval reduction to approximately 3 months (Fig. 1). At our multidisciplinary cranioplasty center, it is customary for all patients with bone flap osteomyelitis to have bone flap removal, scalp débridement, and antibiotic irrigation followed by a mandatory 6-week course of intravenous antibiotics based on intraoperative culture sensitivities. Then, if no signs/symptoms of active infection and/or open scalp wounds are identified by any of the multiple providers who assess the patient during the staged time interval, a second-stage cranioplasty with a prefabricated custom cranial implant is performed at approximately 3 months. However, for those patients with signs of incomplete wound healing, surgery is delayed accordingly.

Our study presented here has several limitations that merit consideration. First, our cohort is of limited size, impacting the power of our analysis. Despite its size, this experience includes a single-surgeon experience at a single academic institution, which helps to remove several possible confounding variables. More importantly, to our knowledge, this is the largest study to date exploring the impact of various time intervals on surgical outcomes in the setting of previous bone flap osteomyelitis. One potentially significant

Fig. 5. Preoperative photographs of a female subject following removal of infected bone flap on oblique (*above*, *left*) and lateral views (*above*, *right*). (*Center*) Intraoperative photographs showing the dissection separating the inferiorly based pericranial-onlay and the transposed fasciocutaneous scalp flap, thereby creating a vascularized pocket (*center*, *left*) into which the implant is rigidly fixated (*center*, *right*). Nine-month postoperative oblique (*below*, *left*) and lateral (*below*, *right*) photographs demonstrating restoration of symmetrical craniofacial contour.

limitation of the analyses in this article is related to the limited sample sizes ($n = 14$ early cranioplasties and $n = 11$ late cranioplasties). For the overall complication rates, our statistical power to detect the observed differences was 19 percent (two-sided $\alpha = 0.05$, $\beta = 0.20$). Conversely, this study with 25 consecutive patients was adequately powered to detect a difference in overall complications of 46 percent (two-sided $\alpha = 0.05$, $\beta = 0.20$), and is coincidentally the exact same size as a similar study published from our same institution 19 years ago.[3] Therefore, although we cannot make the claim

that early delayed reconstruction (i.e., 3-month time interval) is superior to late reconstruction (i.e., 8-month time interval), our analyses do suggest that an early approach does *not* have a markedly higher complication rate (i.e., it is safe) and is efficacious. Future studies with larger cohorts will be needed to identify risk factors that may exclude patients from undergoing early-stage reconstruction.

In summary, our study reports for the first time a low reinfection rate of 4 percent with no significant differences seen in complications following early- compared to late-stage implant-based cranioplasty reconstruction ($p = 0.56$). This preliminary evidence suggests that decreasing the elapsed time interval closer to 90 days may be a viable and safe option for patients with large cranial defects requiring custom cranial implants (Figs. 4, *below* and 5, *below*).

CONCLUSIONS

This retrospective cohort study suggests that a 3-month time interval from osteomyelitic bone flap removal to delayed alloplastic cranioplasty has equivalent outcomes compared to delayed cranioplasties performed at greater than 6-month time intervals with respect to reinfection and overall complication rates. Reduced time intervals from infection to definitive reconstruction provide the patient with an earlier return to normalcy and restored appearance, without the prolonged need for protective helmet therapy. Future studies with larger sample sizes are warranted to confirm the findings of this study.

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PATIENT CONSENT

Patients provided written consent for the use of their images.

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