Timing of cranioplasty: a 10.75-year single-center analysis of 754 patients

Ryan P. Morton, MD,¹ Isaac Josh Abecassis, MD,¹ Josiah F. Hanson, BS,¹ Jason K. Barber, MS,¹ Mimi Chen,¹ Cory M. Kelly, BS,¹ John D. Nerva, MD,¹ Samuel N. Emerson, MD, PhD,¹ Chibawanye I. Ene, MD, PhD,¹ Michael R. Levitt, MD,^{1–3} Michelle M. Chowdhary, MD,¹ Andrew L. Ko, MD,¹ and Randall M. Chesnut, MD¹

Departments of ¹Neurological Surgery, ²Radiology, and ³Mechanical Engineering, University of Washington School of Medicine, Seattle, Washington

OBJECTIVE Despite their technical simplicity, cranioplasty procedures carry high reported morbidity rates. The authors here present the largest study to date on complications after cranioplasty, focusing specifically on the relationship between complications and timing of the operation.

METHODS The authors retrospectively reviewed all cranioplasty cases performed at Harborview Medical Center over the past 10.75 years. In addition to relevant clinical and demographic characteristics, patient morbidity and mortality data were abstracted from the electronic medical record. Cox proportional-hazards models were used to analyze variables potentially associated with the risk of infection, hydrocephalus, seizure, hematoma, and bone flap resorption.

RESULTS Over the course of 10.75 years, 754 cranioplasties were performed at a single institution. Sixty percent of the patients who underwent these cranioplasties were male, and the median follow-up overall was 233 days. The 30-day mortality rate was 0.26% (2 cases, both due to postoperative epidural hematoma). Overall, 24.6% percent of the patients experienced at least 1 complication including infection necessitating explantation of the flap (6.6%), postoperative hydrocephalus requiring a shunt (9.0%), resorption of the flap requiring synthetic cranioplasty (6.3%), seizure (4.1%), postoperative hematoma requiring evacuation (2.3%), and other (1.6%).

The rate of infection was significantly higher if the cranioplasty had been performed < 14 days after the initial craniectomy ($p = 0.007$, Holm-Bonferroni-adjusted $p = 0.028$). Hydrocephalus was significantly correlated with time to cranioplasty (OR 0.92 per 10-day increase, $p < 0.001$) and was most common in patients whose cranioplasty had been performed < 90 days after initial craniectomy. New-onset seizure, however, only occurred in patients who had undergone their cranioplasty > 90 days after initial craniectomy. Bone flap resorption was the least likely complication for patients whose cranioplasty had been performed between 15 and 30 days after initial craniectomy. Resorption was also correlated with patient age, with a hazard ratio of 0.67 per increase of 10 years of age ($p = 0.001$).

CONCLUSIONS Cranioplasty performed between 15 and 30 days after initial craniectomy may minimize infection, seizure, and bone flap resorption, whereas waiting > 90 days may minimize hydrocephalus but may increase the risk of seizure.

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KEY WORDS cranioplasty; timing; infection; resorption; complication; traumatic brain injury

CRANIOPLASTY aims to treat a cosmetic skull defect with either a stored autologous bone flap or a custom synthetic prosthesis. This relatively simple neurosurgical procedure is associated with complication rates of 15%–35%.^{1–23} In efforts to find the most favorable setting to perform cranioplasty, prior investigations have focused on the timing of cranioplasty after initial craniectomy. Most previous reports, however, have been limited to smaller series or pooled analyses with mixed conclusions.

In an attempt to clarify the literature, we present the largest study to date on complications after cranioplasty, focusing specifically on the association between complication rates and the timing of the operation.

Methods

This study was reviewed and approved by the University of Washington's institutional review board. We retro-

ABBREVIATIONS IPH = intraparenchymal hemorrhage; MCA = middle cerebral artery; SAH = subarachnoid hemorrhage; TBI = traumatic brain injury.

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spectively reviewed all cranioplasties performed at Harborview Medical Center, an urban, tertiary care, Level I trauma center, over the past 10.75 years. In addition to relevant clinical and demographic data, the following pre-specified data points were abstracted from the electronic medical record: indication for initial craniectomy, timing of cranioplasty after initial craniectomy, postoperative cranioplasty infection requiring explantation of the bone flap, postoperative hydrocephalus requiring cerebrospinal fluid diversion, new-onset seizure, postoperative hematoma requiring evacuation, autologous bone flap resorption requiring synthetic cranioplasty, and location of discharge (home, rehabilitation facility, or skilled nursing facility).

Statistical analysis was performed using SPSS software version 19 (IBM Corp.). Cox proportional-hazards models were used to analyze variables potentially associated with the risk of infection, hydrocephalus, seizure, hematoma, and bone resorption. Hazard ratios were calculated, and *p* values < 0.01 were considered significant. Tukey's range test and Holm-Bonferroni corrections were used for post hoc comparisons.

Results

Over the 10.75-year study period, 754 cranioplasty procedures were performed. Among the patients who underwent these cranioplasties, 455 were male (60.3%) and the mean age was 44 years (range 1–86 years). The median follow-up after cranioplasty was 233 days. Indications for initial craniectomy included traumatic brain injury (TBI; 51.4%), spontaneous intraparenchymal hemorrhage (IPH; 13.8%), aneurysmal subarachnoid hemorrhage (SAH; 13.5%), malignant middle cerebral artery (MCA) infarction (9.7%), infection after craniotomy (5.2%), brain edema after tumor surgery (2.9%), spontaneous brain abscess (0.7%), and other (2.8%; Table 1).

An autologous bone flap was used in 532 cases (70.6%), whereas a synthetic prosthesis was used in 222 (29.4%). The material used for the synthetic prostheses varied, but polyetheretherketone (PEEK) was the most common.

The 30-day mortality was 0.3% (2 cases), with both deaths resulting from postoperative epidural hematoma. Overall, 24.6% of patients experienced at least 1 complication including infection necessitating explantation of the flap (6.6%), postoperative hydrocephalus requiring a shunt (9.0%), resorption of the autologous flap requiring synthetic cranioplasty (6.3%), seizure (4.1%), postoperative hematoma requiring evacuation (2.3%), and other (1.6%). Upon discharge, 58.7% of patients returned home, 13.8% to a rehabilitation facility, and 27.2% to a skilled nursing facility or adult family home.

Factors Influencing Complications

Infection

When evaluating the association between postoperative complication rates and timing of the cranioplasty, we found the rate of infection was significantly higher if the cranioplasty had been performed < 14 days after the initial craniectomy (HR 3.62, *p* = 0.007, Holm-Bonferroni-adjusted *p* = 0.028). There was no significant difference with any other variable (age, sex, indication for initial craniec-

TABLE 1. Indication for craniectomy in the cranioplasty population at a single institution

Indication	No. of Patients	%
TBI (depressed skull fracture, extraaxial hematoma, intraaxial hematoma, &/or diffuse edema)	388	51.4
IPH (spontaneous or AVM)	104	13.8
SAH	102	13.5
Ischemic stroke w/ malignant edema	73	9.7
Postop infection of previous craniotomy	39	5.2
Brain edema after tumor surgery	22	2.9
Spontaneous brain abscess	5	0.7
Other	21	2.8

AVM = arteriovenous malformation.

tomy, autologous versus synthetic flap, material used for synthetic flap, concomitant shunt placement, and location of discharge). We have previously written in detail about cranioplasty infections regarding the use of synthetic versus autologous flaps.¹³

Hydrocephalus

Hydrocephalus was significantly correlated with time to cranioplasty (OR 0.92 per 10-day increase, *p* < 0.001) and was most common in patients whose cranioplasty had been performed < 90 days after initial craniectomy. Additionally, the initial indication for craniectomy significantly influenced the rate of hydrocephalus (*p* = 0.004), with significant pairwise relationships between SAH (19.6%), TBI (6.2%, *p* < 0.01), and IPH (4.8%, *p* < 0.05; Table 2). Lastly, discharge location was significantly correlated with postoperative hydrocephalus requiring a shunt (*p* = 0.007), with patients discharged to a skilled nursing or rehabilitation facility reporting the highest rates (14.4% and 14.6%, respectively).

Seizure

The indication for initial craniectomy influenced which

TABLE 2. Indication for initial craniectomy versus postoperative hydrocephalus and seizure

Indication for Craniectomy	Postop Hydrocephalus		Postop Seizure	
	%	<i>p</i> Value	%	<i>p</i> Value
TBI	6.2*	0.004	3.1	0.040†
Ischemic stroke	11.0		12.3	
IPH	4.8‡		4.8	
SAH	19.6*‡		2.0	
Brain abscess/empyema	0.0		0.0	
Brain edema	18.2		0.0	
Infection from previous craniotomy	10.3		5.1	
Other	14.3		4.8	

* *p* < 0.01, Tukey pairwise.

† No significance with Tukey pairwise.

‡ *p* < 0.05, Tukey pairwise.

TABLE 3. Complication rates after cranioplasty in published series

Authors & Year	Population	No. of Patients	Infection Rate	Hydrocephalus Rate	Resorption Rate	Seizure Rate	Hematoma Rate	Mortality Rate
Walcott et al., 2013	TBI, stroke	239	12.1	5.0	NR	3.4	3.4	0.0
Chang et al., 2010	SAH, TBI, stroke, tumor, infection, ICH	212	7.1	NR	NR	NR	6.1	0.5
Chibbaro et al., 2011	TBI	147	4.1	NR	NR	NR	0.7	NR
De Bonis et al., 2012	TBI, vascular disease, tumor, elective	218	8.7	NR	5.9	NR	2.8	0.0
Gooch et al., 2009	TBI, stroke, infection	62	11.3	1.6	6.5	1.6	3.2	NR
Sobani et al., 2011	TBI, stroke, tumor	96	3.1	3.1	2.1	15.6	5.2	NR
Stephens et al., 2010	TBI (combat)	108	12.0	NR	NR	7.4	7.4	0.9
Zanaty et al., 2015	SAH, TBI, stroke, EDH/SDH	348	26.4	13.5	NR	14.4	6.9	3.2
Piedra et al., 2012	Stroke	74	10.8	1.4	2.7	NR	4.1	NR
Current study	TBI, stroke, IPH, SAH, infection, tumor, elective	754	6.6	9.0	6.3	4.1	2.3	0.3

EDH/SDH = epidural hematoma/subdural hematoma; ICH = intracranial hemorrhage; NR = not reported.

patients were more likely to develop a first-time seizure after cranioplasty, with those having malignant MCA infarction being the largest subpopulation (12.3%; Table 2). However, there were no significant pairwise relationships after applying Tukey post hoc adjustments. Seizures occurred only in patients whose cranioplasty had occurred more than 90 days after initial craniectomy.

Resorption

When evaluating the 532 cases of autologous cranioplasty, resorption was least likely for patients whose cranioplasty had been performed between 15 and 30 days after initial craniectomy. Resorption was also correlated with patient age, with a hazard ratio of 0.67 per increase of 10 years of age ($p = 0.001$), meaning that younger patients were more likely to experience this phenomenon than older patients. Indication for initial craniectomy did not influence subsequent rates of resorption in our study.

Hematoma

There was no difference with any other variable on the development of a postoperative hematoma requiring evacuation.

Discussion

We have presented the largest series of cranioplasties to date, with a focus on the relationship between cranioplasty timing and postoperative complications. Our complication rates compare favorably to those reported previously (Table 3). To date, no large study has attempted to stringently evaluate the association between the timing of cranioplasty after initial craniectomy and the variety of postoperative complications other than infection. One large systematic review failed to find any statistically significant association with infection when comparing “early” (< 3 months) to “late” cranioplasty.²² However, smaller sample sizes limited the statistical power in that review, and the timing of cranioplasty was categorized into either before or after 3 months from initial craniectomy.

The influence of very early (< 30 days) or ultra-early

(< 14 days) cranioplasty in the current study provides additional information and clinical guidance not previously available due to sample size limitation. Our study attempts to address this problem by reporting single-center results for 754 patients. During the study period, cranioplasties were performed at various dates in the postoperative period. Some providers even performed the cranioplasty < 14 days after the decompression. Often in these ultra-early cases, there was a logistical desire by both the physician and the patient’s family to replace the flap during the primary hospitalization rather than after discharge. Early cranioplasty was also thought to aid in patient mobilization. Our data suggest, however, that performing a cranioplasty in the ultra-early period increases the risk of infection. Waiting to perform the procedure between 15 and 90 days after initial craniectomy is least likely to result in most categories of complications, with the period between 15 and 30 days postcraniectomy being ideal as it helps to minimize infection, seizure, and resorption while still being a relatively short time window after the initial craniectomy to minimize the time that the patient will spend without a bone flap in place and in a helmet. Waiting > 90 days may minimize the risk of hydrocephalus but may also increase the risk of seizure (Fig. 1).

This study has several limitations. First, while the sample size is large, it is still a single-center study. However, the consecutive nature of our review suggests that the proportion of etiology of initial craniectomy is probably representative of the overall cranioplasty population. Additionally, the study’s retrospective nature obviates a proper control group. Prospective studies could further validate our findings. Lastly, the correlation between hydrocephalus and cranioplasty may result from preexisting hydrocephalus not clinically apparent until after cranioplasty placement.

Conclusions

Timing of cranioplasty is related to postoperative complication rates. Infection risk is highest within 14 days of initial craniectomy, hydrocephalus risk is highest within 90 days, and seizure risk is highest after 90 days. Cra-

FIG. 1. Complication rate of cranioplasty versus timing of surgery. d = days; Hydro = hydrocephalus; Sz = seizure.

nioplasty between 15 and 30 days minimizes the risk of infection, seizure, and autologous flap resorption while still minimizing the time the patient will spend without a bone flap.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Abecassis, Barber, Levitt, Chowdhary, Ko, Chesnut. Acquisition of data: Morton, Abecassis, Hanson, Chen, Nerva, Emerson, Ene. Analysis and interpretation of data: Abecassis, Levitt, Chowdhary, Ko, Chesnut. Drafting the article: Abecassis. Critically revising the article: Abecassis, Kelly, Levitt, Ko, Chesnut. Statistical analysis: Barber. Study supervision: Abecassis.

Supplemental Information

Previous Presentations

Portions of this research were presented orally at the Annual Scientific Meeting of the American Association of Neurological Surgeons held in Chicago, Illinois, in April 2016.

Correspondence

Ryan P. Morton, c/o Neuroscience Publications, University of Washington, Box 359924, 325 9th Ave., Seattle, WA 98104.
email: publications@neurosurgery.washington.edu.