Predictors of Clinical Outcomes in Autologous Cranioplasty

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■ BACKGROUND: **Cranioplasty is a common neurosurgical procedure and autologous grafts are preferred due to their aesthetic and biocompatibility benefits. Multiple risk factors are implicated as predictors for neurologic outcome. This study focuses on risk factors that may be associated with complications and analyzes the predictors of neurologic outcomes after autologous cranioplasty.**

■ METHODS: **This is a retrospective observational study conducted at a tertiary care center between 2015 and 2021. Adults with autologous cranioplasty (n = 132) were recruited from procedure logs and the hospital electronic health record. Clinicodemographic parameters, risk factors, and complications were recorded. Neurologic outcomes were measured using the dichotomized Glasgow Outcome Scale (GOS). Primary outcome measure was pre- and post-cranioplasty GOS at the last follow up. Secondary outcome measures were the predicting factors that contributed to enhanced neurologic outcome post-cranioplasty.**

■ RESULTS: **Mean age was 41.4 (standard deviation ± 13.5) years with male predominance (12.2:1). Complications developed in 12.9% (n = 17), with infections in 3.8% (n = 5) and hydrocephalus in 2.3% (n = 3). In bivariate analysis, pre-cranioplasty GOS good grades 4 and 5 ($P < 0.001$), trauma as an indication for decompressive craniectomy (DC) ($P < 0.001$), and early cranioplasty ≤12 weeks ($P = 0.023$) were statistically significant predictors for post-cranioplasty neurologic recovery at follow-up. In a multiple logistic regression model, adjusted odds ratio for pre-cranioplasty GOS was 28.77 (95% confidence interval [CI] 7.21–114.74, $P < 0.001$), for trauma as indication for DC was 5.15 (95% CI 1.65–16.05, $P = 0.003$), and for early cranioplasty ≤12 weeks was 3.04 (95% CI 1.12–8.27 $P = 0.029$).**

■ CONCLUSIONS: **Autologous cranioplasty contributes to a quantifiable neurologic outcome. Pre-cranioplasty neurologic status, cranioplasty done for traumatic DC and early cranioplasty may have potential for enhanced neurologic recovery. Further clinical studies with better evidence may expound upon these findings.**

INTRODUCTION

Decompressive craniectomy (DC) has become increasingly recognized as an effective treatment for increased intracranial pressure due to malignant cerebral edema from head trauma, brain infarction, intracranial hemorrhage, or post-surgical complications.[1,2] As a result, cranioplasty-related procedures are also becoming increasingly common, with a growing body of the evidence.[2-5] In addition to esthetics benefits, cranioplasty tends to promote brain protection and optimizes cerebral hydrodynamic conditions, protects patients from seizures, and

Key words
- Autologous
- Clinical outcome
- Cranioplasty
- Neurologic
- Prognosis
- Predictors

Abbreviations and Acronyms
AOR: Adjusted odds ratio
CI: Confidence interval
DC: Decompressive craniectomy
DM: Diabetes mellitus
EVD: External ventricular drainage
GOS: Glasgow Outcome Scale
HTN: Hypertension
IQR: Interquartile range
SD: Standard deviation
VP: Ventriculoperitoneal

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relieves the syndrome of trephine.[6-10] Cranioplasty also improves neurocognition, relieves psychologic sequelae, and increases social performance.[11-14]

Cranioplasty has recognized complications that include intracranial or graft infection, hemorrhage, pneumocephalus, poor cosmesis, persistent fluid collection, and death.[15,16] The published studies have quoted a wide range of complication rates ranging from 3.3% to 40.8%.[17,18] Multiple risk factors have been implicated including age, indications for DC, time lapse between DC and cranioplasty, repeat operation, antibiotic regimen, use of drains, and type of implant.[19,20] The choice of defect fill material has advanced from use of precious metals to autologous bone, and now includes the use of 3-dimensionally printed synthetic materials.[20,21] Autologous bone flaps are still preferred as these are more convenient, less costly, and offer excellent cosmetic results.[22]

Much of the modern literature regarding cranioplasty analyzes the technical aspects of the procedure (such as bone flap storing procedures, timing of surgical intervention), the use of different materials, or other specific modifications to either the craniectomy or cranial repair, which may influence the cranioplasty.[20,23-25] The complication-related risk factors associated with cranioplasty and their effect on the neurologic outcomes have long been neglected. At present, the appropriate timing of cranioplasty, the ideal material for cranial repair, and possible risk factors associated with complications constitute a matter of debate. This study presents a retrospective review of autologous cranioplasty conducted at a tertiary care center with an emphasis on neurologic outcomes and aims to review risk factors associated with predictors of enhanced neurologic outcome.

METHODS

This is a retrospective observational study with data collection of patients' charts from January 2015 until June 2021 at a tertiary care center. The data were collected from operative logs for patients who underwent standard decompressive craniectomies followed by autologous cranioplasty during the study period. The study was approved by the local institutional review board and patient consent was exempted as the study involved review of existing data without disclosing patient identifiers.

Study Design and Patient Data

The study population included all patients who underwent DC for any reasons including treatment of traumatic and vascular disorders. These patients then underwent cranioplasty or re-implantation of autologous bone flaps. A dichotomized cutoff for early versus late cranioplasty is set at 90 days (12 weeks), as has been previously reported.[25] The patients were alive at the time of the study and did not have any source of infection at the time of cranioplasty. We excluded patients who underwent cranioplasty with any synthetic implants and those operated on for surgical repair of congenital cranial anomalies. Data were obtained from electronic health records for variables including age, ethnicity, comorbid conditions, indications for DC, duration between the DC and cranioplasty, post-cranioplasty complications, pre-cranioplasty Glasgow Outcome Scale (GOS) and postoperative GOS at follow-up.

Bone Flap Preservation and Storage

Per hospital policy, all autologous bone flaps harvested from DC were cryopreserved in a deep freezer at a temperature below −70°C. Before cryopreservation, connective tissues such as pericranium, muscle, fascia, and galea were entirely removed. Before the re-implantation, the autograft was properly identified for the respective patient. The scrub nurse removed autograft bone from the sterile wrapper, washed it with saline, and placed it in a sterile basin container filled with hydrogen peroxide solution. It remained submerged for at least 20–30 minutes at room temperature. The cryopreserved bone was then washed with normal saline after soaking several times in gentamycin solution prior to re-implantation. Prophylactic antibiotics were administered 30–45 minutes before the incision during the cranioplasty; other operative procedure technique varied between different neurosurgeons. A dichotomized threshold for duration of operating time is set at 120 minutes, as has been published as an average timing for autologous cranioplasty in literature.[26] All patients with head trauma were on prophylactic antiepileptic as a standard protocol.[27,28]

Statistical Analysis

Descriptive statistics in the form of mean and standard deviation (SD) (for normally distributed data), or median with interquartile range (IQR) (for data not normally distributed) were calculated for interval variables (e.g., age) as appropriate. Frequency with percentage is reported for categorical variables (e.g., sex). Bivariate analysis of different clinical and demographic variables was performed to find statistically significant predictors of neurologic outcome after cranioplasty. P values were calculated using the Pearson χ^2 test for binary variables and Mann-Whitney U-test was applied to find P values for continuous data. Multiple logistic regression analysis was performed to assess the adjusted relationship between age, sex, diabetes mellitus (DM), hypertension (HTN), number of surgeries, operative time, pre-cranioplasty GOS, indications for DC, time duration between DC and cranioplasty, and good GOS among post-cranioplasty patients. Adjusted odds ratio (AOR) and 95% confidence intervals (CIs) for the AOR were reported. Statistical significance was set at $P < 0.05$ (2-tailed). All statistical analyses were performed using the Statistical Package for Social Sciences (version 27; IBM. Armonk, NY).

RESULTS

Among 132 patients, 69 patients were ≤40 years old (mean 41.4 years, SD ± 13.5 years) with a male predominance (n = 122). Sixty-one patients had associated hypertension and 31 patients had DM preoperatively. Most of the patients (n = 101) were non-Arab and 31 patients were Arab. Trauma was the preoperative indication for DC in 58 versus 74 patients due to non-traumatic reasons including strokes and intracerebral hemorrhages. Mean operative time for cranioplasty procedure remained 124 (SD ± 38.5) minutes with most patients (n = 81) operated on for ≤120 minutes. Most patients (n = 108) underwent one surgery before cranioplasty with mean time between first surgery and cranioplasty of ≤12 weeks (mean 13.1 weeks, SD± 7.8 weeks) in 77 patients and median follow up remained 3 (IQR 2–6) months (**Table 1**). Postoperative complications (n = 17) included infections (n = 5), extradural

hematomas (n = 4), and subgaleal collections (n = 3); intraparenchymal hemorrhage and wound necrosis each developed in 1 patient each (Table 2). Hydrocephalus was observed in 3 patients as a sequala of the initial brain insult. Among the patients with hydrocephalus, all 3 patients have undergone ventriculoperitoneal (VP) shunt placement. All of them had traumatic brain injury initially, 2 patients had ventriculomegaly at time of the cranioplasty, hence an external ventricular drainage (EVD) catheter was inserted during cranioplasty. Both failed weaning from EVD post-cranioplasty and eventually needed a VP shunt. One patient developed hydrocephalus later as manifested by a decrease in level of consciousness. None of the patients has developed new onset seizures after cranioplasty.

In bivariate analysis (Table 3) of dichotomized GOS with clinicodemographic binary variables, indications for DC ($P < 0.001$), duration between DC and cranioplasty ($P = 0.023$) and preoperative cranioplasty GOS ($P < 0.001$) were found to be statistically significant. In multiple logistic regression analysis, after adjusting for confounding variables (including age, sex, DM, HTN, number of surgeries, operative time), the identified significant variables in bivariate analyses (initial GOS, indications for DC, and duration between initial surgery and cranioplasty) remained significant independent predictors associated with good post cranioplasty GOS (Table 4). AOR of the model for preoperative GOS was 28.77 (95% CI 7.21–114.74, $P < 0.001$), 5.15 (95% CI 1.65–16.05, $P = 0.003$) for traumatic DC, and 3.04 (95% CI 1.12–8.27, $P = 0.029$) for the duration between initial surgery and cranioplasty.

Table 1. Summary of Characteristics

Characteristic	Value
1. Age, years	41.4 ± 13.5
≤40	69 (52.3)
>40	63 (47.7)
2. Sex	
• Male	122 (92.4)
• Female	10 (7.6)
3. Comorbidities	
• Diabetes mellitus	31 (23.5)
• Hypertension	61 (46.2)
4. Ethnicity	
• Arab	31 (23.5)
• Non-Arab	101 (76.5)
5. Indication for surgeries	
• Traumatic	58 (43.9)
• Nontraumatic (vascular/tumors/others)	74 (56.1)
6. Operative time, minutes	124.6 ± 38.5
• Up to 120	81 (61.4)
• More than 120	51 (38.6)
7. Number of surgeries before cranioplasty	
• 1	108 (81.8)
• ≥2	24 (18.2)
8. Duration between craniectomy and cranioplasty, weeks	13.1 ± 7.8
• ≤ 12	77 (58.3)
• > 12	55 (41.7)
9. Duration of follow-up, months	3 (2–6)

Results are expressed as mean ± standard deviation, median (interquartile range), or number (percentage).

Table 2. Postoperative Complications

Complication (n = 17)	Frequency (n = 132) Number (%)
None	115 (87.1)
Infections	5 (3.8)
Extradural hematoma	4 (3.0)
Hydrocephalus	3 (2.3)
Subgaleal collections	3 (2.3)
Intraparenchymal hemorrhage	1 (0.8)
Wound necrosis	1 (0.8)
Total complications	17 (12.9)

DISCUSSION

Cranioplasty techniques blend both art and surgical science.[27,29] Although cranioplasties with gold and silver have been documented since the time of the Incas many centuries ago, the first report of cranioplasty by Job Janszoon van Meekeren appeared in 1868.[29-31] Macewen is the father of the modern practice of autologous bone grafting and reported the successful reimplantation of bone pieces into cranial defects in 1885.[29] The diversity of methods proposed for cranium reconstruction from prehistory to modern medicine affirms the engaging nature of the problem.[1,29,30,32]

Autologous Bone for Cranial Reconstruction

Although autologous bone is considered the gold standard material for cranioplasty procedures, there are still some arguments against its use due to its high propensity for reabsorption.[5,20,22] Autologous bone flaps are preferred over newly developed reconstructive materials, because the former are more convenient, offer excellent morphologic fit, and permit bone growth and higher biocompatibility.[20,22,33] Bone storage may be inconvenient since it requires freezing temperatures (below −70°C) or subcutaneous preservation.[34] In comparing methods of bone preservation in the abdominal wall versus cryopreservation, there is no significant difference in postoperative infections in similar surgical risk profiles, and it remains a matter of individual preference and equipment availability.[35] Generally, cryopreservation may be preferred because of the shorter operation time and avoidance of complications with the abdominal pocket, whereas the portability

Table 3. Bivariate Analysis, Relationship of Clinicodemographic Factors With Dichotomized Post-cranioplasty GOS

Variables	Post-cranioplasty GOS		
	Good Grades (4 and 5)	Poor Grades (2 and 3)	*P* Value*
Age, years			
≤40	46 (66.7)	23 (33.3)	0.568
>40	39 (61.9)	24 (38.1)	
Sex			
Male	78 (63.9)	44 (36.1)	0.700
Female	7 (70.0)	3 (30.0)	
Ethnicity			
Arab	22 (71.0)	9 (29.0)	0.382
Non-Arab	63 (62.4)	38 (37.6)	
Comorbidities			
Diabetes mellitus			0.987
• Yes	20 (64.5)	11 (35.5)	
• No	65 (64.4)	36 (35.6)	
Hypertension			
• Yes	40 (65.6)	21 (34.4)	0.793
• No	45 (63.4)	26 (36.6)	
Indications for surgery			
Traumatic	47 (81.0)	11 (19.0)	<0.001
Nontraumatic	38 (51.4)	36 (48.6)	
Operative time, minutes)			
≤120	53 (65.4)	28 (34.6)	0.754
>120	32 (62.7)	19 (37.3)	
Number of surgeries before cranioplasty			
1	71 (65.1)	38 (34.9)	0.698
≥2	14 (60.9)	9 (39.1)	
Duration between craniectomy and cranioplasty, weeks			
≤12	57 (72.2)	22 (27.8)	0.023
>12	28 (52.8)	25 (47.2)	
Pre-cranioplasty GOS			
Good grade (4 and 5)	55 (94.4)	3 (5.2)	<0.001
Poor grade (2 and 3)	30 (40.4)	44 (59.5)	
Total	85 (64.4)	47 (35.6)	
Duration of follow-up, months	3 (2–5.75)	3 (2–8)	0.708†

Results are expressed as number (percentage) or median (interquartile range). Glasgow Outcome scale (GOS) is dichotomized as good (grade 4 and 5) and poor (grade 2 and 3).
**P* value was calculated using the Pearson χ^2 test, unless otherwise noted.
†*P* value was calculated using Mann-Whitney U-test.

Table 4. Bivariate and Multiple Logistic Regression (Identified Significant Factors Associated With Good GOS)

Factor	Unadjusted OR (95% CI); *P* Value	AOR	95% CI for AOR	*P* Value
Pre-cranioplasty GOS				
• Poor grade	1	1		
• Good grade	26.89 (7.69–93.97); <0.001	28.77	7.21–114.74	<0.001
Indications for decompressive craniectomies				
• Nontraumatic (ref.)	1	1		
• Traumatic brain injury	4.05 (1.82–9.0); 0.001	5.15	1.65–16.05	0.003
Duration between initial surgery and cranioplasty, in weeks				
• > 12	1	1		
• ≤ 12	2.39 (1.15–4.96); 0.019	3.04	1.12–8.27	0.029

Multiple logistic regression identified significant factors associated with good GOS, the OR for good GOS was adjusted for all the significant variables in the tables (pre-cranioplasty GOS, indication for decompression, and time delay) and nonsignificant variables (age, sex, diabetes mellitus, hypertension, number of surgeries, operative time, prophylactic antibiotics used, and duration of surgical drain).
Hosmer & Lemshow $\chi^2 = 7.57$; $P = 0.482$ (indicating adequate fit of the model to the data).
AOR, adjusted odds ratio; CI, confidence interval; GOS, Glasgow Outcome Scale; OR, odds ratio.

favors subcutaneous storage.[35,36] In a systematic review, Corliss et al.[37] found no statistically significant differences in terms of infection, resorption, and/or reoperation rate comparing extracorporal cryopreservation versus abdominal pocket storage. Cobbad et al.[22] concluded that autologous bone is still the most reliable, safe, and cost-effective material for use in reconstructive cranioplasty. In our study, we used cryopreservation as a standard method with bone preservation below −70°C for all patients.

Complications in Autologous Cranioplasty

Complication rates for autologous bone cranioplasties range from 0 to 53.3 percent, whereas it is 4.8 to 63.6 percent for alloplastic cranioplasties.[20-22] This encompasses everything from more serious findings of infection, extrusion/reabsorption, to the less common outcomes of hematoma, hydrocephalus, seizure, and chronic pain. Chang et al.[38] found that infection was more common after use of alloplastic materials compared with autologous bone (18.9% vs. 4.6%). Overall, the available literature supports the notion that infection is more common with alloplastic materials.[3,4,20-23,38] The complication rate of 12.9% (n = 17) with overall infection rate of 3.8% (n = 5) in our study is aligned with contemporary data.[3,4,6,17,19] Infections accounted for just over one third of all patients (5 out of 17) who developed complications. Bone resorption was not observed in any of the cryopreserved bone flaps before implantation as most patients (n = 77) underwent cranioplasty in nearly 12

weeks (mean 13.1 ± 7.8 weeks) and no post-cranioplasty resorption was observed in this cohort due to the short duration of follow-up. Hydrocephalus is one of the main complications of decompressive craniectomy, ranging from 11.9% to 36% in adults, with most cases requiring VP shunt placement.[39,40] In our study, only 2.3% (n = 3) of the patients developed hydrocephalus requiring permanent VP shunt. Seizures after cranioplasty have been reported to range from 2.9%–29%.[8,41] No patients with traumatic brain injury developed post-cranioplasty seizure in our cohort except 2 patients who had cranioplasty for non-traumatic indications. This may be due to our standard use of prophylactic antiepileptic in all post-traumatic DC patients for 6 months as its effectiveness has been published in a recent review.[28]

Post-cranioplasty Neurologic Prognosis

Neurologic outcomes after cranioplasty is multifactorial, primarily dependent on indications for DC, quality of neurologic rehabilitation, and support for reintegration into daily life for these patients.[42] In the literature, the rate of good recovery ranged between 36% and 64%.[43] Giese et al. concluded a significant neurologic improvement in the long term after cranioplasty in all patients (42.6%), with a 30 day-mortality rate of 0.49%t.[44] A systematic review and meta-analysis of 7 cranioplasty studies (528 patients) with similar pre- and postoperative assessment of neurologic function confirmed a significant neurologic improvement after cranioplasty (mean follow-up 3–180 days).[43] In our study, there was also significant neurologic improvement ($P \leq 0.001$) based on GOS when we compared preoperative neurologic status with post-cranioplasty dichotomized GOS. In multiple regression analysis, odds of good recovery for GOS grades 4 and 5 was 28.77 (95% CI 7.47–163.56, $P \leq 0.0001$) in comparison with poor grades (2 and 3) after adjusting for identified factors in bivariate analysis. It remains unclear whether neurologic recovery is promoted by cranioplasty or other confounders including the effect of rehabilitation and duration of follow-up. This limitation can only be addressed by direct comparison of DC patients with and without cranioplasty that mandates an ethical equipoise and a long-term follow up.

Predictors of Post-cranioplasty Prognosis

Several heterogenous factors were used to predict clinical outcome, including: patient-centered risks, indications for DC, pre-cranioplasty neurologic status, timing of cranioplasty, post-operative complications, quality of rehabilitation, parameters used for neurologic assessment, and duration of follow-up.[18,19,38] Long-term neurologic outcome of patients undergoing DC differed remarkably when assorting by etiology, ranging from 0%–91%t.[42] In our study, multiple regression analysis of different factors confirmed that the adjusted odds of neurologic outcome were better for traumatic DC (higher odds 5.15, $P = 0.003$) as compared to non-traumatic patients. Posti et al.[45] concluded that a successful cranioplasty with good pre-cranioplasty clinical status predicts a favorable outcome 1 year after cranioplasty, and these results are aligned with our study, showing higher adjusted odds (28.27 times) of neurologic recovery when compared with poor pre-cranioplasty GOS grades. Early cranioplasty (≤3 months) has been associated with enhanced neurologic recovery.[24,25] This is aligned with our study results that showed adjusted odds for early cranioplasty (≤12 weeks) to be 3.04 times with reference to cranioplasty done after 3 months. A recently published consensus statement from the International Consensus Meeting on Post-TBI Cranioplasty endorsed cranioplasties for improved neurologic outcome but stopped short of supporting enhanced recovery related to early cranioplasty.[46]

Limitations

The study has the inherent limitations of being a retrospective review, and data related to some clinical variables were either incomplete or missing. It was limited by a short follow-up duration of 3 months, as most patients were repatriated to their home country, having been expatriate in Qatar. However, the study is powered by a large sample size and the logistic regression model included a wide array of clinical variables.

CONCLUSIONS

Cranioplasty is a common neurosurgical procedure with quantifiable clinical outcomes. There are multiple risk factors for complications but risk of infection after autologous cranioplasty remains low. Pre-cranioplasty neurologic status and cranioplasty done for traumatic DC have comparatively better prognosis while early cranioplasty within 3 months may have a role in enhanced neurologic recovery. Future studies with better clinical evidence are required to consolidate these findings.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Saleh Safi: Conceptualization, Methodology, Resources, Validation, Formal analysis, Writing — original draft, Writing — review & editing, Project administration. **Arshad Ali:** Conceptualization, Methodology, Resources, Validation, Formal analysis, Writing — original draft, Writing — review & editing, Project administration. **Ibrahim Abdelhafez:** Methodology, Project administration. **Abdul Salam:** Validation, Formal analysis, Writing — review & editing. **Talal Alrabayah:** Methodology, Project administration. **Abdulnasser Alyafei:** Methodology, Project administration. **Sirajeddin Belkhair:** Methodology, Project administration.

REFERENCES

1. De Bonis P, Frassanito P, Mangiola A, Nucci CG, Anile C, Pompucci A. Cranial repair: how complicated is filling a "hole"? *J Neurotrauma*. 2012;29:1071-1076.
2. Andrabi SM, Sarmast AH, Kirmani AR, Bhat AR. Cranioplasty: indications, procedures, and outcome—an institutional experience. *Surg Neurol Int*. 2017;8:91.
3. Junior AC, Hamamoto Filho PT, Gonçalves MP, Neto AA, Zanini MA. Cranioplasty: an institutional experience. *J Craniofac Surg*. 2018;29:1402-1405.
4. Liang ES, Tipper G, Hunt L, Gan PY. Cranioplasty outcomes and associated complications: a single-centre observational study. *Br J Neurosurg*. 2016;30:122-127.
5. Mitchell KA, Shay T, Belzberg M, Manson P, Gordon C. Autogenous bone cranioplasty: review of a 42-year experience by a single surgeon. *Plast Reconstr Surg*. 2020;145:1108e-1109e.
6. Dujovny M, Aviles A, Agner C, Fernandez P, Charbel FT. Cranioplasty: cosmetic or therapeutic? *Surg Neurol*. 1997;47:238-241.

7. Paredes I, Alén JAF, Castaño-León AM, et al. Clinical improvement after cranioplasty and its relation to body position and cerebral hemodynamics. *Neurosurg Rev*. 2022;45:1463-1472.

8. Spencer R, Manivannan S, Sharouf F, Bhatti MI, Zaben M. Risk factors for the development of seizures after cranioplasty in patients that sustained traumatic brain injury: a systematic review. *Seizure*. 2019;69:11-16.

9. Jeyaraj P. Importance of early cranioplasty in reversing the "syndrome of the trephine/motor trephine syndrome/sinking skin flap syndrome". *J Maxillofac Oral Surg*. 2015;14:666-673.

10. Yamaura A, Makino H. Neurological deficits in the presence of the sinking skin flap following decompressive craniectomy. *Neurol Med Chir*. 1977; 17:43-53.

11. Agner C, Dujovny M, Gaviria M. Neurocognitive assessment before and after cranioplasty. *Acta Neurochir*. 2002;144:1033-1040.

12. Stefano CD, Rinaldesi ML, Quinquinio C, et al. Neuropsychological changes and cranioplasty: a group analysis. *Brain Inj*. 2016;30:164-171.

13. Corallo F, Marra A, Bramanti P, Calabrò RS. Effect of cranioplasty on functional and neuropsychological recovery after severe acquired brain injury: fact or fake? Considerations on a single case. *Funct Neurol*. 2014;29:273.

14. Di Stefano C, Sturiale C, Trentini P, et al. Unexpected neuropsychological improvement after cranioplasty: a case series study. *Br J Neurosurg*. 2012;26:827-831.

15. Honeybul S, Ho KM. Long-term complications of decompressive craniectomy for head injury. *J Neurotrauma*. 2011;28:929-935.

16. Stephens FL, Mossop CM, Bell RS, et al. Cranioplasty complications following wartime decompressive craniectomy. *Neurosurg Focus*. 2010;28:E3.

17. Shibahashi K, Hoda H, Takasu Y, Hanakawa K, Ide T, Hamabe Y. Cranioplasty outcomes and analysis of the factors influencing surgical site infection: a retrospective review of more than 10 years of institutional experience. *World Neurosurg*. 2017;101:20-25.

18. Godil SS, Shamim MS, Enam SA, Qidwai U, Qadeer M, Sobani ZA. Cranial reconstruction after decompressive craniectomy: prediction of complications using fuzzy logic. *J Craniofac Surg*. 2011; 22:1307-1311.

19. Im SH, Jang DK, Han YM, Kim JT, Chung DS, Park YS. Long-term incidence and predicting factors of cranioplasty infection after decompressive craniectomy. *J Korean Neurosurg Soc*. 2012; 52:396.

20. Shah AM, Jung H, Skirboll S. Materials used in cranioplasty: a history and analysis. *Neurosurg Focus*. 2014;36:E19.

21. Zhang Q, Yuan Y, Li X, et al. A large multicenter retrospective research on embedded cranioplasty and covered cranioplasty. *World Neurosurg*. 2018; 112:e645-e651.

22. Cabbad NC, Stalder MW, Arroyave A, Wolfe EM, Wolfe SA. Autogenous bone cranioplasty: review of a 42-year experience by a single surgeon. *Plast Reconstr Surg*. 2019;143:1713-1723.

23. Sable H, Patel MP, Shah KB. A prospective comparative study of different methods of cranioplasty: our institutional experience. *Indian J Neurosurg*. 2020;9:17-23.

24. Piedra MP, Thompson EM, Selden NR, Ragel BT, Guillaume DJ. Optimal timing of autologous cranioplasty after decompressive craniectomy in children. *J Neurosurg Pediatr*. 2012;10:268-272.

25. Oh JS, Lee KS, Shim JJ, Yoon SM, Doh JW, Bae HG. Which one is better to reduce the infection rate, early or late cranioplasty? *J Korean Neurosurg Soc*. 2016;59:492.

26. Al Shalchy AK. Cranioplasty the use synthetic (acrylic) or autograft. *J Fac Med Baghdad*. 2010;52: 30-31.

27. Chartrain AG, Yaeger K, Feng R, et al. Antiepileptics for post-traumatic seizure prophylaxis after traumatic brain injury. *Curr Pharm Des*. 2017;23: 6428-6441.

28. Wat R, Mammi M, Paredes J, et al. The effectiveness of antiepileptic medications as prophylaxis of early seizure in patients with traumatic brain injury compared with placebo or no treatment: a systematic review and meta-analysis. *World Neurosurg*. 2019;122:433-440.

29. Grant FC, Norcross NC. Repair of cranial defects by cranioplasty. *Ann Surg*. 1939;110:488.

30. Abhay S, Haines SJ. Repairing holes in the head: a history of cranioplasty. *Neurosurgery*. 1997;40: 588-603.

31. Macewen W. Cases illustrative of cerebral surgery. *Lancet*. 1885;125:881-883.

32. Henkel J, Woodruff MA, Epari DR, et al. Bone regeneration based on tissue engineering conceptions—a 21st century perspective. *Bone Res*. 2013;1:216-248.

33. Huang YH, Yang TM, Lee TC, Chen WF, Yang KY. Acute autologous bone flap infection after cranioplasty for postinjury decompressive craniectomy. *Injury*. 2013;44:44-47.

34. Rosinski CL, Chaker AN, Zakrzewski J, et al. Autologous bone cranioplasty: a retrospective comparative analysis of frozen and subcutaneous bone flap storage methods. *World Neurosurg*. 2019; 131:e312-e320.

35. Cheng CH, Lee HC, Chen CC, Cho DY, Lin HL. Cryopreservation versus subcutaneous preservation of autologous bone flaps for cranioplasty: comparison of the surgical site infection and bone resorption rates. *Clin Neurol Neurosurg*. 2014;124: 85-89.

36. Fan MC, Wang QL, Sun P, et al. Cryopreservation of autologous cranial bone flaps for cranioplasty: a large sample retrospective study. *World Neurosurg*. 2018;109:e853-e859.

37. Corliss B, Gooldy T, Vaziri S, Kubilis P, Murad G, Fargen K. Complications after in vivo and ex vivo autologous bone flap storage for cranioplasty: a comparative analysis of the literature. *World Neurosurg*. 2016;96:510-515.

38. Chang V, Hartzfeld P, Langlois M, Mahmood A, Seyfried D. Outcomes of cranial repair after craniectomy. *J Neurosurg*. 2010;112:1120-1124.

39. Nasi D, Gladi M, Di Rienzo A, et al. Risk factors for post-traumatic hydrocephalus following decompressive craniectomy. *Acta Neurochir*. 2018; 160:1691-1698.

40. Nasi D, Dobran M. Can early cranioplasty reduce the incidence of hydrocephalus after decompressive craniectomy? A meta-analysis. *Surg Neurol Int*. 2020;11:94.

41. Shih FY, Lin CC, Wang HC, et al. Risk factors for seizures after cranioplasty. *Seizure*. 2019;66:15-21.

42. Goedemans T, Verbaan D, Coert BA, et al. Neurologic outcome after decompressive craniectomy: predictors of outcome in different pathologic conditions. *World Neurosurg*. 2017;105: 765-774.

43. Malcolm JG, Rindler RS, Chu JK, et al. Early cranioplasty is associated with greater neurological improvement: a systematic review and meta-analysis. *Neurosurgery*. 2018;82:278-288.

44. Giese H, Antritter J, Unterberg A, Beynon C. Long-term results of neurological outcome, quality of Life and cosmetic outcome after cranioplastic surgery: a single center study of 202 patients. *Front Neurol*. 2021;12:1176.

45. Posti JP, Yli-Olli M, Heiskanen L, et al. Cranioplasty after severe traumatic brain injury: effects of trauma and patient recovery on cranioplasty outcome. *Front Neurol*. 2018;9:223.

46. Iaccarino C, Kolias A, Adelson PD, et al. Consensus statement from the International Consensus Meeting on Post-traumatic Cranioplasty. *Acta Neurochir*. 2021;163:423-440.

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