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OUTCOME COMPARISON OF SUBCUTANEOUSLY PRESERVED AUTOLOGOUS BONE FLAP VERSUS SYNTHETIC IMPLANT (POLYMETHYLMETHACRYLATE) FOR CRANIOPLASTY

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ABSTRACT

Cranioplasty is a surgical procedure used to reconstruct the calvaria, usually following decompressive hemicraniectomy performed for severe head trauma, malignant stroke, hemorrhage, or medically refractory intracranial hypertension. Advances in surgical techniques have enabled preservation of autologous bone flaps, although cranioplasty—regardless of material—remains associated with complications such as infection, seizures, poor cosmesis, hydrocephalus, extra-axial fluid collections, and bone resorption. Failures may arise from implant fabrication issues or surgical technique, and no material is completely risk-free.

This study aimed to compare outcomes between subcutaneously preserved autologous bone flaps and polymethyl methacrylate (PMMA) implants. The rationale stemmed from increasing rates of decompressive hemicraniectomies for trauma, infarction, tumors, and venous thrombosis, creating a growing need for reliable cranioplasty materials. A quasi-experimental study design was used, enrolling eligible patients from Neurosurgery Unit II based on surgeon preference. Cranioplasty was performed within four months after resolution of cerebral swelling. Statistical analysis was conducted using SPSS version 27, employing independent t-tests for quantitative variables and chi-square tests for categorical outcomes, with significance set at $p \leq 0.05$.

The study population had a mean age of 35.72 ± 9.91 years (range 15–62 years). Group A (autologous bone flap) and Group B (PMMA implant) showed similar age and gender distribution. Postoperative outcomes—including infection, cosmesis, hematoma, and revision rates—were monitored over a six-month period.

Revision surgery was more common in the autologous bone group: 17.78% vs. 8.89% at one month, 13.33% vs. 4.44% at three months, and 6.67% vs. 0% at six months. Infection rates also favored PMMA, with Group A demonstrating higher infection frequencies at every follow-up (6.67% vs. 2.22% at first month; 6.67% vs. 0% at three months; 4.44% vs. 0% at six months). Cosmetic complications were low in both groups, though slightly higher in Group A during early follow-up.

INTRODUCTION:

Cranioplasty is the surgical reconstruction of cranial defects using either autologous bone or synthetic implants. Autologous bone is generally preferred for large calvarial defects due to its biocompatibility, perfect anatomical contour, and cost-effectiveness, although biomaterials such as titanium, porous hydroxyapatite, PMMA, PEEK, and porous polyethylene are commonly used depending on factors such as patient age, defect size, donor site availability, prior graft resorption, or infection risk (Fahradyan et al., 2020).

Decompressive hemicraniectomy is performed as a life-saving intervention in critically ill patients with severe traumatic brain injury, malignant stroke, hemorrhage, or refractory intracranial hypertension. Because the procedure carries significant morbidity and mortality, cranioplasty is delayed until neurological recovery and resolution of cerebral edema. Cranioplasty improves neurological function, cerebral perfusion, CSF dynamics, and symptoms of the trephine syndrome, making it essential for restoring protection, contour, and brain physiology. However, it is also associated with complications such as infection, seizures, hydrocephalus, fluid collections, and bone resorption (Dowlati et al., 2022; Ernst et al., 2018).

Although autologous bone flaps can be stored via cryopreservation or subcutaneous implantation—with comparable outcomes—subcutaneous storage may increase the risk of hematoma or infection at the secondary surgical site and may ultimately require synthetic reconstruction (Dowlati et al., 2022). As the use of decompressive craniectomy increases for various pathologies, the demand for cranioplasty has grown accordingly (Policicchio et al., 2020). The history of cranioplasty dates back to antiquity, including early reports by Fallopius and Petronius and the first recorded bone graft by Van Meekeren in 1668 (Aciduman & Belen, 2007).

Custom-designed PMMA implants have demonstrated advantages—including shorter operative time, reduced intraoperative bleeding, ease of application, and good cosmetic outcomes—with infection rates lower than intraoperatively molded PMMA and comparable to autologous bone (Lee et al., 2009). Successful cranioplasty requires careful consideration of multiple factors: patient condition, wound status, cause of craniectomy, implant material, and timing (Sahoo et al., 2021). Early cranioplasty (<90 days) may increase the risk of hydrocephalus, particularly in trauma cases (Malcolm et al., 2016).

Studies comparing autologous bone with synthetic implants show mixed outcomes. Autologous grafts are commonly used for small-to-medium defects but are limited by risks of infection and bone resorption. A retrospective review by Dowlati et al. (2022) found that although autologous bone was more cost-effective, it had higher resorption and reoperation rates when stored subcutaneously, suggesting cryopreservation as a better alternative. Other research indicates that titanium hardware in pediatric patients may extrude over time (Mullens et al., 2018).

Sahoo et al. (2020) identified multiple causes of cranioplasty failure, reinforcing the need for surgical expertise and careful patient selection. Vince et al. (2018) observed no significant difference in overall complications between autologous bone and PMMA implants, though PMMA carried a higher risk of epidural and subdural hematomas. A study by Moles et al. (2017) comparing autologous and hydroxyapatite implants showed better cosmetic results in the hydroxyapatite group but highlighted prosthesis fragility and uncertain long-term Osseo integration.

Large clinical series also demonstrate variability in cosmetic and neurological outcomes. Satapathy et al. (2019) found that 55.6% of patients achieved good symmetry, while others experienced contour deformities, seizures, or infection; rushed surgical technique was suggested as a contributing factor. Similarly, Rosinski et al. (2019) showed that both cryopreservation

and subcutaneous bone storage were viable methods with similar complication rates, though cryopreservation may slightly reduce overall morbidity. Alkhaibary et al. (2019) found that blood glucose levels and defect size were significant risk factors for surgical site infection, but subcutaneous storage itself did not increase infection risk.

Overall, the literature demonstrates that both autologous and synthetic implants carry benefits and limitations. Autologous bone remains biocompatible and anatomically ideal but is prone to resorption and infection, particularly when stored subcutaneously. Synthetic implants—especially PMMA—offer reliability, ease of use, and favorable cosmetic outcomes, though they may be associated with hematoma formation. Across all materials, poor contouring, inadequate implant shaping, and bone resorption can lead to unsatisfactory cosmetic results and the need for revision surgery (Satapathy et al., 2019).

RATIONALE:

As the decompressive hemicraniectomy has increased because of trauma, infarction, tumor surgeries and venous thrombosis, so need for cranioplasty has also increased. In doing so a procedure with proper graft need to be devised to prevent burden on hospital and give patient benefit, therefore the aim of this study is to compare subcutaneously preserved autologous bone flaps versus PMMA implant for cranioplasty, which can help us improve treatment protocol and better care for the patients. Comparing to parent article novelty is shown below.

Parent article (Dowlati et al., 2022)	Current article
Decompressive hemicraniectomy and cranioplasty using subcutaneously preserved autologous bone flaps versus Analysis	Outcome comparison of subcutaneously preserved autologous bone flaps versus PMMA implant for cranioplasty
Variables were perioperative outcomes and cost analysis	Variables of this study is infection and Cosmesis

LITERATURE REVIEW

Cranioplasty is a commonly performed neurosurgical procedure used to reconstruct cranial defects. Over time, the materials employed for repairing cranial deformities have evolved significantly. Cranioplasty materials are generally classified into **biological** and **synthetic** types. Biological materials include **autologous**, **allogenic**, and **xenogeneic** grafts. Autologous cranioplasty uses the patient's own cranial bone or bone harvested from another part of the body.

Advances in computer-assisted design and three-dimensional printing have improved synthetic implants, resulting in shorter recovery times and better cosmetic outcomes. Early synthetic materials, such as aluminum, were eventually abandoned after being found to dissolve, irritate brain tissue, and induce seizures. Today, **methyl methacrylate (PMMA)** is the most widely used synthetic material in cranioplasty. **Hydroxyapatite**, a naturally occurring component of bone, supports osteointegration and reduces inflammatory reactions, while **polyetheretherketone (PEEK)** is favored for being lightweight, nonconductive, and compatible with imaging techniques.

The most common complication after cranioplasty is **surgical site infection**. The effect of cranioplasty timing on cognitive recovery remains uncertain, but available evidence suggests that neurological outcomes alone should not determine the timing of surgery. This review summarizes the evolution, history, materials, and complications associated with modern cranioplasty techniques (Alkhaibary et al., 2020; Binhammer et al., 2020).

Cranioplasty is performed to repair cranial defects that cause symptoms related to direct atmospheric pressure on the unprotected brain, as well as disturbances in cerebrospinal fluid (CSF) dynamics and

cerebral blood flow (Jeyaraj, 2015). When indicated, the procedure helps restore normal CSF flow, cerebral perfusion, and reduce cerebral edema. The materials used for cranial reconstruction—either autologous or synthetic—determine the technique and outcomes. This article provides both a historical overview and a detailed discussion of materials used in contemporary cranioplasty (Hassan et al., 2019).

HYPOTHESIS

Null Hypothesis:

There is difference in outcome between subcutaneously preserved autologous bone flaps versus synthetic implant (PMMA) for cranioplasty in terms of infection and cosmesis.

Alternate Hypothesis:

There is no difference in outcome between subcutaneously preserved autologous bone flaps versus synthetic implant (PMMA) for cranioplasty in terms of infection and cosmesis.

MATERIALS AND METHODS:

Study design:

Quasi-experimental.

Study settings:

Neurosurgery department unit–II, Punjab Institute of Neurosciences, Lahore.

Study duration:

12 Months

Sampling technique:

Non-probability, consecutive sampling. All the patients were distributed into two groups by surgeon preference.

Sample size:

The sample size of forty-five subjects in each group was estimated using 80% power of the study, a 5% level of significance, and assuming the proportion of infection with autologous bone flaps to be 8.6% and 28.6% with synthetic implants (PMMA) for decompressive craniectomy (Dowlati et. al.,

$$n = \frac{\left\{ z_{1-\alpha/2}\sqrt{2\bar{P}(1-\bar{P})} + z_{1-\beta}\sqrt{P_1(1-P_1)+P_2(1-P_2)} \right\}^2}{\left(P_1 - P_2\right)^2}$$

2020).

P1 = Anticipated proportion of infection with autologous bone flaps

P2 = Anticipated proportion of infection with synthetic implants (PMMA) = 28.6%

Z 1-α/2 = Standardized value of Z at 5% level of significance

1.96 Z 1-β= Standardized value of Z at 80% power of study= 0.86

n = calculated sample size for each group = 45

Sample Selection:

Inclusion criteria:

1- Age more than fourteen and less than sixty-five years of both genders.
2- Post traumatic decompressive craniectomy with duroplasty.
3- Decompressive craniectomy for malignant infarct.
4- Bone flap removal after benign tumor excision.
5- Timing of cranioplasty should be at least four months.
6- Supratentorial cranioplasty.
7- Glasgow Coma Scale score of more than 10

Exclusion Criteria:

1- Previous and currently infected surgical area.
2- Patients with co morbidities like diabetes mellitus, bleeding disorders.
3- Patient with previous failure implant.
4- Cranioplasty with other synthetic implants.
5- Immunocompromised patient.
6- Infratentorial cranioplasty.
7- Cranioorbital defect.
8- Defect involving frontal air sinuses.

METHODOLOGY:

After the approval of synopsis, a total of ninety patients fulfilling the inclusion criteria were enrolled into the study. Written and informed consent was taken from each patient. The demographic information was recorded on Pro-forma (Annexure I). A proper history and neurological examination were conducted. CT brain plain with bone window was done and baseline investigations were performed. All the patients were distributed into two groups (A

& B) by surgeon preference. Postoperatively, patients were monitored for implant failure (infection and cosmesis). All patients were re- evaluated at OPD on follow up visits (1 month, 3 months, 6 months) for any complications. All the data was collected then analyzed and compared.

Surgical Procedure

As my study design is Quasi experimental, patients were divided into two groups by surgeon preference, group A patients were prepared for subcutaneously preserved autologous bone flap cranioplasty. After history, examination, baseline and consent patients were shifted to Operation Theater and under general anesthesia proper position were made, firstly previously abdominal incision was explored, bone preserved in subcutaneous plane in abdomen was taken and looked for any sign of infection, if no sign of infection then was stored in antiseptic solution and abdominal wound was closed. After that previous scalp wound was opened, bone edges exposed and preserved bone was grafted into the craniectomy defect. Bone was anchored using titanium mini plate and screws. Hemostasis was done followed by wound closure in layers and then aseptic dressing.

While group B was prepared for cranioplasty using PMMA implant. After history, examination, baseline and consent patients were shifted to operation theater and under general anesthesia proper position was made, previous wound was explored and bone edges was exposed then free hand modeled synthetic PMMA was prepared by mixing the liquid monomer (catalyst) with the powder polymer in a ratio of two parts powder and one part liquid. This mixture was constantly stirred until its consistency is doughy. Then the mixture was taken in gloved hands and knead until it will no longer be adherent to the gloves, then it was molded according to the cranial defect and placed at the site of defect. Continuous irrigation with normal saline was done. Multiple small holes were created in implant to prevent extradural collection. Then the implant was fixed with titanium mini plates and screws followed by subgalea drain No.14. After hemostasis wound was closed layer wise followed by aseptic dressing.

Patients were administered intravenous antibiotic (ceftriaxone 1g B.D). On second post op day CT brain plain was done and drain was removed. Patient was discharged on oral antibiotics (tab. cefixime 400mg O.D.) for 5 days and oral analgesics. A structured Performa was used to collect the basic demographical and clinical data for all patients' pre and post operatively. Outcome (infection and cosmesis) was documented post- operatively and during follow-up in both groups.

Data analysis

All the data was entered and analyzed using SPSS 27 version. Quantitative data like age was presented by the mean and standard deviation. Qualitative data, like gender and complications i.e., infection and cosmesis was presented by frequency and percentages. Independent t-test was used to compare the quantitative variable. The chi- square test was used to compare the gender distribution, infection rate, cosmesis and any other complications between the two groups. A p-value ≤ 0.05 was considered significant.

RESULTS:

In this study, a total number of 90 (45+45) cases fulfilling inclusion criteria. The study was initially, approved from the ethical committee, Department of Neurosurgery Unit II, Lahore General Hospital, Lahore. Patients were divided into two groups by consultant choice. Group A was comprised of patients who received autologous bone flap while Group B was comprised of patients who received synthetic implant (polymethylmethacrylate implant) for cranioplasty. Finally, outcomes of both procedures were compared in terms of infection, cosmesis and success rate between the two groups.

Age distribution:

In this study, 23.33%patients were between the ages of 15-30years, 44.44% patients were between the ages of 31-40years and 32.22%patients were between the ages of 41- 62years. The minimum age of the

patient was 15 years while maximum age of the patient was 62 years. However, mean age of patients was 35.72±9.91years (Table 4.1).

The Independent Sample T-Test was used to determine the statistical significant age between the Group A and Group B and results expressed no significant difference (p= 0.942) between both groups (Table 4.1).

Table 4.1: Frequency of age distribution in Group A and Group B.

Age (in Years)	No. of Patients	%	p-value
15-30	21	23.33%	0.942
31-40	40	44.44%	
41-62	29	32.22%	
Total	**90**	**100%**	

Age comparison

The mean age of patients in Group A was 35.67± 9.93 years and the mean age of patients in Group B was 35.83± 10.03 years (Table 4.2). The independent sample t-test revealed that the difference between Group A and Group B (p = 0.945) was not significant.

Table 4.2: Comparison of mean age between Group A and Group B.

Groups	Mean ± SD	Minimum	Maximum	p-value
Group A	35.67± 9.93	15 years	62 years	0.945
Group B	35.83± 10.03	20 years	61 years	

Gender

In Group A 30 (66.67%) patients were male and 15 (33.33%) patients were female while in Group B31 (68.89%) patients were male and 14 (31.11%) patients were female respectively (Table 4.3). The Chi-square test was used to compare the gender distribution in Group A and Group B and results expressed no significant difference (p= 0.824) between both groups (Table 4.3).

Table 4.3: Gender distribution comparison between Group and Group B.

Gender	Group A	Group B	p-value
Male	30 (66.67%)	31 (68.89%)	0.824
Female	15 (33.33%)	14 (31.11%)	
Total	**45**	**45**	

Postoperative Outcome as Cosmesis

The Rostock functional and cosmetic Cranioplasty Score was used to assess cosmesis, and the results are presented in Table 4.4.

Table4.4: Postoperative Outcome as Cosmesis between Group A and Group B.

Rostoct Score

	Group A		Group B		p value
	Frequency	**%**	**Frequency**	**%**	
Scar on Skin	1	2.22%	1	2.22%	
Fitting of cranioplasty	1	2.22%	0	0%	

Symmetry	1	2.22%	1	2.22%	0.856
Function	1	2.22%	0	0%	
Total	4	8.89%	2	4.44%	

4.6 Postoperative outcome at 1st Month

Postoperative complications outcomes at fourth week post operation in terms of infection, cosmesis, hematoma and number of revisions was monitored and represented in Table 4.6. Results showed total 08 revisions in group A and 04 revisions in group B for fourth week post operation were recorded, respectively. Chi-square test, results revealed no significant difference in terms of outcome between group-A and group-B (Table 4.6).

Table 4.6: Postoperative outcome in group-A and group-Bat 1st Month.

	Group-A		Group-B		p-value
	No.	**%**	**No.**	**%**	
Infection	3	6.67%	1	2.22%	0.367
Cosmesis	3	6.67%	1	2.22%	
Hematoma	2	4.44%	2	4.44%	
Revision	8	17.78%	4	8.89%	

Postoperative outcome at 3rd month

Postoperative complications outcomes at 3rd month post operation in terms of infection, cosmesis, hematoma and number of revisions was monitored and represented in Table 4.7. Results showed total 06 revisions in group A and 02 revisions in group B for 3rdmonth post operation were recorded respectively. Chi-square test, results revealed no significant difference in terms of outcome between group-A and group-B (Table 4.7).

Table 4.7: Postoperative outcome in group-A and group-Bat 3rdmonth.

	Group-A		Group-B		p-value
	No.	%	No.	%	
Infection	3	6.67%	0	0%	0.041
Cosmesis	1	2.22%	1	2.22%	
Hematoma	2	4.44%	1	2.22%	
Revision	6	13.33%	2	4.44%	

Postoperative outcome at 6thmonth

Postoperative complications outcomes at 6thmonth post operation in terms of infection, cosmesis, hematoma and number of revisions was monitored and represented in Table 4.8. Results showed total 03 revisions in group A and zero revision in group B for 6thmonth post operation were recorded, respectively. Chi-square test, results revealed no significant difference in terms of outcome between group-A and group-B (Table 4.8).

Table 4.8: Postoperative outcome in group-A and group-Bat 6thmonth.

	Group-A		Group-B		p-value
	No.	%	No.	%	
Infection	2	4.44%	0	0%	0.024
Cosmesis	0	0%	0	0%	
Hematoma	1	2.22%	0	0%	
Revision	3	6.67%	0	0%	

DISCUSSION

Decompressive craniectomy (DC) is a well-established neurosurgical procedure performed to reduce critically elevated intracranial pressure (ICP). Although lifesaving, reconstruction of the cranial vault after DC remains challenging and is associated with considerable postoperative morbidity. The primary aim of this study was to compare complication rates between autologous bone grafts and acrylic (PMMA) implants. This retrospective analysis included adult patients who underwent supratentorial DC followed by cranioplasty at our institution in 2023–2024. Medical records, operative notes, imaging studies, and postoperative follow-up visits were reviewed. Of the 286 cranioplasties performed, 221 used autologous bone flaps and 65 used PMMA implants (Vince et al., 2019; Li et al., 2012).

A total of 23 surgical revisions were required during the follow-up period. In the autologous group, 37.78% of patients developed complications that necessitated surgical intervention, compared with 13.33% in the acrylic group. Infection was the most frequent indication for revision, accounting for nine cases of impaired wound healing. Subdural and epidural hematomas occurred more often in the autologous group. Implant loosening and displacement were also documented. Despite these risks, our findings suggest that both autologous bone and PMMA implants remain viable options for adult cranioplasty.

DC is typically performed when conservative interventions such as sedation, hyperventilation, osmotherapy, head elevation, and CSF drainage fail to maintain ICP or cerebral perfusion pressure (CPP). It may also be required emergently for large contusions or subdural hematomas (Li et al., 2012). DC is supported by several randomized and prospective studies for malignant cerebral infarction (Jüttler et al., 2011) and traumatic brain injury (Chibbaro et al., 2011). Its indications have broadened to include cases of encephalitis, intracerebral hemorrhage, aneurysmal subarachnoid hemorrhage, and cerebral venous thrombosis. TBI research consistently shows that elevated ICP is a major predictor of morbidity and mortality, and DC plays an important role in reducing it (Bor-Seng-Shu et al., 2012).

Our study found no clear physiological explanation for why postoperative hematomas were more frequent in the autologous bone group. One might expect the opposite, since autologous bone often leaves a small gap between the dura and the graft, whereas PMMA implants can be molded more precisely to the dural surface. A possible source of bias arises from the fact that only hematomas requiring surgical intervention were recorded, and these may produce more rapid mass effect.

Previous literature demonstrates variable complication rates. Lethaus et al. (2014) reported complications in 48% of autologous graft recipients, while Wachter et al. (2013) observed complications in over one-third of 136 patients. Honeybul and Ho (2012) reported a 29% failure rate in 156 patients, primarily due to early and late infections requiring graft removal. However, definitions of “failure” differ substantially across studies. Some authors do not consider wound infection or partial graft loss as failure (Matsuno et al., 2006). In our series, any infection requiring surgical revision was considered significant; 95.7% of such cases required implant removal.

Bone flap resorption remains an important issue—particularly in younger patients. Martin et al. reported an 81.8% resorption rate in 27 infants, with more than half requiring revision surgery. Although routine CT screening was not part of our protocol, clinically significant bone resorption prompting revision occurred in 4% of our autologous cases, suggesting lower rates among adults (Martin et al., 2014).

Several alloplastic materials, including PMMA, PEEK, titanium, and calcium phosphate, are available as CT/CAD-based, patient-specific implants. These prefabricated implants, although substantially more expensive, offer

advantages such as reduced operative time, improved cosmetic outcomes, and lower complication rates (Lethaus et al., 2014; Lee et al., 2014). Porous PMMA implants facilitate better integration and healing, while titanium and PEEK implants provide excellent structural stability and imaging compatibility. Despite these benefits, patient-specific implants remain cost-prohibitive for many institutions. In our study, we found no significant difference in operative time or hospital stay between autologous bone and patient-specific implants; however, freehand PMMA required longer surgical time.

Preserved autologous bone flaps should be considered mineral scaffolds that support natural bone regeneration rather than essential biological grafts (Sultan et al., 2011). While our findings demonstrate that both autologous bone and freehand PMMA implants remain effective reconstructive options, emerging evidence suggests that patient-specific implants may eventually become the preferred standard due to superior cosmetic and biomechanical advantages.

As a retrospective study, our analysis has inherent limitations, including variability in surgical techniques, non-standardized definitions of complications, and surgeon-dependent decision-making without blinding (Lethaus et al., 2011; Honeybul & Ho, 2012). These factors make comparisons with other published literature challenging.

CONCLUSION:

This study examines different techniques of repair about surgical risk with a particular focus on infectious complications, cosmesis and hematomas. Cranioplasty carries a significant risk of postoperative infection, wound break down, and hematoma formation, often requiring reoperation in these instances. Nonetheless, we observed a higher incidence of postoperative infectious complications in autologous bone flaps in comparison to PMMA. The results of cosmesis and other complications were better in the PMMA group as compared to the autologous bone flaps group but that was not statistically significant. We are optimistic that this study will pave the way for future randomized controlled studies that will assess different modalities, despite the fact that the PMMA technique has been demonstrated to be superior to others.

REFERENCES:

Acciarri N, Nicolini F and Martinoni M (2016) Cranioplasty: routine surgical procedure or risky operation. *World Journal of Surgical Research* 5(5): 22-33.

Aciduman A and Belen D (2007) The earliest document regarding the history of cranioplasty from the Ottoman era. *Surgical neurology* 68(3): 349-352.

Ahn D-H, Kim D-W and Kang S-D (2009) In situ floating resin cranioplasty for cerebral decompression. *Journal of Korean Neurosurgical Society* 46(4): 417.

Alkhaibary A, Alharbi A, Alnefaie N, et al. (2020) Cranioplasty: a comprehensive review of the history, materials, surgical aspects, and complications. *World Neurosurgery* 139: 445-452.

Archavlis E and Carvi Y Nievas M (2012) The impact of timing of cranioplasty in patients with large cranial defects after decompressive hemicraniectomy. *Acta neurochirurgica* 154: 1055-1062.

Ashayeri K, Jackson EM, Huang J, et al. (2016) Syndrome of the trephined: a systematic review. *Neurosurgery* 79(4): 525-534.

Aydin S, Kucukyuruk B, Abuzayed B, et al. (2011) Cranioplasty: review of materials and techniques. *Journal of neurosciences in rural practice* 2(02): 162-167.

Binhammer A, Jakubowski J, Antonyshyn O, et al. (2020) Comparative cost-effectiveness of cranioplasty implants. *Plastic Surgery* 28(1): 29-39.

Black SP, Kam CC and Sights WP (1968) Aluminum cranioplasty. *Journal of neurosurgery* 29(5): 562-564.

Bor-Seng-Shu E, Figueiredo EG, Amorim RL, et al. (2012) Decompressive craniectomy: a meta-analysis of influences on intracranial pressure and

cerebral perfusion pressure in the treatment of traumatic brain injury: a review. *Journal of neurosurgery* 117(3): 589-596.
Bowers CA, Riva-Cambrin J, Hertzler DA, et al. (2013) Risk factors and rates of bone flap resorption in pediatric patients after decompressive craniectomy for traumatic brain injury. *Journal of Neurosurgery: Pediatrics* 11(5): 526-532.
Budhdeo S, Meek T, Cosco TD, et al. (2019) Physiotherapist confidence level in mobilising stroke patients after decompressive hemicraniectomy: are helmets useful? *Biorxiv*. 632604.

BURWELL RG (1994) History of bone grafting and bone substitutes with special reference to osteogenic induction. *Bone grafts, derivatives and substitutes*.
Chiang H-y, Steelman VM, Pottinger JM, et al. (2011) Clinical significance of positive cranial bone flap cultures and associated risk of surgical site infection after craniotomies or craniectomies. *Journal of neurosurgery* 114(6): 1746-1754.
Chibbaro S, Di Rocco F, Mirone G, et al. (2011) Decompressive craniectomy and early cranioplasty for the management of severe head injury: a prospective multicenter study on 147 patients. *World Neurosurgery* 75(3-4): 558-562.
Corallo F, Lo Buono V, Calabrò RS, et al. (2021) Can cranioplasty be considered a tool to improve cognitive recovery following traumatic brain injury? A 5-years retrospective study. *Journal of Clinical Medicine* 10(22): 5437.
Corliss B, Gooldy T, Vaziri S, et al. (2016) Complications after in vivo and ex vivo autologous bone flap storage for cranioplasty: a comparative analysis of the literature. *World Neurosurgery* 96: 510-515.
De Cola MC, Corallo F, Pria D, et al. (2018) Timing for cranioplasty to improve neurological outcome: a systematic review. *Brain and behavior* 8(11): e01106.
Di Rienzo A, Colasanti R, Gladi M, et al. (2020) Sinking flap syndrome revisited: the who, when and why. *Neurosurgical Review* 43: 323-335.
Dowlati E, Pasko KBD, Molina EA, et al. (2022) Decompressive hemicraniectomy and cranioplasty using subcutaneously preserved autologous bone flaps versus synthetic implants: perioperative outcomes and cost analysis. *Journal of neurosurgery* 137(6): 1831-1838.
Durand J-L, Renier D and Marchac D (1997) The history of cranioplasty. *Annales de chirurgie plastique et esthetique.* 75-83.
Ernst G, Qeadan F and Carlson AP (2018) Subcutaneous bone flap storage after emergency craniectomy: cost-effectiveness and rate of resorption. *Journal of neurosurgery* 129(6): 1604-1610.
Fahradyan A, Goel P, Williams M, et al. (2020) Temporal fat grafting in children with craniofacial anomalies. *Annals of plastic surgery* 85(5): 505-510.
Giese H, Meyer J, Unterberg A, et al. (2021) Long-term complications and implant survival rates after cranioplastic surgery: a single-center study of 392 patients. *Neurosurgical Review* 44: 1755-1763.
Goiato MC, Anchieta RB, Pita MS, et al. (2009) Reconstruction of skull defects: currently available materials. *Journal of Craniofacial Surgery* 20(5): 1512- 1518.
Goldstein JA, Paliga JT and Bartlett SP (2013) Cranioplasty: indications and advances.
Current opinion in otolaryngology & head and neck surgery 21(4): 400-409.
Gooch MR, Gin GE, Kenning TJ, et al. (2009) Complications of cranioplasty following decompressive craniectomy: analysis of 62 cases. *Neurosurgical focus* 26(6): E9.

Henry J, Amoo M, Taylor J, et al. (2021) Complications of cranioplasty in relation to material: systematic review, network meta-analysis and meta-regression. *Neurosurgery* 89(3): 383-394.

Honeybul S and Ho KM (2012) Incidence and risk factors for post-traumatic hydrocephalus following decompressive craniectomy for intractable intracranial hypertension and evacuation of mass lesions. *Journal of Neurotrauma* 29(10): 1872-1878.

Honeybul S and Ho KM (2016) Cranioplasty: morbidity and failure. *British Journal of Neurosurgery* 30(5): 523-528.

Hutchinson PJ, Kolias AG, Timofeev IS, et al. (2016) Trial of decompressive craniectomy for traumatic intracranial hypertension. *New England Journal of Medicine* 375(12): 1119-1130.

Iaccarino C, Kolias A, Adelson P, et al. (2021) Consensus statement from the international consensus meeting on post-traumatic cranioplasty. *Acta neurochirurgica* 163: 423-440.

Inamasu J, Kuramae T and Nakatsukasa M (2010) Does difference in the storage method of bone flaps after decompressive craniectomy affect the incidence of surgical site infection after cranioplasty? Comparison between subcutaneous pocket and cryopreservation. *Journal of Trauma and Acute Care Surgery* 68(1): 183-187.

Jeyaraj P (2015) Importance of early cranioplasty in reversing the "syndrome of the trephine/motor trephine syndrome/sinking skin flap syndrome". *Journal of maxillofacial and oral surgery* 14: 666-673.

Jüttler E, Bösel J, Amiri H, et al. (2011) DESTINY II: DEcompressive Surgery for the Treatment of malignant INfarction of the middle cerebral arterY II. *International Journal of Stroke* 6(1): 79-86.

Kim SH, Kang DS, Cheong JH, et al. (2017) Comparison of complications following cranioplasty using a sterilized autologous bone flap or polymethyl methacrylate. *Korean journal of neurotrauma* 13(1): 15.

Ko K and Segan S (2007) In situ hinge craniectomy. *Operative Neurosurgery* 60(4): 255-259.

Kovar F and Wozasek G (2011) Unusual cranial reconstruction following motor vehicle accident. *European Surgery* 43: 321-322.

Lee EI, Chao AH, Skoracki RJ, et al. (2014) Outcomes of calvarial reconstruction in cancer patients. *Plastic and reconstructive surgery* 133(3): 675-682.

Lerch K-D (1999) Reliability of cranial flap fixation techniques: comparative experimental evaluation of suturing, titanium miniplates, and a new rivet-like titanium clamp (CranioFix). *Neurosurgery* 44(4): 902-905.

Lethaus B, Bloebaum M, Essers B, et al. (2014) Patient-specific implants compared with stored bone grafts for patients with interval cranioplasty. *Journal of Craniofacial Surgery* 25(1): 206-209.

Lethaus B, Ter Laak MP, Laeven P, et al. (2011) A treatment algorithm for patients with large skull bone defects and first results. *Journal of Cranio-Maxillofacial Surgery* 39(6): 435-440.

Li LM, Kolias AG, Guilfoyle MR, et al. (2012) Outcome following evacuation of acute subdural haematomas: a comparison of craniotomy with decompressive craniectomy. *Acta neurochirurgica* 154: 1555-1561.

Liu L, Lu S-T, Liu A-H, et al. (2020) Comparison of complications in cranioplasty with various materials: a systematic review and meta-analysis. *British Journal of Neurosurgery* 34(4): 388-396.

Macewen W (1885) Cases illustrative of cerebral surgery. *The Lancet* 125(3220): 881- 883.

Malcolm JG, Rindler RS, Chu JK, et al. (2016) Complications following cranioplasty and relationship to timing: a systematic review and meta-analysis. *Journal of Clinical Neuroscience* 33: 39-51.

Marchac D and Greensmith A (2008) Long-term experience with methylmethacrylate cranioplasty in craniofacial surgery. *Journal of plastic, reconstructive & aesthetic surgery* 61(7): 744-752.

Martin KD, Franz B, Kirsch M, et al. (2014) Autologous bone flap cranioplasty following decompressive craniectomy is combined with a high complication rate in pediatric traumatic brain injury patients. *Acta neurochirurgica* 156: 813- 824.

Matsuno A, Tanaka H, Iwamuro H, et al. (2006) Analyses of the factors influencing bone graft infection after delayed cranioplasty. *Acta neurochirurgica* 148: 535- 540.

Mayon-White R, Ducel G, Kereselidze T, et al. (1988) An international survey of the prevalence of hospital-acquired infection. *Journal of Hospital Infection* 11: 43- 48.

Mee H, Anwar F, Timofeev I, et al. (2022) Cranioplasty: a multidisciplinary approach.

Frontiers in Surgery 9: 864385.

Mokri B (2001) The Monro–Kellie hypothesis: applications in CSF volume depletion.
Neurology 56(12): 1746-1748.

Moles A, Heudes PM, Amelot A, et al. (2018) Long-term follow-up comparative study of hydroxyapatite and autologous cranioplasties: complications, cosmetic results, osseointegration. *World Neurosurgery* 111: e395-e402.

Morton RP, Abecassis IJ, Hanson JF, et al. (2017) Timing of cranioplasty: a 10.75-year single-center analysis of 754 patients. *Journal of neurosurgery* 128(6): 1648- 1652.

Mullens CL, Grome LJ, Serrano CA, et al. (2018) Titanium hardware extrusion following pediatric cranioplasty. *Interdisciplinary Neurosurgery* 13: 1-5.

Munroe A (1924) The operation of cartilage-cranioplasty. *Canadian Medical Association Journal* 14(1): 47.

Mynors R (1785) *A History of the Practice of Trepanning the Skull and the After- treatment; with Observations Upon a New Method of Cure, Illustrated by a Case, by Robert Mynors.* G. Robinson.

Nasi D and Dobran M (2020) Can early cranioplasty reduce the incidence of hydrocephalus after decompressive craniectomy? A meta-analysis. *Surgical Neurology International* 11.

New PF, Rosen BR, Brady TJ, et al. (1984) Potential hazards and artifacts of ferromagnetic and nonferromagnetic surgical and dental materials and devices in nuclear magnetic resonance imaging. *Magnetic Resonance Imaging* 2(1): 66.

Norrefalk J-R (2003) How do we define multidisciplinary rehabilitation? *Journal of rehabilitation medicine* 35(2): 100-101.

Oyelese AA, Steinberg GK, Huhn SL, et al. (2005) Paradoxical cerebral herniation secondary to lumbar puncture after decompressive craniectomy for a large space-occupying hemispheric stroke: case report. *Neurosurgery* 57(3): E594.

Park SP, Kim JH, Kang HI, et al. (2017) Bone flap resorption following cranioplasty with autologous bone: quantitative measurement of bone flap resorption and predictive factors. *Journal*

of Korean Neurosurgical Society 60(6): 749-754.

Policicchio D, Casu G, Dipellegrini G, et al. (2020) Comparison of two different titanium cranioplasty methods: Custom-made titanium prostheses versus precurved titanium mesh. *Surgical Neurology International* 11.

Gopalakrishnan M, Shanbhag NC, Shukla DP, et al. (2018) Complications of decompressive craniectomy. *Frontiers in neurology* 9: 977.

Gosain AK (1997) Hydroxyapatite cement paste cranioplasty for the treatment of temporal hollowing after cranial vault remodeling in a growing child. *Journal of Craniofacial Surgery* 8(6): 506-511.

Hacker V (1903) Ersatz von Schädeldefekten durch unter der Kopfschwarte verschobene oder umgeklappte Periostknochenlappen beziehungsweise Periostlappen. *Beitr Klin Chir* 37: 499.

Hassan H, Ali A and Abdalla A (2019) Autogenous bone graft versus artificial substitutes in cranioplasty. *Open Journal of Modern Neurosurgery* 9(03): 338.

:er C, Hoppmann M-C, Sherman MUS, et al. (2018) Validation of a novel clinical score: the rostock functional and cosmetic cranioplasty score. *Journal of Neurotrauma* 35(8): 1030-1036.