Cranioplasty: A Comprehensive Review of the History, Materials, Surgical Aspects, and Complications

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Key words
- Cranioplasty
- History
- Materials
- Review

Abbreviations and Acronyms
CSF: Cerebrospinal fluid
DC: Decompressive craniectomy
MMA: Methyl methacrylate
PEEK: Polyetheretherketone

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Cranioplasty is a common neurosurgical procedure performed to reconstruct cranial defects. The materials used to replace bone defects have evolved throughout history. Cranioplasty materials can be broadly divided into biological and synthetic materials. Biological materials can be further subdivided into autologous grafts, allografts, and xenografts. Allografts (bony materials and cartilage from cadavers) and xenografts (bony materials from animals) are out of favor for use in cranioplasty because of their high rates of infection, resorption, and rejection. In autologous cranioplasty, either the cranial bone itself or bones from other parts of the body of the patient are used. Synthetic bone grafts have reduced the operation time and led to better cosmetic results because of the advancement of computer-based customization and three-dimensional printing. Aluminum was the first synthetic bone graft material used, but it was found to irritate neural tissue, induce seizures, and dissolve over time. Acrylic, in the form of methyl methacrylate, is the most widely used material in cranioplasty. Hydroxyapatite is a natural component of bone and is believed to enhance bone repair, resulting in decreased tissue reactions and promoting good osteointegration. Polyetheretherketones are light and nonconductive and do not interfere with imaging modalities. The complication rates of cranioplasty are high, and surgical site infection is the most common complication. The effect of cranioplasty timing on cognitive function remains debatable. However, the timing of cranioplasty is independent of neurologic outcomes. In this article, the history, materials, complications, and evolution of current practices used in cranioplasty are comprehensively reviewed.

INTRODUCTION

Cranioplasty serves not only as a physical barrier to protect cerebral structures and/or cosmetically reshape the cranial bone defect but also as a therapeutic measure to control alterations in the cerebrospinal fluid (CSF), blood flow, and the metabolic demands of the brain.[1-4] Patients who have undergone decompressive craniectomy (DC) and are awaiting cranioplasty are at increased risk of developing trephined syndrome.[1] This syndrome is characterized by neurologic deterioration and sensorimotor deficits after DC that tend to develop as a result of removing a large skull flap.[1] It arises because of direct atmospheric pressure on the unprotected part of the skull and dysregulation of the CSF or cerebral blood flow.[1] When warranted, cranioplasty is performed to allow normalization of the CSF, cerebral blood flow, and edema within the brain.[1] Cranioplasty is classified according to the materials used, which are either autologous or artificial.[5] This article provides a historical overview and discusses the materials used in cranioplasty.

HISTORY OF CRANIOPLASTY

Cranioplasty has progressed a long way since 1668 (Figure 1), when the Dutch surgeon van Meekeren reported in his book, *van Meekeren's Observationes Medico-Chirurgicae*, the first true and successful bone graft, which was performed with bone from a dead dog cranium. The described graft was selected to be large enough to fill a bone defect created by a sword in a nobleman's head.[6] Before this development, Fallopius (1523—1562) described the use of a gold plate to replace the bone over the violated dura, which was considered the first historical description of cranioplasty.[6] Most of the other ancient attempts were descriptions of dressings placed over the exposed meninges and were not true forms of cranioplasty.[6,7]

The concepts of autografts, allografts, and xenografts were first defined by a French surgeon named Ollier (1859).[8] In 1821, Walther[6] documented the first use of autografts in cranioplasty by replacing a bone plug over a trepanated bone. Walther's work was followed by several other successful attempts in 1885 by Macewen, the father of modern bone grafting, and in 1888 by Burrell.[6,8-10] However, delayed healing was noted for such grafts and was not specifically addressed in the reports.[6] This issue was pointed out and reported, at first, by Muller in 1890.[6,11] Muller[11] was the first to use a single flap (of skin, periosteum, and the skull outer table) for the repair of

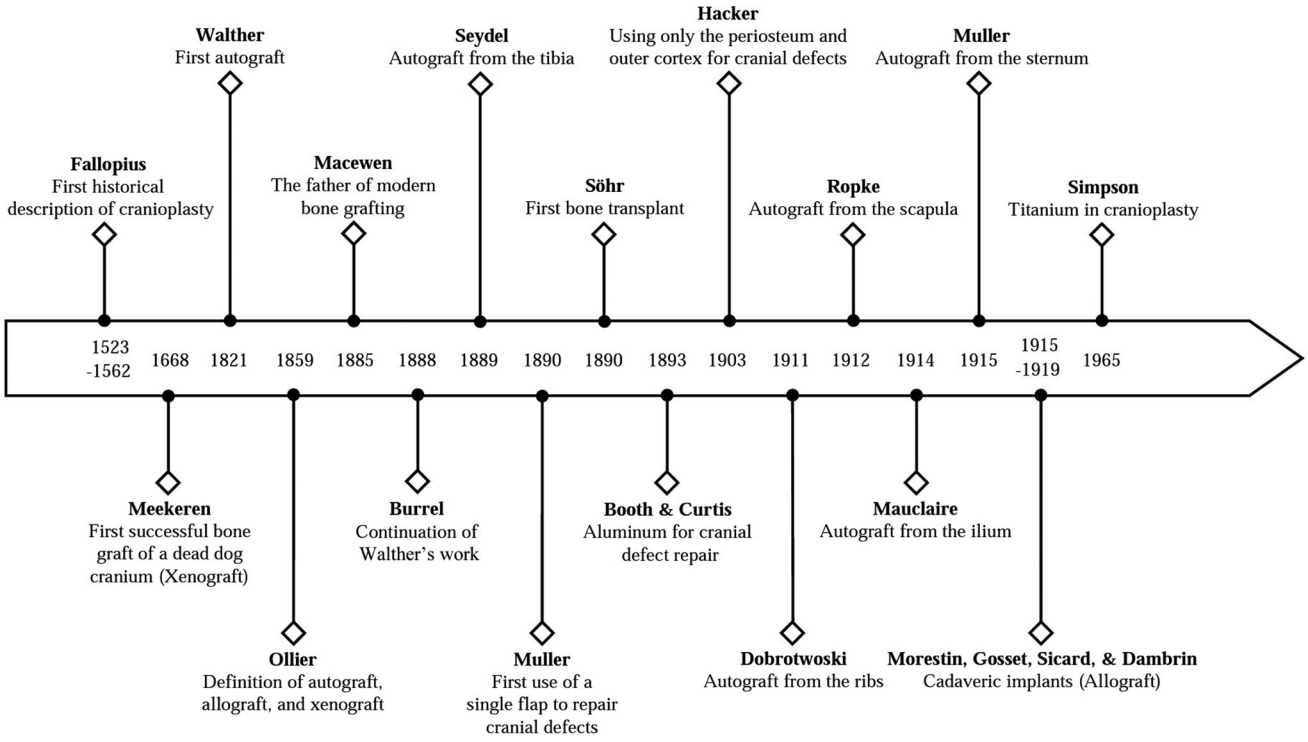

Figure 1. Historical evolution of cranioplasty.

cranial defects. A modification was made to Muller's work by Hacker (1903), who used only the periosteum and the outer cortex for the repair of cranial defects.[6,12] Throughout history, different types of bone have been used.[13] Autografts have been used from the tibia (by Seydel 1889), ribs (by Dobrotwoski 1911), scapula (by Ropke 1912), ilium (by Mauclaire 1914), and sternum (by Muller 1915).[6,14-16] In 1890, the first bone transplant was performed by Söhr, who used the cranial external tabula without the periosteum.[13,17,18] Tibial bone was also used, and one of the earliest patient tibial transplants was performed by Axhausen, who treated 27 patients.[18] Tibial bone is now rarely used because it is difficult to contour and harvest.[13] In addition, ribs were used commonly in the past but are no longer used because of the high risk of respiratory complications.[18,19] Despite their significant advantages, autografts alone cannot always meet the aesthetic requirements of cranioplasty or be used for large complicated cranial defects.[6]

Between 1915 and 1919, Morestin, Gosset, Sicard, and Dambrin introduced cadaveric implants (allografts).[6,20-22] Because they are limited by the increased risk of infection and unfavorable bone resorption, allografts are no longer used in cranioplasty.[6] In addition, bone transplants from many species of animals (xenografts) have been used in repairing cranial defects since the first case reported by van Meekeren in 1668.[6,23-25] However, there was inadequate evidence to support their use in consideration of the satisfactory outcomes of the use of autografts and bone substitutes.[6,26]

Because of their advantages of adequate strength and malleability, metallic bone substitutes have been used for cranioplasty.[6] Although the outcomes were unfortunate, in 1893, Booth and Curtis[27] used aluminum as a substitute for bone in cranial defect repair. Aluminum was able to provide the desired cosmetic and functional outcomes, as noted by Black et al. (1968) after its accidental use but failed because of its epileptogenicity and irritative properties.[6,28] The use of gold in cranioplasty was limited by its high cost and the failure of the pure metal to maintain its strength.[6,29] Similarly, the use of platinum was abandoned because of its costs.[6] The use of other metallic bone substitutes, including silver, lead, vitallium, and tantalum, as bone substitutes was unsuccessful because of unanticipated disadvantages, technical difficulties, and side effects.[6,15,27,30,31] Titanium was first used by Simpson (1965) and has continued to be used for cranioplasty via the computer-assisted design of molded titanium implants.[6,26,32,33]

Other bones, such as the sternum, ilium, and scapula, were used previously, but they were difficult to harvest and resulted in a high risk of complications.[13,34] The first artificial bone graft was used after World War II, and the first artificial material used was acrylic.[35]

MATERIALS USED FOR CRANIOPLASTY

Cranioplasty materials are divided broadly into 2 main groups: 1) biological and 2) synthetic. Biological materials are further subdivided into autologous grafts, allografts, and xenografts. Allografts (bony materials and cartilage from cadavers) and xenografts (bony materials from animals) are out of favor for cranioplasty because of their very high rates of infection, resorption, and rejection.[22,36] Furthermore, the success

of autologous grafts and synthetic materials caused these other options to become obsolete. Bone flap replacement by using an autologous graft is usually the first and most common option for cranioplasty after decompressive procedures. It has a low rejection rate in hosts because of its increased biogenic compatibility, reduced chance of fracture, and its ability to be molded and integrated into the bones of pediatric patients as they grow.[37] It is best suited for small to medium skull defects smaller than 75 cm^2, because larger defects have a greater chance of failure.[38] Furthermore, it is cheap and has good cosmetic results, especially in frontal defects, because it fits the defect naturally. The most common complications of the use of autologous bone flaps are infection and resorption.

The materials used to replace bone defects have evolved throughout time. Initially, the choice of materials was based on the patient's social status.[39] Now, the choice depends on multiple factors, including patient age, size, location of the defect, surgeon preference, and the primary reason for performing craniectomy.[13,39-44]

Xenografts

Xenografts were introduced early in cranioplasty, and canines were the first sources of xenografts.[36,39] Animal bones from dogs, rabbits, apes, and other animals were also used, but xenografts were soon replaced by other materials.[36,39]

Allografts

Allografts of tissues such as cartilage and bone were also used.[36] Cartilage was discovered to have a lower infection rate; however, it was not strong enough to protect the neural tissue.[45] Cadaver bone allografts had comparable strength to that of bone autografts but resulted in a higher infection rate.[22]

Autografts

Autografts are widely used and considered the gold standard because of their reduced infection rate and cost and improved host immune response.[39,46] Tibial bone was the first autograft used, followed by the ribs, iliac crest, scapula, sternum, fascia, and fat.[13,45] The use of removed cranial bone became popular, especially after the advancement of bone preservation methods.[39,47] Bone is preserved either by cryopreservation or by preservation within subcutaneous abdominal pockets.[39] Both methods are equivalent after nontraumatic craniectomy.[48] However, the use of subcutaneous abdominal pockets is preferred after traumatic craniectomy because it results in a lower infection rate and is more cost effective.[48-50] Autografts carry the risk of necessitating reoperation and replacement by other materials because of the risk of bone resorption, especially in the pediatric age group, and bone breakdown.[37,39,51]

Synthetic Bone Grafts

Synthetic bone grafts began to be used because of the decreased risks of infection, resorption, and reoperation compared with those of bone autografts.[52,53] In addition, the use of synthetic bone grafts has reduced the operation time and led to better cosmetic results because of the advancement of computer-based customization and three-dimensional printing.[46]

Metals. Aluminum was the first metal used as a synthetic bone graft, but it was found to irritate the neural tissue, induce seizures, and dissolve over time.[27,39] Gold was not cost effective, silver was not strong enough, and tantalum was difficult to acquire; therefore, metals were not used for a long time.[39,54]

Methyl Methacrylate. Methyl methacrylate (MMA) was found to be strong, radiolucent, nonirritating, and nonconductive.[39,55] However, in addition to its limited expansion properties, it was also found to result in a high risk of infection, degradation, and fragmentation.[39,52,56,57] It shows better resistance and compression properties than hydroxyapatite.[58] The main disadvantages are the risk of the fracture of the implant in larger defects and a high failure rate in the long-term as a result of lack of integration into bone because of the inert nature of MMA. Blum et al.[56] reported a complication rate of 23% at 8 years follow-up. MMA has a high infection rate of 12.7% compared with that of other materials and is similar to autologous flaps.[52] Furthermore, MMA is not used in pediatrics because it does not accommodate skull growth. Acrylic in the form of MMA is the most widely used material in cranioplasty.[13,59,60] Reconstructive surgeries are commonly performed by plastic surgeons in craniofacial aesthetic surgery.[58] Polymethyl methacrylate use continued for adults craniofacial reconstructions with satisfying outcomes as reported by Marach et al.[58] in a long-term outcomes series (1998–2001).

Hydroxyapatite. Hydroxyapatite is a natural component of bone. It has macropores and osteogenic properties, allowing it to be integrated into bone in animal models.[6] It can be used in pediatrics because of its expansion properties and ability to be contoured to the skull shape.[39] Hydroxyapatite has been widely used because of its expansion properties, nonirritating chemical composition, and flexibility for contouring.[39] However, in addition to its low tensile strength, it has a high risk of infection and fragmentation and shows limited osteointegration.[39,50] Hydroxyapatite is a material present in human tissue and is therefore believed to enhance bone repair, produce fewer tissue reactions, and show good osteointegration.[13,59-61] However, it does not provide sufficient mechanical protection.[61] For this reason, patients with hydroxyapatite are advised to avoid risky activities until bone repair is complete.[61]

Titanium Mesh. Titanium mesh can be combined with other synthetic materials, such as MMA or hydroxyapatite, to enhance cosmetic results, or it can be used alone.[39] In addition to its superior cosmetic results compared with those of other materials used in cranioplasty, it has the lowest infection rate.[39,52] However, it was found to be heat conductive and is considered expensive.[33,43,62-64] Titanium is an inert material that has high biocompatibility; however, it can still conduct heat or cold and produce artifacts on imaging.[39,62]

Alumina Ceramics. Alumina ceramics are now widely used because of their strength, decreased infection rate, improved cosmetic results, and chemical stability; however, their high cost has reduced their use.[39,52,54]

Polyetheretherketone. Polyetheretherketone (PEEK) implants can be customized

according to the craniectomy defect with high accuracy.[39,65] They are light and nonconductive and do not interfere with imaging modalities.[39,65] However, they are subject to extrusion, show limited osteointegration, and are expensive.[39] Custom-made PEEK implants show the best cosmetic results. They are designed to fit cranial defects accurately using three-dimensional printers.[65] However, they are the most expensive implants among all types and lack osteogenic properties. This factor increases the risk of dislodgment and infection because of the lack of integration into the surrounding bone.[39] Furthermore, foreign body reaction was previously reported.[39] PEEK implants are a good choice for larger defects or defects in fronto-orbitotemporal areas, especially when the use of autologous bone flaps is a possible option.[40,66]

SURGICAL ASPECTS

Fixation Techniques

The procedure of bone flap fixation should be safe, inexpensive, time efficient, and aesthetically acceptable.[67] The optimal fixation technique produces no or minimal artifacts on neuroradiologic imaging and requires less use of foreign materials.[67]

Sutures. Sutures can be applied to fixate bone flaps with a reasonable protective capacity.[68] Sutures cannot mechanically provide a strong stabilizing attachment of the bone flap to the cranium because they are connected only by a low-grade force of friction.[69] In addition, using sutures may cause recurrent dislocation of the bone plates and subsequent bone flap depression or protrusion.[70] However, they are time efficient compared with wires.[70]

Wires. Stainless steel wires are comparatively stronger than sutures in terms of fixation.[70] They can be placed by drilling several holes in the bone flap and the adjacent bone edges of the skull.[71] The wire is subsequently passed through the skull then in the holes of the bone flap. The wires are twisted until they are perfectly taut.[71] The extra wire is then cut and buried into the hole of the skull edge to allow for fixation.[71] However, the use of wires can be limited by their associated local scalp pain in some cases.[72] With the advent of computed tomography and magnetic resonance imaging, wires have fallen out of favor and have been replaced by sutures, because they can cause artifacts on neuroimaging.[69,73]

Miniplates. Miniplates have been recently used and proved to be successful in neurosurgery because of their biocompatibility and osteointegrative properties.[70,74] They are available in sizes as thin as 0.3 mm.[74] Therefore, bone indentation to hide the surface thickness is not required, resulting in excellent cosmetic outcomes.[74] Compared with wires, miniplates have been shown to be superior, with 40% reduction of operative time.[74] However, they are expensive and can be rarely associated with transcranial migration of the miniplates.[69-71,75] In patients with thin scalps, miniplates can cause skin irritation and subsequent disfiguration of the skin contour.[69] This side effect is commonly caused by the sharp edges of the miniplates and the protrusion of their screw heads.[69]

Hinged Craniectomy

Cranioplasty can be considered as the subsequent staged-procedure after DC.[76,77] In situ craniectomy is a procedure that allows outward movement of the bone flap relative to the accommodation of the brain swelling.[77] In this technique, the bone flap is positioned so that the inferior edge is fixed to the cranial bone (i.e., hinged), whereas the superior edge is kept unattached.[77] Considering that the bone flap is kept in place, secondary reconstruction can be subsequently performed under a local anesthetic, avoiding the need to store the bone flap via cryopreservation or in the patient's own subcutaneous tissue.[77] Because the long-term outcome of the hinged craniectomy technique remains undetermined, further randomized controlled trials are required to validate its efficacy.[78]

Floating Cranioplasty

Cerebral decompression can be performed using in situ floating cranioplasty.[76] This procedure maintains the function of the bone flap and allows accommodation of cerebral swelling, reducing the need for a major secondary reconstruction via cranioplasty.[76] Resin implants can be molded intraoperatively and fixed loosely with sutures to allow for smooth movement of the bone flap according to the degree of brain swelling.[76] This procedure can be advantageous to the elderly population and patients who have experienced unfavorable outcomes, because it provides a protective barrier to the brain without the need for secondary cranioplasty.[76]

TIMING OF CRANIOPLASTY

The timing of the use of cranioplasty material after initial surgery has been poorly discussed in the literature except for the replacement of autologous bone flaps. Bone resorption or aseptic osteonecrosis is an important complication of autologous cranioplasty. Studies of this issue have been controversial in relation to the timing of cranioplasty because of study heterogeneity and the involvement of multiple confounders. Certain retrospective studies showed that late cranioplasties were associated with aseptic osteonecrosis of the flap,[79] whereas others showed that early cranioplasty increased the risk of osteonecrosis[80-82]; nevertheless, most of these studies failed to confirm such an association, and no difference between early and late cranioplasty was observed for the development of aseptic osteonecrosis, and firm conclusions on this association are lacking.[83,84]

The timing and selection of grafts can also be influenced by the cause of the initial injury. Patients who undergo surgery for traumatic brain injury may receive autologous flaps early for structural support and cosmesis, whereas patients with stroke may undergo intensive rehabilitation while waiting for custom-made PEEK implants in certain neurosurgical centers. With the exception of autologous bone flaps, timing is less important when selecting the appropriate material for cranioplasty, and other important factors should be considered, including patient age, cost, defect size, defect shape and complexity, skin viability, the need to repeat cranioplasties, material availability, and cosmesis.

STORAGE TECHNIQUES

Many storage methods have been used when performing cranioplasty.[13] These methods aim to preserve the bone flap and maintain its sterile condition/osteogenic capacity for later reconstruction in cranioplasty.[6] Traditionally, bone flaps are preserved by either cryopreservation (storage of the bone flap at extremely low temperatures) or storage of the bone flap in subcutaneous pockets in the abdomen.[50,85,86] The latter was first performed by Kreider in 1920.[87] The difference between both methods in terms of the risk of infection is almost identical, although cryopreservation is the most commonly used method in the literature.[81]

COMPLICATIONS

Bone Flap Resorption

Resorption of the bone flap (aseptic osteonecrosis) is a well-recognized complication after cranioplasty, especially in the pediatric population.[51] Its incidence ranges from 7.2% to 50%, with a higher incidence in the pediatric age group.[37,62,88] This technique requires reoperation and the use of synthetic grafts as replacements.[51,62] Factors proved to increase the risk of bone resorption are multiple fractures, bone fragmentation, larger defect size, younger age, and the presence of ventriculoperitoneal shunts.[37,38,51,81,89] Bone flap resorption may result in a large defect, resulting in an increased risk of damage to the brain or unacceptable cosmetic properties for the patient.[51] The timing of cranioplasty and the storage methods used are still controversial, with conflicting results regarding bone resorption. These factors should be considered when selecting autologous bone flaps for the first procedure; cranioplasty and synthetic materials should be used when late osteonecrosis is anticipated.[89] Bowers et al.[51] retrospectively evaluated 54 pediatric patients who underwent cranioplasty after DC. Approximately 50% of the patients developed bone flap resorption. These investigators identified several independent risk factors for bone flap resorption. The most significant risk factors included the presence of underlying contusion, comminuted skull fracture, or a permanent ventriculoperitoneal shunt, posttraumatic hydrocephalus, age $\leq$2.5 years, and bone flap infection.[51] The investigators recommended that children who present with one of these risk factors be observed closely for any signs of bone flap resorption. When bone flap resorption occurs, revision cranioplasty using a synthetic material may offer an excellent alternative option.[51]

Infection

The rate of surgical site infection after DC/cranioplasty ranged from 2.3% to 20%.[90-92] In a systematic review by Becking et al.[93] comparing autologous cranioplasties versus alloplastic cranioplasties, the overall risk of infection was found to be 5.6%. However, depending on the materials used in cranioplasty, the risk of infection varies; autologous cranioplasty was found to have the highest risk (6.9%), and hydroxyapatite cranioplasty (3.3%) had the lowest risk of infection.[93] In another study,[46] infection was found to be the most common complication, with a risk of 8.7%, and an additional risk of infection in patients subjected to bifrontal cranioplasty versus unilateral hemispheric or bihemispheric cranioplasty was observed. The predictors of surgical site infection after autologous cranioplasty were the size of the skull defect and blood glucose levels.[94]

Hydrocephalus

There are multiple causes that may contribute to hydrocephalus in patients undergoing cranioplasty after DC, including intraventricular hemorrhage, subarachnoid hemorrhage, or the DC itself. Post-DC hydrocephalus was evident in 2%–29% of patients.[95] Two systematic reviews showed an increased risk of hydrocephalus after early cranioplasty,[96,97] which might be attributed to precranioplasty hydrocephalus and the fact that late cranioplasty may provide more time for the spontaneous resolution of hydrocephalus.[96,97]

CSF DYNAMICS

It is well established that DC alters the circulation of CSF.[3] The dynamics of the local blood flow and cerebral metabolic demand can be significantly disturbed secondary to DC.[3,4,98] Performing cranioplasty after DC can reduce physiologic changes and subsequently improve the neurologic status of the patient. Such patients greatly benefit from cranioplasty to reverse/halt any clinical deterioration.[2,99,100] Alperin et al.[101] reported that CSF flow and pressure increased after cranioplasty. DC of a large cranial defect causes ipsilateral ventricular dilatation, which disrupts the CSF flow.[102] A disadvantage of DC is that the effects of atmospheric pressure on the boneless scalp can produce sunken skin flap syndrome, causing low cortical perfusion and, in turn, contributing to cerebral metabolism disorders that affect venous drainage.[103]

COGNITIVE FUNCTION

The effect of cranioplasty timing on cognitive function is still an area of debate. There are multiple confounding factors that come into play, including neuropsychological rehabilitation, the timing of the surgery, surgical technique, and cognitive assessment tools. Early cranioplasty was found to improve cognitive function by restoring CSF hydrodynamics, intracranial compliance, and cerebral blood flow when neurocognitive changes are at their peak.[4,104] However, Su et al.[105] found that improvement in cognitive function was observed in patients who had neuropsychological rehabilitation. A meta-analysis by De Cola et al.[106] concluded that the optimal timing to ensure the best cognitive outcome is between 3 and 6 months, if patients are undergoing neuropsychological rehabilitation. On the other hand, Huang et al.[107] and Corallo et al.[108-110] reported that the timing of cranioplasty is independent of neurologic outcomes.

OUR EXPERIENCE

In our institution, cranioplasty is performed from autologous bone using subcutaneous abdominal pockets or cryopreservation methods. These methods have been used for several years and we are satisfied with their outcome. Performing autologous cranioplasty using subcutaneous abdominal pockets is a cost-effective neurosurgical procedure that can provide low-resourced neurosurgeons worldwide with better evidence for a common procedure. In addition, we have been applying miniplates for bone flap fixation for several years in our institution, with excellent cosmesis. In our practice,

we have noticed that the timing of cranioplasty (early [<3 months] vs. late [>3 months]) after DC does not seem to affect the neurologic outcome as well as postoperative complications. We believe that timing is of less significance when performing cranioplasty, and other parameters should be taken into consideration (e.g., age, cost, defect size, materials availability, and storage/fixation techniques).

CONCLUSIONS

The materials used to replace bone defects in cranioplasty have evolved over time. The selection of the optimal material depends on multiple factors, including patient age, the size and location of the defect, surgeon preference, and the primary reason for undergoing craniectomy. Multiple storage methods have been described for cranioplasty to preserve bone flaps and maintain their sterile condition/osteogenic capacity for later reconstruction.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Ali Alkhaibary: Conceptualization, Writing - original draft, Writing - review & editing. **Ahoud Alharbi:** Writing - original draft, Writing - review & editing. **Nada Alnefaie:** Writing - original draft, Writing - review & editing. **Ahmed Aloraidi:** Supervision, Writing - review & editing. **Sami Khairy:** Conceptualization, Supervision, Writing - original draft, Writing - review & editing.

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