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Autograft and Implant Cranioplasty in Pediatric Patients

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Abstract---*The use of implants in pediatric cranioplasty is still debatable. Many surgeons prefer to use autologous bone grafts than implants due to previous concerns that implants have a higher risk of infection, allergic response, and are not biocompatible as an autologous bone graft. However, recent studies showed that several implant materials have a similar infection rate following cranioplasty or might be lower compared to autologous bone. Moreover, several studies also reported a high rate of bone flap resorption in autograft cranioplasty, particularly in patients below the age of 8 years, thus requiring revision surgery with an implant as a substitute in most cases. Implant materials also have advantages in several conditions that make them more suitable than autologous bone grafts. This literature review is expected to give information about the type of implant materials that can be used as an alternative to substitute autologous bone grafts in certain conditions*.
Keywords---*autograft, cranioplasty, implant, infection, revision.*

Introduction

Cranioplasty is a reconstructive procedure to close a defect in the calvarial bone. Cranioplasty can be performed directly at the end of surgery requiring craniotomy for example in cases of trauma, excision of tumor involving calvarial bone structure, infection, and congenital defect or after the period following craniectomy (Abu-Ghname et al., 2019). Based on the material, two types of cranioplasty are currently used, autograft (organic) and implant (synthetic organic and inorganic) cranioplasty. Autograft cranioplasty commonly uses previous bone flaps from the defect site or can be taken from other sites of the body such as from costae (most common), iliac crest, scapula, or

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tibial bone (Aydin et al., 2011; Goldstein et al., 2013). Meanwhile, titanium mesh, polymethylmethacrylate (PMMA), polyetheretherketone (PEEK), and polyethylene are materials that are widely used for implant cranioplasty (Fu et al., 2016; Badhey et al., 2017).

Autologous bone graft is more favored by many surgeons in cranioplasty than implants even if the source of bone is limited, especially in pediatric patients, and thus collecting the bone graft from the other side of the body might be harmful or inconvenient for the patients (Buchanan, 2019). This is due to the previous belief that implants have a higher rate of infection and might cause allergic or immune response following surgery compared to autograft cranioplasty, aside from the cost aspect (Feroze et al., 2015; Salam et al., 2018). However, several studies have shown that the rate of infection and revision following surgery were not significantly different between several types of implant materials compared to autologous bone graft (Fu et al., 2016; Bykowski et al., 2019; Matsuno et al., 2006). While many studies have reported the outcome of autograft compared to implant cranioplasty directly, there are still not many that reported and discussed it in pediatric patients. This paper review will discuss the comparison of autograft and implant cranioplasty particularly in the pediatric patient that has distinctive features from the adult (Wood et al., 2006).

Method

This literature reviews all articles or studies related to the topics about cranioplasty using autologous bone graft and implant materials, particularly in pediatric patients. Distinctive features of pediatric patients and types of material used for cranioplasty in pediatric patients were then discussed further.

Result and Discussion

Aim of cranioplasty

Cranioplasty is mainly performed to close the defect of calvarial bone. The small size of the calvarial defect might not cause any cosmetic problems. However, a large cranial defect or a defect located in the frontal area often causes aesthetic discomfort for the patient. Cranioplasty is also important to protect the brain under the defect from mechanical trauma (Salam et al., 2018; Bykowski et al., 2019). In large calvarial defects, the dynamics of cerebral blood flow and cerebrospinal fluid are often altered and might cause many neurological symptoms (Dujovny et al., 1997). Vertigo triggered by head's position changes, cephalgia, tinnitus, cognitive and memory impairments as well as focal neurological deficits is some symptoms that are often observed in patients with large cranial defect, thus known as a trephined syndrome (Honeybul et al., 2013). Therefore, cranioplasty is important not only for cosmetic reasons but also for therapeutic purposes.

Timing in cranioplasty

Time for cranioplasty is mainly dependent on the patient's condition and the indication of surgery. Cranioplasty can be performed right away at the end of the surgical procedure in cases of tumor excision, head trauma, intracranial hemorrhage evacuation, and closure defect in congenital abnormalities (Kuo et al., 2004). Cranioplasty should not be performed or postponed in certain conditions. In refractory intracranial hypertension, intracranial and extracranial problems of the patient should be treated first before doing the cranioplasty. In case of infection at the site of the defect, cranioplasty should be postponed until the infection problem is solved, thus preventing infection complications following surgery (Konofaos & Wallace, 2019). Cranioplasty could be considered unnecessary in conditions where the defect is small (size less than 2 cm) and particularly located at the temporal so that can be covered and protected by the muscle above it (Shah et al., 2014).

Cranioplasty following decompressive craniectomy could be performed after 6 weeks until 1 year after the previous surgery (Baumeister et al., 2008). However, it is recommended to do autograft cranioplasty using previously-stored bone flap in pediatric patients in less than 6 weeks after previous decompressive craniectomy procedure to prevent bone flap resorption afterward (Piedra et al., 2012). Further, cranioplasty should be performed after the age of 1 year to increase spontaneous ossification where alloplastic cranioplasty is the only available option (Grant et al., 2004).

Characteristics of pediatric as a consideration in cranioplasty

Cranioplasty in pediatrics generally has the same purpose as in the adult. This procedure is essential especially in pediatric patients with large calvarial defects to prevent brain growth alteration by restoring cerebrospinal fluid and blood flow dynamics as well as the atmospheric pressure of the intracranial components (Bykowski et al., 2019; Dujovny et al., 1997).

The strategy and technique of cranioplasty applied in adults cannot be fully implemented in pediatric patients. Dura mater and cranium are still growing mostly from birth until the age of 8 years. In addition, the diploic space of calvarial bone in pediatric patients below 4 years is not well developed yet, thus cranioplasty using split calvarial bone grafting is not feasible (Bykowski et al., 2019). The thin condition of the skin might be problematic for bone flap preservation under subgaleal. If the bone flap is too large it might cause tension of the skin above, thus causing skin necrosis and infection (Diniari & Aryani, 2022). Therefore, the strategy and technique for cranioplasty in pediatric patients should reconcile with the condition of each patient. The timing of the cranioplasty procedure after decompressive craniectomy also should be well considered. If the cranioplasty is performed too long after previous surgery the bone flap might not perfectly fit, and the contour might not ideal anymore to the defect due to the growth of the skull. Another important factor that should be considered is bone flap resorption or osteolysis as the main complication of autograft cranioplasty in pediatric patients, particularly in patients below 8 years, thus requiring revision procedure with implant material (Feroze et al., 2015; Grant et al., 2004; Martin et al., 2014). Therefore, the strategy or techniques of cranioplasty in pediatric patients should reconcile the condition of each patient.

Autograft cranioplasty in pediatric

Autologous bone graft is still favorable material in cranioplasty. The autologous bone graft used for cranioplasty is mainly from a previous bone flap removed in surgery requiring craniotomy or decompressive craniectomy. In some cases, autologous bone graft used in cranioplasty can be obtained from calvarial bone adjacent to the defect or other parts of the body such as costae, tibia, scapula, and iliac crest (Aydin et al., 2011; Bykowski et al., 2019). Aside from the cost aspect, the advantages of using autologous bone graft in cranioplasty include high biocompatibility, osteoconductive and merging well with surrounding bone structures, and relatively not causing or triggering inflammation or immune response compared to implant materials (Bykowski et al., 2019).

Bone flap from previous craniectomy procedures is commonly stored under the skin adjacent to the operation site (subgaleal) or at the abdominal site in adult patients. This method is practical because the patient can undergo surgery in other facilities if the patient moves out to other places. However, this method might not be feasible in pediatrics especially those who have thin skin or with large bone flap. Another method to preserve bone flap is cryopreservation in an ultra-low temperature freezer (Rocque et al., 2013; Yadla et al., 2011). Unlike subgaleal or abdominal preservation methods, cryopreservation does not cause any discomfort for the patient. However, this method is potentially having a higher risk of infection that might be due to an unsterile process in packaging the bone flap or malfunction of the freezer (Inamasu et al., 2010).

A major complication of autograft cranioplasty in pediatrics is bone flap resorption. A study conducted by Martin et al. reported that 16 out of 18 pediatric patients experienced bone flap resorption at 6-12 months following cranioplasty and 8 of them are requiring revision surgery to substitute bone flap with implant materials (Martin et al., 2014). Interestingly, more than 80% of pediatric patients who experienced bone flap resorption were aged below 8 years. This even might be related to the growth phase of children where the metabolism of the skull is relatively high due to heat expansion. The rate of bone flap resorption is highest at the early phase of growth, from birth to the age of 2 years where intracranial volume is expanding almost 83% from adult size. This resorption rate will significantly decline in age ranging from 8 to 14 years. Meanwhile, in children aged 15 to 18 years where their skull is completely developed, bone resorption is rarely observed (Martin et al., 2014; Rocque et al., 2013; Bowers et al., 2013).

Implant cranioplasty in pediatric

Implant cranioplasty can be an alternative when cranioplasty using autologous bone graft is not feasible. In case of infection, tumor, and trauma when the bone structure should be removed or cannot be put back, implant materials might be the only option for cranioplasty (Manor et al., 2009). This is also applied when the autologous bone flap from the previous cranioplasty is resorbed (Grant et al., 2004; Martin et al., 2014). Implant materials can also be considered as an alternative for cranioplasty in pediatric patients with large cranial defect (size more than 75 cm^2), aged below 8 years, and limited bone graft resources to close the defect (Grant et al., 2004; Martin et al., 2014). Implant materials also have some advantages over autologous bone grafts including no risk of resorption, durability,

and adjustable to defect size as well as cranial contour for each patient (Abu-Ghname et al., 2019; Salam et al., 2018).

The advanced technologies have introduced many implant materials that are relatively saved and can be used for cranioplasty. Although the ideal material for cranioplasty in pediatric is still debatable, several materials are commonly used in pediatric cranioplasty, including polymethylmethacrylate (PMMA), hydroxyapatite, titanium mesh, polyetheretherketone (PEEK), and polyethylene (Bykowski et al., 2019; Singh et al., 2021).

Polymethylmethacrylate (PMMA)

PMMA is a polymerized ester derived from acrylic acid. It was found in 1939 and broadly tested as cranioplasty material in the 1940s. PMMA has a durability that is equal to bone structure and has better resistance to stress or compression than hydroxyapatite (Marchac & Greensmith, 2008). PMMA also has more distinctive features including unlimited resources, practical, can be adjusted in size and contour shape, inexpensive, heat resistant, tend to radiolucent in X-ray, and is more inert than metal. Therefore, the use of metal has been abandoned and replaced by PMMA (Aydin et al., 2011). PMMA needs to be mixed with a monomer before being used, thus surgeons need to be careful with the exothermic reaction that can potentially cause burn injuries (Lee et al., 2012). Nowadays, 3-D modeling technology in cranioplasty allows to design and print of PMMA before surgery based on the defect of the patient. Therefore, the customized PMMA with 3-D modeling could minimalize the potential risk of injury and shorten the time needed for surgery (Feroze et al., 2015; Morales-Gómez et al., 2018).

Hydroxyapatite

Hydroxyapatite is a calcium phosphate mineral, a bioactive material that can be found in bone structures (Aydin et al., 2011). Hydroxyapatite is known to have a minimal risk of triggering an immune response and has good compatibility with surrounding bone structures. It can also be easily formed to deliver fine aesthetic outcomes. However, hydroxyapatite is fragile and has a low resistance to pressure. Therefore, hydroxyapatite can be combined with another material like titanium mesh to overcome its vulnerability (Teixeira et al., 2010; Martini et al., 2012). The structural integrity of hydroxyapatite also can be affected by cerebrospinal fluid and blood, thus decreasing its osteoconductive property with surrounding bone structures (Grant et al., 2004).

Titanium mesh

Titanium is a non-corrosive material and does not induce an inflammatory response, thus having a low risk of infection following surgery and a good cosmetic outcome (Langford et al., 2020). Titanium is a material with high flexibility and resistance to pressure. Titanium mesh is also reported to have the lowest risk of infection compared to the other implant materials and autologous bone graft in cranioplasty (Fu et al., 2016; Matsuno et al., 2006). The advanced technology in 3D modeling can also be applied for titanium mesh to design and customize its shape, thus it will give a good cosmetic outcome even in the large cranial defect (Shah et al., 2014).

Polyetheretherketone (PEEK)

PEEK is a semi-crystalline polymer with a radiolucent feature and is chemically inert (Lethaus et al., 2012). PEEK has hardiness, thickness, and elasticity that equal calvarial bone. PEEK can also be placed precisely at the site of the calvarial defect without using any mini plates (Jonkergouw et al., 2016). PEEK will not show any artifact in computed tomography (CT-scan) or magnetic resonance imaging (MRI). This synthetic material is relatively light, not too compact, and not sensitive to temperature changes so that more comfortable for the patient (Lethaus et al., 2012). Unfortunately, PEEK is relatively expensive so many surgeons prefer to use any materials that are more affordable (Jonkergouw et al., 2016).

Polyethylene

Polyethylene is a component commonly used for isolator wire in a plane. Polyethylene has characteristics of easily molded with heat, porous surface, and biocompatible. The porous surface of polyethylene allows early vascularization to occur followed by soft tissue formation and collagen deposition, thus making this material relatively safe from infection (Aydin et al., 2011). Polyethylene with high density is now being developed to allow

better soft-tissue growth. Polyethylene is reported to have a low risk of complication following cranioplasty (Fu et al., 2016; Bykowski et al., 2019).

Autograft Vs implant cranioplasty in pediatric

Many studies have been conducted in studying the outcomes of implant materials for cranioplasty compared to autograft cranioplasty. However, there are only a few studies that directly compare the outcomes between autograft and implant cranioplasty in pediatric patients (table 1). Rate of infection and revision following cranioplasty surgery are the key parameters that can be observed for the outcomes and for consideration whether the materials are safe or not.

Table 1
Studies that directly compare the outcomes of autograft and implant cranioplasty in pediatric patients

Author (year)	Age (month)		Cranioplasty (%)			Infection (%)		Need for revision (%)		Description
	Mean	min-max	Autograft	Implant	Total	Autograft	Implant	Autograft	Implant	
Josan et al. (2005)	97.2	1.4 – 180	28 (87.5)	4 (12.5)	32	3 (10.7)	0	5 (17.9)	0	**Autograft:** - Full-thickness bone flap = 20 - Split calvarial = 8 **Implant:** PMMA = 3, Titanium plate = 1
Martin et al. (2014)	115.85	1 – 204	20 (60,6)	13 (39,4)	33	2 (10)	1 (7,7)	8 (40)	3 (23,1)	**Autograft:** Bone flap = 20 **Implant:** PMMA = 13
Gilardino et al. (2015)	127.2	48 – 192	15 (75)	5 (25)	20	0	0	2 (13,3)	0	**Autograft:** Split bone grafts = 15 **Implant:** PEEK = 5
Fu et al. (2016)	88.8	12 – 228	11 (26.83)	30 (73.17)	41	0	0	1 (9)	0	**Autograft:** - Split calvarial = 7 - Bone particulates = 4 **Implant:** - Polyethylene = 9 - PMMA = 15 - PEEK = 2 - Alloplastic unspecified = 1 - Titanium = 3

PMMA Polymethylmethacrylate; **PEEK** Polyetheretherketone; total cases of cranioplasty using autologous bone graft only and implant material only as well as total cases of infection and revision during the follow-up period.

The infection rate of implant materials from all studies was quite low, with only 1 case of infection that was reported (PMMA) from 52 cases whereas autograft had 5 out of 74 cases. For revision rate, the total of revision in implant cranioplasty was 3 cases (PMMA) whereas autograft had 16 cases (Weeden & Paprosky, 2002). Revision surgery in all studies was caused by osteolysis, infection, the disintegration of the graft, and fractured material for fixation (Fu et al., 2016; Martin et al., 2014; Josan et al., 2005; Gilardino et al., 2015). The high rate of revision in autograft cranioplasty was mostly due to osteolysis or bone flap resorption. In a study conducted by Martin et al., a patient that experienced bone flap resorption was mostly below the age of 8 years (Martin et al., 2014). This might be related to the high metabolism of the skull where the skull is still expanding (Rocque et al., 2013; Bowers et al., 2013). In implant cranioplasty, the cases of revision were due to infection so the previous implant need to be removed and replaced after the infection had been treated (Dhami et al., 2020).

Conclusion

Pediatrics have characteristics that make it different from an adult. Many considerations should be taken to decide the ideal material that will be used for cranioplasty depending on the patient's conditions. Implant materials like PMMA, titanium mesh, PEEK, and polyethylene could be used as an alternative or substitute in pediatric patients if an autologous bone graft is not feasible. A proper follow-up should be taken to evaluate patients' conditions and possible complications.

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