FACTORS AFFECTING GRAFT INFECTION AFTER CRANIOPLASTY IN DEPARTMENT OF NEUROSURGERY HOSPITAL KUALA LUMPUR

By

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LIST OF ABBREVIATIONS

≤ - equals to or less than	**H_2O- water**
≥ - equals to or more than	**ICP- intracranial pressure**
3D – three dimension	**IV- intravenous**
COTDS – computerised operating theatre documentation system	**NaCl- sodium chloride**
CSF- Cerebrospinal fluid	**MRI- magnetic resonance imaging**
CT Scan- computed tomograghy scan	**PEEK- polyether ether ketone**
GCS- Glasgow coma score	**PMMA- ploymethyl methacrylate**
HIV- Human Immunodeficiency virus	**STO- suture to open**
HKL – Hospital Kuala Lumpur	**WHO- world health organisation**

Abstract

Background:

Cranioplasty, one of the oldest surgical procedure used for cranial defect repair. It has undergone many evolution over time to find ideal technique and material to improve patient's prognosis. The most common complication post cranioplasty is graft infection. It may poses substantial burden of disease for both patients and healthcare services in terms of morbidity, mortality and economic cost. Therefore this study is to determine factors affecting graft infection after cranioplasty procedure.

Objectives:

This study was done to determine incidence of graft infection after cranioplasty procedures in Hospital Kuala Lumpur in 2012 and factors affecting graft infection rate.

Methodology:

Observational cross-sectional case study on the patients who have undergone cranioplasty procedure at Hospital Kuala Lumpur (HKL) over period of 1 year (2012). Identified 172 patients included in the study. A total of 105 (61.8%) cases were autologous bone and 67 (38.2%) were acrylic cranioplasty. Patients' case notes were reviewed and relevant demographic, clinical, surgical treatment documented. Graft infection is defined according to the Center for Disease Control and Prevention definitions. Statistic analysis if Fisher exact and Pearson chi-square test were used to determine factors associated with outcome.

Result:

A total of 5 infected graft have been identified among 172 cases included in the study, resulting in an overall infection rate of 2.9%, within this infection rate involving acrylic is 3 (4.5%) and 2(1.9%) in autologous bone. There was high proportion of male patients undergoing cranioplasty, 118 (or 68.6%) where female were 54 (or 31.4%). Primary pathology in majority of patients was due to trauma seen in 126 (or 73.2%) where non trauma contribute to 46 cases (or 26.8%). Patients undergone a single cranial procedure prior to cranioplasty were 123 (or 71.5%) and whereas the balance 43 (or 28.5%) patients underwent multiple cranial procedures. Majority of the patients underwent cranioplasty 90 days after decompressive craniectomy were performed, 114 (or 66.3%) and 58 (or 33.7%) had cranioplasty before 90 days. Patients that undergone cranioplasty mostly have GCS more than 8, 137 (or 79.7%) and GCS less than 8 were 35 (or 20.3%). The prevalence (proportion) of infection rate between group bone and acrylic are not significantly different ($P = 0.379$). Therefore, there is no significant association between these group and infection rate. The prevalence of infection rate between gender showed no significant different as well where $P = 0.327$ ($P<0.05$). Thus, we have no significant evidence to conclude that the association between gender and infection rate exist. While testing for association between infection rate and other variables under interest individually, which is mechanism of injury, number of procedure, timing, and GCS; the proportion of infection rate between those variables are not significantly different where the P value are 0.326; $P = 0.140$; $P = 0.664$; and $P = 0.585$ respectively. All this P-value are more than 0.05, thus the association between these variables and infection rate are not significant.

Conclusion:

Cranioplasty is a surgical procedure for anatomical reconstruction, brain protection and cosmetics. Infection rate overall for cranioplasty is relatively low, 2.9%. When comparing infection rate of graft material, gender, primary pathology, number of procedures, time interval, and GCS pre cranioplasty, no significant difference noted.

Abstrak

Latar belakang.

Kranioplasti adalah satu prosedur pembedahan yang tertua untuk pemulihbaikan kecacatan tengkorak. Ia telah mengalami beberapa evolusi bagi mencapai teknik dan material yang ideal untuk memperbaiki prognosis pesakit. Komplikasi yang paling kerap berlaku adalah jankitan kuman terhadap graf. Ia boleh menyebabkan bebanan penyakit kepada pesakit dan perkhidmatan kesihatan dari segi mobiditi, kematian dan kos rawatan. Oleh itu ,pengetahuan mengenai factor yang mempengaruhi jangkitan kuman kepada graf membolehkan kita mengamalkan langkah – langkah berjaga –jaga untuk mengurangkan kadar jangkitan.

Objektif.

Tesis ini bertujuan untuk mengenalpasti kadar jangkitan kuman kepada graf kranioplasti dan faktor – faktor yang mempengaruhi kadar tersebut.

Metodologi.

Tesis ini mengetengahkan satu kajian pemerhatian ‘cross-section’ yang telah dijalankan keatas pesakit dewasa di HKL pada tahun 2012.Sejumlah 172 pesakit telah memenuhi syarat- syarat kajian,di mana 105 (61.8 %) telah melakukan tulang autologous dan 67 (38.2 %) menggunakan acrylic sebagai bahan kraniplasti. Data pesakit dikumpul ,jangkitan kuman kepada graf didefinasikan mengikut definasi yang dikeluarkan oleh Center for Disease Control and Prevention. Analisis statistik yang dijadualkan adalah fisher exact dan pearson chi-square untuk menentukan factor yang berkait rapat dengan jangkitan kuman.

Keputusan.

Daripada analisis didapati sejumlah 5 jangkitan kuman pada graf di kenalpastii berlaku daripada 172 kes, iaitu 2.9% daripada kadar tersebut, 3 adalah daripada acrylic (4.5%) dan 2 (1.9%) adalah daripada tulang autologous.Majoriti pesakit adalah lelaki iaitu 118(68.6%) manakala pesakit perempuan adalah hanya 52(31.4%). Majoriti patologi adalah trauma yang merangkumi 126(73.2%)manakala bukan trauma merangkumi 46(26.8%). Jumlah pesakit yang menjalani pembedahan hanya satu prosedur pembedahan sebelum kranioplasti adalah 123

(71.5%)manakala selebihnya adalah 43(28.5%) menjalani prosedur kranial lebih daripada sekali. Pesakit yang menjalani kranioplasti selepas 90 hari 'decompressive craniectomy' dilakukan adalah seramai 114(66.3%) dan sebelum 90 hari seramai 58(33.7 %). Kebanyakkan pesakit yang menjalani kranioplasti 137(79.7%) adalah yang skor GCS lebih daripada 8/15, manakala pesakit yang GCS kurang daripada 8/15 adalah 35(20.3%). Tetapi ,analisa statistic menunjukkan tiada hubungkait diantara jenis graf yang digunakan ,jantina ,patologi ,bilangan prosedur,jangka masa dan GCS dengan kadar jangkitan kuman pada graf selepas kranioplasti. Kesemua p-value adalah lebih daripada 0.05. Oleh itu ia tidak signifikan.

Kesimpulan.

Kranioplasti adalah satu prosedur pembedahan untuk pemulihan anatomi, pemulihan otak dan kosmetik. Kadar keseluruhan jangkitan untuk kranioplasti secara relatifnya adalah rendah iaitu 2.9%.apabila di bandingkan kadar jangkitan mengikut bahan graf,jantina,patologi,bilangan prosedur ,jangka masa dan GCS sebelum kranioplasti adalah tidak signifikan.

INTRODUCTION

Cranioplasty is defined as a surgical repair of acquired or congenital cranial defects. It is performed mainly for anatomical reconstruction, brain protection and cosmetics. Commonly, cranioplasty is performed following craniectomy or decompressive craniectomy for traumatic brain injury. Performing a cranioplasty and in essence is an art, aimed at reconstructing skull defects, and poses certain challenges to neurosurgeons. The procedure requires good anatomical knowledge and meticulous surgical techniques, and when performed well, results in good outcome in terms of cosmetics and anatomical protection. On the other hand, when performed incorrectly, it may lead to potential serious complications such as extradural or subdural collection, graft infection, graft failure, post operative hematoma, edema and seizures.

Cranioplasty like any surgical procedure is associated with complications. The common complications include, surgical site infecction, graft infection, graft failure, and poor cosmesis. Among this graft infection appears to be the most common complication documented in various centers throughout the years. Over the years, the procedure has evolve both in terms of procedural techniques and materials to improve outcome Despite improvement in surgical techniques and materials, rate of graft infection still remains significant. Many factors have been attributed to graft infection including graft type, duration of surgery, patient's premorbid condition, underlying disease as well operating room sterility and environment.

Surgical site infection, defined as infection resulting in surgical implantation of a bone flap, is a feared complication occurring in cranioplasty. This study aims to identify rate of infection in cranioplasty utilizing autologous cryopreserved bone graft and methyacrylate graft as well as factors associated with graft infection among cranioplasty patients.

CHAPTER ONE: BACKGROUND OF STUDY

The practice of cranioplasty dates back to the prehistoric Inca Culture in 3,000 BC in Peru. Cranioplasty was first documented by Fallopius (Robert M Redfern 2007) who described repair using gold plates. The use of the first bone graft was documented by van Meekeren(Kurz LT 1989). The first documented autologous bone graft cranioplasty was performed by Walthers in 1821(Carson, Goodrich et al. 2014). During the late 19th century, the histologic sequence of what in now termed as osteoinduction and osteoconduction was first discovered, and this led to various experimentation in use of bone graft substitues for cranioplasty. Survival of implanted bone graft depends on reaction of surrounding tissue and functional contact between bones.

Cranioplasty is commonly done for skull defects following craniectomies for traumatic brain injury and cerebrovascular ischemic events. Other reasons where cranioplasty may be required include cases of infiltrating tumours, post operative edema for non traumatic cases and congenital cases of craniosynostosis. Cranioplasty serves various functions, including anatomical reconstruction, restoration of brain hemodynamic condition, protective barrier for brain, cosmetic appearance and patient self esteem. Recent studies have shown that cranioplasty also results in functional recovery of neuronal tissue, and thus serves a significant functional purpose as well. (Walcott et al 2013)

Contraindications for cranioplasty include the presence of hydrocephalus, infection, and brain swelling. In children below 4 years old, if there is an intact dura mater, cranium can achieve self closure

Timing of cranioplasty differs between institutions. In most cases, cranioplasty is performed in a delayed fashion, between 3 months to 9 months after the initial surgery.(Satya Bhusan Senapati, et al. 2012) The timing of surgery depends on various factors. In the early post operative period, on going inflammatory and healing process results in exudates within the surgical site, friable granulation tissue and capillaries resulting in reduce strength within the surgical margins. Cranioplasty done within this period may result in development of complications such as infection, hematoma and wound dehiscence. Furthermore, hemodynamic changes within cerebral vasculature and parenchyma has yet to compensate for the absence of skull in the early stages following decompressive craniectomies, and this may lead to development of hydrocephalus, cerebral edema and hemorrhagic contusions following cranioplasty. Furthermore, surgical dissection in cases done earlier than 6 months has been noted to be challenging due to inadequate resolution of ongoing inflammatory process which results in poor demarcation of clear anatomical planes. This results complications of parenchymal injury and increased blood loss after surgery. Thus most centres perform cranioplasty after a time period of 3 months.

Timing of surgery is also influenced by flap storage in cases of autologous cranioplasty. Storage in subcutaneous abdominal fat results in increase incidence of bone resorption after periods exceeding 6 months, thus necessitating cranioplasty within this period. Storage in cryopreservation results in constricted in terms of space and cost, tilting the balance toward early cranioplasty. Recent findings has shown functional recovery of neuronal tissue following cranioplasty, thus favouring early cranioplasty. The need for cosmetic repair and anatomical protection in patients whom have achieved neurological recovery following craniectomies plays an influencing factor in timing of surgery. A large series published by Rish et al in 2009(Rish MN 2009) noted a higher rate of complications in cranioplasty done within 1 to 6 months, while cranioplasty done after 12 to 18 months had a lower complication rate. Waiting to perform cranioplasty is important to prevent the development of devitalized autograft or allograft infections. Recent literature in support of early cranioplasty report a reduce incidence of bone resorption, sinking flap syndrome, hydrocephalus and graft infection rate (Odom GL 1952). Essentially, the timing of cranioplasty should depend on patient's neurological status and recovery as a primary indicator.

Autologous bone is still considered as graft of choice in cranioplasty. Bone flap removed during initial craniectomies are re-implanted in cranioplasty. Autologous bone has the advantage of an ideal geometric fit to the defect, lack of immune reaction and reduce risk of infection transmission. It is also readily available and has the potential to grow. These bone graft are either stored subcutaneously in the abdominal fat area or crypreserved during the interval between craniectomy and cranioplasty. In the past, the practice of autoclaving bone or boiling bone prior to implantation was used, but this is currently not practiced as the practice results in destruction of essential bone proteins and minerals, essential for osteoconduction. (Mankin HJ 1996)Other sites of autologous graft include the inner table of the cranium, by use of spilt calvarial grafting, first described in 1839 (Robert M Redfern 2007). This technique results in a pleasing cosmetic appearance, following the contours of the skull. Split-thickness skull cranioplasty are biocompatible, which are easy harvested and with less infection and reaction risks. For this reason, it is considered a good option for cases with high risk of infection. In pediatric patients whom skull growth is continuing, split-thickness skull grafts showed integration and cooperated with the remolding skull, in contrast to fixed nonbiologic materials which resulted in restricted growth of the skull and deformities in adult ages. However, when a large defect is present, split calvarial graft may not be adequate, and are less stable in strength.

Cadaveric grafts were used during the World War I due to their elastic nature and high resistance to infections.(Robert M Redfern 2007) But with time, their use decreased because it did not show calcification as expected and did not provide enough mechanical protection, high infection rates and risk of transmission of infections.

Apart from cranial grafts, other common sites for grafting include the ribs, which is still common on practice in this era. Historically, grafts from tibia, sternum, scapula and fat have been experimented and used for cranioplasty. The use of ribs as substitues was popularized at the beginning of the 20th century(Am. Shah and 2014). However, many surgeons do not prefer using ribs, because of the intra- and postoperative complications of the technique, such as deformities of thorax and respiratory problems.

Autologous bone can be preserved either by cryopreservation or by implantation in subcutaneous abdominal fat. Both methods are currently in use, and have been reported as equally efficacious methods for bone storage. Dry freeze in -70°C is an accepted way to keep bone flaps sterile and ready to use. This technique keeps the matrix architecture of bone intact and ready to use. But this technique does not prevent the bone from "dying." Saving the craniotomy flap in the fatty tissue of the abdomen was first described by Kreider in 1920. (Constantino PD 1994) This method is no more as popular as it was first described, because the need for a second surgery arises, the scar tissue in abdomen occurs, and osteogenic capacity of the bone is never as it is expected. Some authors are not in favour of cryopreservation, citing various reasons include cost, loss of osteoconduction properties and a higher infection rate and recommend storage of bone in subcutaneous fat region(Seckin Aydin 2011). Similarly, various authors are in favour of cryopreservation, citing incidence of bone resorption and implant site complications among other factors.(Matsuno A 2006, Sang-Hyuk Im 2012, Satya Bhusan Senapati, et al. 2012)

Autologous bone transplant are however not without complications, among those reported were bone flap resorption, graft infection and implant failure. Matsuno et al (Matsuno A 2006) reported a higher incidence of bone graft infection in autologus bone grafts compared to synthetic materials used in cranioplasty.

Synthetic materials are considered as an alternative to autologous bone grafts, largely to overcome or prevent complications assoaciated with autologous bone grafts such as infections, bone resorption, donor site complications and reduced strength as well as malleability for cosmetic appearance. Synthetic materials were first experimented with during the onset of World War I and II, to treat patients with skull deformities resulting from penetrating injuries.(Carson, Goodrich et al. 2014) The ideal material should be radiolucent, resistant to infection, non thermoconductive, malleable to fit, resistant to degradation and inexpensive. Over time various materials have been used, researched and experimented with. Among them are use of metals dating back to onset of World War 1. Metals were preferred largely because it was strong, malleable and can be sterilized. Aluminium were initially used, but were found to be poor substitute as it was prone to infection, induced seizures, irritates surrounding tissue and undergoes disintegration (Carson, Goodrich et al. 2014). Gold and silver was also experimented with during world war 1 and 2, but various reasons such as its high cost, reaction to surrounding tissue and poor malleability made them unpopular over time. Tantalum was then experimented with during the second world war, and proved to be effective as it was resistant to tissue infection, corrosion and infection, but was expensive and conducted heat resulting in heat induced headaches among patients(Elephterios, et al. 2010).Titanium, a metallic alloy, has high strength and malleability, non corrosive, low risk of infection and good cosmetic results. It is also relatively cheaper, bioacceptable, and radiolucent after mixing with other metals.Various authors have reported similar experiences with titanium for cranioplasty, and currently titanium is the preferred metal for cranioplasty.(Mathias PG 1997, Elephterios, et al. 2010, Carson, Goodrich et al. 2014)

Apart from metal alloys, alloplastic materials were also experimented with for use as substitutes in cranioplasty. Methyl-methacrylate was initialy used during World War 2, initially as acrylic resins in dental prosthesis. Acrylate was fist discovered in 1939, and extensive research and experimentation over the years that followed resulted in acrylate being used commonly in cranioplasty. Acrylic has some advantages above metal substances; it is easy to shape, lighter in weight, radiates less heat, and radiolucent. Methyl mathacrylate is a polymerized esther of acrylic, with strength comparable to bone. Acylic is preferable to metal because it is strong, inert, heat resistant, radiolucent, malleable, and adheres to tissue without causing a reaction. Acrylate had traditionally been moulded by hand since the 1970's. (Enrique Caro‑Osorio and 2013, Carson, Goodrich et al. 2014)With current developments, acrylate can be moulded using 3D tehnology to offer a perfect fit and better cosmetic results. (Mathias PG 1997) Despite these advantages, acrylate has a higher risk of extrusion, fragmentation and infection. Fragmentation leads to loss of strength and potential development of complications. Matsuno et al demonstrated an infection trate of 12.7% in his series (Cheng TA 2000, Matsuno A 2006).

Apart from acrylate, hydroxyapatite is another alloplastic material commonly used in cranioplasty. Hydroxyapatite is naturally occurring calcium phospahate compound found in bone, and manufactured synthetically as ceramic.(Am. Shah and 2014) The advantages of hydroxyapatite are minimal tissue reaction, increased bone repair, easy malleability and good osteointegration. In contrast to acylate which does not expand with a growing skull, hydroxyapatite does and can be used in paediatric population. However, it is weak compound, that fractures easily, and has high infection rates.(Sanan A 1997). It also does not demonstrate osteointergrative changes when implanted. Recently, porous structure gave this material more osteointegrative state and its use with titanium mesh to increase its durability.It is suggested that patients with hydroxyapatite cranioplasty should stay away from trauma until total bone repair.

Polyetheretherketone (PEEK) is a semicrystalline polymer that is radiolucent and inert. These implants have strength, thickness and can be moulded into the defect directly without further anchoring implants. PEEK implants are advantageous, as they are translucent and do not create artefacts on CT or MRI, it is light weight and non conductive. PEEK implants are commonly used nowadays in cranioplasty as they can be design or moulded using computer generated 3D technology to form a perfect fit for the defect. The disadvantage of PEEK implants are that they are expensive and lack osteointegration, and has a higher risk of extrusion because it does not incorporate with surrounding existing bone.

Current research trends has shifted towards development of molecular biology by using bone growth factors to improve the ability of patient to regenerate bone.(Mathias PG 1997) With evolving biomedical technology, new materials are available to be used by the surgeons. Although many different material and techniques had been described, there is still no consensus about the best material, and ongoing researches on both biologic and nonbiologic substitutions continue to develop the ideal reconstruction materials.

Various complications following cranioplasty have been reported in literature, and broadly these can be categorized as surgical related or material related. The commonest complications reported following cranioplasty include graft infection, bone resorption, intracranial hematomas, brain edema, hydrocephalus, post operative seizures, worsening of neurological status post operative, sinking flap and donor site morbidities.(Am. Shah and 2014) Various factors have been attributed to development of complications. Among them are types of graft used, methods of preservation of bone grafts, surgical timing and techniques, underlying etiology ,multiple craniotomy procedures as well as patients overall condition in terms of neurological recover, nutritional status and hygiene. The risk and factors associated with complications have been extensively analyzed by various institutions and authors, however, a general consensus regarding this topic has yet to be reached.

CHAPTER TWO: LITERATURE REVIEW

The first reported successful cranioplasty was performed in 1668 by the Dutch physician Job Janzoon van Meekren (Constantino PD 1994). In modern Neurosurgery there has been an increasing interest in decompressive craniectomies following head trauma and acute ischemic stroke (JT 1996, Carson, Goodrich et al. 2014). Decompressive craniectomies following head trauma have been shown to reduce the intracranial pressure (ICP) in patients with refractory intracranial hypertension, and may also affect the outcome(Prolo DJ 1979, Fernyhough JC 1992). Surviving patients undergoing decompressive craniectomies are obligated to undergo a second procedure with surgical repair of the cranial defect (cranioplasty). Two of the most commonly used materials are autologous bone grafts or polymethylmethacrylate (PMMA). At our institution both these materials have been used for cranioplasty. In our experience cranioplasty is a procedure associated with a high rate of complications. This has also been recognized by others, and immediate postoperative complications have been reported to be as high as 34%(Robert M Redfern 2007). Complications may include infection, postoperative haematomas and bone resorption. The timing of surgery in relation to the previous decompressive craniectomy and preferred material to be used for a cranioplasty is still debated (GR 1996, Je Il Ryu 2005, Yadl a S 2011). Our aim is to evaluate both short term and long term complications in patients underwent cranioplasty following a decompressive craniectomy. We also aimed to compare the rate of complications in patients operated using autologous bone versus PMMA and investigate possible predictors of complications.

There are four characteristics that an ideal bone graft material should exhibit which include: (i) osteointegration, the ability to chemically bond to the surface of bone without an intervening layer of fibrous tissue;(JT 1996) (ii) osteoconduction, the ability to support the growth of bone over its surface;(JT 1996) (iii) osteoinduction, the ability to induce differentiation of pluripotential stem cells from surrounding tissue to an osteoblastic phenotype;(Kopylov P 1999)and (iv) osteogenesis, the formation of new bone by osteoblastic cells present within the graft material.(Lotz JC 1997)

Only autologous bone graft satisfies all of these requirements. Allograft is osteointegrative and osteoconductive and may exhibit osteoinductive potential, but it is not osteogenic because it contains no live cellular component. Synthetic bone graft substitutes currently possess only osteointegrative and osteoconductive properties.

Autograft, Autologous cancellous bone graft is the most effective bone graft material possessing all four characteristics. Few mature osteoblasts survive the transplantation but adequate numbers of precursor cells do.(JT 1996) It is from these precursor cells that the osteogenic potential is derived. Limitations include the increased operative time, limited availability and significant morbidity related to blood loss, wound complications, local sensory loss and, most importantly, chronic pain.(Constantino PD 1994) Donor site pain persisting for more than 3 months has been reported in up to 15% of patients having an iliac graft harvested. The amount of pain seems to be proportional to the extent of dissection required to obtain the graft.(GR 1996)

Allograft, as an alternative offers the same characteristics as autograft with the exclusion of osteogenic cells. It does possess osteoinductive properties but these may not be recognized