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Surgical Outcome of Ex-vivo Preserved Autologous Cranioplasty - A Novel Approach

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Autologous cranioplasty is an increasingly common procedure performed in neurosurgical centers following a decompressive craniectomy. Available evidence on the safety of autologous bone flap preservation and cranioplasty is limited due to a large diversity in study conducted, nature of pathology and reported outcomes.

In this Institutional Review Board-approved retrospective observational study, patients who underwent neurosurgical intervention as "craniectomy followed by cranioplasty" at the Department of Neurological Surgery, Kathmandu Medical College Teaching Hospital were enrolled retrospectively from 1st May 2012 to 30th April 2019. The craniectomy bone flap was preserved ex-vivo, dipped in spirit solution in deep freeze, then autoclaved prior to cranioplasty. Data were collected from the hospital's electronic database. Information analyzed included patient age, sex, indication for craniectomy, interval between craniectomy and cranioplasty, length of hospital stay, peri-operative complications and mean time of follow-up. Patients who underwent a cranioplasty following removal of an infected bone flap after a craniotomy were excluded from the study. Associated complications were assessed and statistical analysis was performed using a Fisher's exact test.

There were a total of 210 patients with 92 vascular, 58 post traumatic. With all these surgeries undergone we had 9% complication rate, all of whom underwent cranioplasty later than four weeks of primary surgery ($p = <0.0001$).

Ex-vivo preservation and autoclaving of bone flap is a simple technique with significant benefits in our hospital and national scenario with significantly less financial burden to patients.

Key words: Autologous, Bone flap preservation, Cranioplasty, Decompressive craniectomy, Ex-vivo, Freeze

Autologous cranioplasty is an increasingly common procedure performed in neurosurgical centers following a decompressive craniectomy (DC). The number of cranioplasties performed has increased over the last years, reaching 20-25 per million inhabitants per year in 2010 (in Europe, Middle East, and Africa)[1].

It has been estimated that cranial reconstructions are performed at a rate of 25 per 1 million people[2]. Publications concerning cranioplasties will benefit by a standardized reporting of surgical procedures, outcomes and graft materials used[3].

Autologous bone flap cranioplasty is the gold standard and the most commonly used materials in cranioplasty in reconstruction of cranial defects.[4] However, the morbidity associated with their harvest, additional time required, the need for a second surgical site, the limited hospital resources and supplies has led to the search for newer substitutes. A traditional method is to place the bone flap in a subcutaneous pocket at the abdominal wall till retrieval for cranioplasty.[5] Alternatively, craniectomy bone flaps can be stored at a hospital Skull Bone Bank in a freezer at -80 ^{0}C (with an acceptable range of -70 ^{0}C to -90 ^{0}C)[6] under aseptic technique, also known as cryopreservation. The unavailability of a safe freezer container and adequate bone bank facilities in most hospitals is the main reason why this technique is not widely practiced.

We have introduced an ex-vivo preservation of bone flap dip immersed in spirit solution and stored in deep freeze compartment in regular fridge. It is a simple and cheap alternative to other techniques and could be proceeded in any institution that provides autoclaving sterilization service prior to cranioplasty.[5] To the best of our knowledge, there has been no such publication yet, so we called it a "novel technique". We had been successfully conducting cranioplasty with such stored and autoclaved bone. This study aims to perform an audit of ex-vivo preservation of craniectomy bone flap, along with a comprehensive review of literature in regards to clinical outcomes after cranioplasty. We designed a retrospective study to evaluate the effectiveness of our method after cranioplasty with the autologous bone.

Methods and Materials

In this KMCTH IRC/ethics Institutional Review Board-approved study, patients who were admitted and underwent decompressive craniectomy and cranioplasty in Department of Neurological Surgery KMCTH, were enrolled retrospectively, over a 7-year period between May 2012 and April 2019. Data were collected from the hospital's electronic database, minimum up to 6 months post cranioplasty. Individual patient consent were not required as the study was undertaken as an audit. Two groups were identified arbitrarily—those who had received an 'early' cranioplasty, defined as less than 4 weeks from craniectomy, and those who received a 'late' cranioplasty, defined as more than 4 weeks from craniectomy.

Data registration was done in the designated performa, prepared for the study. Registration of baseline and clinical data started on admission in the hospital, Department of Neurological Surgery, KMCTH. These collected data were entered in the Statistical Package for the Social Sciences (SPSS) data sheet, subjected for descriptive statistics, diagrams and the needful test. Statistical analysis were done using SPSS computer software version 15.0. The p value of < 0.05 was taken as statistically significant.

Information analyzed include patient age and sex, indication for craniectomy, interval between craniectomy and cranioplasty, associated complications. Patients who underwent a cranioplasty following removal of an infected bone flap after a craniotomy were excluded from the study. Statistical analysis was performed using a Fisher's exact test.

Results

There was a total of 210 patients who underwent decompressive craniectomy with autologous cranioplasty during this seven years of study period. The age ranges from 18 to 63 years with mean age of presentation being 45 years. Altogether there were 168 Males (80%) and 42 females (20%). Most of the primary surgeries underwent were emergency (n=190; 90%) with elective surgery being 20 (10%). Among all surgeries, they could be categorized as traumatic brain injury 60 (28.5%), hemorrhagic stroke 57 (27%), ischemic stroke 40 (19%), subarachnoid hemorrhage (post aneurysm clipping and trauma) 40 (19%), tumor 12 (6%) and venous sinus thrombosis 1(0.5%) . (Fig. 1)

Patients underwent cranioplasty in an average of 6 weeks following the primary decompressive craniectomy surgery, with range 21 days to 6 months, and a median of 4 weeks. Among all the patients 180 had early cranioplasty and 30 patients had late cranioplasty. Mean time duration of surgery was 120 mins, with range from 45 mins to 180 mins. Longer operative duration in late group was due to time consuming dissection of scalp layers from dura. Most of the patients underwent cranioplasty during the same period of admission as for primary cranial surgery, in early cranioplasty group. Those discharged presented with good pre-surgical status and low pre-surgical risk. Preoperatively 168 (80%) could be categorized as GOS 4 or 5 and ASA scale 1 or 2. Most of the procedures

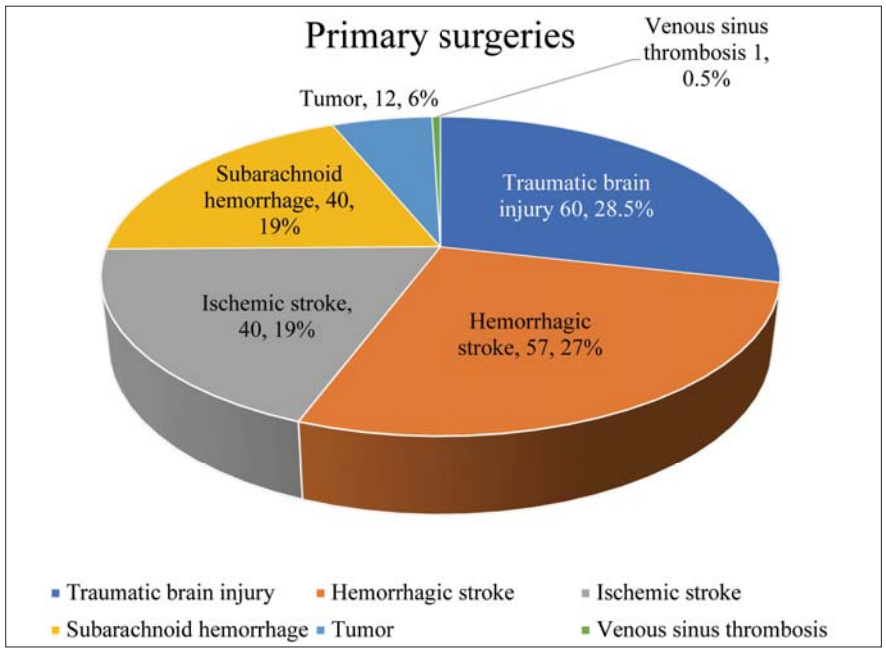

Figure 1: Description of Primary surgeries

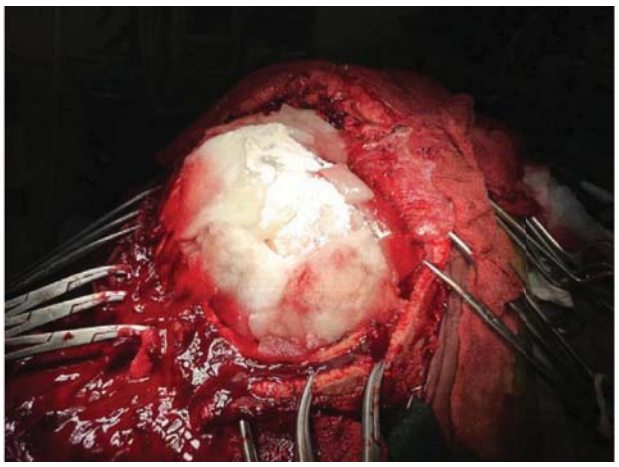

Figure 2: Topical sprinkling of vancomycin powder over, surgical site covered with bagel before skin closure

were undertaken under general anesthesia however 10 patients, who were cooperative with GOS 5, ASA scale 1; cranioplasty was done awake, under local anesthesia without any difficulty.

Post-surgical procedure in most of the patients topical vancomycin powder was used except for 40 of the patients (Fig. 2). All the patients received a single dose of antibiotics preoperatively and no antibiotics postoperatively. The bone was fixed with titanium miniplates and screws.

There were postoperative complication seen in 19 patients, with complication rate of 9% (p = <0.001), all in late cranioplasty group (Table 1).

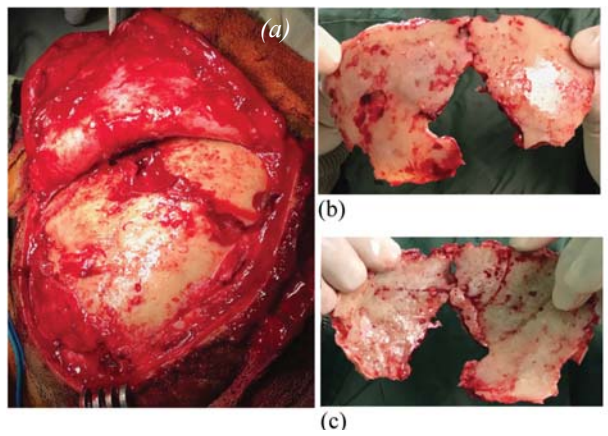

Figure 3: Surgical site infection: (a) Intraoperative osteomyelitic bone with pathological fracture and bone resorption, (b) outer view of the skull bone removed, (c) inner view of the skull bone removed.

	Total patients	complications	P value
Early cranioplasty	180	0	<0.0001
Late cranioplasty	30	19	
Total	210	19 (9%)	

Table 1. Complications in cranioplasty

Complication evident were pseudo-meningocele in 10, surgical site infection (SSI) in 4 (Fig. 3, Fig. 4), extradural hematoma (EDH) in 3, subdural hematoma (SDH) in 2(Fig. 5).

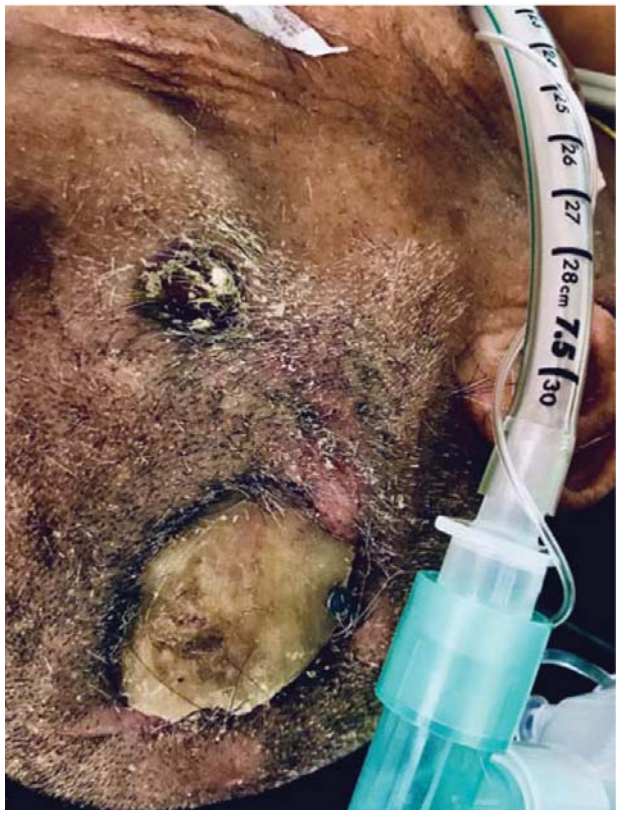

Figure 4: Exposed R parieto-frontal bone flap due to necrosed overlying skin

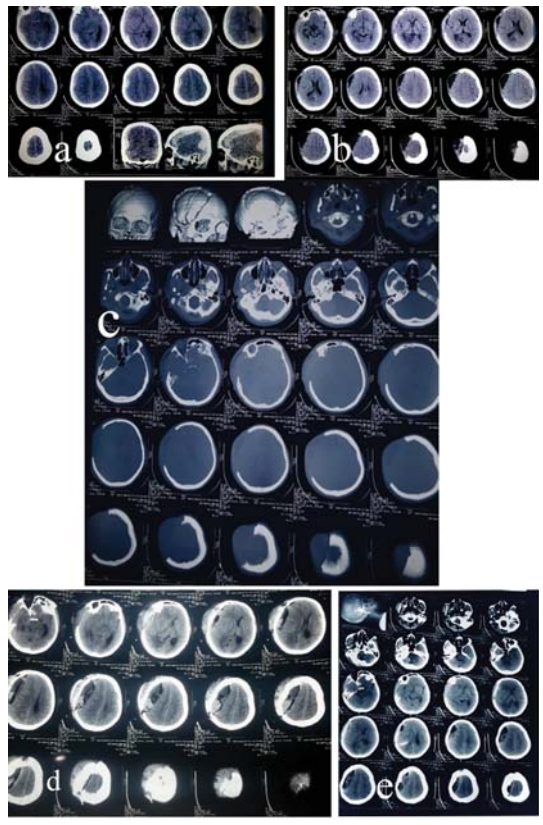

Figure 5: Complication in cranioplasty (a) R Preop acute subdural hematoma; (b) 4 weeks Post-op pseudomeningocele; (c) Bony frame, post craniectomy; (d) Immediate post cranioplasty epidural, sub-dural and sub-galeal hematoma; (e) Post emergency evacuation of hematoma

They were managed accordingly with, tight compression bandage, antibiotics along with removal of bone flap and evacuation of hematoma and other needful surgical intervention. With this late cranioplasty group has prolonged duration of hospital admission; mean stay being 15 days (range 10 – 42 days) in hospital.

Discussion

Flap preservation in deep freezer storage was introduced in the 1950s to reduce the rate of infection.[7,8] However, this method has been correlated with devitalization of tissue and an increased future risk of resorption.[9] In our study we preserved all bone flaps ex-vivo. Biomechanical studies reveal that freezing and thawing have little effect on the mechanical properties of the human skull.[10] Storage of the flap in an abdominal pocket, requires a second surgical site, adding the additional risk of abdominal surgical site infection with resultant flap contamination. The poor systemic condition of patient and associated co-morbidities warrant subcutaneous preservation of autologous bone, at times. Clinical review by Brian et al,[11] has found no statistically significant differences in clinical outcomes(infection, resorption, reoperation) when comparing storage methods for these two bone flap preservation. This study suggests that both strategies may be used safely and successfully.

Autologous bone is relatively inexpensive, easy to obtain, exhibits good fit and contour, presents no risk of disease transmission, offers biological reconstruction with minimal donor site morbidity.[12] The SSI rate after cranioplasty with autologous bone has been reported to be approximately 3-30%[13] with a bone resorption rate from 4% to 22.8%.[14,15] In our study we had complication rate of 9% ($p = <0.001$), which is comparable with international standard of complication rate in delayed cranioplasty.

It is important to keep the graft absolutely aseptic during storage as studies have shown that bacteria can survive freezing. However, it is difficult to eradicate contamination completely and therefore, the frozen bone must be processed to rule out the chances of infection. The commonly used sterilizing methods are autoclaving, gaseous ethylene oxide, alcoholic soaking and gamma radiation.[16,17] The frozen bone graft was autoclaved

immediate prior to cranioplasty, in the present study. Autoclave is easily available in most of the hospitals. Matsuno et al.[18] cryopreserved autologous bone flap in 100% ethanol at −20 °C and sterilised the flap in an autoclave before cranioplasty. Bone flap infection was noted in 25.9% of patients in his study. The autoclaving of autologous bone has been introduced to decrease the risk of SSI; however, several studies have shown disparate results regarding its effects.[19]

In our set up, as the graft is autoclaved, it does not have any viable cells and bone morphogenetic proteins, there by lacking osteogenic potential. So graft healing by osteogenesis and osteoinduction is ruled out. However, haversian systems are still present in autoclaved bone to provide a frame work for osteoconduction. Osawa et al[20] revealed that freezing and autoclaving had only minimal effects on bone structure. Sieving of the graft should be carried out as it not only facilitates uniform sterilization but also permits escape of collected fluid, in growth of fibrous tissue and revascularization following reconstruction. Another important factor in revitalization of autoclaved bone is the exact fitting of the graft and stable fixation using low profile biocompatible titanium bone plate and screws.[21]

The ideal time for cranioplasty post decompressive craniectomy is still controversial,[22] with conflicting view as to which has better outcome and postop result.[23] Quah B et al suggests there being no significant difference in infection risk for patients undergoing early (< 12 weeks) or late cranioplasty after non-infection related craniectomy.[22] We kept our cranioplasty procedure as early as possible from 3 weeks post craniectomy to the earliest as per resolution of cerebral edema. As per our experience earlier the cranioplasty better the tissue planes for surgical dissection thus reducing surgical procedure and less dural tear, which corelates with the recent experience mentioned in international publications. Recent studies have proposed post infection cranioplasty at 12 weeks after osteomyelitic bone flap removal instead of the greater than 6 month time intervals previously agreed upon.[24] Early cranioplasty as early as 1 week post-decompression was successfully performed after radiographic evidence of resolution of cerebral edema.[25]

Overall complication rates in cranioplasty procedures have been reported to be approximately 4% to 15% in large series.[24] The average rate of cranioplasty infection is approximately 7.9%.[23] This is comparable to our study with complication rate of 9%. Several studies have shown that there is no significant difference in infection rates between autologous and alloplastic cranioplasty.[26] The cranioplasty flap is an unlikely source of influence in surgical infections, but rather the complexity of the injury with involvement of contaminated wounds appears to be a stronger determinant. Another factor that can influence risk of infection is proximity of cranioplasty reconstruction to the frontal sinus, as this has been shown to be an independent risk factor for infection.[27]

Postoperative epidural hematoma (Fig. 5D) is a less common complication, occurring at a rate of approximately 3.5%.[28] The use of both sub-galeal and subdural drains does not result in a significantly lower rate of hematoma formation, thus enforcing the well-known principle that drains do not prevent hematoma formation. In patients presenting with a history of bleeding dyscrasias, it is helpful to consult a hematologist to assist with perioperative anticoagulation management.[29] Bone flap resorption is an overall low risk, but has been seen with both abdominal banking and cryopreservation. It has been shown to be increased when cranioplasty is delayed[14,30] and when the bone flap is large (>120 cm^2),[31] or comminuted.

Being retrospective study, there definitely is need of prospective study with inclusion of more number of cases. There might be some applicable potential bias that might have affected our result as it is single center study without any control. Similarly, this study could have been specific if there has been correlation of the final outcome to the comorbidities that patient had, indication of the surgeries, diagnosis, etc. As we had included all routine and emergency surgical cases in this analysis. It is possible that patient-related factors, indications and diagnosis, may influence surgical outcome. However, findings of this present study has encouraged us to proceed with further study prospectively, thus including detail variables like length of hospital stay ,duration of surgery, and other confounding factors.

Conclusion

Our technique of autologous cranioplasty has been comparable with outcomes mentioned in the international literatures. It has significant benefits in our hospital and national scenario with significantly less financial burden to patients with better surgical results. Cranioplasty should be performed early, as long as clinical conditions are good and the patient has resolved the cerebral edema. Given the impressive outcomes of the present study, it can be concluded that autologous skull bone flap, freeze stored and autoclaved is a safe and effective reconstruction material for cranioplasty. However, a prospective multicentric randomized controlled study is necessary to confirm our findings.

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