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ORIGINAL RESEARCH

Retrospective Comparative Analysis of Frozen and Subcutaneous Bone Flap Storage Methods for Autologous Bone Cranioplasty

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ABSTRACT

Aim: Retrospective Comparative Analysis of Frozen and Subcutaneous Bone Flap Storage Methods for Autologous Bone Cranioplasty. **Material and methods:** A retrospective study was conducted, authorized by the institutional review board, to identify all adult patients who had autologous bone cranioplasty after craniectomy. we examined the electronic medical records of these patients to gather various demographic information such as sex, race, and age. They also collected baseline characteristics including smoking status and body mass index (BMI). Additionally, we recorded any medical conditions the patients had, such as osteoporosis, diabetes, and a history of cancer, as well as other conditions like chronic obstructive pulmonary disease, hypertension, congestive heart failure, peripheral vascular disease, stroke (hemorrhagic and ischemic), myocardial infarction, coronary artery disease, coronary artery bypass grafting, and chronic kidney disease. The Glasgow Coma Scale score before and after surgery, as well as the modified Rankin Scale score before and after surgery, were also recorded. Furthermore, the charts were used to determine various acute surgical complications such as hospital-acquired infection (HAI), surgical site infection, deep vein thrombosis, pulmonary embolism, hematoma, and cerebrospinal fluid leak. **Results:**The duration of follow-up for the 40 patients who had subcutaneous storage was 443.45± 25.78 days, whereas it was 355.76± 15.76 days for the patients who underwent frozen storage. The two groups had comparable baseline characteristics, with the exception of BMI, which showed a statistically significant difference when comparing both demographics and comorbidities (Tables 1 and 2). The average BMI of the population stored in frozen bone (27.87 ±3.57) was significantly higher (P = 0.02) than the population stored subcutaneously (24.77 ±3.76). The time of surgery for cranioplasty utilizing bone kept in the belly (182.71±8.87 minutes) was substantially greater (P < 0.001) compared to surgeries using autologous bone preserved in the freezer (114.64 ± 7.66 minutes). The only other significant difference (P = 0.02) was observed in the placement of a ventriculoperitoneal shunt (VPS). The subcutaneous storage population had a much higher occurrence of VPS placement during the cranioplasty procedure (42.4%) compared to the frozen storage population (11.67%). However, VPS placement before the cranioplasty procedure (in a separate procedure) was more common in the frozen storage population (23.33%) than in the subcutaneous storage population (10%). **Conclusions:** Both subcutaneous and cryopreservation are viable and possibly comparable choices for storing the bone flap after craniectomy.

Keywords: subcutaneous, cryopreservation,bone flap, craniectomy

INTRODUCTION

Cranioplasty is a surgical treatment that involves repairing a defect in the skull by incorporating material into the damaged area of the bone[1]. Cranioplasty is performed when the underlying condition that led to the first craniectomy has been treated and stabilized. This condition is commonly caused by cerebral edema after a cerebrovascular accident, traumatic brain injury, or brain tumor[2-4]. The indications for cranioplasty include providing protection for the underlying brain tissue, improving physical appearance, and, in certain situations, it becomes medically necessary to prevent atmospheric pressure from affecting cranial fluid dynamics (as shown in the syndrome of trephine)[1].

The materials used for correcting the cranial defect may be classified into two distinct categories: autologous bone or synthetic substitutes. Autologous bone refers to the use of the patient's own skull fragment that is extracted after craniectomy. This method is a more affordable and biologically compatible option compared to synthetic materials[5]. Cranioplasty is often performed at a later time after the first craniectomy, thus it is important to determine how to store the patient's own bone flap. There are two commonly used ways for storing autologous bone flaps: cryopreservation, which involves storing the bone flap in a specific freezer according to a predetermined protocol, or subcutaneous storage in the abdominal cavity, where the bone flap is preserved in the compartment above the fascia. Previous studies have generally shown that the advantage of one approach over another in terms of patient outcomes is not significant, particularly when it comes to the integrity of the bone flap's capacity to generate new bone tissue. At now, the choice of storage method is determined by evaluating the distinctions between cryopreservation and subcutaneous storage, as shown by references [5-8]. Consequently, the storage of autologous-bone flaps is a contentious issue in neurosurgery and ultimately determined by the surgeon's discretion.

MATERIAL AND METHODS

A retrospective study was conducted, authorized by the institutional review board, to identify all adult patients who had autologous bone cranioplasty after craniectomy. Due to the retrospective nature of the study, patient agreement for recruitment was not necessary. we examined the electronic medical records of these patients to gather various demographic information such as sex, race, and age. They also collected baseline characteristics including smoking status and body mass index (BMI). Additionally, we recorded any medical conditions the patients had, such as osteoporosis, diabetes, and a history of cancer, as well as other conditions like chronic obstructive pulmonary disease, hypertension, congestive heart failure, peripheral vascular disease, stroke (hemorrhagic and ischemic), myocardial infarction, coronary artery disease, coronary artery bypass grafting, and chronic kidney disease. The current medications the patients were taking, such as steroids, aspirin, clopidogrel, warfarin, and other anticoagulants, were also documented. we also noted various operative characteristics, such as the length of surgery, blood loss, use of prophylactic antibiotics, cranial defect size, autologous bone storage method, and ventriculoperitoneal shunt placement. The Glasgow Coma Scale score before and after surgery, as well as the modified Rankin Scale score before and after surgery, were also recorded. Furthermore, the charts were used to determine various acute surgical complications such as hospital-acquired infection (HAI), surgical site infection, deep vein thrombosis, pulmonary embolism, hematoma, and cerebrospinal fluid leak. Other factors such as resorption, readmissions, reoperations, cranioplasty flap infection, cranioplasty flap removal, length of stay under neurosurgical management, and discharge destination for all patients were also determined. All identified patients were included in the research irrespective of the duration of follow-up.

METHODOLOGY

It is crucial to note that all patients who had their bone flap kept under the skin were treated by one attending surgeon, whereas the patients whose bone flap was frozen were treated by various attending surgeons. This is mostly due to the fact that surgeons at our institution have a preference for placing the bone subcutaneously in all cranioplasty procedures. This preference is not influenced by the patient's disease pathology, medical history, or any other circumstances related to their hospital stay. However, because to its nature as an academic hospital and the duration of 5 years during which these instances occurred, several resident doctors were involved in the surgical teams for both the subcutaneous and frozen cranioplasties.

In regards to the subcutaneous storage technique, the rough edges of the flap were made smooth using rongeurs. If the bone flap was particularly large, it was divided. Then, it was wrapped in gel film to prevent the formation of adhesions. Finally, it was placed with the curved surface facing the incision in a pocket located just above the abdominal fat.

The autologous bone flaps, which were intended to be maintained in a specialized deep freezer, were cleansed by the scrub specialist to remove any attached tissue. Subsequently, they were immersed in the suitable antibiotic solution for a duration of 10 minutes. The bone was then inserted into an inner bag made by Cranioloc (Instant Systems, Inc, Norfolk, VA) and stored in a freezer maintained at a temperature of 40◦C. Before immersing the bone fragment in the antibiotic solution, the whole fragment was swabbed to collect samples for microbiological cultures. If the culture test showed positive results, the flap was discarded. Before implantation, frozen bone was thawed to room temperature in a sterile saline and antibiotic solution, sequentially.

STATISTICAL ANALYSIS

We employed c2 tests to assess and compare various categorical patient demographic and operative characteristics, such as sex, race, smoking status, preoperative antibiotics, preoperative steroids, anticoagulation, ventriculoperitoneal shunt (VPS) type, defect size, and indication for surgery. Additionally, we used c2 tests to compare all comorbidities between the groups. We used t-tests to compare several continuous demographic and operational parameters, such as age, expected blood loss, surgery length, and the time gap between craniotomy and cranioplasty. The c2 tests were used to examine the univariate occurrence of readmissions, reoperations, and complications between the groups,

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while a t test was utilized to assess the overall duration of stay between the groups. Additionally, multivariable logistic regression was used to evaluate the occurrence of readmission, reoperations, and complications across different groups. Furthermore, multivariable linear regression was utilized to compare the overall duration of hospital stay among these groups. For all studies involving several variables, the variables used were the ones that maximized the quality of the model, as determined by the Akaike information criterion. All demographic and operative factors were considered as potential confounders. The threshold for statistical significance was established at a P-value of less than 0.05, and all statistical analysis was conducted using SPSS version 25.0.

RESULTS

Demographic information, presence of other medical conditions, and details on the surgical procedure. A total of 100 individuals who had craniectomy at a tertiary academic medical facility were identified during a 5-year retrospective assessment. These patients obtained cranioplasty using their own bone. For 40 of the patients, the bone flap that was taken out during craniectomy was preserved under the skin (in the patient's belly), whereas the remaining 60 flaps were frozen and stored in the bone bank. The duration of follow-up for the 40 patients who had subcutaneous storage was 443.45± 25.78 days, whereas it was 355.76± 15.76 days for the patients who underwent frozen storage. The two groups had comparable baseline characteristics, with the exception of BMI, which showed a statistically significant difference when comparing both demographics and comorbidities (Tables 1 and 2). The average BMI of the population stored in frozen bone (27.87 ±3.57) was significantly higher (P = 0.02) than the population stored subcutaneously (24.77 ±3.76). The time of surgery for cranioplasty utilizing bone kept in the belly (182.71±8.87 minutes) was substantially greater (P < 0.001) compared to surgeries using autologous bone preserved in the freezer (114.64 ± 7.66 minutes) (Table 1). The only other significant difference (P = 0.02) was observed in the placement of a ventriculoperitoneal shunt (VPS). The subcutaneous storage population had a much higher occurrence of VPS placement during the cranioplasty procedure (42.4%) compared to the frozen storage population (11.67%). However, VPS placement before the cranioplasty procedure (in a separate procedure) was more common in the frozen storage population (23.33%) than in the subcutaneous storage population (10%). In addition, the implantation of VPS at any stage in relation to the cranioplasty surgery was more frequent in the subcutaneous storage group compared to the frozen storage group. Significantly, there was no notable disparity (P = 0.31) in the reasons for craniectomy between the two groups. In both groups, craniectomy was carried out in over 90% of patients due to bleeding or malignant edema after an ischemic stroke. Immediate and severe problems The incidence of all problems examined was higher in the subcutaneous storage group compared to the frozen storage group, with the exception of cranioplasty infection and resorption (Table 3).

In our research population, particular complications related to cranioplasty, such as resorption, bone-flap infection, graft fracture, and skull fracture, were rare occurrences (Table 3). Among the 100 patients examined, only one instance of resorption was observed. This happened in a patient whose bone flap was preserved in a frozen state and was detected on day 556 following the cranioplasty procedure. The submerged flap was extracted and substituted with a synthetic implant 692 days following the autologous bone cranioplasty. The patient who had resorption was a 50-year-old individual who underwent cranioplasty. The time interval between craniectomy (performed for bleeding) and cranioplasty was 161 days. The cranioplasty procedure included a 10-cm incision. The patient did not have a ventriculoperitoneal shunt (VPS) and did not experience any additional problems. It is worth mentioning that the incidence of autologous bone flap infection was comparable in both groups, and all instances were managed by removing the infected bone flap. No instances of either graft or skull fracture were seen after cranioplasty. It is important to mention that in 2 individuals, the bone that was being stored under the skin was taken out from the belly before the cranioplasty procedure. One patient required removal due to infection of the subcutaneous pocket containing the bone. In this instance, the bone was extracted, treated according to hospital policy, preserved by freezing, and then sterilized using autoclaving before being used for cranioplasty. This subject was examined using the frozen storage cohort. The second patient had a procedure in which their bone was extracted from their belly and disposed of owing to erosion. This patient had cranioplasty using a synthetic plate, and as a result, was excluded from any analysis. A single patient with factor XI deficiency had a hemorrhage in the location where the abdomen was stored, but the bone was not extracted and was ultimately used for the cranioplasty.

Table 1. Basic parameter of the participants

Parameter	Total	Subcutaneous	Frozen	P Value
Total patients	100	40	60	
Gender				0.33
Male	32	11	21	
Female	68	29	39	

Age, years		51.1	50.4	
Body mass index		24.77±3.76	27.87±3.57	0.02
Smoking status				
Yes	53	27	26	0.14
No	47	13	34	
Operative characteristics				
Days to cranioplasty		83.61±5.56	98.65±4.98	0.11
Surgery duration, minutes		182.71±8.87	114.64±7.66	<0.001
Blood loss		115.99±6.68	126.66±7.54	0.26
Prophylactic antibiotics	89	31	58	0.23
Steroids	11	9	2	0.32
VPS placement				0.02
Before	20	6	14	
During	24	17	7	
After	4	3	1	
None	52	14	38	
Cranioplasty size, cm				0.22
<10	36	25	11	
>10	64	15	49	
Indication for craniectomy				
Hemorrhage	68	24	44	0.31
Stroke and malignant edema	21	10	11	
Traumatic brain injury	6	3	3	
Malignant edema after tumor biopsy	3	2	1	
Tumor biopsy	2	1	1	
Anticoagulants				0.25
Aspirin	13	6	7	0.32
Clopidogrel	2	0	2	0.72
Warfarin	9	5	4	0.34
Other	26	11	15	0.67
Any	40	10	30	0.45
Multiple	10	8	2	0.46

Table 2. Comorbidities of Patients with Subcutaneous and Frozen Storage

Comorbidities	Total (N =100)	Subcutaneous (n =40)	Frozen (n =60)	P Value
Hypertension	60	20	40	0.21
Diabetes				0.23
DM1	10	3	7	
DM2	5	2	3	
Coronary artery disease	11	2	9	0.16
Congestive heart failure	10	2	8	0.18
Peripheral vascular disease	10	3	7	0.33
Cancer	9	1	8	0.13
Myocardial infarction	9	2	7	0.16
Chronic kidney disease	7	1	66	0.34
Chronic obstructive pulmonary disease	4	2	2	0.22
Coronary artery bypass graft	3	2	1	0.13
Osteoporosis	1	0	1	0.26

Table 3. Postoperative Complications for Patients with Subcutaneous Versus Frozen Storage

Postoperative Complications	Total	Subcutaneous	Frozen	Multivariable
Readmission	16	7	8	0.33
Reoperation	15	8	7	0.16
Length of stay, days	10.43±1.54	9.06±1.65	11.66±1.67	0.67
Hospital-acquired infection	14	8	6	0.27
Cranioplasty infection	7	2	5	0.12
Cranioplasty removal	7	2	5	0.13
Hematoma	7	5	2	0.11

Deep vein thrombosis	4	3	1	0.19
Pulmonary embolism	3	2	1	0.45
Cerebrospinal fluid leak	1	1	0	0.34
Resorption	1	1	0	0.32

Table 4. Reasons for Reoperation

Reason for Reoperation	Total (% of Reoperations)	Subcutaneous (% of Reoperations)	Frozen (% of Reoperations)
Hematoma/fluid evacuation	9	7	2
Cranioplasty removal	9	2	7
Redo cranioplasty (infection)	4	1	3
SSI management	2	1	1
Redo cranioplasty (resorption)	1	0	1
VPS placement	1	1	0
Hardware removal	1	0	1
Total	27	12	15

DISCUSSION

In order to provide accurate comparison between the subcutaneous and frozen storage techniques of autologous bone following craniectomy, it is crucial that the baseline demographics and comorbidities of these two groups be comparable, despite the retrospective nature of the data (Table 1, 2). Only two preoperative characteristics, race and BMI, showed statistically significant differences between the two groups. The Body Mass Index (BMI) may operate as a single risk factor that contributes to an elevated risk of medical complications, therefore impacting the results of surgical procedures.The given text is the list [9,10]. Contrary to expectations, our data found no correlation between higher BMI and worse surgical complications. The comparability of grounds for craniectomy in both groups allows for a direct comparison of the two techniques of storing bone flaps. However, the higher percentage of VPSs seen in patients with subcutaneous bone storage may have affected outcomes since previous studies have linked the existence of VPSs with a higher incidence of problems, including infection, the need for revision surgery, and a faster rate of bone resorption.[11] It is important to mention that the decision to use the subcutaneous mode of the bone flap during cranioplasties is solely based on the surgeon's training and personal preference, and is not influenced by any specific patient factors such as their medical condition, demographics, or risk factors. Therefore, all patients who undergo craniectomy by this surgeon will have their bone flap stored subcutaneously. In addition, this particular surgeon specializes only in treating cerebrovascular disorders, namely ruptured arteriovenous malformations and ruptured aneurysms, which often result in a greater probability of developing hydrocephalus that may need the use of a shunt in the future. This may account for the increased number of VPSs allocated to the subcutaneous category. Due to the intricate nature of vascular problems that need surgical treatment, these procedures are frequently more time-consuming and complicated. As a result, it is difficult to make definitive conclusions on the difference in operation time between the two storage systems. Undoubtedly, the cranioplasty procedure takes more time in the subcutaneous storage group since it requires more preparation, harvesting of the bone flap, and preparation of the bone flap before it can be finally placed. Utilizing more time-efficient surgical procedures is advantageous, since research has shown that longer cranioplasty operations are associated with a higher risk of infection [12,13]. Furthermore, it is important to mention that the duration between craniectomy and cranioplasty had no impact on the results. Nevertheless, there is substantial data indicating that doing cranioplasty within a 14-day period after craniectomy leads to worse outcomes[14]. Ultimately, there were no notable disparities in the incidence of surgical complications between the subcutaneous and frozen storage groups, as shown in Table 3. having the exception of 2 complication rates, all other complication rates were higher in the subcutaneous group. However, this observation might be attributed to the larger number of patients having a VPS. The higher incidence of complications in the subcutaneous group contradicts a recent (2016) comparative analysis of the literature. This analysis found that patients who had cryopreserved bones had a higher rate of infection and reoperation, although these differences were not statistically significant. In the end, the technique used to store the bone flap did not have a significant impact on the surgical complications of cranioplasty.

The variables HAI (hospital-acquired infection) and duration of stay were significantly affected by preoperative factors that were gathered in this research. Initially, there was a correlation between being female and having a higher likelihood of acquiring a HAI. This is likely due to the fact that female patients are more susceptible to urinary tract infections (UTIs) because they have a shorter urethra. In our data, 50% of the HAIs (10 in total) in female patients were UTIs, while none of the 3 male patients who contracted a HAI had a UTI. Furthermore, the likelihood of HAI was shown to be higher as individuals became older, a conclusion that is well supported in the existing body of research[16]. Expanding the extent of the craniectomy was linked to a longer hospital stay, which may be indirectly ascribed to a bigger region of damage (hemorrhage or malignant edema after a stroke) and resulting neurological impairment.

The ultimate and most significant factor affecting both healthcare-associated infections (HAI) and length of stay is the implantation of a VPS, since its timing may be modified. The positioning of the VPS before the cranioplasty was shown to significantly elevate the risk of HAI and prolong the duration of hospitalization. The placement of VPS during the cranioplasty procedure, however, merely led to a notable increase in the duration of hospitalization. Thus, if VPS installation is necessary for conditions such as hydrocephalus, hydrocephalus ex vacu, subgaleal fluid accumulation, or fullness of the flap, we suggest doing VPS and cranioplasty together. Theoretically, placing the shunt simultaneously can prevent the need to manipulate the final location of the shunt catheter tip, which could lead to shunt malfunction. It also avoids altering the cerebrospinal fluid dynamics in the absence of a bone flap, which can result in the syndrome of trephine. Lastly, it eliminates the need for reoperation in a surgical site that has undergone multiple prior surgeries. However, doing surgery simultaneously takes more time and raises concerns about the possibility of shunt infection owing to the extended duration of the surgical procedure.

The incidence of complications specific to cranioplasty was quite low and showed no significant difference between the two groups. Within the whole group, there was just one instance of resorption. This occurred in a 50-year-old male with a cranial defect of 10 centimeters, who did not have a VPS or any other difficulties. Therefore, the resorption rate was calculated to be 1.1%. The resorption rate reported in earlier studies varied between 5% and 17%[17-20], which is much higher than the rate mentioned here.

The infection incidence did not differ significantly between subcutaneous and frozen bone-flap preservation. Ultimately, both the subcutaneous and frozen preservation of the autologous bone flap have comparable risk profiles. An additional danger to the patient associated with subcutaneous storage, but not with frozen storage, is the potential for issues arising from storing the bone in the belly. Three individuals had difficulties associated with the intra-abdominal storage of the bone, and all three of these instances were managed with surgical intervention. Two patients had abdominal bone flap removal, one due to infection and the other due to erosion. Additionally, a third patient experienced hematoma formation at the storage location. There was no indication of heightened risk in the patient who had their bone removed due to erosion, as their BMI was 29 during the surgery. The surgeon who conducted the craniectomy removed the sharp edges of the bone flap using rongeurs, divided large grafts into two pieces, and positioned the rounded edge towards the incision to minimize the risk of erosion. Finally, the patient who experienced hematoma had a deficiency of factor XI. As a result, we advise against using the subcutaneous storage method in patients who are at a higher risk of bleeding, unless there is a specific reason to use subcutaneous storage due to the knowledge that their care (cranioplasty) will be carried out at a different medical facility. The problems associated with storing the bone-flap in the abdominal pocket do not exist when the bone is cryopreserved. This additional danger to the patient and the possible increase in expenses of future procedures must be taken into account when comparing these two approaches.

While the difference is not statistically significant, it is important to mention that the incidence of reoperation in patients who had cranioplasty with autologous bone flap stored subcutaneously was more than twice as high as in patients whose bone was cryopreserved[21]. Contrary to current comparative examination of the literature, cryopreservation led to reoperation rates that were more than double those of subcutaneous storage. In addition, the overall reoperation rate was higher compared to the rate reported in the same paper[15]. After doing a multivariable analysis, no prognostic indicators were found for the two most prevalent causes for reoperation: hematoma/fluid evacuation and cranioplasty removal for infection. Nevertheless, it is worth mentioning that among the patients in the frozen storage group, 3 out of 4 showed a tendency towards longer surgery, which was associated with the need for cranioplasty. Similarly, 1 out of 2 patients in the subcutaneous storage group also exhibited this trend. This observation is significant because previous studies have demonstrated that prolonged surgical duration is linked to a higher likelihood of surgical site infection.[13]

CONCLUSIONS

Both subcutaneous and cryopreservation are viable and possibly comparable choices for storing the bone flap after craniectomy. Both approaches have a very comparable risk profile for individuals who undergo cranioplasty using their own bone transplant. Although the outcomes are comparable, our conclusion is that frozen storage is more advantageous due to its somewhat lower complication rates and the avoidance of the tiny but significant risk of complications at the subcutaneous storage location. Subcutaneous storage serves a distinct purpose for patients who are receiving treatment at distant medical facilities from where the cranioplasty will take place, lack insurance coverage to finance a synthetic graft, and are unreliable in attending follow-up appointments.

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