Comparison between subcutaneous pocket and cryopreservation method for storing autologous bone flaps in developing bone flap infection after cranioplasty, a prospective observational multicenter study of 100 cases

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Research

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Abstract

Background

Following a craniotomy, harvested bone flap, if available, is stored for future cranioplasty. There are two different methods for bone banking: subcutaneous pocket in abdominal wall and cryopreservation in a refrigerator. This study is designed to evaluate risk of developing infection in each group, retrospectively.

Methods

In this prospective observational multi-center study, one hundred (100) patients who underwent cranioplasty with autologous bone flap were divided into two groups of 50 patients. Rate of clinical post-operative infection and possible associated risk factors were analyzed with statistical measures. The data check lists parameters were indication of DC, CP vs SP, interval between craniotomy and cranioplasty, post-operative hospitalization duration, new morbidities and possible mortalities. The data were analyzed by an expert bio-statistician with proper bio-statistical methods (p<0.05)

Results

Four (4) patient in cryopreservation group (50 patients) had post-operative bone flap infection (8%). In subcutaneous pocket method no post-operative infection after cranioplasty was noticed, which are not statistically significant (p=0.054). Over-all post-operative infection rate was 4%.

Conclusion

There were no significant differences in post-operative infection rate between cryopreservation versus subcutaneous pocket method in storing bone flaps. Older age maybe associated with infection development after cranioplasty.

Background

there are many circumstances that a surgeon removed a bone flap out of a patients calvaria, which is known as decompressive craniectomy (DC), in order to reduced intra-cranial pressure (ICP). e.g. diffuse brain edema, acute subdural hematoma (ASDH), epidural hematoma (EDH), severe brain contusions, intra-cranial hemorrhage (ICH), cerebro-vascular infarctions (CVA), space-occupying lesions (SOL) with mass effect (1,2,3).

cranioplasty is a procedure that the cranial defect is repaired by autologous/prosthetic calvaria flap and has both cosmetic and neuro-biologic rationalities (4). the autologous bone flap is the cheapest and the easiest way to reconstruct the calvaria after decompressive craniectomy, but the harvested bone requires specific condition to be free from infections and reusable (3, 5). The interval between a decompressive craniotomy and cranioplasty procedure is determined by surgeons considering many factors, most
importantly general condition of the patient and degree of current brain edema. It is usually possible to be performed between 3 weeks to months after the primary decompression (3).

There are two major methods to store the harvested bone flap after decompressive craniectomy: subcutaneous preservation (SP) and cryopreservation (CP) (3, 6, 7).

In SP method bone flap is kept between subcutaneous fat layer of the abdominal wall and underlying fascia. In CP method, the bone flap will be frozen in -70 C in a freezer.

Post-operative complications of cranioplasty are versatile, including surgical site infection (SSI), autolysis of the bone flap, bone reabsorption and hydrocephalus.

SSI after every procedure and most importantly craniotomy and cranioplasty has major impacts on the patient, hospitalization duration, morbidities and health-service costs. If bone flap after cranioplasty is deemed to be infected, it must be removed, the wound should be irrigated and debrided, antibiotics via intra-venous route should be administered and at least after a 4–6 weeks the patient should be followed up until any evidence of infection resolves and proper time for the second cranioplasty could be determined (3, 8).

This study was designed to compare post-cranioplasty infection incidence after CP and SP methods for cranioplasty procedure and emphasize adjustable risk factors in the patients to prevent in the later groups of the patients.

**Methods**

In this prospective observational multi-center study, the patients who had a decompressive craniectomy by any indication and underwent a following cranioplasty with autologous bone flap, who were hospitalized in Al-Zahra referral hospital, Amin general hospital, Montazeri general hospital between 2013–2018 were enrolled into the study.

It must be mentioned that despite the general recommendation to store bone flap in CP method in a -70 C refrigerator, we kept them in a -28 C freezer.

Post-cranioplasty infection was defined as “any clinical evidence denoting infection, including: fever, erythema, cellulitis, secretions, SSI, change in neurological status which can be attributed to an infective intra-cranial process, Post-op follow up Brain CT findings suggest any evidence of abscess formation or infectious process.”. If a patient had clinical evidence of post-operative infectious status, he or she would be hospitalized, Intra-venous antibiotics administered and if indicated, flap should be removed and tissue culture would be prepared for microbiology lab.

According to inclusion criteria, 50 patients in each CP and SP method arm enrolled. All of them have been followed for 2 years in a rational interval, all of them had received same antibiotic regimen post-operatively.
Post-operative antibiotic regimen that was used in this study was Vancomycin 1 gr IV q12hrs x3 days + Ceftazidime 1gr IV q8hrs x3 days with proper renal adjustments.

The data check lists parameters were indication of DC, CP vs SP, interval between craniotomy and cranioplasty, post-operative hospitalization duration, new morbidities and possible mortalities. The data were analyzed by an expert bio-statistician with proper bio-statistical methods (p < 0.05).

Results

In CP method, post-operative infection incidence was 8% (four in fifty CP patients). In SP there was no post-operative infection event that results in 0% infection incidence. In comparison of two CP and SP method, there was no meaningful difference in post-operative infection incidence. (p = 0.059). Over-all incidence of Post-operative infection was 4% (four in one hundred patients).

The most common cause of decompressive craniotomy was trauma (82%)., tumors and CVA were the other prevalent etiologies of the primary DC.

The prevalence of post-cranioplasty bone flap infection in traumatic patients was 3.7% and in non-traumatic patients was 5.6% (p = 0.612).

The youngest patient was 5 years-old and the oldest was 73. mean-age of the patients was 35 years and 6 months. mean-age in post-operative infection group was 50.25 years and in non-infected was 34.93 years which was statistically significant(p = 0.048).

Eighty-two percent (82%) of the patients were male and eighteen percent (18%) were female. post-operative infection rate in male and female was 3.6% and 5.5%, respectively.

The longest time interval between primary craniotomy –to-cranioplasty was 14 months, the shortest was 1 month and the mean time interval was 4 months.

The mean time interval between primary craniotomy –to-cranioplasty in post-operative infection cases was 7.25 months which was significantly different in non-infected (≈ 4 months) cases. (p = 0.069).

Mean hospital-stay duration days, after cranioplasty in both infected (before the occurrence of the infection) and non-infected cases was approximately equal,4 days.

Table-1: demographic data distribution in CP and SP method. cp = cryopreservation, sp = subcutaneous pocket
| Variable                                | SP method | CP method |
|-----------------------------------------|-----------|-----------|
| Male: female                            | 9:41      | 9:41      |
| Age(years)                              | 35.88 ± 14.37 | 35.20 ± 16.17 |
| Hospitalization duration(days)          | 5.16 ± 1.87 | 3.3 ± 0.87 |
| Flap storage duration(months)           | 3.22 ± 1.98 | 5.44 ± 3.91 |

Table 2: demographic data distribution in presence or absence of flap infection.

| variable                                | infection | number | Mean value | Standard deviation(SD) | p-value |
|-----------------------------------------|-----------|--------|------------|-------------------------|---------|
| age                                     | negative  | 96     | 34.93      | 15.061                  | 0.048   |
|                                         | positive  | 4      | 50.25      | 12.842                  | 0.048   |
| Flap storage length                     | negative  | 96     | 4.21       | 3.292                   | 0.069   |
|                                         | positive  | 4      | 7.25       | 0.957                   | 0.069   |
| Post-cranioplasty hospitalization duration | negative | 96     | 4.27       | 1.732                   | 0.244   |
|                                         | positive  | 4      | 3.25       | 0.500                   | 0.244   |

Table 3: variables associated with flap infection

| variable                                | Bone Flap infection | p-value |
|-----------------------------------------|---------------------|---------|
|                                         | yes                 | no      |
| Primary decompressive craniectomy etiology | 3                   | 79      | 0.603   |
| Traumatic = 81                          |                     |         |
| Non-traumatic = 22                      | 1                   | 21      | 0.603   |
| Method of bone flap preservation        | SP = 50             | 0       | 50      | 0.041   |
|                                         | CP = 54             | 8       | 46      | 0.041   |
| gender                                  | Male = 82           | 3       | 79      | 0.560   |
|                                         | Female = 18         | 1       | 17      | 0.560   |
Discussion:

Post-cranioplasty bone flap infection is a clinical serious condition due to its consequences, including meningitis, brain abscess formation, encephalitis, system inflammation and sepsis. Thus, high index of suspicion and low diagnostic-threshold would be rational (8).

In review of literature bone flap infection rate after cranioplasty ranges from 5.9%-22%. In review of literature, Post-operative infection after CP method is stated to be 2-25.9% and SP method 2.3–18% (8,9,10,11,12).

In a retrospective study of 70 patients, Inamasu and colleagues, reported that post-cranioplasty bone flap infection rate in CP and SP method was 16.1% and 5.1%, respectively that had no statistical significance. they also declared that CP method in traumatic patient had a higher incidence of post-operative infection (13).

Another similar study performed by the Cheng and associates had similar results in CP versus SP method and in prevalence of infection in traumatic versus non-traumatic cases. in our study there was no significant differences in traumatic and non-traumatic cases. Both of these studies lack in non-traumatic cases (2).

these finding maybe of selection bias concern because the number of non-traumatic cases in these studies, including us, are fewer than traumatic cases and the results maybe are not completely reliable and distributable. further studies with higher non-traumatic cases are required to clarify this obscurity.

Pooi-Pooi Cheah and colleagues, performed an 18-months follow up in cranioplasty patients and reported no significant difference in CP and SP method complications (10).

in this study CP and SP infection rates were 8% and 0%, respectively which are not statistically significant.

According to demographic data, older age is associated with higher infection rate which can be attributed to many factors, including comorbidities, longer hospital staying, previous use of antibiotics, possible immune suppression state in elderly patients and other factors that are not in the scope of this study and requires future studies.

Conclusion:

According to recent review of literatures and this study, there are no differences post-operative infection rate after cranioplasty in each CP and SP method and the method of preservation is best determined by the local hospital facilities and the patient condition.

Elder age maybe concerning in development of post-operative infection after cranioplasty but more dedicated studies with prospective design and higher number of patients are required to determine the
possible reasons of this hypothesis.

**List Of Abbreviations**

subcutaneous preservation (SP), and cryopreservation (CP), decompressive craniectomy (DC), intra-cranial pressure (ICP), acute subdural hematoma (ASDH), epidural hematoma (EDH), intra-cranial hemorrhage (ICH), cerebro-vascular infarctions (CVI), space-occupying lesions (SOL), surgical site infection (SSI)

**Declarations**

**Ethics approval and consent to participate**

This study was conducted using archived data of patients and was approved by School of Medicine - Isfahan University of Medical Sciences ethics committee:

1. Changiz Tahereh, Director of University, Regional Research Ethics Committee, Isfahan University of Medical Sciences and Health Services
2. Haghjooy Javanmard Shaghayegh, secretary of University, Regional Research Ethics Committee, Isfahan University of Medical Sciences and Health Services
3. Emami Najafi Dehkordi Mohammad Hasan, Director of Institutional Research Ethics Committee, School of Medicine, Isfahan University of Medical Sciences and Health Services

Approval ID: ir.mui.rec.1396.3.714

**Consent for publication**

Not applicable

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors can confirm that all relevant data are included in the article and/or its supplementary information files

**Competing interests**

The authors declare that they have no competing interests

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Authors' contributions

MS helped with gathering data and analyzing the data and was a major contributor in writing the manuscript. AS executed the study and was a contributor in writing the manuscript. AK helped with analyzing the data and writing the manuscript. SM gathered the data for the manuscript.

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