Effect of cranioplasty timing on the functional neurological outcome and postoperative complications

Ahmed Aloraidi, Ali Alkhaiyary, Ahoud Alharbi, Nada Alnefaie, Abeer Alaglan, Abdulaziz AlQarni, Turki Elarjani, Ala Arab, Jamal M. Abdullah, Abdulaziz Oqalaa Almubarak, Munzir Abbas, Ibtesam Khairy, Wedad H. Almadani, Mohammed Alowhaibi, Abdulaziz Alrifi, Sami Khairy, Ahmed Alkhani.

1College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia, 2King Abdullah International Medical Research Center, Riyadh, Saudi Arabia, 3Division of Neurosurgery, Department of Surgery, Ministry of National Guard - Health Affairs, Riyadh, Saudi Arabia, 4University of Miami, Department of Neurological Surgery, Miami, FL, USA, 5Department of Neurosurgery, Prince Sultan Military Medical City, Riyadh, Arabia, 6Prince Mohammed Medical City, Jouf, Saudi Arabia, 7Faculty of Applied Medical Sciences, Jazan University, Jazan, Saudi Arabia, 8National Center for Evidence Based Healthcare, Saudi Health Council, Riyadh, Saudi Arabia.

E-mail: Ahmed Aloraidi - loraheidiah@ngha.med.sa; Ali Alkhaiyary - alkhaiyary@hotmail.com; Ahoud Alharbi - lharbi1ahoud@gmail.com; Nada Alnefaie - adacsl92@gmail.com; Abeer Alaglan - laglanab@ngha.med.sa; Abdulaziz Alqarni - lgarniab@ngha.med.sa; Turki Elarjani - elarjani@gmail.com; Ala Arab - la_arab@yahoo.com; Jamal M. Abdullah - drjamael.abbullah@gmail.com; Abdulaziz Oqalaa Almubarak - aalmubarak89@gmail.com; Munzir Abbas - limonzir2008@yahoo.com; Ibtesam Khairy - btesamk2016@gmail.com; Wedad H. Almadani - adanithw@gmail.com; Mohammed Alowhaibi - ohaibidr@yahoo.com; Abdulaziz Alrifi - larifi100@hotmail.com; Ahmed Alkhani - lkhaniah@ngha.med.sa; Sami Khairy - rsami2009@hotmail.com

*Corresponding author:
Ali Alkhaiyary,
College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia.
alkhaiyary@hotmail.com

ABSTRACT

Background: The optimal timing for performing cranioplasty and its effect on functional outcome remains debatable. Multiple confounding factors may come into role; including the material used, surgical technique, cognitive assessment tools, and the overall complications. The aim of this study is to assess the neurological outcome and postoperative complications in patients who underwent early versus late cranioplasty.

Methods: A retrospective cohort study was conducted to investigate the neurological outcome and postoperative complications in patients who underwent cranioplasty between 2005 and 2018 at a Level I trauma center. Early and late cranioplasties were defined as surgeries performed within and more than 90 days of decompressive craniectomy, respectively. The Glasgow Outcome Score (GOS) and modified Rankin scale (mRS), recorded within 1 week of cranioplasty, were used to assess the neurological outcome.

Results: A total of 101 cases of cranioplasty were included in the study. The mean age of the patients was 31.4 ± 13.9 years. Most patients (n = 86; 85.1%) were male. The mean GOS for all patients was 4.0 ± 1.0. The mean mRS was 2.2 ± 1.78. Hydrocephalus was noted in 18 patients (early, n = 6; late, n = 12; P = 0.48). Seizures developed in 28 patients (early, n = 12; late, n = 16; P = 0.77).

Conclusion: The neurological outcome in patients who underwent early versus late cranioplasty is almost identical. The differences in the rates of overall postoperative complications between early versus late cranioplasty were statistically insignificant. The optimal timing for performing cranioplasty is mainly dependent on the resolution of cerebral swelling.

Keywords: Bone flap, Comparison, Glasgow Outcome Scale, Modified Rankin scale

INTRODUCTION

Although cranioplasty is a common neurosurgical procedure, it carries a high complication rate. The complication rates of cranioplasty may reach up to 34%. These complications include...
infection, hygroma, hydrocephalus, seizures, reoperations, intracranial hemorrhage, bone resorption, flap depression, and wound dehiscence. The factors that may increase or contribute to postoperative complications depend on patients' demographics, comorbidities, surgical procedures, and the underlying disease.\cite{1,8,10,20,26}

Considering the high complication rates of cranioplasty, it is necessary to compare the neurological outcome relative to the timing of cranioplasty after decompressive craniectomy (DC). The purpose of the present study is to assess the neurological outcome and postoperative complication rates among patients who underwent early versus late cranioplasty at a major Level I trauma center.

MATERIALS AND METHODS

Patients' eligibility and study setting

This is a retrospective cohort study, reviewing the neurological outcome and postoperative complications, in cranioplasty patients. Data were collected for all eligible cranioplasties performed between January 2005 and December 2018 at King Abdulaziz Medical City, Riyadh, Saudi Arabia. King Abdulaziz Medical City is a Level I trauma center serving Riyadh region and receives referrals from all over the country. King Abdulaziz Medical City was one of the main contributors to DC in diffuse traumatic brain injury (TBI) (DECRA Trial).\cite{18}

All patients who underwent cranioplasty, preserved in the abdominal pocket, during the specified period were included in the study. The exclusion criteria were; patients with congenital cranial defects repaired by cranioplasty, patients who had nonautologous cranioplasty, and patients who had more than 50% of the defect replaced with nonautologous bone even in the presence of his/her bone. In addition, all patients who did not have documented primary outcome postoperatively or on follow-up visits were excluded from the study.

Data collection

Data were retrieved from the archives of the neurosurgery department using two distinct methods; medical record files from 2005 to 2015 and the hospital’s electronic system from 2016 to 2018. Data included patients' demographics (age, gender, and body mass index [BMI]) and postoperative complications (hydrocephalus, hygroma, seizure, sunken flap syndrome, and long-term mortality). The primary indications for performing DC were TBI and malignant cerebral infarction. Comorbidities refer to the confirmed diagnosis of diabetes, hypertension, or cancer. Early and late cranioplasties were defined as surgeries performed within and more than 90 days of DC, respectively.

Long-term mortality was defined as death after 6 months of cranioplasty. Figure 1 illustrates the month in which cranioplasty was performed after DC for all patients.

The Glasgow Outcome Score (GOS) and modified Rankin scale (mRS) were calculated to assess the neurological outcome. The GOS and mRS were recorded within 1 week of performing cranioplasty. The GOS is scored as follows: (1 = Death), (2 = Persistent vegetative state), (3 = Severe disability), (4 = Moderate disability), and (5 = Good recovery).\cite{20} The mRS is scored as follows; (0 = No symptoms), (1 = No significant disability despite symptoms), (2 = Slight disability), (3 = Moderate disability), (4 = Moderately severe disability), (5 = Severe disability), and (6 = Dead).\cite{26}

Statistical analysis

Data were coded and entered into IBM SPSS (version 23, IBM Corporation, Armonk, New York, United States). Descriptive statistics were performed to present categorical data as frequencies and percentages. Mean and standard deviation were calculated for numerical variables including; age, GOS, mRS, BMI, and intensive care unit stay. The independent sample T-test was performed to calculate the mean differences in numerical data between early versus late cranioplasty. The Chi-square test was performed to assess the association between categorical data and the timing of cranioplasty. The statistical significance level of the P-value was set at 0.05.

Ethical considerations

Ethical approval was obtained from the Institutional Review Board at King Abdullah International Medical Research Center (KAIMRC), Ministry of National Guard - Health Affairs (NGHA), Riyadh, Saudi Arabia. Patients' identities were kept concealed and deidentified. The study was noninterventional and retrospective in nature.

RESULTS

A total of 101 cases of autologous cranioplasty were included in the study. The mean age of the patients was 31.4 ± 13.9 years. The duration of follow-up for all patients following cranioplasty was 474.3 ± 649.1 days. The mean GOS for all patients was 4 ± 1. The mean mRS was 2.2 ± 1.78. Most patients (n = 86; 85.1%) were male. The mean BMI was 24.0 ± 6.0 kg/. Most cranioplasty cases were performed late (n = 60; 59.4%). Approximately one-quarter of the patients (n = 26; 25.7%) required external ventricular drainage (EVD) insertion. A total of 19 patients (18.8%) were committed to shunt dependency surgery, that is, ventriculoperitoneal shunt. Table 1 outlines the demographics of all patients who underwent autologous cranioplasty.
Among the cohort who underwent early cranioplasty, most decompressive craniectomies (n = 32; 78%) were performed within 24 h of admission. A total of 23 (56%) cases of decompressive craniectomies were right sided in the early cranioplasty group. TBI was the indication to perform DC in around two-thirds (n = 26; 63.4%) of the patients. In contrast, in the late cranioplasty cohort, a total of 14 (23.3%) patients underwent DC after 24 h of presentation to the emergency department. A total of 9 (15%) patients underwent bifrontal DC. The most frequent indication of DC was TBI (n = 38; 63.3%). [Table 2] compares the characteristics of DC between early versus late cranioplasty.

The mean age of patients who underwent early versus late cranioplasty was 32.0 ± 14.9 and 31 ± 13.3 years, respectively (P = 0.71). The mean BMI in early cranioplasty was 22.9 kg/m² as opposed to 24.9 kg/m² in late cranioplasty. The mean GOS for patients who underwent early and late cranioplasty was 4.1 ± 1.0 and 4.0 ± 1.0, respectively (P = 0.64). The mean mRS for patients with early cranioplasty was 2.2 ± 1.7. Patients who underwent late cranioplasty had an average mRS of 2.3 ± 1.7. [Table 3] compares the average of continuous variables in relation to cranioplasty timing.

Hydrocephalus was identified in a total of 18 patients (early, n = 6; late, n = 12; P = 0.48). Hygroma developed in three patients (early, n = 2; late, n = 1; P = 0.56). A total of 28 patients presented with seizures postoperatively (Early, n = 12; Late, n = 16; P = 0.77). Sunken flap syndrome was noted in three patients (early, n = 0; late, n = 3; P = 0.29). Long-term mortality was encountered in two patients (early, n = 1; late, n = 1; P = 0.78). [Table 4] outlines the details of the bivariate analysis of cranioplasty timing against postoperative complications.

**DISCUSSION**

The present study investigated the association of the neurological outcome and postoperative complications relative to the timing of cranioplasty at a Level I trauma center. The overall postoperative complication rates between patients who underwent early versus late cranioplasty were statistically insignificant. The neurological outcome, assessed by the mRS and GOS, was not affected by cranioplasty timing. The P-values in the subgroups, early versus late, were statistically insignificant. In our institutional experience, the optimal timing for performing cranioplasty is dependent on the resolution of cerebral swelling.
Although the definition of early cranioplasty varies in the literature, early cranioplasty is commonly set at 90 days after DC. Therefore, in the present study, the 90-day cutoff definition was applied. As a result, patients were classified into two groups. All bone flaps after DC were implanted in subcutaneous abdominal pockets in the present study. In our practice, bone flaps are fixated using miniplates with excellent cosmetic results. While some institutions have abandoned autologous implantation of bone flaps, preservation of bone flaps in abdominal pockets can be safely performed with satisfactory outcomes. In addition, being a trauma center, the majority of our patients (≈2/3) had severe TBI, leading to malignant cerebral edema. Therefore, it is noteworthy to mention that the mRS and GOS are expected to slowly improve overtime after DC. As a result, the mRS and GOS were recorded after cranioplasty and not after DC.

Surgical site infection is one of the main risks complicating cranioplasty and has a significant impact on the reported outcome and patient's recovery. We recently published a paper with a cohort of our patients who underwent cranioplasty from a previous study to be associated with increased infection rates. It has been reported in a previous study that the timing of cranioplasty is not associated with increased risk of infection. Several systematic reviews compared early (<3 months) versus late (>3 months) cranioplasty in regard to the infection rate. In a systematic review of Yadla et al., the rate of infection in early versus late cranioplasty was statistically insignificant. The effect of timing on the rate of infection in cranioplasty is still debatable.

### Table 2: Characteristics of decompressive craniectomy between early versus late cranioplasty.

| Variable                  | Timing* | Early (n=41) | Late (n=60) | P-value |
|---------------------------|---------|--------------|-------------|---------|
|                          |         | n  %        | n  %        |         |
| Time to decompressive craniectomy (h) |          |             |             |         |
| <24                       | 32      | 78          | 46          | 76.6    | 0.29    |
| >24                       | 9       | 21.9        | 14          | 23.3    |         |
| Side of decompressive craniectomy |         |             |             |         |
| Right                     | 23      | 56          | 26          | 43.3    |         |
| Left                      | 16      | 39          | 25          | 41.6    |         |
| Bifrontal                 | 2       | 4.8         | 9           | 15      |         |
| Indication of decompressive craniectomy |         |             |             |         |
| Traumatic brain injury    | 26      | 63.4        | 38          | 63.3    |         |
| Malignant cerebral infarction | 15      | 36.5        | 22          | 36.6    |         |

*Early cranioplasty is defined as surgery performed within 90 days of decompressive craniectomy.

### Table 3: Comparison between cranioplasty timing versus continuous variables.

| Variable        | Timing* | Early (n=41) | Late (n=60) | P-value |
|-----------------|---------|--------------|-------------|---------|
|                |         | Mean        | SD          | Mean    | SD     |         |
| Age            |         | 32.0        | 14.9        | 31.0    | 13.3   | 0.71    |
| Body mass index|         | 22.9        | 6.0         | 24.9    | 5.9    | 0.12    |
| Glasgow Outcome Scale |         | 4.1        | 1.0         | 4.0     | 1.0    | 0.64    |
| Modified Rankin scale |       | 2.2        | 1.7         | 2.3     | 1.7    | 0.74    |
| Follow-up duration‡ |     | 315.6      | 607.2       | 582.6   | 659.3  | 0.04    |
| Intensive care unit‡ |     | 4.7        | 7.9         | 6.8     | 13.1   | 0.35    |

*Early cranioplasty is defined as surgery performed within 90 days of decompressive craniectomy. †The significance level at <0.05. ‡The follow-up duration is calculated in days from the day of cranioplasty until the last visit to the clinic. The length of stay in the intensive care unit is calculated in days. SD: Standard deviation.

### Table 4: Analysis of cranioplasty timing against the risk of postoperative complications.

| Variable                  | Timing* | Early (n=41) | Late (n=60) | P-value |
|---------------------------|---------|--------------|-------------|---------|
|                          |         | n  %        | n  %        |         |
| Hydrocephalus              |         |             |             |         |
| No                        | 35      | 85.3        | 48          | 80      | 0.48    |
| Yes                       | 6       | 14.6        | 12          | 20      |         |
| Hygroma                   |         |             |             |         |
| No                        | 39      | 95.1        | 59          | 98.3    | 0.56    |
| Yes                       | 2       | 4.9         | 1           | 1.7     |         |
| Seizure                   |         |             |             |         |
| No                        | 29      | 70.7        | 44          | 73.3    | 0.77    |
| Yes                       | 12      | 29.3        | 16          | 26.7    |         |
| Sunken flap syndrome      |         |             |             |         |
| No                        | 41      | 100         | 57          | 95      | 0.29    |
| Yes                       | 0       | 0           | 3           | 5       |         |
| Long-term mortality†      |         |             |             |         |
| No                        | 40      | 97.5        | 59          | 98      | 0.78    |
| Yes                       | 1       | 2.5         | 1           | 1.6     |         |
| External ventricular drain |     |             |             |         |
| No                        | 29      | 70.7        | 46          | 76.6    | 0.50    |
| Yes                       | 12      | 29.2        | 14          | 23.3    |         |
| Ventriculoperitoneal shunt |     |             |             |         |
| No                        | 34      | 82.9        | 48          | 80      | 0.71    |
| Yes                       | 7       | 17          | 12          | 20      |         |

*Early cranioplasty is defined as surgery performed within 90 days of decompressive craniectomy. †Significance level at <0.05. ‡Long-term mortality is defined as death after 6 months of cranioplasty.
In the present study, the risk of postoperative hydrocephalus, necessitating EVD insertion or ventriculoperitoneal shunt dependency, between both groups was statistically insignificant. Undoubtedly, subsequent surgical procedures following cranioplasty can affect the overall neurological outcome and drastically increase the length of stay. Of note, hydrocephalus is a common complication after cranioplasty, and it was reported to be higher in patients undergoing early cranioplasty compared to patients undergoing late cranioplasty.[6,33,34,35,44] On the other side, it was shown that there is insignificant increase of hydrocephalus among patients undergoing early cranioplasty.[7] There was no significant increase in intracranial hematoma and subdural fluid collection in patients undergoing early cranioplasty.[14,37,38]

Hydrocephalus may start to develop secondarily to the disturbance in the dynamics of cerebrospinal fluid.[29] Several studies reported the incidence of hydrocephalus after cranioplasty. Some studies defined hydrocephalus as the need of ventriculoperitoneal shunt insertion.[31,35,42,49] On the contrary, other studies defined hydrocephalus as the finding of dilated ventricles on CT images with[6] or without[13] neurological deficit or poor improvement. The incidence of hydrocephalus reported by these studies was 5.6% (range 1.4–12.2%).[6,13] The early cranioplasty group had a higher incidence of hydrocephalus (7.8%) while the late cranioplasty group had an incidence of 3.6%.[29] The results of a previous study concluded that early cranioplasty (<90 days) had greater incidence of hydrocephalus than late cranioplasty (>90 days).[29]

A systematic review of Xu et al. compared early versus late cranioplasty.[44] A total of nine studies were included to investigate the overall complications, seven of which studied the infection rates.[5,6,11,14,34,35,37,49] There was no difference between early versus late cranioplasty in terms of complications. Three articles analyzed the rate of hydrocephalus.[6,34,35] Early cranioplasty patients had higher postoperative hydrocephalus rates. Four articles[6,34,35,37] analyzed intracranial hemorrhage rates and three articles analyzed subdural fluid collection rate.[34,37,38] There were no differences between intracranial hemorrhage rates and subdural hygroma rates.

Zheng et al. conducted a systematic review and a meta-analysis to investigate the effectiveness of early versus late cranioplasty.[50] Their meta-analysis included a total of 413 patients who had cranioplasty following traumatic DC.[50] In terms of postoperative complications, no difference was noted between early versus late cranioplasty.[50] This is concurring with the findings of the present study.

Seizure is a major well-established complication following cranioplasty. New-onset seizure following cranioplasty was estimated to be 5–6%.[31,39] Early seizure occurring within the first 24 h after cranioplasty comprised 37%, 16% within the 1st week, and 47% after the 1st week.[43] Yap et al. published a study in 2018 where they investigated the incidence of postcranioplasty seizure among patients who underwent cranioplasty in their institute.[47] Out of 336 patients who had no previous history of seizures, 89 patients (26.5%) had new onset seizures.[47] Similarly, in the present study, seizures developed in 27% of patients who had cranioplasty, concurring with the results of Yap et al.[47] Although seizures are one of the most serious complications after cranioplasty, their incidence in both groups (early vs. late) was statistically insignificant.

The risk of seizure among patients who underwent cranioplasty has been associated with multiple factors. Previous TBI, hemorrhagic stroke, or neurological sequelae before cranioplasty increase the risk of developing seizure.[27] Being a male, developing infection after cranioplasty, and older age have been also reported to increase the risk of seizure.[48] However, male gender and older age were shown to be independent risk factors in multiple studies[20,22,25,33,41] and increased age was associated with a higher risk of complications.[11] Bitemporal and convexity cranioplasties were also associated with seizure, but the association was not statistically significant.[48] Surgery following cranioplasty for evacuation of hematoma has been associated with increased risk of seizure, but it was also reported to be insignificant.[48]

Timing of cranioplasty has been shown to be insignificant predictor for developing seizure following cranioplasty.[31] However, other studies showed increased risk of seizure in patients who underwent late cranioplasty.[28,43] Some studies also showed the benefits of early cranioplasty in minimizing the risk of seizure.[32,40] In contrast, a systematic review concluded that seizure was more common in patients who underwent early cranioplasty compared to patients who underwent late cranioplasty.[46] Regardless of the timing of cranioplasty, the use of prophylactic antiepileptic medications was shown to decrease the risk of postoperative seizure.[46]

A systematic review by De Cola et al. showed that motor improvement occurs in the early cranioplasty group, coupled with improved other parameters, such as cognition.[18] In another study by Archavlis et al., their results were improved neurologically, including motor power if cranioplasty is performed within 7 weeks, compared to later than 7 weeks.[4] Corallo et al. in two of their studies showed that motor improvement does occur in cranioplasty, regardless of the timing.[16,17] The speculative mechanism of why motor improvement occurs is mainly due to postcranioplasty physical therapy, precluding the timing difference of cranioplasty on motor improvement. Multiple systematic studies showed the overall positive benefits of early cranioplasty on motor function, with similar side effect profile in early and late cranioplasty.[18,30]
In addition, extensive physical therapy postcranioplasty is essential to positively influence the motor component of patients. Being a major trauma center, a comprehensive rehabilitation program may be required while awaiting for cranioplasty. This serves to facilitate recovery and improve the occupational status of the patient. At our institute, all patients are referred to a physical therapy program within 48 h of admission for DC/cranioplasty to ensure early rehabilitation. Those patients are evaluated daily for motor improvement, functional capacity, and neurological outcome. In the present study, postoperative GOS and mRS between both groups were statistically insignificant, indicating a similar neurological outcome.

Finally, there are a few limitations that need to be acknowledged before interpreting the results of the current study. First, the retrospective design of the study renders it liable to selection and information bias. Second, as all patients had autologous cranioplasty, patients with nonautologous cranioplasty were excluded from the study, limiting the overall number. In addition, the risk of bone flap resorption could not be investigated as a possible postoperative complication of cranioplasty due to the variation in the measurement. However, innumerable efforts were taken to address the obstacles in the current study. Despite these limitations, the present study highlighted the importance of investigating the neurological outcome and postoperative complications from a comparative perspective.

CONCLUSION

The neurological outcome in patients who underwent early versus late cranioplasty is almost identical. The differences in the rates of overall postoperative complications between early versus late cranioplasty were statistically insignificant. These findings are consistent with the previous published literature. When performing cranioplasty, timing is of less significance. Therefore, other clinical parameters, influencing the neurological outcome and postoperative complications, should be taken into consideration. Further multicenter, prospective studies investigating the neuropsychological outcome pre/postoperatively in relation to cranioplasty timing are required.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Conflicts of interest

There are no conflicts of interest.

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