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Factors Affecting Optimal Time of Cranioplasty: Brain Sunken Ratio

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Objective: After a rigorous management of increased intracranial pressure by decompressive craniectomy (DC), cranioplasty (CP) is usually carried out for functional and cosmetic purposes. However, the optimal timing of CP remains controversial. Our study aims to analyze the relationship between the optimal timing of CP and the post-operative complications.
Methods: From January 2013 to December 2015, ninety patients who underwent CP in a single institution were analyzed. We set the independent variables as follows: 1) patient characteristics; 2) the time interval between the DC and CP; 3) operation time; 4) anesthesia time; and 5) pre-operative computed tomography (CT) findings such as a degree of sunken brain by ratio of A (the median length from scalp to midline) to B (the length from midline to inner table of skull at this level). The dependent variables of this study are the event of post-operative complications.
Results: The overall complication rate was 33.3%. There was no statistical significance in the time interval between the DC and CP in the groups with and without complications of CP (p=0.632). However, there was a significant statistical difference in the degree of sunken brain by ratio (A/B) between the two groups (p<0.001).
Conclusion: From this study, we conclude that it is better to determine the optimal timing of CP by the pre-operative CT finding than by the time interval between the DC and CP. Hereby, we suggest a potentially useful determinant of optimal timing of CP.

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KEY WORDS: Complication · Cranioplasty · Decompressive craniectomy.

Introduction

Decompressive craniectomy (DC) is often performed as a potential life-saving procedure in patients suffering from elevated intracranial pressure (ICP) because of brain swelling due to traumatic brain injury (TBI), cerebral infarction, subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), and for other reasons. Though DC is increasingly performed, its efficacy is still highly controversial.[5,15-18,24] After DC, cranioplasty (CP) has been performed universally as a protective and cosmetic procedure. And CP has been reported to facilitate neurological recovery and to improve cerebral blood flow (CBF), cerebrospinal fluid (CSF) hydrodynamics, and metabolic activity after DC.[12] On the other hand there are often complications such as hemorrhage, wound problem, infection, CSF leaks, in patients who underwent a CP.

Many neurosurgeons questioned the traditional delayed timing of CP (3–6 months after DC) and tried to explore the advantages of cranial repair at an early stage (1–3 months after DC) in terms of complications and neurological function outcomes.[3,9,19] Nevertheless, the optimal timing of CP remains controversial. The aim of this study is to measure the proper CP timing based on the degree of brain swelling

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after DC rather than a simple passage of time.

Materials and Methods

Study design

From January 2013 to December 2015 we performed 90 CP procedures in patients who previously underwent DC. We set the independent variables as follows: 1) patient characteristics; 2) the time interval between the DC and CP; 3) operation time; 4) anesthesia time; and 5) pre-operative computed tomography (CT) findings such as a degree of sunken brain by ratio of A (the median length from scalp to midline) to B (the length from midline to inner table of skull at this level) at the CT section of maximum size craniectomy (Figure 1). The dependent variables of this study are the event of post-operative complications such as hemorrhage, infection, abnormal wound healing, CSF leakage, hygroma, and hydrocephalus.

Clinical management

Autologous bone graft was used whenever available. Bone flaps were cryo-preserved in the hospital bone bank after DC and were immersed in povidone iodine solution for 30 minutes before replacement. When no bone graft was available, for example, when a patient was transferred from other institutions, acrylic or titanium plate was used. Prophylactic intravenous cefotetan (2 g) was given on induction.

FIGURE 1. Computed tomography (CT) of brain before the cranioplasty. The brain sunken ratio is calculated as the ratio of A (the median length from scalp to midline) to B (the length from midline to inner table of skull at this level) at the CT section of maximum size craniectomy.

Statistical analysis

Data are expressed according to the properties of the variable. Continuous variables are presented as mean and standard deviation. Categorical variables are presented as frequency and percentage. In order to compare two groups, we performed the two-simple *t*-test or chi-square test (Fisher's exact test) as appropriate. Logistic regression analysis was used to identify the factors to predict complications and the result were expressed as odds ratio (OR) with 95% confidence interval (CI). A *p*-value less than 0.05 was considered statistically significant and all statistical analyses were conducted using SPSS (version 21; IBM Corp., Armonk, NY, USA).

Results

Out of 90 participants, 30 cases reported complication, reaching the overall complication rate at 33.3%. Patient characteristics of the complication group and the non-complication group, the time interval between the DC and CP, operation time, anesthesia time, and pre-operative CT findings are summarized in Table 1. Complications were observed in 30 patients, including hemorrhage, infection, wound problem, CSF leakage, hygroma, and hydrocephalus. Of the patients with complications, 17 patients had post op hemorrhage, and 7 patients received re-opration. The 8 patients had a wound problem and two of them underwent infection and received re-operation. The hydrocephalus was observed in 2 patients, only one patient was received ventriculoperitoneal (VP) shunt insertion later. CSF leakage was observed in 2 patients but no CSF leakage was observed without special procedures such as lumboperitoneal (LP) insertion. Of the 90 patients, 83 received CP with autologous bone and bone repositioning occurred in 3 of the patients, and autologous bone was changed to artificial bone. It was concluded that the group who had a history of liver disease and who underwent DC because of ICH experienced a higher rate of complication and this is statistically significant. Moreover, the mean sunken ratio was 0.909 and the difference of this measure between the group who suffered complication and who didn't was statistically significant as the ratio from the earlier group being 0.809 and close to 1 (0.959) from the latter group. It was also observed that midline shifting was more severe with the group who suffered complication but the difference deemed to be statistically insignificant as the figure was at -1.337 compared to the other group who showed -1.201.

The difference in DC-CP interval days observed from both groups did not appear statistically significant although average days of the group with no complication was shorter. (122.9 vs. 139.1). Patients who underwent CP within two months suffered less complication rate (17.4%) compared to those undergoing late procedures post 2 months. Similarly, the complication rate was lower when CP was performed within 3 months versus after 3 months but the difference was not statistically significant. It has also been demonstrated that patients who underwent CP within 2 months suffered less complication rate compared to those undergoing within 3 months. Table 2 summarizes that in case of complications from CP (hemorrhage, infection, wound problem, CSF leakage, hygroma and hydrocephalus), out of DC-CP interval, operative time, anesthesia time, Midline shifting, and sunken ratio, only sunken ratio was associated with increased risk of hemorrhage. Table 3 shows that based on a multi-variated analysis, only in the case of DC performed by spontaneous ICH and sunken ratio statistically different outcome.

Discussion

CP is performed after DC, which saves the lives of patients

TABLE 1. Comparison of clinical factors according to post-operative complications

	Total	Without complication (n=60)	With complication (n=30)	*p*-value
Gender (male)	52 (57.8%)	33 (63.5%)	19 (36.5%)	0.451
Age	52.6 (18.6)	52.3 (19.0)	53.1 (18.1)	0.855
History				
Hypertension	35 (38.9%)	21 (60.0%)	14 (40.0%)	0.285
Diabetes mellitus	15 (16.7%)	10 (66.7%)	5 (33.3%)	1.000
Liver disease	3 (3.3%)	0 (0.0%)	3 (100.0%)	0.035*†
Alcohol	17 (18.9%)	12 (70.6%)	5 (29.4%)	0.703
Smoking	15 (16.7%)	10 (66.7%)	5 (33.3%)	1.000
Antiplatelet agent	8 (8.9%)	5 (62.5%)	3 (37.5%)	1.000*
Etiology				
Disease	35 (38.9%)	22 (62.9%)	13 (37.1%)	0.541
SAH	17 (18.9%)	14 (82.4%)	3 (17.6%)	0.128
ICH	9 (10.0%)	2 (22.2%)	7 (77.8%)	0.006*†
Infarction	10 (11.1%)	6 (60.0%)	4 (40.0%)	0.726*
TBI	55 (61.1%)	38 (69.1%)	17 (30.9%)	0.541
SDH	36 (40.0%)	25 (69.4%)	11 (30.6%)	0.648
EDH	8 (8.9%)	6 (75.0%)	2 (25.0%)	0.714*
ICH	10 (11.1%)	7 (70.0%)	3 (30.0%)	1.000*
Hemicraniectomy	87 (96.7%)	58 (66.7%)	29 (33.3%)	1.000*
Bifrontal craniectomy	3 (3.3%)	2 (66.7%)	1 (33.3%)	1.000*
Pre-OP VP shunt	10 (11.1%)	7 (70.0%)	3 (30.0%)	1.000*
DC-CP interval (day)	133.7 (150.7)	139.1 (170.3)	122.9 (102.2)	0.632
DC-CP interval (before 2 month)	23 (25.6%)	19 (82.6%)	4 (17.4%)	0.060†
DC-CP interval (before 3 month)	50 (55.6%)	35 (70.0%)	15 (30.0%)	0.453
OP time (min)	150.1 (44.9)	151.5 (45.1)	147.3 (45.1)	0.678
ANE time (min)	219.8 (52.5)	223.0 (54.6)	213.4 (48.2)	0.418
Pre-OP CT finding				
Midline shifting (mm)	−1.337 (2.78)	−1.201 (2.61)	−1.609 (3.11)	0.514
Sunken ratio‡	0.909 (0.18)	0.959 (0.17)	0.809 (0.16)	<0.001†
Using artificial bone	7 (7.8%)	4 (57.1%)	3 (42.9%)	0.682*
Intra-OP V-P shunt	3 (3.3%)	2 (66.7%)	1 (33.3%)	1.000*

*Fisher's exact test, †statistical significance based on two-sample *t*-test or chi-square test ($p < 0.05$), ‡ratio of A (the median length from scalp to midline) to B (the length from midline to inner table of skull at this level). OP: operation, SAH: subarachnoid hemorrhage, ICH: intracranial hemorrhage, TBI: traumatic brain injury, SDH: subdural hemorrhage, EDH: epidural hemorrhage, VP: ventriculoperitoneal, DC-CP: decompressive craniectomy to cranioplasty, ANE: anesthesia, CT: computed tomography

TABLE 2. Subtype of complications after cranioplasty

	Hemorrhage (n=17)	Infection (n=2)	Wound problem (n=8)	CSF leakage (n=2)	Hygroma (n=6)	Hydrocephalus (n=2)
DC-CP interval	0.847	0.600	0.616	0.783	0.377	0.905
OP time	0.968	0.478	0.717	0.897	0.187	0.615
ANE time	0.985	0.539	0.816	0.760	0.085	0.539
Midline shifting	0.234	0.454	0.892	0.494	0.751	0.494
Sunken ratio†	<0.001*	0.214	0.693	0.969	0.439	0.217

*Statistical significance based on two-sample *t*-test or chi-square test ($p<0.05$), †ratio of A (the median length from scalp to midline) to B (the length from midline to inner table of skull at this level). DC-CP: decompressive craniectomy to cranioplasty, OP: operation, ANE: anesthesia, CSF: cerebrospinal fluid

TABLE 3. Multivariated analysis according to independent variables

	OR (95% CI)	*p*-value
ICH	6.777 (1.127–40.758)	0.037*
SAH	0.473 (0.102–2.182)	0.337
DC-CP interval 2 month	2.832 (0.600–13.356)	0.188
DC-CP interval 3 month	1.124 (0.354–3.563)	0.843
Antiplatelet medication	0.418 (0.066–2.644)	0.354
Sunken ratio†	0.007 (0.000–0.198)	0.004*

*Statistical significance based on ($p < 0.05$), †ratio of A (the median length from scalp to midline) to B (the length from midline to inner table of skull at this level). OR: odds ratio, CI: confidence interval, ICH: intracranial hemorrhage, SAH: subarachnoid hemorrhage, DC-CP: decompressive craniectomy to cranioplasty

suffering from elevated ICH due to brain swelling caused by various reasons. Though the indications for and the clinical value of DC are still under research, the procedure it is still performed widely across the world.[23,27] Consequentially, CP is also being increasingly performed. While CP was initially considered to play protective and cosmetic roles only, recent studies have recognized that CP provides neurological function improvements.[4,8,14] In addition, DC is known to bring about changes in oxygen and glucose, which affect the normal cerebral function and the metabolic rate, the velocity of cerebral metabolism, and the regional CBF.[11] Theoretically, therefore, it can be expected that a performance of CP can reconstitute all of the changes mentioned above and improve patients' overall neurological state.[6] It has also been proven that CP can improve cardiovascular-related functions, which consequently expedites the blood flow velocities in the ipsilateral middle cerebral artery and internal carotid artery and ultimately increase the CBF.[11] However, the complication rate of CP is higher than other types of intracranial operations. The overall complication rate after CP was 33.3% in our study. Chang and associates[7] recently published a series with an overall complication rate of 16% following CP. Gooch and colleagues[13] reported complications after CP requiring surgical treatment in 16 of 109 patients (14.7%). CP has many complications, including central nervous system infection, hydrocephalus, intracranial hematoma and subdural fluid collection, which will prolong the hospitalization, lead to unfavorable prognosis and even death.[10] It was also found that the risk of post-operative wound infection was higher particular in the case of CP performed after a TBI. This is because TBIs are commonly admitted with injuries to the skin leading to secondary infections or contamination.[22]

As mentioned already, CP is a necessary post-DC procedure. But because of its high complication rate, many studies have been conducted on the factors that influence the occurrence of post-CP complications.

Quite a number of researches argue that implant materials have an important role in post-CP complications.[25] Normally, using patients' own bones is preferred as they yield better cosmetic results, have a low risk of immunological rejection, and have bone reconstruction and blood vessel revascularization effects.[1] Nevertheless, because autologous bone flap, CP still has a high rate of complications in case of TBI patients,[21] new synthetic materials, though expensive, such as three-dimensional (3D) printing using computer-aided design technologies have been developed to offer excellent cosmetic results.[2] Moreover, from a meta-analysis perspective, there is no significant difference in the infection rate between autograft and allograft.[26]

Studies are also in full-swing about the relationship between the time of CP performance and post-operative complications. Some recent reports claim that an early CP is better for patients.[3] According to the study of Liang et al.[20] early CP is safe and leads to neurological improvements. But the study lacked detailed information in relation to the rate of complications after intracranial surgeries. The study of Chang et al.[7] reported that the complication rate was lower for the group that received early CP. Chang et al.[7] added that the craniotomy conducted in the early stages did not significantly increase the rate of complications, and that no correlation between the timing of CP and post-operative complications could be found.[13] In other words, the optimal timing of CP still remains a controversial topic.

Existing studies defined three months as the cutoff time for early CP and delayed CP. But our study determined two cutoff times; it studied patients who underwent CP within two months and those within three months. The rate of complications for patients who underwent CP within two months after DC was 17.4%. While this figure was lower than the figure for the group of patients who underwent CP after two months, it was not statistically significant. The rate of complications for patients who received CP within three months was 30.0%. While this figure was also lower than the figure for patients who underwent CP after three months, it was not statistically significant. By comparing the two cutoff groups, we found that those who received CP within two months had a lower complication rate than that of three months. In other words, the rate of complication was lower for the group patients who received CP early.

Unlike previous studies, this study took into consideration not only the time DC-CP interval day arithmetically but also pre-operative CT findings such as the brain's midline shifting and sunken ratio in order to come up with the optimal timing of CP. The mean midline shifting was -1.201 mm and -1.609 mm for the complication group and the non-complication group, respectively. While the result showed that a lower midline shifting was related to a lower rate of complications, it was the not statistically significant.

Also, the mean sunken ratio was 0.959 and 0.809 for the non-complication group and the complication group, respectively, which was statistically significant. The result showed that a sunken ratio to 1 (at least 0.909) led to a lower rate of complications, which was statistically significant. This result suggests complications can be reduced if CP is conducted when the pre-operative CT shows that there is low level of sinking in the brain. However, in other complications except for postoperative hemorrhage, no statistical significance was found with brain sunken ratio. This result suggests that perhaps the optimal CP timing is when the CT scan shows that there is no severe sinking of the brain, rather than simply a few days after DC, as the speed of brain's sinking differs from patient to patient. The rate of complications, especially postoperative hemorrhage, may effectively be reduced if CP is performed when the sunken ratio is close to 1. Naturally, a continuous brain CT would have to be conducted on the patients after DC.

The limitations of this study are as follow: First, the study was retrospective, meaning that the patient selection was not based on randomization. Second, patients in this study cannot represent all patients universally as the study was conducted on patients in a single center. A larger-scale study that can represent the whole thus needs to be conducted in the future to supplement this shortcoming. Third, the sunken ratio which was used as a tool to measure the level of brain swelling was not calculated 3D but 2D. Therefore, finding the volume factor by analyzing 3D CT scan and using that in future studies would yield results with a broader representation.

Conclusion

Despite many existing studies, the optimal timing of CP performance is still a controversial topic. The findings of this study leads to the assumption that making the decision on the optimal CP timing based on not simply the DC-CP interval days but on the sunken ratio is effective in decreasing post-CP hemorrhagic complication. Identify the indications and the clinical value of sunken ratio through a larger scale study that can represent the whole would be needed in the future.

■ The authors have no financial conflicts of interest.

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