

Optimal Timing and Complications of Cranioplasty: A Single-Center Retrospective Review of 109 Cases

Young-Mook Kim, Taejoon Park, Sang-Pyung Lee, Jin-wook Baik, Kyoung-Soo Ryou, Seong-Hwan Kim

Department of Neurosurgery, Halla Hospital, Jeju, Korea

Received: September 29, 2020

Accepted: October 7, 2020

Corresponding Author:

Tae-Joon Park, M.D.

Department of Neurosurgery,
Halla Hospital, 65, Doreong-ro,
Jeju, Korea

Tel: +82-64-740-5412

Fax: +82-64-740-5676

E-mail: Viamorti@hanmail.net

Objective

Cranioplasty is the surgical repair of decompressive craniectomy. Although cranioplasty is performed for cosmetic and functional benefits, and is a simple surgical procedure, it is usually associated with a relatively high complication rate, ranging from 10% to 50%.

Methods

This was a retrospective review of 109 patients who had undergone a cranioplasty over a period of 10 years. At our institution, the time period were classified into very early (<30 days), early (between 30-60 days), late (between 60-90 days), and more late (>90 days) interventions based on the time period before cranioplasty. We evaluated postoperative complications and the relationship between their occurrence and the timing of the cranioplasty.

Results

The overall complication rate in this study was 44%. Hydrocephalus was the most common complication (34.9%), followed by infections (6.4%), hematoma (4.6%), and others such as seizure (0.9%) and headache (0.9%). Infections were the only complications whose incidence increased with the early timing of the cranioplasty. The incidence of hematoma increased with the late timing of cranioplasty and was probably a result of its prolonged operation time ($p=0.007$). The incidence of hydrocephalus was not associated with cranioplasty timing but the indication of craniectomy and the number of revision surgeries performed before cranioplasty. ($p=0.046$)

Conclusion

Cranioplasty is associated with high rate of complication and the incidence of the complications vary with the timing of the operation. There are many advantages of early cranioplasty that can be redeemed if strict measures are taken, while performing the surgery, to prevent postoperative infections.

Keywords: Cranioplasty; Complication; Optimal Timing; Infection; Hydrocephalus

INTRODUCTION

Cranioplasty is the surgical procedure used to repair surgical

skull defect secondary to decompressive craniectomy. When a medically refractory intracranial hypertension occurs (such as brain trauma, spontaneous intracranial hemorrhage, malignant in-

farction, injuries with a cerebral edema like subdural hemorrhage or epidural hemorrhage), decompressive craniectomy is known to be the therapeutic strategy that is effective in helping the patients survive. Decompressive craniotomy helps to control intracranial pressure and maintain cerebral perfusion^{1,13,20,30}.

Cranioplasty is performed to protect the brain from mechanical assault, for cosmetic reasons, and to prevent complications of skull defect like the sinking skin flap syndrome^{2,11,18}. It is known to improve cerebrospinal fluid dynamics and it sometimes accelerates neurologic recovery^{1,11,15,17}.

Cranioplasty can be divided into early cranioplasty and late cranioplasty depending on its timing after the decompressive craniectomy. Although there are small differences, a time of 2 or 3 months is used as a reference to distinguish between early and late timings in most cases^{8,11,15,19,20,24,26,30}. Depending on the situation, there are cases in which the surgery is performed very early (< 1 month) or ultra-early (< 14 day)²⁴. However, there is no clear-cut consensus on the timing of the cranioplasty¹³. The timing reference used depends on the trends of the implications of the timing of the surgery.

Although cranioplasty is a relatively simple neurosurgical procedure, the incidence of complications is known to be very high, reaching up to 10% to 50%^{1,11,20,24}. The types of the complications vary; they include infections, intracranial hemorrhage, hydrocephalus, seizure, bone resorption, and extra-axial fluid collection^{18,20,24}. According to some reports, the types of complications differ depending on the timing of the surgery^{13,15,20,24}.

There have been attempts to determine the appropriate timing of the surgery by investigating the relationship between the timing of the surgery and the complications^{20,24,27}. Some studies claim that early cranioplasty induces more complications and that late cranioplasty is more advantageous^{10,27}, while others have grouped frequent complications per timing period by categorizing the timing of each complication^{15,24}. Many studies are recently suggesting that early cranioplasty is better by stating that there is no strong correlation between the timing of the cranioplasty and complications^{19,30}. These studies instead emphasize on the benefits of early cranioplasty^{1,7,9,11,16,20,28,30}.

Mostly, early cranioplasty was performed in this study. This study aimed to examine the complications of early cranioplasty and to compare and analyze the results with previous findings.

MATERIALS AND METHODS

This study compared all patients who had a cranioplasty procedure after undergoing decompressive craniectomy for various reasons, during the 10-year period between June 2010 and June 2020. Indications for the decompressive craniectomy were malignant ce-

rebral infarcts (27 cases, 24.8%), subarachnoid hemorrhage (SAH) due to aneurysmal rupture (25 cases, 23%), intracerebral hemorrhage (7 cases, 6.4%), arteriovenous malformations (2 case, 1.8%), and traumatic brain injury (48 cases, 44.0%). Comparative analyses were also performed between the complications of each indication. As earlier reported, the main complications after cranioplasty included symptomatic hemorrhage, bone flap infection, symptomatic hygroma, and symptomatic hydrocephalus requiring implantation of a ventriculoperitoneal (VP) shunt^{1,18}. In this study, the predictors of the frequent complications were identified by using data collected retrospectively while focusing on the aforementioned complications.

Data collection

This study included all patients who underwent a cranioplasty after undergoing decompressive craniectomy in the author's hospital during the above mentioned 10-year period. The patients' evolution reports and radiologic data were retrospectively collected in this study. The patients' demographic characteristics, the etiology of the brain injury, the timing of cranioplasty, and the clinical outcome were analyzed to bring out the frequency of the complications as function of these factors. Outpatient records were used for patients who were discharged or transferred. The patients' history and laboratory data were also used. The maximum follow-up duration was established at 2 months and the clinical outcomes and surgical outcomes at 2 months were investigated.

Cranioplasty timing was divided into early timing and late timing using the benchmark of 60 days post-craniectomy^{8,20,26,27}. A cranioplasty that was performed before 30 days was considered as a very early timing for cranioplasty. Furthermore, a cranioplasty performed after 90 days was considered as more late timing for cranioplasty.

The preparation and processing for the cranioplasty bone flap were as follows: The bone material was used was categorized as autologous bone or synthetic prosthesis. In accordance with the Bone Bank Management Regulations, autologous bones were processed at a constant temperature of -80°C and stored frozen in the bone bank (ultra-low temperature freezer, MDF-US2V, SANYO, JAPAN). It was thawed from one hour before the cranioplasty. Then, it was submerged into pure povidone and then mixed with saline and vancomycin for 15 minutes each before being washed to be used in the cranioplasty²⁶.

In cases where the use of a synthetic bone flap was involved, the artificial bone flap arrived from the manufacturer to the hospital 2 days beforehand. This artificial bone flap was sterilized in a vacuum speed autoclave (HS-1606VD) machine set at 134°C for twenty minutes. Further, one hour before the surgery, it was sub-

merged into pure povidone and then mixed with saline and vancomycin for 15 minutes each before being washed to be used in the cranioplasty.

Clinical outcome

To assess the clinical outcomes, 2 widely used scales were used: the Glasgow Coma Scale (GCS) and the GOS. The patient's condition immediately before the cranioplasty was assessed using the 2 scales. Further, 2 months after the surgery, the 2 scores were re-evaluated and compared to examine the changes in each score⁷.

Surgical outcome

The surgical outcomes after the cranioplasty were analyzed while focusing on the complications that occurred after the surgery. Comparative analyses were performed for complications that are frequent after cranioplasty and require additional management. These included hydrocephalus, infection, and hematoma. Complications such as seizure and headache were included as "Others." In particular, subdural hygroma was similar to external hydrocephalus and thus was included under hydrocephalus. The frequencies and prevalence rates of these complications were comparatively analyzed with different variables such as the timing of the surgery and the indication of the surgery.

Statistical analysis

Statistical analysis was performed using the software IBM SPSS Statistics 21.0 (IBM Corporation) and results with $p < 0.05$ were considered statistically significant. Additionally, chi-squared analysis was performed to test for associations with complications via meta-analysis.

Because this was an observational study, formal approval was given by the institutional Ethical Review Board of our hospital and patients' consent was not required.

RESULTS

Patients' characteristics

A total of 109 consecutive patients underwent a cranioplasty between June 1, 2010 and June 1, 2020. The cranioplasties were performed after a median delay of 49 days (7–167 days) post decompressive craniectomy. The indications of decompressive craniectomy in these patients were malignant cerebral infarct (24.8%), aneurysmal SAH (22.9%), traumatic brain injury (43.1%), intracerebral hemorrhage (6.4%), and arteriovenous malformation (1.8%) (Table 1).

In this study, among patients who underwent a cranioplasty, a total of 44 % (48 out of 109) had at least one complication. This

outcome was significant compared to the previously reported prevalence of complications (10-50%) in other studies. Among these complications, infection necessitating explantation of the flap comprised 6.4% (7/109), postoperative hydrocephalus requiring a shunt comprised 34.9% (38/109), postoperative hematoma requiring evacuation comprised 4.6% (5/109), and others including seizure and headache comprised 1.8% (2/109) of the cases.

Among the 109 patients, 107 (98.2%) used an autologous bone graft and 2 (1.8%) used a synthetic prosthesis bone flap. In both cases, titanium material and Polyether ether ketone material were used for performing the cranioplasty.

Clinical outcome

Concerning the GCS score, preoperative GCS score and 2-month postoperative GCS score were assessed. In general, the GCS score of all patients who underwent a cranioplasty showed a general increase from an average preoperative GCS score of 10.7 to an average postoperative GCS score of 11. Although the difference was small, the increase was greater for the late timing group (Table 1).

The average GOS score assessed 2 months after the cranioplasty showed no differences when compared to the GOS before the cranioplasty (Table 1).

Timing of cranioplasty

Among the 109 patients, 5.5% (14/109) patients corresponded to very early timing (< 30 days), 59.6% (65/109) patients corresponded to early timing (30-60 days), 22% (24/109) patients corresponded to late timing (60-90 days), and 5.5% (6/109) patients corresponded to more late timing (> 90 days). The mean time lapse between the decompressive craniectomy and cranioplasty was 49 days \pm 23 (7-167 days). There was no statistically significant association between the demographic data of the patients (age, sex, etc.) and the clinical outcomes (GCS, GOS), time of cranioplasty, type of implant, and presence of VP shunt (Table 2).

A shunt was placed to treat hydrocephalus on 30 patients. On average, the VP shunt was placed after 28 ± 31 (0-157) days after the cranioplasty.

Number of surgeries before the cranioplasty

The cases, which required additional surgeries, due to rebleeding or cerebral edema progression, after the decompressive craniectomy and before the cranioplasty, were analyzed. The average number of additional surgeries other than the decompressive craniectomy was 2.6 (range, 1–9). The relationship between the number of surgeries and the complications was examined. While there was no particular association with other complications, the prevalence of

Table 1. Characteristics of 109 patients undergoing cranioplasty after decompressive craniectomy

Character	Total (n=109)	Without complication (n=57)	Complication (n=52)	p-value
Gender (M:F) (%)	1.5 : 1	1.8:1	1.3:1	0.261
Age (Mean±SD)	52.6(±16.1)	51.7(±17.3)	53.8(±14.27)	
Underlying ds.				
HTN	31	17	14	0.604
DM	9	6	3	0.613
Etiology				
TBI	48	24	24	0.643
Infarction	27	20	7	0.062
SAH	25	11	16	0.215
ICH	7	4	3	0.930
Others	2	0	2	0.801
Timing of cranioplasty (day)	49.2(±23.1)	47.6(±25.0)	51.4(±20.1)	
Very early	14	12	2	0.028*
Early	65	36	29	0.391
Late	24	13	11	0.810
More late	6	3	3	0.656
Op time (min)	121±51.9	112.0±52.1	132.8±50.1	0.211
Op count (n)	2.7±1.2	2.4±1.0	3.1±1.4	0.087
Bone flap				
Autologous (n)	107	64	43	
Allograft (n)	2	0	2	
GCS				
Pre (mean±SD)	10.8(±2.9)	11.6(±2.5)	9.4(±3.0)	
Post (mean±SD)	11.4(±3.2)	12.4(±2.7)	10.0(±3.4)	
GOS				
Pre (mean±SD)	3.1(±1.0)	3.4(±1.0)	2.6(±0.8)	
Post (mean±SD)	3.1(±1.0)	3.4(±1.0)	2.6(±0.8)	

M: male, F: female, ds.: diseases, HTN: hypertension, DM: diabetes mellitus, TBI: traumatic brain injury, SAH: subarachnoid hemorrhage, ICH: intracerebral hemorrhage, OP: operation, min: minute, n: number of patient, GCS: Glasgow coma scale, GOS: Glasgow outcome scale, pre: pre-operative, post: post-operative. The GOS was scored as follows: 1 = dead, 2 = vegetative state, 3 = dependent and disabled, 4 = independent, 5 = return to work.

*The complication has low statistical significance at the very early timing.

Table 2. Postoperative complication rate by etiology

Variable	TBI (n=48)	Infarction (n=27)	SAH (n=25)	ICH (n=7)	Others (n=2)	All (n=109)
Age (year) (Mean±SD)	47.1±17.6	62.4±13.6	53.6±8.3	46.14±18.4	62±18.3	52.6±16.1
Meantime of CP (days)	46.6±27.5	48.51±21.4	51.64±14.9	57.85±24.8	57.5±5.0	49.17±23.9
Op time (min)	125.7±47.6	125.8±49.9	103.2±41.3	106.7±27.2	119±31.1	121.1±51.9
Complication (n, (%))	24 (50.0)	7 (25.9)	16 (64)	3 (27.5)	2 (100)	52 (47.7)
Hydro	20 (41.7)	3 (11.1)	13 (52)	1 (14.3)	1 (50.0)	38 (34.9)
Infection	3 (6.3)	2 (7.4)	2 (8.0)	0	0	7 (6.4)
Hematoma	1 (2.1)	0	1 (4.0)	2 (28.6)	1 (50.0)	5 (4.6)
Others	0	2 (7.4)	0	0	0	2 (1.8)
Time to CP						
Very early	9 (18.8)	4 (14.8)	1 (4)	0	0	14 (12.8)
Early	28 (58.3)	15 (53.6)	17 (68)	4 (57.1)	1 (50)	65 (59.6)
Late	7 (14.6)	7 (25.9)	6 (24)	2 (28.6)	1 (50)	23 (21.1)
More late	4 (8.3)	1 (3.7)	1 (4)	1 (14.3)	0	6 (5.7)

TBI: traumatic brain injury, SAH: subarachnoid hemorrhage, ICH: intracerebral hemorrhage, others: arteriovenous malformation, CP: cranioplasty, Op: operation, min: minute, n: number of patient, hydro: hydrocephalus.

hydrocephalus significantly increased with increase in the number of surgeries ($p = 0.046$) (Table 3).

Operation time

The mean operation time (duration) of the cranioplasty procedure was 121.1 ± 51.9 minutes. The relationship between the operation time and the postoperative complications was examined. There was no particular association between the operation time and the incidence of complications, even for infections ($p = 0.633$).

However, when the relationship between the timing of the cranioplasty operation and the operation time (duration) was examined, the operation time needed to perform the surgical procedure significantly increased with increased delay of the cranioplasty ($p = 0.009$) (Table 3).

Complications

Among the 109 patients who underwent cranioplasty, hydrocephalus was observed in 38 patients (32.1%). A VP shunt was placed in all the cases except for 8 patients. Among these patients, the VP shunt was placed after the cranioplasty in 23 cases and the VP shunting procedure was performed simultaneously with cranioplasty in the remaining 7 cases. For the 8 cases where the VP shunt was not placed, the surgery could not be performed because the caregivers' refused to give their consent. This was because of the relative worsening of the patients' clinical status.

Although there was no significant association between the timing of cranioplasty and hydrocephalus, traumatic brain injury (51.4%) and spontaneous arachnoid hemorrhage (31.4%) among the initial indications of decompressive craniectomy comprised 82.8% of all the cases of hydrocephalus. Furthermore, as previously stated, there was a statistically significant correlation between the number of revision surgeries before the cranioplasty and the preva-

lence of hydrocephalus. ($p = 0.046$) (Table 4.)

Postoperative infections after the cranioplasty were observed in 6 cases (5.5%). Concerning the relationship between infections and the timing of the cranioplasty, the prevalence rate of infections was higher in the cranioplasty performed in the very early and early timing groups compared to those of the other timing groups (Fig. 1). However, there were no statistical significance. Additionally, risk factors of infections that were suggested in many previous studies (3,11,25,29) (underlying diseases, systemic infection, operation time, etc.) were also investigated. No clear relationships were found (Table 4) and there were no statistically significant association found with the preoperative laboratory data (Table 5).

A revision surgery was performed due to rebleeding after cranioplasty in 4 cases (3.7%). In terms of the relationship between a hemorrhagic event and the cranioplasty timing, it was observed that later timing of the cranioplasty was associated with a greater frequency of hemorrhagic event, and this was a statistically significant finding ($p = 0.009$). There were no statistically significant associations found for other variables.

For other complications, there was 1 case each of seizure (0.9%) and of headache (0.9%). Because the numbers of cases were small for these, it was not possible to compare the differences to the cranioplasty timing.

DISCUSSION

The DECRA and RESCUEICP's randomized controlled trials^{3,19} and the DECIMAL, DESTINY, and HAMLET randomized controlled trials showed that decompressive craniectomy significantly treated intracranial hypertension and was associated with an increase in survival rates in traumatic brain injury and spontaneous ischemic or hemorrhagic stroke^{23,24,25}.

Table 3. The incidence rate of Complication and Meta-analysis results by time

Variable	Very early (<30days) (n=14, 12.8%)	Early (30-60days) (n=65, 59.6%)	Late (60-90days) (n=24, 22.0%)	More late (>90days) (n=6, 5.5%)	All (n=109)	P value (n=109)
Gender (M:F)	1.8:1	1.2:1	2.3:1	2:1	1.5:1	
Age (Mean±SD)	46.5±20.1	54.84±15.1	52.09±14.1	45.5±23.1	52.6±16.1	
Complication (n, (%))	3 (21.4)	34 (52.3)	12 (50)	3 (50)	52 (47.7)	
Hydrocephalus	2 (14.2)	26 (40.0)	8 (33.3)	2 (33.3)	38 (34.9)	0.382
Infection	1 (7.1)	5 (7.7)	1 (4.2)	0	7 (6.4)	0.849
Hematoma	0	1 (1.5)	3 (12.5)	1 (16.7)	5 (4.6)	0.058
Others	0	2 (3.1)	0	0	2 (1.8)	0.710
Mean duration (day)	21.0±6.4	42.1±8.0	68.7±7.4	113.3±27.1	49.2±23.1	
Op time (min)	99.2±38.0	115.9±46.8	124.5±45.5	115.7±27.4	121.5±51.9	0.009*

*It has statistical significance that the operation time becomes shorter as the time of operation gets earlier.

Table 4. Postoperative Complications of Meta-Analysis

Character	Hydrocephalus (n=38, 34.9%) (p-value)	Infection (n=7, 6.4%) (p-value)	Hematoma (n=5, 4.6%) (p-value)	Others (n=2, 1.8%) (p-value)	All (n=109) (p-value)
Age (year) (Mean±SD)	53.2±13.8 (0.508)	52.6±17.1 (0.702)	57.2±16.3 (0.065)	60±24.0 (0.176)	53.8±14.3 (0.438)
Sex (M:F)	1.1:1 (0.716)	0.75:1 (0.350)	1.5:1 (0.986)	1:1 (0.986)	1.3:1 (0.261)
Operation time (min)	129±59.6 (0.323)	148.1±51.8 (0.709)	103.4±29.7 (0.200)	161.5±20.5 (0.290)	119.7±52.8 (0.203)
Numbers of operation	3.2±1.4 (0.046*)	4.1±2.3 (0.151)	2.6±0.9 (0.792)	2±0 (0.543)	2.7±1.2 (0.082)
Underlying ds.					
HTN	11 (0.857)	2 (0.454)	2 (0.628)	0 (0.139)	15 (0.604)
DM	2 (0.935)	0 (0.412)	0 (0.492)	0 (0.329)	2 (0.613)
Time to cranioplasty					
<60DAYS	29 (0.530)	7 (0.418)	1 (0.007*)	2 (0.158)	39 (0.440)
<90DAYS	37 (0.947)	8 (0.509)	5 (0.146)	2 (0.581)	52 (0.762)

M: male, F: female, min: minute, ds.: diseases, HTN: hypertension, DM: diabetes mellitus, TBI: traumatic brain injury, SAH: subarachnoid hemorrhage, ICH: intracerebral hemorrhage.

*Statistically less hematoma occurred in the case of surgery before 60 days.

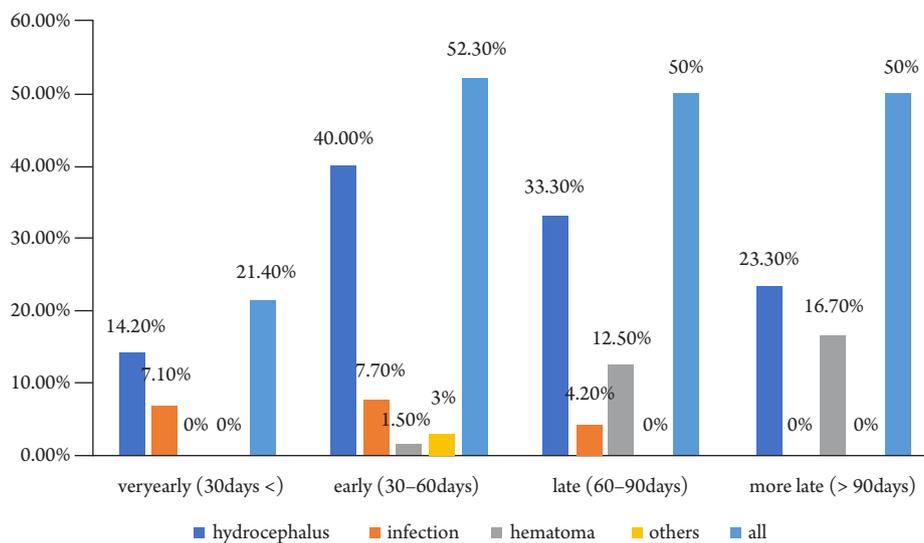


Fig. 1. The incidence rate of complications by timing (%).

The first reported cranioplasty was performed in 1668¹⁾. Thereafter, most neurosurgeons performed cranioplasty as a routine neurosurgical procedure to treat the surgical skull defect after a decompressive craniectomy¹⁰⁾. This of course is done for cosmetic reasons and to protect the brain from external mechanical insult⁶⁻⁸⁾. However, it also helps to prevent the sinking skin flap syn-

drome (a complication of cranial defect) and paradoxical herniation, which can cause coma or even death^{3,17)}. Furthermore, there are reports showing that cranioplasty also accelerates restoration of brain parameters such as cerebrospinal fluid circulation, dynamics of local cerebral blood flow, and cerebral metabolic rate of oxygen and glucose, ultimately enabling the recovery of cognitive, behav-

Table 5. Timing and Etiology and risk of preoperative Infection hematologic analysis result

Variable	WBC mean (K/ul)	ESR mean (mm/Hr)	CRP mean (mg/dl)
Time to CP			
Very early	7.7±1.7	25.4±17.8	1.2±1.4
Early	6.9±2.0	32.0±24.1	1.4±1.7
Late	7.1±2.3	39.2±28.1	2.2±4.3
More late	5.7±1.4	33.8±21.0	0.5±0.4
Etiology			
TBI	7.4±2.0	33.0±25.7	1.5±3.0
Infarction	6.4±2.3	33.6±23.6	1.3±1.4
SAH	6.5±1.5	30.6±19.1	1.5±2.1
ICH	7.7±2.0	45.0±36.2	2.1±3.1
Others	7.1±1.4	23.0±25.5	1.0±0.3

TBI: traumatic brain injury, SAH: subarachnoid hemorrhage, ICH: intracerebral hemorrhage, others: arteriovenous malformation.

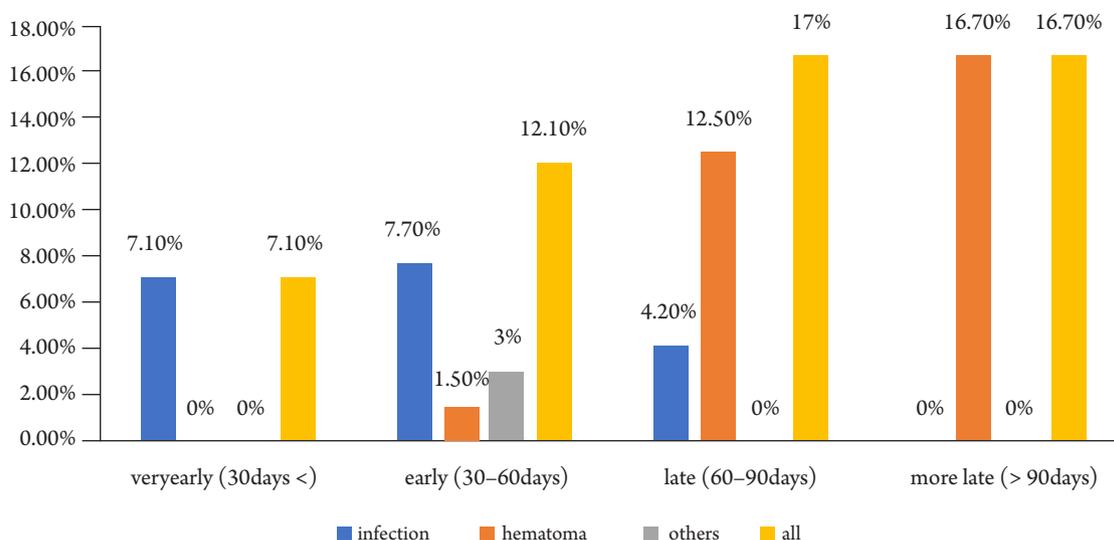


Fig. 2. The incidence rate of complications by timing excluding hydrocephalus.

ioral, and motor functions^{3,9,14,26}.

Therefore, it appears evident to stipulate that it would be beneficial to perform the cranioplasty as early as possible. However, it is not that simple in reality. Although cranioplasty is a relatively simple neurosurgical procedure, the complication rate is reported to be up to 10-50%^{4,9,13}. Also, there have been claims that early cranioplasty is associated with greater complications and, consequently, is more detrimental to the patient¹¹. Although some studies claim that there are different types of complications depending on the timing of the cranioplasty and that the timing of the cranioplasty and the complication rate is unrelated, the appropriate timing of cranioplasty is still controversial^{3-5,10,13}.

A gross examination of the 109 cases of cranioplasty that were analyzed in this study showed that the cranioplasties were mostly performed in the early timing (30-60 days), accounting for 59.6%

(65/109) of the cases. Furthermore, the complications rate was highest in the early timing (30-60 days), accounting for 52.3% (34/65). Among the complications, hydrocephalus was the most frequent complication and accounted for 73.1% (38/52) (Table 3) (Fig. 1).

However, we cannot conclude from these findings that most complications occur in the cranioplasties performed at the early timing and that hydrocephalus is the most common complication. The reason being the fact the hydrocephalus most frequent complication of cranioplasty was not associated with operative timing but the other factors, such as the cause of craniectomy and the number of revision surgery. In other word, the trends of complications for each timing must be evaluated by the prevalence without hydrocephalus.

The reason was the fact that the most frequent complications of

hydrocephalus in cranioplasty were not related to the timing of surgery but related to other factors such as the cause of craniectomy and the number of revision surgeries. That was, the propensity for each timing complication should be assessed by prevalence without hydrocephalus.

The results of investigating the prevalence of complications after cranioplasty in association with the timing of the operation revealed the following:

Firstly, complications were most frequent in the late timing 16.6% (4/24) when it come to the prevalence of complication without hydrocephalus and there was a little different from that in the more late timing. Although no statistical significance was observed ($p=0.382$), it was observed that the incidence rate of the complications tended to be higher in the late timing (60days or later) group of cranioplasty except for hydrocephalus.

First, complications were highest at 16.6% (4/24) when the prevalence of complications without hydrocephalus was late timing, which was slightly different from the late period. No statistical significance was observed ($p=0.382$), but a tendency for a higher incidence of complications was observed in the late timing (60 days or longer) group of cranioplasty excluding hydrocephalus (Fig. 2).

Secondly, as shown in the results of this study, there were associations between the timing of the cranioplasty and each of the frequent complications. The relationship between hydrocephalus and the cranioplasty timing showed no large differences in the prevalence rates of hydrocephalus between early timing (40.0%) and late timing (33.3%) groups. As mentioned before, traumatic brain injury and SAH among the initial indications of the decompressive craniectomy accounted for 82.8% of the cases with hydrocephalus. As such, it appears that the cause of craniectomy, which is the initial condition of the patient's disease, had a stronger relationship than the operation timing. This finding is in line with the studies explaining the mechanism of hydrocephalus (by the mass effect of blood clots and the obstruction by inflammation-mediated adhesions of the ventricle)^{4,5,23}. Additionally, there was a statistically significant association between the prevalence of hydrocephalus and the number of revision surgeries performed between the decompressive craniectomy and the cranioplasty ($p=0.046$). In other words, it is possible that the prevalence of the hydrocephalus is not strongly related to the timing of the cranioplasty.

The evaluation of the relationship between the prevalence of post cranioplasty infection and the timing of the cranioplasty showed that infections were not quite different between in very early timing cranioplasties (< 30 days) (7.1%) and the infection rate in the early timing (30-60 days) (7.7%) were also higher compared to the late timing (0.7%). Although these findings were not

statistically significant (p value = 0.084), this suggests that more infections can occur if the cranioplasty is performed before 60 days. This is in line with the findings by Cheng et al.⁶) and Kim et al.¹⁴) This implies that one must be cautious about infections when performing early timing cranioplasty in earlier timings, and especially in very early timing cranioplasty^{15,22,24}). This study also examined the relationship between previously reported data^{6,12,25,26}), infection factors, demographic information, underlying disease, graft material, and preexisting and post cranioplasty infection and found no statistical significance. In particular, this study did not find a significant difference between incidence of infections and the duration of the cranioplasty as suggested by Lim et al.²⁵) ($p=0.709$).

This study also examined the relationship between the timing of the cranioplasty and the prevalence of revision surgeries due to bleeding after the cranioplasty. It was found that the prevalence of rebleeding increased with an increase delay in the timing of the cranioplasty. Although this finding was not statistically significant, this could be explained by the fact that the duration of operation lengthened with increasing delay in the timing ($p=0.009$). Also, adverse events occur more frequently during dissection because adhesion are more common in later surgeries^{1,19,30}). These trends found in this study are different from the findings of Ryan et al. They found that the timing of the operation and the occurrence of hematoma are not strongly related. However, this finding is in line with the trends mentioned by Patrick et al.²⁷), and suggests that more attention should be given to bleeding control during surgery because the prevalence rate of bleeding increases with delayed surgery.

While it has been reported that the trends of the complications after the cranioplasty differ with timing^{15,24}), the trends found in this study did not match the trends found in previous studies. However, these findings suggest that it cannot be easily concluded that the complications after cranioplasty are related to the timing of the cranioplasty and that the surgeons must be cautious about certain complications at specific timings^{11,21}).

There are already many known advantages of performing an early cranioplasty. First, early cranioplasty contributes to the recovery of the normal cerebrospinal fluid circulation³), decreased cerebral blood flow and disturbed brain metabolism could be restored^{9,14-17}). Furthermore, there are improvements in neurocognitive and neurological functions as a result. Not only that, early cranioplasty allow an easy dissection of tissue planes as there is less scar tissue thus, shortening the duration of the surgery³). Furthermore, early cranioplasty decreases the time during which the patient is at risk of incurring another injury without a bone flap in place⁴). It is known that this can enable more active rehabilitation and reduce the length and cost of hospital stay through a quicker recovery^{2,3,4}).

CONCLUSION

Cranioplasty after decompressive craniectomy is associated with high complication rate and the incidence of the complications vary with the timing of the operation. There are many advantages of early cranioplasty, and we can make use of these advantages by performing the surgery while taking strict measures to prevent post-operative infections.

There are some limitations of this study. Despite the fact that the data collected was promising, data analysis was retrospective. Therefore, the study suffers from the drawbacks of retrospective analysis. It is possible that the underlying pathology heterogeneity that led to decompressive craniectomy has biased the complication rates after cranioplasty. In addition, these results represent only a single-center experience.

NOTES

Conflict of interest

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Tasiou A, Vagkopoulos K, Georgiadis I, Brotis AG, Gatos H, Fountas KN. Cranioplasty optimal timing in cases of decompressive craniectomy after severe head injury: a systematic literature review. *Interdisciplinary Neurosurgery* 2014;1:107–111.
2. Di Rienzo A, Colasanti R, Gladi M, Pompucci A, Della Costanza M, Paracino R, Esposito D, Iacoangeli M. Sinking flap syndrome revisited: the who, when and why. *Neurosurg Rev* 2020;43:323–335.
3. Cheah PP, Rosman AK, Cheang CK, Idris B. Autologous Cranioplasty Post-Operative Surgical Site Infection: Does It Matter if the Bone Flaps were Stored and Handled Differently? *Malays J Med Sci* 2017;24:68–74.
4. Chen K-H, Lee CP, Yang YH, Yang YH, Chen CM, Lu ML, et al. Incidence of hydrocephalus in traumatic brain injury : a nationwide population-based cohort study. *Medicine (Baltimore)* 2019;98:1–8.
5. Chen S, Luo J, Reis C, Manaenko A, Zhang J. Hydrocephalus after subarachnoid hemorrhage: pathophysiology, diagnosis, and treatment. *Biomed Res Int* 2017;2017:Article ID 8584753.
6. Cheng YK, Weng HH, Yang JT, Lee M, Wang T, Chang C. Factors affecting graft infection after cranioplasty. *J Clin Neurosci* 2008;15:1115–1119.
7. Corallo F, Cola MCD, Buono VL, Marra A, Luca RD, Trinchera A, et al. Early vs late cranioplasty: what is better? *Int J Neurosci* 2017;127:688–693.
8. Archavlis E, Nievas MC. Kranioplastik nach supratentorieller dekompressiver Kraniektomie : Wann ist der Zeitpunkt optimal? [Cranioplasty after supratentorial decompressive craniectomy: when is the optimal timing]. *Nervenarzt* 2012;83:751–758.
9. Fodstad H, Love JA, Ekstedt J, Friden H, Liliequist B. Effect of cranioplasty on cerebrospinal fluid hydrodynamics in patients with the syndrome of the trephined. *Acta Neurochir* 1984;70:21–30.
10. Goedemans T, Verbaan D, Veer Ovd, Bot M, Post R, Hoogmoed J, et al. Complications in cranioplasty after decompressive craniectomy: timing of the intervention. *J Neurol* 2020;17:1–9.
11. Oh JS, Lee KS, Shim JJ, Yoon SM, Doh JW, Bae HG. Which one is better to reduce the infection rate, early or late cranioplasty? *J Korean Neurosurg Soc* 2016;59:492–497.
12. Jin SW, Kim SD, Ha SK, Lim DJ, Lee H, You HJ. Analysis of the factors affecting surgical site infection and bone flap resorption after cranioplasty with autologous cryopreserved bone: the importance of temporalis muscle preservation. *Turk Neurosurg* 2018;28:882–888.
13. Beauchamp KM, Kashuk J, Moore EE, Bolles G, Rabb C, Seinfeld J, Szentirmai O, Sauaia A. Cranioplasty after postinjury decompressive craniectomy: Is timing of the essence? *J Trauma* 2010;69:270–274.
14. Kim YW, You DS, Kim DS. The infection rate in case of cranioplasty according to used materials and skull defect duration. *J Korean Neurosurg Soc* 2001;30:216–220.
15. Iaccarino C, Koliass AL, Roumy LG, Fountas K, Olufemi Adeleye A. Cranioplasty following decompressive craniectomy. *Front Neurol* 2019;10:1357.
16. Liang W, Xiaofeng Y, Weiguo L, Gang S, Xuesheng Z, Fei C, et al. Cranioplasty of large cranial defect at an early stage after decompressive craniectomy performed for severe head trauma. *J Craniofac Surg* 2007;18:526–532.
17. Dujovny M, Agner C, Aviles A. Syndrome of the trephined: theory and facts. *Crit Rev Neurosurg* 1999;9:271–278.
18. Malcolm JG, Rindler RS, Chu JK, Grossberg JA, Pradilla G, Ahmad FU. Complications following cranioplasty and relationship to timing: a systematic review and meta-analysis. *J Clin Neurosci* 2016;33:39–51.
19. Mark P, Piedra P, Brian TR. Timing of cranioplasty after decompressive craniectomy for trauma. *Surg Neurol Int* 2014;5:1–5.
20. Piedra MP, Ragel BT, Dogan A, Coppa ND, Delashaw JB. Timing of cranioplasty after decompressive craniectomy for ischemic or hemorrhagic stroke. *J Neurosurg* 2013;118:109–114.

21. Gooch MR, Gin GE, Kenning TJ, German JW. Complications of cranioplasty following decompressive craniectomy: analysis of 62 cases. *Neurosurg Focus* 2009;26:E9.
22. Datti R, Cavagnaro G, Camici S. Stainless steel wire mesh cranioplasty: ten years' experience with 183 patients (100 followed up). *Acta Neurochir (Wien)* 1985;78:133–135.
23. Vinas Rios JM, Sanchez-Aguilar M, Kretschmer T, Heinen C, Medina Govea FA, Jose Juan SR, Schmidt T. Predictors of hydrocephalus as a complication of non-traumatic subarachnoid hemorrhage: a retrospective observational cohort study in 107 patients. *Patient Saf Surg* 2018;12:13.
24. Ryan P, Morton M, Isaac Josh Abecassis M, Josiah F, Hanson B, Jason K, et al. Timing of cranioplasty: a 10.75-year single-center analysis of 754 patients. *J Neurosurg* 2018;128:1648–1652.
25. Im SH, Jang DK, Han YM, Kim JT, Chung DS, Park YS. Long-term incidence and predicting factors of cranioplasty infection after decompressive craniectomy. *J Korean Neurosurg Soc* 2012;52:396–403.
26. Yang SM, Park HK, Cho SJ, Chang JC, Park SQ, Kim RS. The current analysis of the risk factors for bone graft infection after cranioplasty. *Korean J Neurotrauma* 2013;9:57–63.
27. Schuss P, Vatter H, Marquardt G, Imöhl L, Ulrich CT, Seifert V, Güresir E. Cranioplasty after decompressive craniectomy: the effect of timing on postoperative complications. *J Neurotrauma* 2012;29:1090–1095.
28. Winkler PA, Stummer W, Linke R, Krishnan KG, Tatsch K. The influence of cranioplasty on postural blood flow regulation, cerebrovascular reserve capacity, and cerebral glucose metabolism. *Neurosurg Focus* 2000;8:e9.
29. Zanaty M, Chalouhi N, Starke RM, Chitale R, Hann S, Bovenzi CD, et al. Predictors of infections following cranioplasty: a retrospective review of a large single center study. *ScientificWorldJournal* 2014;2014:356042.
30. Zheng F, Xu H, Spreckelsen Nv, Stavrinou P, Timmer M, Goldbrunner R, et al. Early or late cranioplasty following decompressive craniotomy for traumatic brain injury: a systematic review and meta-analysis. *J Int Med Res* 2018;46:2503–2512.