Cognitive and Functional Outcomes of Early Versus Delayed Cranioplasty after Decompressive Craniectomy

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Abstract

Introduction Delay in doing cranioplasty (CP) after decompressive craniectomy (DC) may cause motor, cognitive, and language deficits. Studies show doing CP before developing such symptoms helps in improving the outcome. CP improves cerebrospinal fluid (CSF) dynamics and cerebral blood flow, which may lead to better cognitive and functional outcome.

Objective The aim of the study was to assess cognitive and functional outcomes of early versus delayed cranioplasty (DCP) after DC.

Methodology This was a prospective observational study on 42 patients aged over 16 years and up to 70 years, who had undergone CP after DC for severe traumatic brain injury in in-patient and outpatient department of neurosurgery at a tertiary care hospital in Bhubaneswar, Odisha, India from the period of March 01, 2016 to December 31, 2017. Cognitive and functional outcomes were compared in early and DCP groups in preoperative and follow-up period at 1 month, 3 months, and 6 months. Early cranioplasty (ECP) was within 2 months, and DCP was beyond 2 months.

Results Total sample size under this study was 42; 21 in ECP and 21 in DCP group. Mean age was 41.40 ± 15.95 years. The age distribution was quite young with 38.1% in 30 to 49 age group and had very high proportion of males (85.7%).This analysis revealed that both the ECP and DCP groups have resulted in significant improvement in mini-mental state examination (MMSE) and Glasgow Outcome Scale Extended (GOSE) score after CP. But in the ECP group, there has been steady and significant improvement in MMSE and GOSE score at different follow-ups starting from postoperative 1 month in MMSE score and from 3 months up to 6 months in GOSE score.

Conclusion Neurosurgeon should evaluate and carefully monitor each individual case and take up CP as early as possible with suitable indication.

Keywords
- ► decompressive craniectomy
- ► early cranioplasty
- ► delayed cranioplasty
- ► cognitive outcome
- ► functional outcome

Introduction

Traumatic brain injury is a significant public health problem worldwide in the form of major cause of death and disability. It is the most common cause of death and disability in children and young adults.[1] Decompressive craniectomy (DC) is a life-saving operation for severe brain edema with impending brain herniation due to severe head injury.[2–4] A large bone flap is left out to allow brain tissue to expand and thus to lower intracranial pressure (ICP).[2] DC leaves a bony skull defect. It exposes brain tissue to atmospheric

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pressure and disturbs physiological brain perfusion[5] and cerebrospinal fluid (CSF) flow[6] and exposes to later neurological symptoms, such as epileptic seizures[7]. Delay in doing cranioplasty (CP) after DC may cause motor, cognitive and language deficits, which often resolve after cranial reconstruction. CP is an essential surgery not only to satisfy patients' external defects, but also to improve patient's functional outcome.[8] It improves CSF dynamics and cerebral blood flow (CBF), which may lead to better cognitive and functional outcome.[9–24]

Historically, CP has been recommended at least 3 months after initial craniectomy, but CP can be done after 5 to 8 weeks in selected patients. CP when done early may allow easier discrimination of the various tissue layers and obviates blood loss. The optimal timing for performing a CP seems to play an important role not only in avoiding procedure-associated complications, but also in the neurological outcome of these patients. General improvements in neurological function and CBF following CP have also been reported.[25] Delayed cranioplasty (DCP) might lead to increased rates of persistent communicating hydrocephalus.[26] Despite the fact that CP is a time honored, straight-forwarded procedure, it is still associated with a relatively high complication rate, ranging between series from 12 to 50% in previous literatures.[27–30] CP by autologous bone and by a variety of alloplastic materials have been employed to restore the skull defect including polyethylethylketone (PEEK), polymethyl methacrylate (PMMA), hydroxyapatite, polyethylene, and more recently, titanium. Several parameters, such as the initial underlying pathology, the biotechnological characteristics of the bone graft, and the technical aspects of the CP technique, have been associated with the occurrence of complications in CP cases. In the above backdrop, an attempt has been made through observational study to see the outcomes in terms of cognitive and functional status after CP in a tertiary care hospital where good numbers of cases are performed every year. This study will provide insight to the clinicians and neurosurgeons in better management and innovations related to CP after DC.

Aims and Objectives

The aim of the study is to assess cognitive and functional outcomes of early versus DCP after DC.

Material and Methods

This was a prospective observational study on patients who have undergone CP after DC for severe traumatic brain injury in the department of neurosurgery at a tertiary care hospital in Bhubaneswar, Odisha, India from March 01, 2016 to December 31, 2017. Research ethics board approval has been obtained for this study. All patients aged over 16 years and up to 70 years, who presented for CP after DC for severe traumatic brain injury, constituted the study population.

The exclusion criteria constitute patients who have undergone CP by other than autologous method, patients who have undergone CP complicated with cranial infection, and those who have undergone CP after DC for head injury associated with previous stroke.

The patients presenting with indication for CP were evaluated for inclusion and exclusion criteria for the study and patients who had undergone CP within 2 months were taken as early cranioplasty (ECP) patients, and patients who had undergone CP after 2 months were taken as DCP patients.

Apart from the routine systemic examination, laboratory and radiological evaluation, all patients were evaluated before CP as per operative protocol for CP, and after fulfilling required check points, they were posted for CP such as no systemic infection, healthy scalp wound and abdominal wound, and no brain swelling. Preoperative Glasgow Coma Scale (GCS), Glasgow Outcome Scale Extended (GOSE), and mini-mental state examination (MMSE) were recorded for each patient. CP was done under general anesthesia in supine position and head tilted to opposite side of the operative site. Scalp and abdominal sites were scrubbed and draped, 2% xylocaine with adrenaline after dilution was infiltrated along the line of incision, scalp incision was given on previous scar and scalp flap reflected from dura, all edges of skull bone defect were cleaned properly, dura was made free from the inner table of the native skull, and then harvested bone from abdominal wall was taken out and repositioned anatomically and fixed with miniplate and screw. After achieving hemostasis and putting subgaleal suction drain, scalp wound was closed in layers. Subgaleal stitches were done by polyglactin 2–0 suture, and scalp wound was closed by polyamide 2–0 suture. Abdominal wound was also closed after securing hemostasis in layers. Postoperatively, recovery, seizure, scalp flap necrosis, and mortality associated with procedure were noted for each patient. Computed tomography (CT) scan of brain was routinely done after CP to look for intracranial complications such as epidural hematoma (EDH), subdural hematoma (SDH), intracerebral hemorrhage (ICH), cerebral edema, hydrocephalus, and subdural hygroma. We usually discharge the patient on third postoperative day. The first follow-up was done after 1 week, and then patients were asked to come for follow up in 1 month, 3 months, and 6 months. An observation chart was prepared for each patient, and pre-CP MMSE and GOSE recorded. Post-CP MMSE and GOSE were repeated at 1 month, 3 months, and 6 months and were compared with the previous score. Data on demographic profile, clinical history, general examination, local examination, and nervous system examination (with respect to GOSE, MMSE, and GCS) at different follow-ups were collected through data collection Proforma. Informed consent was obtained from the patient or authorized guardian/caretaker of the patient.

Statistical Methods

Statistical analysis was done using IBM statistics SPSS 24.0. For significant difference the cut-off '*p*' value was < 0.05. The association of categorical variables, such as age group and gender with ECP and DCP, was done using cross tabulation procedure along with chi-square test of independence.

Observations

To study the cognitive and functional outcomes of ECP versus DCP after DC, observations were made on 21 cases each of

ECP and DCP. Data were analyzed following appropriate statistical procedure. Out of total 42 cases, 14 (33.3%) were in 19 to 29 age group, 16 (38.1%) in 30 to 49 age group, and 12 (28.6%) in 50 or > 50 of age. Age distribution in ECP and DCP groups were not significantly different (p = 0.33). This implied that both groups are matched by age distribution. Out of 42 subjects, 36 (85.7%) were males, and the remaining 6 (14.3%) were females. The distribution of sex in both groups, ECP, and DCP was not significantly different (p = 0.378). The ECP and DCP groups were matched by sex distribution.

Time difference is a critical feature of ECP and DCP. In the ECP group, the median value of time difference between DC and CP was 39 days with minimum time difference 21 days and maximum 58 days. In DCP group, the median value of time difference between DC and CP was 80 days with minimum time difference 62 days and maximum 150 days.

Cognitive Outcomes

The MMSE score is a measure of cognitive function of the subject. The analysis of comparison of MMSE by group at different follow-ups is presented in ►**Table 1**. The analysis revealed that at preoperative both the groups were having insignificant difference in MMSE score, but at subsequent follow-ups, it was found that ECP had better MMSE score than the DCP had.

Functional Outcomes

In the present study, the median GOSE score for CP done before 2 months (ECP) and after 2 months (DCP) have shown significant improvement in 3 months and 6 months over the previous follow-ups and also over baseline value. However, the improvement in GOSE score was higher for the ECP than for DCP. At 6 months, the median GOSE score for ECP was 7, and for DCP, it was 5 (p = 0.000). Comparison of GOSE score as an indicator of functional outcome is represented in ►**Tables 2** and **3**.

Postoperative Complication

In the DCP, no complication was observed in postoperative period; however, in ECP group, there was one case of seizure, ICH, and EDH each. ►**Table 4** presents postoperative complication in two groups.

Discussion

The related literatures indicated that there is hardly any study which compares cognitive and functional outcomes of ECP versus DCP after DC and comparative indication for the same. There is need to conduct such study in different setting to arrays the scientific knowledge in this area based on evidence. The related literature on CP did not draw any conclusion regarding optimal timeframe for CP for better outcome. Researcher could not locate comparative study of ECP versus DCP in Indian context. This is an area which needs to be highlighted.

The present observational study has brought out the detailed indications and outcomes of ECP and DCP. These findings need to be triangulated with the research conducted in different places and time for validation. Besides the clinical implications and the messages for the scientific community, these need to be discussed at length. The present study found that distribution of age was quite young in the study population and had a very high proportion of males (85.7%). The mean age of sample subjects was 41.40 ± 15.95 years. Andrabi et al (2017) found that the maximum patients were in the age group of 21 to 30 years, i.e., 30.93% (n = 73). Mean age of the patients was 33.44 years.[31] They also found a young age distribution of such patients. The reason behind this is that young males are more getting RTA leading to severe TBI.

In the present study, there were 21 cases of ECP out of which 13 had indications such as left DC with sinking flap (SF) and 8 had right DC with SF. There were 21 cases of DCP of which 14 were left DC, 6 were right DC, and 1 B/L frontal DC. Time difference is a critical feature of ECP and DCP. In the ECP group, the median value of time difference between DCP and CP was 39 days with minimum time difference of 21 days and maximum 58 days. In the DCP group, the median value of time difference between DC and CP was 80 days with minimum time difference of 62 days and maximum 150 days. All the patients were having cognitive impairment. None of the patient had swelling in the brain, surgical site infection, and systemic infection preoperatively. We did ECP within 2 months on 21 patients as they were fit to undergo CP, and moreover, they were showing cognition and functional impairment. All patients of ECP were having SF. Previous 12 weeks criteria to undergo CP came down to 3 weeks in

Table 1 Comparison of MMSE score by groups at different follow-ups

		MMSE			
Time period	Groups	Median	Q1	Q3	t, p
Preoperative	Early cranioplasty	22	20	23.50	t = 1.262 p = 0.214
	Delayed cranioplasty	20	16.50	22.50	
Postoperative 1 month	Early cranioplasty	24	22	25	t = 2.170 p = 0.036
	Delayed cranioplasty	22	16	23	
Postoperative 3 months	Early cranioplasty	25	24	26	t = 2.242 p = 0.031
	Delayed cranioplasty	23	20	24	
Postoperative 6 months	Early cranioplasty	26	25	27	t = 2.705 p = 0.010
	Delayed cranioplasty	23	20	25	

Abbreviation: MMSE, mini-mental state examination.

Table 2 Comparison of GOSE score between groups at different follow-ups

		GOSE score			
Time period	**Group**	**Median**	**Q1**	**Q3**	***t*, *p***
Preoperative	Early cranioplasty	5	5	6	$t = 5.582$ $p = 0.000$
	Delayed cranioplasty	4	3	4	
Postoperative 1 month	Early cranioplasty	5	5	6	$t = 5.520$ $p = 0.000$
	Delayed cranioplasty	4	3	4	
Postoperative 3 months	Early cranioplasty	6	6	7	$t = 5.688$ $p = 0.000$
	Delayed cranioplasty	4	4	5	
Postoperative 6 months	Early cranioplasty	7	6	8	$t = 6.472$ $p = 0.000$
	Delayed cranioplasty	5	4	5	

Abbreviation: GOSE, Glasgow Outcome Scale Extended.

Table 3 GOSE score comparison by group

		Early cranioplasty		Delayed cranioplasty		Total		
GOSE score	**Status**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**χ^2, *p***
Preop	Severe	4	19	21	100	25	59.5	$\chi^2 = 28.56$ $p = 0.000$
	Moderate	16	76.2	0	0	16	38.1	
	Lower good recovery	1	4.8	0	0	1	2.4	
Postop 1 month	Severe	4	20	21	100	25	61	$\chi^2 = 27.552$ $p = 0.000$
	Moderate	15	75	0	0	15	36.6	
	Lower good recovery	1	5	0	0	1	2.4	
Postop 3 months	Severe	3	15	12	57.1	15	36.6	$\chi^2 = 13.384$ $p = 0.001$
	Moderate	9	45	9	42.9	18	43.9	
	Lower good recovery	8	40	0	0	8	19.5	
Postop 6 months	Severe	1	5	9	42.9	10	24.4	$\chi^2 = 16.582$ $p = 0.000$
	Moderate	7	35	11	52.4	18	43.9	
	Lower good recovery	12	60	1	4.8	13	31.7	

Abbreviations: GOSE, Glasgow Outcome Scale Extended; preop, preoperative; postop, postoperative.

Table 4 Postop complications in both groups

	Early cranioplasty		Delayed cranioplasty		Total		
Postop complications	**No.**	**%**	**No.**	**%**	**No.**	**%**	**χ^2, *p***
No complications	18	85.7	21	100.0	39	92.9	$\chi^2 = 3.231$ $p = 0.357$
Seizure	1	4.8	0	0.0	1	2.4	
ICH	1	4.8	0	0.0	1	2.4	
EDH	1	4.8	0	0.0	1	2.4	
Total	21	100.0	21	100.0	42	100.0	

Abbreviations: EDH, epidural hematoma; ICH, intracranial hemorrhage; Postop, postoperative.

our study. Patients who were not fit to undergo CP within 2 months due to persistent brain swelling or some medical illness underwent DCP. They were either not fit or not fulfilling the criteria to undergo CP within 2 months. Previous literature suggested to do CP as soon as patients met the criteria to undergo CP. [20,22,27,32]

Beauchamp et al suggested CP during the initial hospital admission, as soon as there is resolution on a CT scan of brain swelling outside of the cranial vault with concurrent clinical examination. This occurs as early as 2 weeks post craniectomy and should lower the overall cost of care by eliminating the need for additional hospital admissions since early intervention lowers the overall cost of care.[20]

In our study, all the patients were having cognitive impairment. None of the patient had swelling in brain, surgical site infection, and systemic infection preoperatively. They were chosen as per their merit for CP because delaying CP invites more complications in future.

Chun et al stated that ECP allows safer surgical dissection of the DC site tissues, resulting in reduced blood loss and minimization of any operative adverse events.[22] The mean interval for CP in their study was 28.6 days after the first operation (DC). In our study, the mean time interval between DC and ECP was 39.2 days, with median 39 days, and the earliest was 21 days. The synthesis of the present study along with other review of literature revealed that CP should be performed at the earliest possible time depending upon the indication.

The MMSE score is a measure of cognitive function of the subject. The analysis revealed that preoperatively, both the groups were having insignificant difference in MMSE score, but in the subsequent follow-ups, it was found that ECP had improved the MMSE score at a faster pace than did the DCP. In our study, at preoperative stage, the median MMSE score in ECP and DCP was 22 and 20, respectively. The median score between the two groups was not significantly different at base level, but at postoperative follow-ups, the median MMSE score improved faster and better than that of DCP. At 6 months, the median MMSE score for ECP was 26, corresponding median MMSE score for DCP was 23, and the difference was significant ($p = 0.010$). Many studies have been published regarding the improvement in cognitive outcome after CP,[21,22,33,34] which states better cognitive outcome in ECP, which corroborates to the findings of our study. Songara et al (2016) showed in their study that median value for MMSE was having significantly higher value for CP done earlier than 3 months than CP done beyond 3 months.[22] Thus, ECP has chance of faster and better improvement in cognitive function than DCP has.

GOSE score has been used worldwide as a functional measure after head trauma. In present study, the mean and median GOSE score for CP done before 2 months (ECP) and after 2 months (DCP) have shown significant improvement in 3 months and 6 months over the previous follow-ups and also over baseline value. However, the improvement in GOSE score was higher for the ECP than for the DCP. At 6 months, the median GOSE score for ECP was 7, and that for DCP was 5 ($p = 0.000$). The severity of disability in terms of GOSE score has shown significantly better improvement in ECP cases than in DCP cases. Shahid et al (2018) studied the effect of CP following DC on GOSE score and found that prior to CP, 9 (26.5%) patients had GOSE score of 5 and 25 (73.5%) patients had GOSE scores of 4, whereas post CP, all 34 (100%) patients had improved to GOSE scores of 5.[35] Songara et al (2016) studied neurocognitive outcome in ECP patients after DC. The neurocognitive improvement after CP was more remarkable in the ECP group in terms of GOSE.[22] This finding is in term with the findings of the present study. They have compared the results of CP done before 3 months and after 3 months and found better functional outcome for the CP done before 3 months. This also is in consistency with our findings. But we have taken CP as early as 2 months to define ECP. Therefore, we can conclude that the ECP has an advantage in terms of functional outcome than DCP.

In our study, no complication was observed in postoperative period of the DCP group; however, in ECP group, there was one case of seizure, ICH (death), and EDH each. We did CP by autologous bone in both groups, and complication rate in ECP was 14.28%, but if we analyze the rate of complication in our study, overall complication rate was 7.14%—seizure 2.38%, EDH 2.38%, and ICH 2.38%. Xu et al (2015) showed that ECP had no significant difference in overall complications, infection rates, intracranial hematoma, and subdural fluid collection. However, ECP significantly reduced the duration of CP. The postoperative hydrocephalus rates were significantly higher in the ECP group. They concluded that ECP can only reduce the duration of operation, but cannot reduce the complications of patients and can even increase the risk of hydrocephalus.[36] Chang et al found that the overall complication rate was 16.4% (35 of 213 patients).[21] Patients 0 to 39 years of age had the lowest complication rate of 8% ($p = 0.028$). For patients 40 to 59 years of age and older than 60, complication rates were 20 and 26%, respectively. Patients who received autologous bone graft placement had a statistically significant lower risk of postoperative infection (4.6 versus 18.4%; $p = 0.002$). Patients who underwent CP with a 0 to 3 months interval between operations had a complication rate of 9%, 3 to 6 months 18.8%, and > 6 months 26%. They concluded that the overall rate of complications related to CP after craniectomy is not negligible, and certain factors may be associated with increased risk. The CP-associated complication rates between early (< 3 months), and late (> 6 months) CP was significantly higher among patients undergoing late CP.[37] Chaturvedi et al (2016) studied and analyzed complications following CP after DC, retrospectively, and found that mortality rate was 1.35% and overall complication rate 31%.[38] In the study of Andrabi et al. (2017), complications were noted in 15.25% ($n = 36$) of the patients; wound infection/dehiscence 6.78% ($n = 16$) was the most common complication encountered.[31] In our study, complications were at par with previous literature, and one case of mortality was due to intracerebral hemorrhage (had history of hypertension) followed by prolonged mechanical ventilation leading to ventilator-associated pneumonia, so that cannot be attributed to CP. This study has been done with certain limitations since the analysis was done with patients from a single center in limited time leading to a limited sample size. Further prospective and multi-center study will strengthen the usefulness of ECP after DC as well as the relationship between the timing of CP, the neurological outcome, and the postoperative complications in patients with traumatic brain injury.

Conclusion

Based upon the analysis and interpretation of our results and critical review of related literature, the following conclusions are drawn. CP has to be followed after DC, but the time frame for the CP after DC varies from patient to patient, so CP should be performed as early as possible if favorable indications are present. In our study, the earliest being 21 days and within 56 days in early group and in delayed group, respectively, CP were done between 60 and 150 days. In both groups, the cognitive and functional parameters were not different at base level, but for the 21-day group with the ECP have indicated significantly better cognition and functional outcomes than in the DCP cases. Therefore, treating neurosurgeon should evaluate and carefully monitor each individual case and take up CP as early as possible with suitable indication.

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Conflict of Interest

There is no conflict of interest.

Disclosure

None.

Contribution of the Authors

Conception, design of study, and acquisition of data: Dr. Arun Kumar, Biswaranjan Nayak, Prafulla Kumar Sahoo, and Dr. Debabrat Biswal; analysis and/or interpretation of data: Biswaranjan Nayak, Dr. Sushant Kumar Patro, Dr. Krishnamurthy BH, Abhijeet CR, Balwant Singh, Himanshu Bhusana Nyak, and Dhanwantari Shukla.

Declaration of Authors

The manuscript has been read and approved by all the authors, the requirements for authorship as stated earlier in this document have been met, and each author believes that the manuscript represents honest work.

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