Complication Rates in Early Versus Late Cranioplasty—A Fourteen-Year Single-Center Case Series

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BACKGROUND: Cranioplasty (CP) following decompressive craniectomy (DC) is a common neurosurgical procedure for cranial cosmesis and protection. There is uncertainty regarding the complication rates and potential benefits related to the timing of CP.

OBJECTIVE: To investigate the impact of the timing of CP on complication rates for different etiologies of DC.

METHODS: A retrospective chart review was performed of all CP cases between 2004 and 2018 for traumatic and nontraumatic indications of DC. Demographics, clinical characteristics, and complications were collected. Early and late CP were defined as replacement of the bone flap at $\leq$90 and $>$90 d following DC, respectively.

RESULTS: A total of 278 patients were included, receiving 81 early and 197 late CPs. When analyzing all patients, early CP was associated with a statistically significant higher odds of any complication (odds ratio [OR]: 3.25, $P < .001$), reoperation (OR: 2.57, $P = .019$), hydrocephalus (OR: 6.03, $P = .003$), and symptomatic extra-axial collections (OR: 9.22, $P = .003$). Subgroup analysis demonstrated statistically significant higher odds of these complications only for the CP trauma subgroup, but not the nontrauma subgroup. The odds of complications postCP demonstrated a statistically significant decrease of 4.4% for each week after DC (Unit Odds Ratio [U-OR]: 0.956, $P = .0363$).

CONCLUSION: In our retrospective series, early CP was associated with higher odds of postoperative complications compared to late CP in the trauma subgroup. Greater care should be taken in preoperative planning and increased vigilance postoperatively for complications with this potentially more vulnerable subpopulation. Future prospective controlled trials are needed to elucidate optimal timing for CP.

KEY WORDS: Cranioplasty, Complications, Hydrocephalus, Infection, Decompressive craniectomy, Traumatic brain injury

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Cranioplasty (CP) following decompressive craniectomy (DC) is an elective neurosurgical procedure important for cranial cosmesis and protection. However, optimal timing of CP remains controversial[1-3] and can occur weeks, months, or years following the original DC. The potential importance of optimizing the timing of CP has been highlighted by several recent studies reporting benefits associated with early CP. These include but are not limited to improved cerebral blood flow and improved neurological outcomes, which would support performing procedures as early as possible to optimize patients' recovery from their neurological injuries.[2] Several studies have also reported fewer infections, seizures, and resorption with early CP.[2,4,5] A recent systemic review and meta-analysis reported improved neurological outcomes with CP regardless of

ABBREVIATIONS: BMI, body mass index; **CDG,** Clavien-Dindo grade; **CP,** cranioplasty; **CSF,** cerebrospinal fluid; **DC,** decompressive craniectomy; **EAC,** extra-axial collections; **GCS,** Glasgow Coma Scale; **HCP,** hydrocephalus; **HH,** Hunt and Hess score; **ICH,** Intracerebral Hemorrhage Score; **NIHSS,** National Institutes of Health Stroke Scale; **OR,** odds ratio; **SAH,** subarachnoid hemorrhage; **SD,** standard deviation; **U-OR,** unit odds ratio; **VPS,** ventriculoperitoneal shunt

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timing, as well as statistically significant association with better outcomes in early CP patients.[2] However, these findings are in contrast to other studies that have reported no significant difference or higher rates of hydrocephalus (HCP) and infection associated with early CP.[5-7] It is unclear whether the complication types and rates remain favorable for earlier procedures compared to later timepoints, and may, in fact, vary based on brain injury etiology.

While the prospect of optimizing neurological outcomes is appealing, the effect of earlier CP on complications and the role of the original etiology for DC remains unclear. The present study aims to examine our institution's experience with patients who received both DC and subsequent CP to investigate associations between the timing of CP, original etiology for DC, and complication rates. Here, we report 278 patients who underwent both the procedures at our institution.

METHODS

Study Design and Patient Population

Patients that underwent CP after DC between 2004 and 2018 for traumatic or nontraumatic indications (ischemic stroke, intracerebral hemorrhage, and aneurysmal subarachnoid hemorrhage) were retrospectively identified. Patients that underwent DC at an outside institution or received DC for other indications (eg, tumor and infection) were excluded. Independent reviewers abstracted demographic and clinical data from the chart including age at CP, sex, indication for DC, time to CP, complications, follow-up, CP material, and CP location. Patient comorbidities assessed included obesity (body mass index [BMI] > 30), diabetes, hypertension, and smoking status (current, former, never). Only patients who underwent follow-up for both DC and CP at our institution were included in the present study. Length of follow-up was compared between the early and late subgroups (Table 1). In addition, baseline clinical severity scores were recorded at the time of presentation as appropriate for the presenting pathology including Glasgow Coma Scale (GCS),[8] Intracerebral Hemorrhage Score (ICH),[9] National Institutes of Health Stroke Scale (NIHSS),[10] and Hunt and Hess Score (HH).[11] The Clavien-Dindo grade (CDG) was used to classify complication severity following CP into minor (CDG <= 2) or major (CDG > 2).[12] All patients were assessed from the time of admission to CP to the last available follow-up. No cut-off was implemented. CDG was assessed by 3 data abstractors agnostic to the performed statistical analyses based on objective metrics as per Clavien et al.[12] Any disputes were resolved by consensus agreement. This study was conducted with the approval of the institutional review board and ethics committee. Patient consent was not required for this retrospective cross-sectional study. This study was conducted in accordance with STROBE reporting guidelines for cross sectional studies.[13]

Definitions

Complications following CP included infection, wound dehiscence, need for reoperation, HCP, ischemic stroke, bone flap resorption, and symptomatic extra-axial collections (EAC) that required surgical intervention. Reoperation was defined as any subsequent surgical intervention required to address complications, including wound revision, debridement for infection, evacuation of EACs, or repeat CP. HCP was defined as postCP HCP requiring placement of a ventriculoperitoneal shunt (VPS) but was not counted as a reoperation. Early and late CPs were defined as replacement of the bone flap or prosthesis ≤90 and >90 d following DC, respectively.[7]

Statistical Analysis

Continuous variables were described with means, standard deviation (SD), and compared with 2-tailed *t*-test where appropriate. Categorical variables were compared using Pearson's chi-squared test or Fisher's exact test where appropriate. Univariate logistic regression was used to examine the impact of CP timing and initial clinical severity scores on complication rates. For all statistical tests, $P < .05$ was considered statistically significant. All statistical analyses were performed using SAS JMP Pro (Version 14.0.0; Cary, North Carolina).

RESULTS

Demographics and Comorbidities

A total of 278 patients were included in the study (Figure 1), with 81 early and 197 late CPs. Baseline patient characteristics are summarized in Table 1. There was a greater proportion of CPs performed for initial trauma indication in the early CP group compared to the late CP group. In addition, we found that a higher proportion of patients had a history of diabetes and obesity in the late group. No statistically significant differences between age, sex, smoking status, follow-up, CP material, CP Location were found between the early and late groups. To investigate whether there was a change in the overall proportion of early or late CPs conducted from 2004 to 2018, we conducted a logistic regression of years vs CP timing and found no statistically significant association (Unit Odds Ratio [U-OR]: 1.14, $P = .0714$).

Complication Rates

A total of 51 patients (18.3%) experienced at least 1 complication following CP, regardless of timing. The most common complication was reoperation (11.2%, n = 31). There were 19 infections (6.8%), 13 patients with HCP (4.7%), 9 wound dehiscences (3.2%), 9 EACs (3.2%), and 6 resorptions (2.2%). No patients suffered an ischemic stroke. Patients were further assessed for associations between baseline comorbidities and CP location and we found no statistically significant associations between comorbidities and overall complications (**Supplemental Table 1**). In addition, we conducted a univariate logistic regression to investigate the impact of patient BMI on overall complications and found no statistically significant difference (U-OR: 2.47, $P = .339$).

Complications Rates—Early vs Late

The complication rates were compared between early and late groups. Complication frequencies and odds ratios for all patients and stratified by CP timing are outlined in Table 2. Patients with early CP had a significantly higher rate (32.1%) and odds of any complication compared with late CP (12.7%; odds ratio [OR]:

TABLE 1. Baseline Patient Characteristics

Age	Total N = 278	Early N = 81	Late N = 197	*P* value[a]
Mean (SD)	43.7 (16.0)	43.4(18.37)	43.8 (15.0)	.865
Sex				
Female	92 (33.1%)	27 (33.3%)	65 (33%)	1
Male	186 (66.9%)	54 (66.7%)	132 (67%)	
Time to cranioplasty (wk)				
Mean (SD)	24.8 (26.2)	8.5 (3.1)	31.5 (28.4)	–
Follow-up (mo)				
Mean (SD)	8.6 (15.1)	7.3 (9.7)	9.1 (16.8)	.248
Indication for DC				
Trauma	142 (51.1%)	51 (63%)	91 (46.2%)	**.011**[b]
Nontraumatic	136 (49%)	30 (37%)	106 (53.8%)	
ICH	39 (14%)	11 (13.6%)	28 (14.2%)	
Ischemic Stroke	69 (24.8%)	8 (9.8%)	61 (30.9%)	
aSAH	28 (10.1%)	11 (13.6%)	17 (8.6%)	
CP material				
Bone	260 (93.5%)	77 (95.1%)	183 (92.9%)	.601
Prosthesis	18 (6.5%)	4 (4.9%)	14 (7.1%)	
CP location				
LHC	118 (42.4%)	34 (42.0%)	84 (42.6%)	1
RHC	157 (56.5%)	46 (57.0%)	111 (56.3%)	
Bifrontal	3 (1.1%)	1 (1.0%)	2 (1.0%)	
Smoking status[c]				.420
Current	64 (24.7%)	16 (23.2%)	48 (25.3%)	
Former	77 (29.7%)	17 (24.6%)	60 (31.6%)	
Never	118 (45.6%)	36(52.2%)	82 (43.2%)	
Hypertension				.066
No	144 (51.8%)	49 (60.5%)	95 (48.2%)	
Yes	134 (48.2%)	39 (39.5%)	102 (51.8%)	
Diabetes				**.031**
No	241 (86.7%)	76 (93.8%)	165 (83.8%)	
Yes	37 (13.3%)	5 (6.2%)	32 (16.2%)	
Obesity[c]				**.001**
No	215 (78.5%)	71 (91.0%)	144 (73.5%)	
Yes	59 (21.5%)	7 (9.0%)	52 (26.5%)	

Standard deviation (SD), decompressive craniectomy (DC), Intracerebral Hemorrhage Score (ICH), aneurysmal subarachnoid hemorrhage (aSAH), cranioplasty (CP), left hemicranium (LHC), right hemicranium (RHC).
[a]Continuous and categorical variables in early vs late groups were evaluated using a 2-tailed *t*-test and Fischer's exact test, respectively.
[b]Comparing number of traumatic and nontraumatic indications for DC in early vs late cranioplasty groups.
[c]Information on smoking status was available for 259 of 278 patients, and information on BMI was available for 274 of 278 patients.
Bolded values indicate statistical significance.

3.27, $P < .001$). This remained true for several specific complications, including reoperation (early: 19%, late: 7.7%, OR: 2.80, $P = .01$), HCP (early: 11.4%, late: 2.1%, OR: 6.11, $P = .002$), and EAC (early: 8.9%, late: 1.0%, OR: 9.33, $P = .003$). There were no statistically significant associations with infection, wound dehiscence, ischemic stroke, and resorption.

Subgroup Analysis—Traumatic and Nontraumatic Indications

The early CP group demonstrated a higher distribution of traumatic brain injury patients (63%) compared to the late subgroup (46.2%), ($P = .017$, Table 1). Consequently, a subgroup analysis of early vs late CPs by traumatic and nontraumatic etiologies was performed to evaluate whether the traumatic etiology accounted for the higher complication rates seen in the early subgroup. The early CP trauma subgroup was associated with a statistically significant higher odds of any complication (early: 38.8%, late: 8.9%, OR: 6.49, $P < .001$), reoperation (early: 20.4%, late: 6.7%, OR: 3.59, $P = .024$), HCP (early: 16.3%, late: 2.2%, OR: 8.58, $P = .004$), and EAC (early: 12.2%, late: 1.1%, OR: 12.42, $P = .008$). There were no statistically significant associations with infection, wound dehiscence, ischemic stroke, and resorption in this subgroup analysis (Table 3).

In addition, when comparing the total complications in the traumatic and nontraumatic populations irrespective of CP

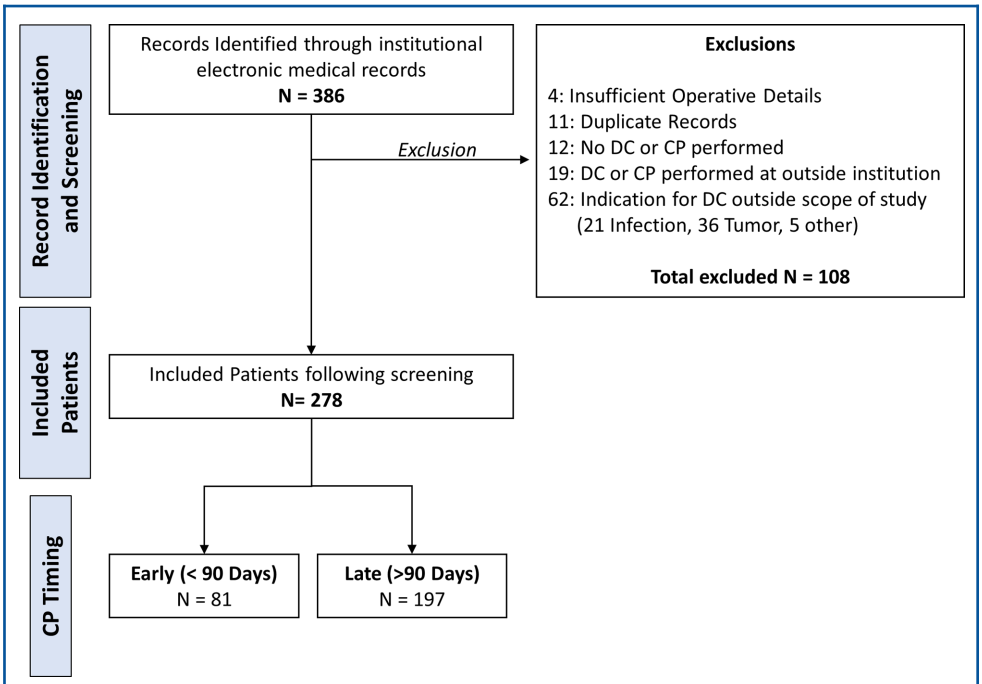

FIGURE 1. *Patient flowchart. Patient records were screened to identify patients who underwent both decompressive craniectomy (DC) and cranioplasty (CP) as per the inclusion criterion of the present retrospective study.*

TABLE 2. Effect of Early Cranioplasty on Complication Rates in All Patients

Complication	Total N = 278	Early N = 81	Late N = 197	OR[a]	95% CI	*P*-value[b]
Any	51 (18.3%)	26 (32.1%)	25 (12.7%)	3.25	1.73-6.09	**<.001**
Infection	19 (6.8%)	9 (11.1%)	10 (5.1%)	2.34	0.91-5.99	.113
Dehiscence	9 (3.2%)	2 (2.5%)	7 (3.6%)	0.69	0.14-3.38	1.000
Reoperation	31 (11.2%)	15 (18.5%)	16 (8.1%)	2.57	1.20-5.49	**.019**
HCP	13 (4.7%)	9 (11.1%)	4 (2.0%)	6.03	1.80-20.19	**.003**
Ischemic stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)	NC	–	–
Resorption	6 (2.2%)	2 (2.5%)	4 (2.1%)	1.22	0.22-6.80	1.000
EAC	9 (3.2%)	7 (8.9%)	2 (1.0%)	9.22	1.87-45.41	**.003**

HCP (hydrocephalus), EAC (extra-axial collection), OR (odds ratio), CI (confidence interval), NC (not-calculated).
[a]Odds ratios provided describe odds of respective complication in early vs late cranioplasty.
[b]*P*-values provided for 2-tailed Fisher's exact test comparing early vs late cranioplasty for each complication. Bolded values are indicated as statistically significant where $P < .05$.

timing, there was no statistically significant difference (trauma: 19.0%, nontraumatic: 17.7%, OR: 0.91, $P = .877$). The length of follow-up compared between trauma and nontrauma groups demonstrated no statistically significant difference ($P = .67$). We further did not detect statistically significant differences between the early trauma and late trauma groups with regard to sex, age, length of follow-up, smoking status, diabetic status, hypertension, GCS score, CP material, and CP location. We did observe a higher proportion of patients with obesity in the late trauma subgroup (early trauma: 4%, late trauma: 19%, $P = .019$).

Impact of Timing on Complication Rates

To further examine the impact of time to CP following DC on complication rates, a univariate logistic regression was performed for all patients regardless of etiology (**Supplemental Table 2**). In the pooled analysis, the odds of developing any complication decreased by 3.04% for each week that the CP was delayed from the time of the initial DC, but was not statistically significant (U-OR: 0.983, $P = .107$). In the trauma subgroup, the odds of any complication demonstrated a statistically significant 4.43% weekly decrease with CP delay (U-OR: 0.956, $P = .036$).

TABLE 3. Trauma Subgroup Analysis on Effect of Early Cranioplasty on Complication Rates

DC indication	Complication	Total N = 142	Early N = 51 (35.9%)	Late N = 91 (64.1%)	OR[a]	95% CI	*P* value[b]
Trauma	Any	27 (19.0%)	19 (37.3%)	8 (8.8%)	6.16	2.45-15.48	**<.001**
	Infection	7 (5.0%)	5 (9.8%)	2 (2.2%)	4.84	0.90-25.90	.098
	Dehiscence	2 (1.4%)	1 (2.0%)	1 (1.1%)	1.80	0.11-29.40	1.000
	Reoperation	16 (11.3%)	10 (19.6%)	6 (6.6%)	3.46	1.18-10.16	**.026**
	HCP	10 (7.0%)	8 (15.7%)	2 (2.2%)	8.28	1.69-40.66	**.004**
	Ischemic stroke	0 (0.0%)	0 (0%)	0 (0%)	NC	–	–
	Resorption	5 (3.5%)	1 (2.0%)	4 (4.4%)	0.44	0.05-4.00	.654
	EAC	7 (4.9%)	6 (11.6%)	1 (1.1%)	12	1.40-102.71	**.009**
		N = 136	**N = 30 (22.1%)**	**N = 106 (77.9%)**			
Nontraumatic	Any	24 (17.7%)	7 (23.3%)	17 (16%)	1.59	0.59-4.30	.416
	Infection	12 (8.8%)	4 (13.3%)	8 (7.5%)	1.88	0.52-6.75	.300
	Dehiscence	7 (5.2%)	1 (3.3%)	5 (5.7%)	0.57	0.06-4.97	1.000
	Reoperation	15 (11%)	5 (16.7%)	10 (9.4%)	1.92	0.60-6.12	.321
	HCP	3 (2.2%)	1 (3.3%)	2 (1.9%)	1.79	0.16-20.48	.530
	Ischemic stroke	0 (0.0%)	0 (0.0%)	0 (0.0%)	NC	–	–
	Resorption	1 (0.7%)	1 (3.3%)	0 (0%)	NC	–	–
	EAC	2 (1.5%)	1 (3.3%)	1 (1.0%)	3.62	0.22-59.67	.394

DC (decompressive craniectomy), HCP (hydrocephalus), EAC (extra-axial collection), OR (odds ratio), CI (confidence interval), NC (not-calculated).
[a]Odds ratios provided describe odds of respective complication in early vs late cranioplasty.
[b]*P*-values provided for 2-tailed Fisher's exact test comparing early vs late cranioplasty for each complication. Bolded values are indicated as statistically significant where $P < .05$.

Clavien-Dindo Grade, Baseline Clinical Scores, and Comorbidities

We examined the distribution of None or Minor Complications (CDG <= 2) and major complications (CDG > 2) in all patients as well as traumatic and nontraumatic groups (**Supplemental Table 3**). Among all patients, a statistically significant association with major complications was found in the early CP group (early: 27.2%, late: 9.1%, $P = .0002$). This association remained in the early CP trauma subgroup (early: 33.3%, late: 8.8%, $P = .0004$) but not the nontraumatic subgroup ($P = .3209$). We found no significant association between severity of neurological status on admission (ICH, GCS, NIHSS, HH) and complication rates (**Supplemental Table 4**), as well as for trauma patients when stratified by mild, moderate, or severe injury (not presented).

DISCUSSION

Key Results and Interpretation

The results of the present study demonstrate that in our 14-yr single center experience, early CP was associated with significantly higher odds of overall complications, reoperation, HCP, and EAC compared to late CP. This finding persisted only in the trauma subgroup, but not in the nontraumatic subgroup. Notably, the odds of complications decreased by 4.4% for each week the CP were delayed after the initial DC in trauma patients. These results suggest that optimal timing of CP for complication avoidance may, in fact, be different for different etiologies of neurological injury. Thus, our interpretations of these findings is that the use of early CP in patients with a traumatic etiology for their DC may be at higher odds for complications, and waiting to perform a CP may reduce the risk of certain complications (Figure 2). Importantly, the reader should be cautioned from the conclusion of whether early or late CP is "better" or "worse" purely from our single-center retrospective experience (see: Limitations). Instead, moving forward clinical decision making must rely on the purported advantages and disadvantages of CP timing based on the body of literature.

Generalizability

While the generalizability of our study is limited due to its retrospective nature, our results are similar to several previous studies. A recent study by Goedemans et al[14] of 145 patients reported higher rates of overall complications in early CP (30%) compared to late CP (>90 d; 3%). The largest single-center study to date is that of Morton et al,[6] who reported their 10-yr experience on CP timing (n = 754). In their study, they found that HCP was most common in their pooled analysis among patients who underwent CP at <90 d after DC. They report a statistically significant association with development of HCP in their trauma subgroup. Further subgroup analyses discovered that this was true for not only trauma patients, but also patients with subarachnoid hemorrhage (SAH) and intraparenchymal hemorrhage. Our present study reported an HCP rate among all patients of 11.4% with early CP (<90 d) and 2.1% with late CP (>90 d), and noted a statistically significant difference, which persisted only in the trauma subgroup. Morton et al also examined HCP at

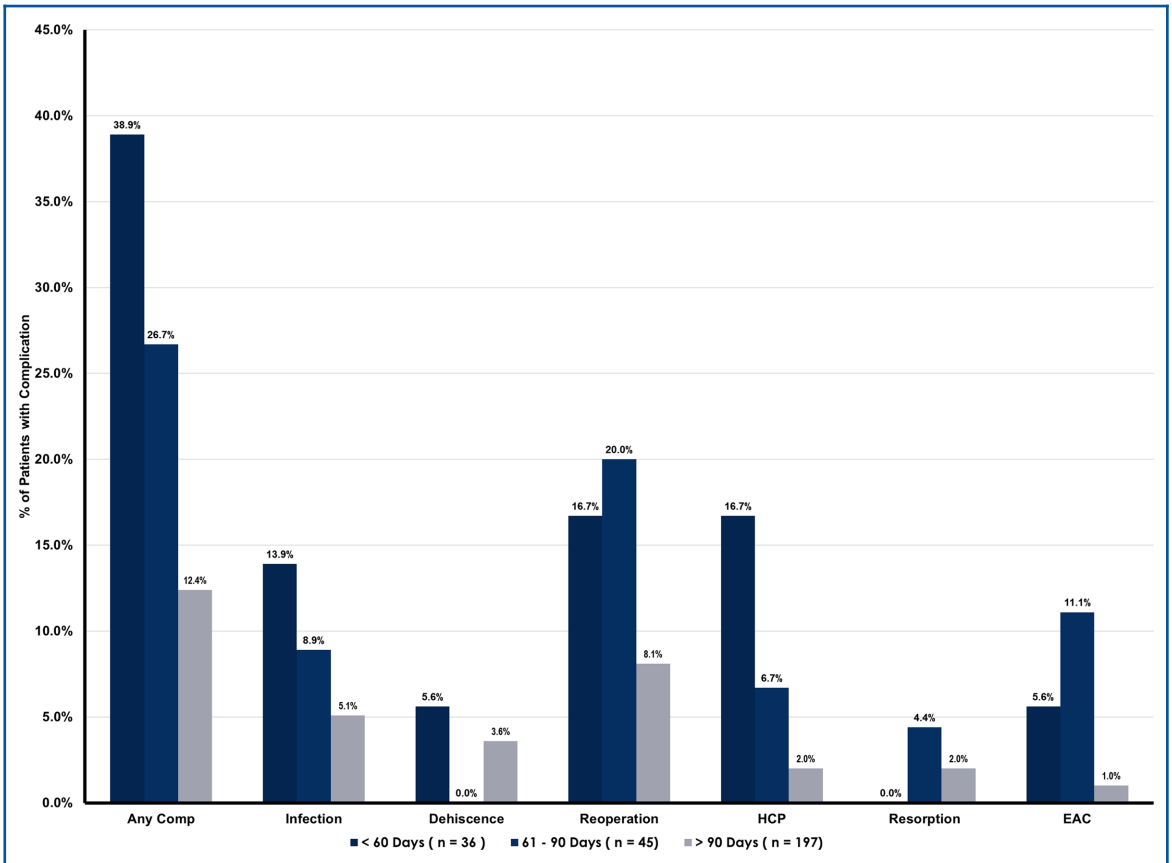

FIGURE 2. *Distribution of complications following CP performed at different time intervals. Patients were grouped based on timing of CP at either <60 d (n = 36 patients), 61 to 90 d (n = 45), or >90 d (n = 197) post DC. The relative frequency of patients who experienced any complication, infection, dehiscence, reoperation, HCP, resorption, or EAC is presented for each time range.*

several timepoints regardless of etiology, reporting rates of 29% (<14 d), 21% (15-30 d), 20% (31-42 d), 13% (42-90 d), and 4% (>90 d). In addition, Morton et al reported a statistically significant decrease in the odds of HCP for every 10-d post DC in their pooled analysis of all indications for DC (U-OR: 0.92, $P < .001$). Our present study found similar results in the trauma subgroup (4.4% decrease in complication odds for each week of CP delay), but the pooled analysis irrespective of etiology did not reach statistical significance. Our findings are also in agreement with 2 recent systematic reviews examining this topic.[7,15]

Numerous studies have further reported heterogenous findings regarding the timing of CP and respective complications.[2,6,7,15-18] For example, Morton et al[6] also reported that the rate of infection was significantly higher in patients who underwent CP at less than 14 d. This is consistent with studies that have reported higher infection rates among patients undergoing earlier CP.[19,20] Our present study did find a greater odds of infection in the early CP group (OR: 2.36), but did not reach statistical significance ($P = .11$). Other studies have reported no differences in complications, including infection and HCP in early vs late CPs.[21-23] In order to achieve a consensus regarding the question of optimal timing for CP and complications that is appropriately generalizable, a prospected randomized trial with appropriate sample size is needed.

The Question of Optimal Timing

The motivation for performing a CP is multiform. In addition to restoring cranial cosmesis and brain protection, there is some evidence in the literature that CP may improve neurological outcomes.[2,21,24] It stands to reason that surgeons might wish to perform a CP as soon as possible to optimize patients' rehabilitation potential, without putting the patient at increased risk of complication. The optimal timing of CP remains an open question. The heterogeneous findings in the literature regarding complication rates suggest that perhaps this timepoint is different for different patients. The most obvious characteristic to consider is the etiology of the neurological injury, as the pathophysiology of brain injury and development of cerebral edema that necessitates DC in the first place can lead to variable pathways to cellular dysfunction and death. This is supported by the fact

that there were higher odds of complications only in trauma patients undergoing early CP in our study, but not other groups. Other studies have attempted to hone in on the reason for this and found an association between presence of any preoperative cerebrospinal fluid (CSF) disturbance[1,23,25] or traumatic acute subdural hematoma[14] with increased complications rates. It is also possible that severity of the underlying traumatic injury influences later complications, as suggested by previous studies.[7] In our study, we attempted to assess if the severity of the initial pathology was associated with postCP complications but we found no significant associations (**Supplemental Table 3**).

Given the heterogeneity of the evidence, the question of optimal CP timing likely depends on a number of factors, including the original indication for DC, as influenced by its respective pathophysiology and baseline injury severity. Other patient-specific variables including past medical history may also contribute.[26] At present, there is no standard guideline for deciding when a CP should be performed. This decision is largely made on a case by case basis and influenced by both clinical and nonmedical factors. Most surgeons clinically variably assess the fullness of the skin flap and radiographic metrics to determine favorability of CP. Timing of CP can also be influenced by social factors such as patient or family preferences, complexity of patients' social situation, or convenience of operative scheduling.[6,14] It will be necessary to develop an objective metric and evidence that supports clinical decision making when choosing the right time to perform a CP, if the goal is to optimize neurological recovery and minimize complications. One option is to devise a multivariate clinical scoring system that utilizes patient characteristics, clinical data, radiological metrics, CSF dynamics, and severity scores to devise a model that maximizes the benefits of earlier CP while limiting potential drawbacks. This effort would best be executed by a cooperative multi-institutional effort for appropriate statistical power, development, and subsequent validation in a prospective fashion.

Limitations

There are several important limitations to this present study. While this series has a substantial number of patients allowing for robust statistical analysis, it is a single-institution study, which limits its generalizability. Its retrospective nature means a lack of control, so it is certainly possible that patients undergoing earlier CP were at higher risk for complications, regardless. In the present study, a higher proportion of patients in the late group had baseline comorbidities of diabetes and obesity. We also compared baseline demographics of early vs late trauma patients, and found a higher proportion of obesity in the late trauma patients. However, the multiplicity of this type of further subgroup analysis is a limitation of this study. While these are unlikely to be protective characteristics for the late subgroup, this highlights the heterogeneity of the groups due to the retrospective design and the importance of conducting a prospective trial with matched clinical metrics.

Other important factors to consider include insurance status, the clinical course from DC, and the elective decision to perform CP at a particular time point. Indeed, some patients who undergo DC following a trauma do not expediently return for a CP, thereby potentially presenting a cohort in the late CP group that may have fewer comorbidities and are less likely to incur respective complications. In addition, as with any long-term retrospective study, the involvement of staff, surgical personnel, and individual decision making cannot be controlled. Lastly, while the length of follow-up did not differ in a statistically significant fashion, a prospective trial would be better suited to appropriately assess complication rates across groups. Future studies should consider randomizing CP timing delay for eligible patients.

CONCLUSION

In our retrospective series, early CP was associated with higher odds of any postoperative complication, reoperation, HCP, and extra-axial-collection compared to late CP, which was most true for the trauma subgroup. The nontrauma subgroup did not demonstrate differences in complication rates with respect to early or late CP. These results suggest the use of early CP in patients with a traumatic etiology for their DC may be at a higher risk for certain complications. Greater care should be taken in preoperative planning and increased vigilance postoperatively for complications with this more vulnerable subpopulation. Future prospective controlled trials are needed to elucidate optimal timing for CP.

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Supplemental Table 1. Complication rates by CP location and baseline comorbidities. Abbreviations: Left hemicranium (LHC), right hemicranium (RHC). **P*-values of chi-square tests. **Information on smoking status was available for 259 of 278 patients, and information on BMI was available for 274 of 278 patients.

Supplemental Table 2. Time to cranioplasty and odds of complications. Logistic regression of time to cranioplasty (in wk) vs development of any complication. Abbreviations: N (number of patients), OR (odds ratio), U-OR (unit odds ratio). *U-OR provided describes the change in odds of any complication for each week CP is delayed post DC. ***P*-values provided for chi-square test. Bolded values are indicated as statistically significant where $P < .05$.

Supplemental Table 3. Association of early cranioplasty with major complications. Abbreviations: N (number of patients), CDG (Clavien-Dindo grade), CP (cranioplasty). **P*-values provided for 2-tailed Fisher's exact test comparing early and late groups and number of patients with CDG > 2 events. Bolded values are indicated as statistically significant where $P < .05$.

Supplemental Table 4. No association between initial severity of score and odds of any complication. Logistic regression of initial score vs development of any complication for patients who had recorded respective scores. One trauma patient and 5 ischemic stroke patients did not have recorded scores. Abbreviations: N (number of patients), OR (odds ratio), HH (Hunt and Hess Score), ICH (Intracerebral Hemorrhage Score), NIHSS (National Institutes of Health Stroke Scale), GCS (Glasgow Coma Scale). *U-OR provided describes the change in odds of any complication for each unit change in clinical score. ***P*-values provided for chi-square test. Bolded values are indicated as statistically significant where $P < .05$.