Complications following cranioplasty: incidence and predictors in 348 cases

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OBJECT The factors that contribute to periprocedural complications following cranioplasty, including patient-specific and surgery-specific factors, need to be thoroughly assessed. The aim of this study was to evaluate risk factors that predispose patients to an increased risk of cranioplasty complications and death.

METHODS The authors conducted a retrospective review of all patients at their institution who underwent cranioplasty following craniectomy for stroke, subarachnoid hemorrhage, epidural hematoma, subdural hematoma, and trauma between January 2000 and December 2011. The following predictors were tested: age, sex, race, diabetic status, hypertensive status, tobacco use, reason for craniectomy, urgency status of the craniectomy, graft material, and location of cranioplasty. The cranioplasty complications included reoperation for hematoma, hydrocephalus postcranioplasty, postcranioplasty seizures, and cranioplasty graft infection. A multivariate logistic regression analysis was performed. Confidence intervals were calculated as the 95% CI.

RESULTS Three hundred forty-eight patients were included in the study. The overall complication rate was 31.32% (109 of 348). The mortality rate was 3.16%. Predictors of overall complications in multivariate analysis were hypertension (OR 1.92, CI 1.22–3.02), increasing age (OR 1.02, CI 1.00–1.04), and hemorrhagic stroke (OR 3.84, CI 1.93–7.63). Predictors of mortality in multivariate analysis were diabetes mellitus (OR 7.56, CI 1.56–36.58), seizures (OR 7.25, CI 1.238–42.79), bifrontal cranioplasty (OR 5.40, CI 1.20–24.27), and repeated surgery for hematoma evacuation (OR 13.00, CI 1.51–112.02). Multivariate analysis was also applied to identify the variables that affect the development of seizures, the need for reoperation for hematoma evacuation, the development of hydrocephalus, and the development of infections.

CONCLUSIONS The authors’ goal was to provide the neurosurgeon with predictors of morbidity and mortality that could be incorporated in the clinical decision-making algorithm. Control of a patient’s risk factors and early recognition of complications may help practitioners avoid the exhaustive list of complications.

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KEY WORDS cranioplasty complication; infection; seizure; mortality rate; cranioplasty morbidity; reoperation; hematoma

CRANIOPLASTY is more than a cosmetic repair of cranial defects; it is part of the rehabilitation process following a patient’s neurological injury. Recent studies have shown that cranioplasty may improve the patient’s psychological status, social performance, and neurocognitive functioning.1,14,19,21 The factors that contribute to periprocedural complications, including patients’ demographic information, comorbidities, surgical procedure, and underlying disease, need to be thoroughly evaluated. Previous studies that were intended to answer these questions were limited by their design or by their sample size. Our aim was to evaluate risk factors that predispose patients to an increased risk of cranioplasty complications. Recent evidence in the literature emphasizes patient-specific factors over surgery-specific factors as major predictors of cranioplasty complications.47,51 It is also becoming evident that surgical treatment for cranioplasty complications is associated with additional surgical procedures.17,46 In this study, we evaluated the association between patient-specific factors and complications fol-
following cranioplasty surgery. We also evaluated whether some complications increase the risk of developing others. Finally, we studied factors that are associated with patient death following cranioplasty.

**Methods**

**Study Design**

The Thomas Jefferson University Hospital Institutional Review Board approved the study protocol. We queried a prospectively maintained database of patients who had undergone cranioplasty at our institution between January 2000 and December 2011. The study included all patients who underwent a craniectomy for traumatic brain injury (TBI), subdural hematoma, hemorrhagic or ischemic stroke, epidural hematoma, and subarachnoid hemorrhage (SAH). The aim of the study was to identify the predictors of infections, seizures, hydrocephalus, and hematoma in the postoperative setting (in vascular patients specifically). We selected our patients to be comparable, as much as possible, in their baseline risks and pathological entity. Therefore, we excluded patients with craniotomy for seizure, infectious disease, and tumors.

**Variables Studied**

Patient demographic data including age and sex were collected, in addition to the following medical comorbidities: smoking history, hypertension, diabetes mellitus (DM), therapeutic indication for craniectomy (reason for craniectomy), urgency of the therapeutic craniectomy, and the cranioplasty graft material. Complications related to the cranioplasty were identified as postoperative hematoma requiring reoperation, infection of the cranioplasty graft, postcranioplasty hydrocephalus, postcranioplasty seizure, and death.

The variables were defined as follows. 1) Diabetes mellitus: any patient who has been diagnosed with DM Type 1 or Type 2. Patients were not stratified according to hemoglobin A1C level. 2) Hypertension: any patient who has been diagnosed with Stage 1 or more hypertension. Patients were not stratified to controlled versus uncontrolled hypertension. 3) Smoking: any patient who had smoked in the past, regardless of the number of pack-years. A patient who stopped smoking after the craniectomy was still counted as a smoker. 4) Graft material: categorized as autologous or synthetic. 5) Urgency of craniotomy: categorized into urgent versus elective. 6) Location: convexity cranioplasty, bifrontal cranioplasty, suboccipital cranioplasty. 7) Postcranioplasty seizure: any patient who experienced a seizure after the cranioplasty operation. 8) Reoperation for hematoma: any intracranial hematoma that occurred after the cranioplasty and required an operation for evacuation. 9) Postcranioplasty hydrocephalus: a hydrocephalus that developed after the cranioplasty, documented by a CT scan. 10) Postcranioplasty infection: any case of graft infection that needed to be removed or any case in which infection was suspected and antibiotic therapy was administered for more than 2 weeks, regardless of culture results. 11) Race: Caucasian, African American, Asian, and Hispanic. 12) Reason for craniectomy: SAH, TBI, nontraumatic epidural hematoma, nontraumatic subdural hematoma, ischemic stroke, and hemorrhagic stroke.

**Statistical Analysis**

Data are presented as the mean and range for continuous variables, and as frequency for categorical variables. Analysis was performed using the unpaired t-test, chi-square, or Fisher exact tests as appropriate. Univariate analysis was used to test covariates predictive of cranioplasty complication. Interaction and confounding was assessed through stratification and relevant expansion covariates. Factors that were predictive in univariate analysis (p < 0.15) were entered into a multivariate logistic regression analysis. Probability values of ≤ 0.05 were considered statistically significant. Statistical analysis was performed with Stata version 10.0 software (StataCorp LP). Confidence intervals were calculated as the 95% CI.

**Results**

**Baseline Characteristics**

We enrolled 348 patients in our study. Patient demographic data and surgical indications are included in Table 1. The mean age (± SD) was 46.5 ± 12.7 years. The proportion of male patients in the study was 50.86%. The majority of the patients were Caucasians (72.99%), followed by African Americans (16.09%), Hispanics (6.90%), and Asians (4.02%). Diabetic patients constituted 14.94% (52 of 348) of the study population. The proportion of patients with hypertension was 54.31% (189 of 348), and the proportion of smokers was 47.13% (164 of 348). The majority of patients received autologous bone graft (67.24%). The most common indication for craniectomy was SAH (52.01%) followed by stroke (27.01%) and TBI (18.96%).

**TABLE 1. Characteristics of 348 patients who underwent cranioplasty**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>177</td>
</tr>
<tr>
<td>Female</td>
<td>171</td>
</tr>
<tr>
<td>Mean age (yrs) ± SD</td>
<td>46.5 ± 12.7</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>254</td>
</tr>
<tr>
<td>African American</td>
<td>56</td>
</tr>
<tr>
<td>Hispanic</td>
<td>24</td>
</tr>
<tr>
<td>Asian</td>
<td>14</td>
</tr>
<tr>
<td>Smoking status</td>
<td>164 smokers</td>
</tr>
<tr>
<td>Diabetic status</td>
<td>52 patients w/ DM</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>189 patients w/ hypertension</td>
</tr>
<tr>
<td>Craniectomy indication</td>
<td></td>
</tr>
<tr>
<td>SAH</td>
<td>181</td>
</tr>
<tr>
<td>TBI</td>
<td>66</td>
</tr>
<tr>
<td>Stroke</td>
<td>94</td>
</tr>
<tr>
<td>EDH/SDH</td>
<td>7</td>
</tr>
</tbody>
</table>

EDH = epidural hematoma; SDH = subdural hematoma.
Predictors of Overall Complications

We studied the association between each of the following variables—age, sex, race, hypertension, DM, smoking status, reason for craniotomy, urgency status, and cranioplasty location—and the development of any complication postcranioplasty. The list of complications was as follows: reoperation for hematoma evacuation, postcranioplasty hydrocephalus, postcranioplasty seizures, and postcranioplasty infection.

The overall complication rate was 31.32% (109 of 348). The mortality rate was 3.16%. Table 2 lists the proportion of each complication encountered. Univariate predictors included in multivariate analysis were age, DM, hypertension, and hemorrhagic stroke. Univariate analysis applied for graft material type showed no difference between synthetic and autologous bone graft (OR 1.34; p = 0.20). In multivariate analysis, hypertension (OR 1.92, CI 1.22–3.02), increasing age (OR 1.02, CI 1.00–1.04), and hemorrhagic stroke (OR 3.84, CI 1.93–7.63) predicted complications (Table 3).

Predictors of Postcranioplasty Hydrocephalus

Multivariate logistic regression analysis identified increasing age (OR 1.05, CI 1.01–1.08), therapeutic indication for SAH (OR 2.04, CI 1.16–3.58), and therapeutic indication for TBI (OR 2.12, CI 1.23–3.65) as significant predictors of postcranioplasty hydrocephalus development, whereas male sex was found to have a protective effect (OR 0.39, CI 0.19–0.80) (Table 4). Smoking was associated with postoperative hydrocephalus (OR 1.91, p = 0.001) in univariate analysis, but the association was no longer significant in multivariate analysis (OR 1.89, CI 0.94–3.80). The other variables (race, hypertension, DM, urgency status, graft material, cranioplasty location) did not affect the risk of hydrocephalus development in univariate analysis, and therefore were excluded from multivariate analysis.

Predictors of Reoperation for Hematoma Evacuation

Multivariate logistic analysis (Table 5) identified male sex (OR 2.87, CI 1.13–7.25), African American race (OR 3.82, CI 1.50–9.72), and hypertension (OR 3.72, CI 2.93–5.30) as predictors of subsequent reoperation for hematoma evacuation. Right-sided hemispheric craniectomy was associated with a higher risk in univariate analysis, but the risk was no longer significant when multivariate analysis was applied (OR 4.32, CI 0.98–19.00). Emergency status, smoking, diabetic status, age, graft material, and reason for craniectomy were not associated with reoperation for hematoma evacuation in univariate analysis, and were therefore excluded from the multivariate analysis.

Predictors of Infection

All patients who underwent cranioplasty have received perioperative cefazolin. We also evaluated whether postcranioplasty hydrocephalus and reoperation for hematoma evacuation could affect the risk of infection, as long as these complications preceded the infection of the graft. Univariate analysis revealed that increasing age (OR 3.37, p = 0.05), DM (OR 1.84, p < 0.05), hemorrhagic stroke (OR 5.27, p < 0.05), postcranioplasty hydrocephalus (OR 1.91, p < 0.05), and reoperation for hematoma evacuation (OR 2.67, p = 0.051) were predictive of infection. Bilateral convexity cranioplasty showed a higher rate of infection when compared with suboccipital, bifrontal, and unilateral convexity cranioplasty (OR 12.01, p < 0.05) in univariate analysis. Sex, race, hypertension, smoking, graft material, and urgency status did not increase the risk of infection. In multivariate analysis (Table 6), bilateral convexity cranioplasty (OR 14.41, CI 1.52–36.66), postcranioplasty hydrocephalus (OR 1.90, CI 0.99–3.65; p = 0.05), and hemorrhagic stroke (OR 4.33, CI 1.66–11.34) remained associated with a higher risk of infection, whereas reoperation for hematoma evacuation showed a higher trend (OR 1.90, p = 0.054) but was not statistically significant (not shown).

Predictors of Seizure

We excluded from the analysis any patient who had experienced a seizure before the cranioplasty or any patients who were receiving antiepileptic drugs (AEDs). The large majority of patients who were temporarily receiving AEDs were no longer taking these drugs by the time of cranioplasty. Patients who were receiving long-term AEDs were excluded from the analysis, because they had experienced a seizure before cranioplasty or had a base-

### Table 2. Postcranioplasty complications and their proportions

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Most Common Indication</th>
<th>Overall</th>
<th>Seizures</th>
<th>Surgical Site</th>
<th>Hydrocephalus</th>
<th>Overall Infection</th>
<th>Superficial Infection</th>
<th>Deep Infection</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>348</td>
<td>SAH (52%)</td>
<td>31.32%</td>
<td>14.37%</td>
<td>6.90%</td>
<td>13.51%</td>
<td>26.43%</td>
<td>14.94%</td>
<td>11.49%</td>
<td>3.16%</td>
</tr>
<tr>
<td>Broughton et al., 2014</td>
<td>87</td>
<td>TBI (46%)</td>
<td>30.0%</td>
<td>5.7%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee et al., 2013</td>
<td>236</td>
<td>TBI (60.17%)</td>
<td>25.92%</td>
<td>14.81%</td>
<td>1.65%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wachter et al., 2013</td>
<td>136</td>
<td>TBI (38.2%)</td>
<td>30.1%</td>
<td></td>
<td>6.6%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gooch et al., 2009</td>
<td>62</td>
<td>TBI (66%)</td>
<td>33.8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tbody>
</table>

### Table 3. Predictor of complications on multivariate analysis

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR</th>
<th>p Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>1.92</td>
<td>&lt;0.005</td>
<td>1.22–3.02</td>
</tr>
<tr>
<td>Increasing age</td>
<td>1.02</td>
<td>0.029</td>
<td>1.00–1.04</td>
</tr>
<tr>
<td>Hemorrhagic stroke</td>
<td>3.84</td>
<td>&lt;0.001</td>
<td>1.93–7.63</td>
</tr>
</tbody>
</table>
line disease (epilepsy) for which they were being treated with the drugs. Therefore, none of the patients analyzed in the seizure cohort was receiving AEDs at time of the cranioplasty surgery.

We also evaluated whether postcranioplasty infection, reoperation for hematoma, and postcranioplasty hydrocephalus affected the risk of seizures, provided they occurred before the seizure’s onset. Univariate analysis revealed the following variables to be associated with a higher risk of postcranioplasty seizure: male sex (OR 2.37, p < 0.05), older age of > 60 years (OR 1.02, p < 0.05), bifrontal and convexity cranioplasty location when compared with suboccipital (OR 9.43, p < 0.05), decompressive hemicraniectomy (DHC) for trauma (OR 3.22, p < 0.05), cranioplasty site infection (OR 4.54, p < 0.05), and reoperation for hematoma evacuation (OR 3.40, p < 0.05). Smoking, hypertension, DM, race, and urgency status did reach statistical significance. There was no difference in seizure rate between patients who had a synthetic graft and those who had an autologous bone graft. In multivariate analysis (Table 7), male sex (OR 2.35, CI 1.14–4.85), increasing age (OR 1.04, CI 1.01–1.07), and cranioplasty graft infection (OR 4.12, CI 2.07–8.20) were associated with a higher risk of postcranioplasty seizure development. Trauma (OR 2.18, CI 0.93–5.09; p = 0.07) and cranioplasty location (OR 2.86, CI 0.93–8.81; p = 0.06) showed a trend of increased risk but did not achieve statistical significance.

Predictors of Mortality

We tested the following predictors: age, sex, race, diabetic status, hypertensive status, smoking, reason for craniectomy, urgency status of craniectomy, location of cranioplasty, graft material type, reoperation for hematoma evacuation, hydrocephalus postcranioplasty, graft infection, and seizure postcranioplasty. In multivariate analysis (Table 8), only DM (OR 7.56, CI 1.56–36.58), seizures (OR 7.25, CI 1.23–42.79), bifrontal cranioplasty (OR 5.40, CI 1.20–24.27), and repeated surgery for hematoma evacuation (OR 13.00, CI 1.51–112.02) predicted death.

| TABLE 4. Multivariate analysis of hydrocephalus predictors |
|----------------|---|---|---|
| Predictors     | OR | p Value | 95% CI |
| Male sex       | 0.39 | 0.010 | 0.19–0.80 |
| Increasing age | 1.05 | 0.004 | 1.011–1.08 |
| Smoking        | 1.89 | 0.073 | 0.94–3.80 |
| SAH            | 2.04 | 0.013 | 1.16–3.58 |
| TBI            | 2.12 | 0.007 | 1.23–3.65 |

Discussion

Overview of Cranioplasty Complications

Cranioplasty is associated with a relatively high overall complication rate, estimated between 15% and 36.5%. Further, 25%–76% of patients with postcranioplasty complications may need additional procedures to correct these complications. Therefore it is of paramount importance to understand, prevent, and treat the complications as they arise. The overall complication rate in our study was relatively high because the list of complications that we included was more exhaustive than in previous series. Another reason is that the definition of infected cranioplasty was not limited to cases that required reoperation. The complications in our study were as follows: postcranioplasty hydrocephalus, reoperation for hematoma evacuation, superficial and deep infection, new-onset seizure, and death. We did not include subgaleal fluid collection, bone desorption, and wound dehiscence that was not due to infection. The most common cause of craniectomy was SAH, followed by stroke, and then by TBI (the last being the most common cause of DHC in the literature). The aim of this study was to determine the most important predictors of complications and death.

Patient-specific and surgery-specific factors are historically reported to be the most important determinant of complications following cranioplasty. Recently, most studies have reported limited contributions of surgery-specific factors or implant material on the overall complication rate following cranioplasty. In addition, the data on time interval have been contradictory. Predictors of mortality have not been previously thoroughly examined. In our study, in addition to demographic data, we included in the analysis smoking status, hypertension, DM, the reason for cranioplasty, the urgency of the procedure, and graft type.

Demographic Information and Associated Comorbidities

We found that increased age and hypertension were as-
associated with higher risk of complications. Smoking was associated with an increased risk of hydrocephalus development in univariate analysis, and showed a strong trend in multivariate analysis. A recent study by Wachter et al. identified smoking and older age (> 60 years) as factors associated with cranioplasty complications.46 These authors did not find sex to be a significant variable. We found that diabetic patients had a higher risk of death. Male patients had a higher rate of seizure, whereas females had a higher risk of hydrocephalus. Older age was also associated with seizure and hydrocephalus. Neurosurgeons should therefore recognize these factors (age, sex, DM, and smoking) as possible predictors of postoperative complications and take all necessary preventive measures.

Location of Cranioplasty

Patients with convexity cranioplasty had a higher risk of infections and postoperative hematoma requiring reoperation for evacuation when compared with bifrontal and suboccipital cranioplasties. We also found bifrontal cranioplasty to be associated with a higher risk of both seizure and death. Bifrontal defect was identified by Gooch et al.17 to be the only location significantly associated with cranioplasty complications. The authors postulated several reasons for this finding, such as a longer incision, a longer operative time, less soft-tissue coverage, and a possible violation of the frontal sinus. Indeed, frontal sinus breach has been reported to increase the risk of infection after cranioplasty.6,28

Timing, Infection, and Hydrocephalus

The timing of surgery is one of the most controversial topics in cranioplasty.4,31 Some studies have shown that patients who had early cranioplasties had better functional outcomes,3,5,46 whereas several others have shown that early cranioplasty (3–6 months) is associated with higher complication rates and worse outcomes,3,4,8,10,26,35,42 including hydrocephalus, increased intracranial pressure, and infection. Other studies have shown that late cranioplasty is associated with a higher risk of complications.17,38,42,48 Finally, recent studies, including a meta-analysis, have shown no difference in complication rates between early and late cranioplasties.5,24,39,51 We did not account for the timing of cranioplasty in our study because our patients underwent early operation unless there was a convincing need to delay it, such as the presence of wound dehiscence, hydrocephalus, or evidence of persistent brain swelling. We balanced the wait for maximal neurological improvement with early intervention to prevent hemodynamic changes in the CSF and cerebral blood flow that may occur if the flap was left out for a prolonged period of time.5 Still, the large majority of our patients have undergone early cranioplasty (within 3 months). We found no significant association of age, sex, DM, and mechanism of injury (SAH, trauma, ischemic stroke) with postcranioplasty infection, which is consistent with the published literature.22,29 Reoperation for hematoma showed no significant effect in our study, even though the need for multiple procedures has been shown to increase the risk of cranioplasty site infection.29,43,47 On the other hand, Cheng et al.’s work9 showed that the number of procedures does not affect the risk of graft infection following cranioplasty.

We found hemorrhagic stroke to be predictive of infection. One reason would be shared risk factors between stroke and infection, such as DM and smoking.15,45 Even though it has been proven that DM40 and smoking46 increase the risk of surgical infection, the association did not achieve statistical significance in our study. We believe that the lack of a significant effect of smoking and DM might be related to the fact that stratification did not account for present and past smokers, as well as controlled and uncontrolled DM. In many of our patients their DM was controlled, and many had quit smoking after experiencing a stroke or an SAH. Quitting smoking and controlling DM have been known to decrease the patient’s risk of developing postsurgery infection.16,32 Cranioplasty has been reported to contribute to the development of persistent hydrocephalus requiring permanent CSF flow diversion.45 We found that female sex, increasing age, and craniectomy for SAH increased the risk of postcranioplasty hydrocephalus.

Postcranioplasty Hemorrhage

Postcranioplasty hemorrhage includes epidural, subdural, and intraparenchymal hematomas that required reoperation.6,17,36 Postcranioplasty hemorrhage has been previously explained by many mechanisms, the most important of which is persistent bleeding by a scalp artery,36 along with a negative transluminal pressure caused by a subgaleal drain.37 Gooch and colleagues17 found that bifrontal cranial defect was associated with a need for reoperation, including infection and hematoma evacuation. The authors, however, only studied the complications that occurred within 30 days of surgery. In our study, convexity location showed a trend of higher risk of reoperation for hematoma evacuation when compared with suboccipital and bifrontal locations. Other significant risk factors in multivariate analysis were male sex and African American race. Although this finding may be due to the presence of hypertension, this factor was controlled for in multivariate analysis, which suggests that male sex and African American race are independent predictors of hemorrhage. The problem with subjecting a patient to another surgery is the increased risk of further complications8 and the increased length of hospital stay. Indeed, in our study, patients undergoing another operation for hematoma evacuation had a significantly higher mortality rate.

Postcranioplasty Seizures

Seizures that follow cranioplasty surgery might be the

### TABLE 8. Multivariate analysis of predictors of mortality

<table>
<thead>
<tr>
<th>Predictors</th>
<th>OR</th>
<th>p Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>7.56</td>
<td>0.012</td>
<td>1.56–36.58</td>
</tr>
<tr>
<td>Bifrontal cranioplasty</td>
<td>5.40</td>
<td>0.028</td>
<td>1.20–24.27</td>
</tr>
<tr>
<td>Postcranioplasty seizures</td>
<td>7.25</td>
<td>0.029</td>
<td>1.238–42.79</td>
</tr>
<tr>
<td>Reop for hematoma evacuation</td>
<td>13.00</td>
<td>0.020</td>
<td>1.51–112.02</td>
</tr>
</tbody>
</table>

*OR = Odds Ratio, CI = Confidence Interval*
result of the underlying cause, the DHC surgery, or the cranioplasty operation itself. Surgery might produces free radicals, disturb the ionic balance, and manipulate the cerebral parenchyma, all of which have been postulated as mechanisms for postoperative seizure formation.25,48 In the literature, TBI, hemorrhagic stroke, and neurological deficits before cranioplasty increased the risk of seizures.25 In our study, we found that male sex, cranioplasty infection, and older age were significantly associated with seizures. Furthermore, seizure itself was significantly associated with death. On univariate analysis, reoperation for hema-
toma evacuation was a predictor of seizure (OR 3.40, p < 0.05), but the association was no longer significant on multivariate analysis. Male sex and older age have been described as independent factors for first adult seizure in the general population.18,20,23,31,44

Other Predictors

Graft material (synthetic vs autologous) failed to show any significant association with seizure, infection, death, or any other complication. The Glasgow Coma Scale, pre-
operative Barthel Index, and the Coma Remission Scale may predict the risk of cranioplasty complications.4,46 Even
though the risk of infection with autologous graft can get relatively high (up to 33%),12,33,34,52 many studies, including ours, suggest no difference in the infection rate between synthetic and autologous grafts.9,47

Limitations and Strengths of the Study

The limitations of this study are the retrospective de-
gign; a possible selection bias; and the lack of stratification of diabetic, smoker, and hypertensive patients. The study also did not include any surgery-specific risk factor. We did not study the association between the timing of cranioplasty and outcomes, although this might affect the results. The strength of the study is the long-term follow-
up and the large size of the cohort, allowing for a robust statistical analysis. Both the long follow-up and the large number of patients allowed the evaluation of rare complications.

Conclusions

Cranioplasty complications include infections, hydro-
cephalus, multiple operations, seizures, and even death. The independent predictors of mortality in the present series were DM, postcranioplasty seizure, reoperation for hema-
toma evacuation, and therapeutic indication for hemorrhagic stroke. Male sex could predispose a patient to seizures and additional operations. African American race also seemed to play a role in the development of hematoma requiring operation. Other important findings were the asso-
ciation of bilateral convexity cranioplasty with infec-
tions. Finally, old age was a predictor of postcranioplasty seizure. Our goal was to provide the neurosurgeon with predictors of morbidity and mortality that could be incor-
porated in the clinical decision-making algorithm. Control of the patient’s risk factors and early recognition of complications may help avoid the exhaustive list of complications. Prospective multicenter trials are needed to settle the controversial question of risk factors.

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### Author Contributions


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