Clinical Research

Cranioplasty after decompressive craniectomy. A prospective series analyzing complications and clinical improvement

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A B S T R A C T

Background: Cranioplasty is carried out for cosmetic reasons and for protection, but it may also lead to some neurological improvement after the bone flap placement. Complications of cranioplasty are more frequent than expected for a scheduled neurosurgical procedure. We tried to identify factors associated with both complications and improvement after cranioplasty.

Methods: We prospectively studied the cranioplasties performed in our hospital from November 2009 to November 2013. Patients whose initial reason for bone removal was tumor infiltration were excluded. Demographic, clinical and radiological data were collected. The NIH Stroke Scale and Barthel Self-Care Index scores were obtained both before and within 72 h after cranioplasty. The outcome measures were the occurrences of complications and clinical improvement.

Results: Fifty-five cranioplasties were performed. The material used for the cranioplasty was autologous bone in 42 cases, polyetheretherketone (PEEK) in 7 and methacrylate in 6. The average size of the bone defect was 69.5 (19.5–149.5) cm². The time elapsed between decompressive craniectomy and cranioplasty was 309 (25–1217) days. There were 10 complications (7 severe and 3 mild), an 18.2% complication rate. Statistically significant risk factors of complications were identified as a Barthel ≤70 (Odds ratio [OR] 22; 2.5–192; P = 0.005), age over 45 years (OR 13.5; 1.5–115; P = 0.01) and early surgery (<85 days; OR 8: 1.69–37.03, P = 0.004). After multivariate analysis, Barthel ≤70 and age over 45 years remained independent predictors of complications. Twenty-two (40%) of the 55 patients showed objective improvement. Early surgery (<85 days) increased the likelihood of improvement (OR 4.67; 1.05–20.83; P = 0.035). Larger bone defects seemed to be related with improvement, but differences in defect size were not statistically significant (75.3 vs 65.6 cm²; P = 0.1).

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Síndrome arachnoid decompressive. Timing

Complicaciones

the refractory clínica clave: del hemorrhage those trefinado can this injury in this a improvement (DC) or the improvement neuroquirúrgico programado. Se han tratado de identificar los factores asociados tanto a la aparición de complicaciones como de mejora neurológica.

Métodos: Se han analizado prospectivamente las craneoplastias realizadas en nuestro centro desde noviembre del 2009 hasta noviembre del 2013. Los pacientes sometidos a craneomía decompresiva (CD) por infiltración tumoral no fueron incluidos. Se recogieron datos demográficos, clínicos y radiológicos. La escala NIHSS y Barthel fueron medidas en cada paciente antes y dentro de las primeras 72 h tras la cirugía. Las medidas -resultado- fueron la aparición de complicación y/o mejora clínica.

Resultados: Se realizaron 55 craneoplastias. El material utilizado para las plastias fue el propio hueso en 42 casos, PEEK en 7 y metacrilo en 6. El tamaño medio del defecto óseo fue de 69,5 (19,5–149,5) cm². El tiempo medio transcurrido desde la CD hasta la plastia fue de 309 (25–1.217) días. Hubo 10 complicaciones (7 graves, 3 leves), lo que supone una tasa de complicaciones del 18,2%. Una puntuación de Barthel ≤70 (OR: 22; 2,5–192; P = 0,005), la edad por encima de 45 años (OR: 13,5; 1,5–115; P = 0,01), y la cirugía temprana (≤85 días, OR: 8; 1,69–37,03, P = 0,004) fueron identificados como factores de riesgo estadísticamente significativos de la aparición de complicaciones. Tras el análisis multivariante, el Barthel ≤70 y la edad mayor de 45 años permanecieron como predictores independientes de complicaciones. Veintidós (40%) de 55 pacientes presentaron mejoría clínica objetiva. La cirugía temprana (<85 días) aumentó la probabilidad de mejoría (OR: 4,67; 1,05–20,83; P = 0,035). El mayor tamaño de defecto óseo parece relacionarse con la aparición de mejoría, pero las diferencias en tamaño entre los que mejoraron y los que no, no resultó estadísticamente significativa (75,3 vs 65,6 cm², P = 0,1).

Conclusiones: La tasa de complicaciones de la craneoplastia es mayor que la de otros procedimientos neuroquirúrgicos electivos. Una edad mayor, una peor situación funcional (entendido como peor puntuación en la escala Barthel) y la cirugía temprana (menos de 85 días) son factores de riesgo de complicación. Por otro lado, la craneoplastia produce un beneficio clínico más allá de la protección y la mejora estética. La cirugía temprana y los defectos óseos mayores parecen aumentar la probabilidad de mejora clínica.

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Craneoplastia tras craneomía descompresiva. Serie prospectiva analizando complicaciones y mejora clínica

RE SUM E N

Antecedentes: La craneoplastia es un procedimiento que se realiza por motivos estéticos y de protección, pero que además puede producir cierta mejora neurológica tras la reposición del colgajo óseo. Las complicaciones del procedimiento son más frecuentes de lo esperado para un procedimiento neuroquirúrgico programado. Se han tratado de identificar los factores asociados tanto a la aparición de complicaciones como de mejora neurológica.

Métodos: Se han analizado prospectivamente las craneoplastias realizadas en nuestro centro desde noviembre del 2009 hasta noviembre del 2013. Los pacientes sometidos a craneomía decompresiva (CD) por infiltración tumoral no fueron incluidos. Se recogieron datos demográficos, clínicos y radiológicos. La escala NIHSS y Barthel fueron medidas en cada paciente antes y dentro de las primeras 72 h tras la cirugía. Las medidas -resultado- fueron la aparición de complicación y/o mejora clínica.

Resultados: Se realizaron 55 craneoplastias. El material utilizado para las plastias fue el propio hueso en 42 casos, PEEK en 7 y metacrilo en 6. El tamaño medio del defecto óseo fue de 69,5 (19,5–149,5) cm². El tiempo medio transcurrido desde la CD hasta la plastia fue de 309 (25–1.217) días. Hubo 10 complicaciones (7 graves, 3 leves), lo que supone una tasa de complicaciones del 18,2%. Una puntuación de Barthel ≤70 (OR: 22; 2,5–192; P = 0,005), la edad por encima de 45 años (OR: 13,5; 1,5–115; P = 0,01), y la cirugía temprana (≤85 días, OR: 8; 1,69–37,03, P = 0,004) fueron identificados como factores de riesgo estadísticamente significativos de la aparición de complicaciones. Tras el análisis multivariante, el Barthel ≤70 y la edad mayor de 45 años permanecieron como predictores independientes de complicaciones. Veintidós (40%) de 55 pacientes presentaron mejoría clínica objetiva. La cirugía temprana (<85 días) aumentó la probabilidad de mejoría (OR: 4,67; 1,05–20,83; P = 0,035). El mayor tamaño de defecto óseo parece relacionarse con la aparición de mejoría, pero las diferencias en tamaño entre los que mejoraron y los que no, no resultó estadísticamente significativa (75,3 vs 65,6 cm², P = 0,1).

Conclusiones: La tasa de complicaciones de la craneoplastia es mayor que la de otros procedimientos neuroquirúrgicos electivos. Una edad mayor, una peor situación funcional (entendido como peor puntuación en la escala Barthel) y la cirugía temprana (menos de 85 días) son factores de riesgo de complicación. Por otro lado, la craneoplastia produce un beneficio clínico más allá de la protección y la mejora estética. La cirugía temprana y los defectos óseos mayores parecen aumentar la probabilidad de mejora clínica.

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Introduction

Decompressive craniectomy (DC) is a life saving procedure performed in those patients suffering intracranial hypertension (ICH) refractory to medical treatment. Several underlying conditions like traumatic brain injury (TBI), spontaneous subarachnoid hemorrhage (SAH) or malignant cerebral infarction, among others, can lead to this situation. The relative increase in the use of this procedure and the improvement of the survival rate make us face a growing number of patients that might need a cranioplasty.

Classically, the benefits of a cranioplasty were protection and cosmetics. Nevertheless, there is an increasing number of publications sustaining that cranioplasty may produce a neurologic improvement, and an improvement in cerebral blood flow, cerebrospinal fluid (CSF) dynamics and cerebral metabolism.1-17

On the other hand, cranioplasty is not a procedure exempt of complications. In fact, the published rates of complications...
are considerably higher than the rest of the scheduled neurosurgical procedures. Varieties of factors, like the time elapsed from the DC, the material used, or the underlying pathology, have been related to the appearance of complications\cite{18-48}; although results are often contradictory.

We have prospectively analyzed a series of cranioplasties in order to determine the actual incidence of clinical improvement after surgery, the rate of complications, and their possible risk factors.

Materials and methods

We have prospectively studied the cranioplasties performed in a tertiary reference center in Spain from November 2009 to November 2013. Demographic data, like age, sex or medical comorbidities, were collected. The reason to perform a DC was recorded, as well as the time elapsed until the cranioplasty. Those DC performed for tumor infiltration of the bone, or infections of a bone flap after a scheduled craniotomy were excluded. The area of the defect was calculated by measuring the largest diameter ($D_1$) and its perpendicular one ($D_2$), and the surface of an ellipse formula ($D_1/2 \times D_2/2 \times \pi$) was used. This study was revised and approved by the ethical committee of the hospital (Reference: CEIC n.: 11/089).

Surgical procedures

In our department, swab cultures are taken from the bone during the DC, and then the bone flap is stored in a tissue bank at −80 °C temperature. The durotomy is C or X shaped, and the dural closure is performed with biologic substitute either on lay (Duragen®) or stitched up (Tutapatch®) according to the surgeon preference. In the bifrontal DC the falx cerebri is sectioned. No biological glues or any other sealants are routinely used.

The Cranioplasty is carried on a variable time after the DC, once the underlying pathology that led to the decompression had resolved. The timing of the cranioplasty varies according to the preference of the surgeon. Some rather perform the surgery as soon as it is considered safe, while others prefer to move the patient to a rehabilitation or nursing facility and operate when the patient has recovered partially.

The material used for the cranioplasty is the autologous bone flap, unless the swab cultures were positive, or the bone flap was deteriorated in the moment of harvesting. If the bone flap was not available, then computed-designed PEEK (polyetheretherketone) implants, or acrylic cement manually shaped implants were used. A subgaleal drain is routinely used during 24–72 h. Antibiotic prophylaxis is performed with 2 g of cefazolin 15–60 min before the skin incision and 6 h after it. According to the surgeon preference, the antibiotic administration may be extended for up to 72 h after the surgery.

The use of a ventriculoperitoneal shunt (VPS) is reserved for those patients presenting obvious preoperative ventricular enlargement, and it is done synchronously with the cranioplasty. Those patients with a ventricular size on the higher limit of normality (Evan’s index between 0.3 and 0.4), or with subdural fluid collections, are operated upon without VPS implantation (a lumbar drain or ventricular puncture is used before or during the procedure to avoid excessive pressure on the brain parenchyma), because, in our experience, most of them evolve to resolution of the CSF disarrangements after the surgery.\cite{49} In case of a persistent or progressive ventricular dilatation, a shunt is placed in a second operation.

A brain CT is performed after the cranioplasty in every patient before being discharged.

Outcome variables

Clinical improvement

A score on the National Institutes of Health Stroke Scale (NIHSS) and the Barthel index were recorded for every patient on the week before the cranioplasty, and within 72 h after the surgery. Objective improvement was defined as an improvement of at least 1 point in the NIHSS or 5 in the Barthel index.

Same wise, the subjective improvement was recorded by asking either the patient directly or his caregivers if the patient was unable to answer. To quantify this improvement the unpleasant symptoms for the patient not amenable to objective measure were recorded, but the esthetic improvement was not taken into account. Those symptoms were very diverse, like headaches, dizziness, insomnia, vague discomfort, and have been grouped under the term subjective symptoms.

Complications

Every complication of the procedure was recorded, and they were grouped as mild (healing problems of the wound, or superficial infections confirmed by culture that required antibiotic treatment, but not revision surgery with bone flap removal), or severe (neurological worsening, infection that requires bone flap removal, and hemorrhage of the surgical field requiring revision surgery). The hematomas diagnosed in the control CT scan producing no symptoms and requiring no intervention were not considered as a complication. Long-term bone flap reabsorptions were recorded, but not considered as complications.

Statistics analysis

The software SPSS® Statistics version 20.0 was used for the data analysis. An unpaired t-test was used for parametric statistics analysis between quantitative parameters and the presence of complication or clinical improvement. Associations with categorical variables were explored using the $\chi^2$ test or the Fisher’s exact test (when expected cell sizes were smaller than 5). Results with $P<0.05$ were considered statistically significant. In a second step a multivariate analysis was performed to find independent predictors for postoperative complications, or clinical objective improvement after CP using a binary logistic regression. Variables with significant $P$ values in univariate analyses, or that had been considered to be clinically relevant, were considered as potentially independent variables in the multivariate analysis.
Results

Patients characteristics

Fifty-five cranioplasties were performed, in 37 men and 18 women. The average age was 42.8 years (17–73). The reason for DC was TBI in 28 (50.9%), 24 primary DC, and 4 due to ICTH refractory to medical treatment, intracerebral hemorrhage in 12 (21.8%), 6 hypertensive, 3 aneurysmatic, and 3 due to an arteriovenous malformation rupture, 6 (10.6%) malignant infarction of the MCA, 2 (3.6%) for reabsorption of a previous bone flap, and 7 (12.7%) because of infection of previous flap (5 of those were decompressed initially for a subdural acute hemorrhage, 1 hypertensive hemorrhage and 1 secondary to AVM rupture; the bone flap was replaced, but had to be removed later on because of an infection).

The material used for the cranioplasty was autologous bone in 42 cases, PEEK in 7, and methacrylate in 6. The DC were 30 (54.6%) right sided, 18 (32.7%) left sided, and 7 (12.7%) bifrontal. At the moment of the surgery the average score of the NIHSS scale was 5.9 (range 0–33) and the Barthel was 71 (range 5–100). The mean GOS at discharge was 3.85.

The average size of the bone defect was 69.5 cm² (standard deviation 24.5 cm²; median 73.51 cm²; range 19.5–149.5 cm²; asymmetry coefficient 0.23). The average size of the largest diameter was 9.81 cm (SD 2.29; median 10.5; asymmetry coefficient –1.66). The time elapsed between DC and cranioplasty was 309 days (SD 237 days, median 268 days, range 25–1217 days, asymmetry coefficient 1.42, Chart 1).

Complications

Of the 55 patients, there was a postoperative death secondary to a massive pulmonary thromboembolism, 3 days after the surgery. It is hard to establish if both events were related, or if it was due to the prolonged time lying in bed. Since antithrombotic prophylaxis is withheld for 48 h around the surgery, we must assume that there is a causative effect between both events.

Besides the death, there were 3 mild complications, 2 of which were wound infections that resolved after proper antibiotic treatment; and the other was a wound breakdown with CSF leakage, resolved after lumbar drain and wound revision. There were 6 severe complications, 5 of which were bone flap infections that required removal of the implant, and another one that was neurological worsening due to an intraventricular hemorrhage secondary to a ventricular puncture during the procedure. It sums up a total of 10 cases of morbidity or mortality, which accounts for a 18.2% complication rate. 7 patients suffered an infection (2 mild, 5 severe) caused by methicillin sensitive Staphylococcus aureus (MSSA) in 3 cases, methicillin resistant SA (MRSA) in 2 cases, Staphylococcus epidermidis in 1 case, and Serratia marcescens in 1 case.

Of the factors studied, the average age was higher in those who suffered complications (56 vs 49.9 years old, 95% CI P = 0.002). We selected 45 years old as a cut point, and the Odds Ratio of suffering a complication in the older group was 13.5 (1.5–115, P = 0.01). We identify a statistic tendency of the complications occurring to those being operated earlier (195 vs 335 days, 95% CI P = 0.067). When we divided the patients in early (<85 days) and late (>85 days) surgery, the OR of suffering a complication in the early group was 8 (1.69–37.03, P = 0.004). According to the clinical situation before surgery, patients who suffered a complication had lower NIHSS and Barthel scores (average Barthel for patients with complications 43; average Barthel for patients without complication 77 (P < 0.01). If we set a Barthel score of dependency (Barthel ≤ 70) as a cut point, the odds ratio of suffering a complication was 22.1 (2.5–192.9, P = 0.005) on those scoring lower. If we exclude from the analysis the patients who had suffered a previous infection, the three factors remained statistically significant (Early surgery ≤ 85 days: OR 8.5; 1.69–42.76, P = 0.004. Age older 45: OR 16; 1.8–141.94, P = 0.002. Barthel ≤ 70: OR 3; 1.92–4.67, P < 0.001). About the material used, there were complications in 8 out of 42 (19%) autologous bone, 2 out of 6 methacrylate (33%) and in none of the 7 PEEK. Neither the reason for the DC (Table 1), nor the aforementioned material (Table 2), nor the size of the bone defect, nor the need of a VPS showed statistical correlation with the complications rate. In the multivariate analysis using a logistic regression, a Barthel ≤ 70 (OR 23.64,
95% CI 2.45–229, P = 0.006) and the age over 45 years-old (OR 14.6, 95% CI 1.46–146, P = 0.022) were independent predictors of complications (if we exclude the patients with a previous infection, only age older than 45 remained an independent factor, OR 25.16; 1.77–356.2, P = 0.017). Time to cranioplasty as a continuous variable showed a tendency but it was no longer statistically significant. The constant of equation was −5.35 (a), the b of the Barthel (b1) was 3.162, and the b of age was 2.68 (b2); so the probability of suffering a complication being older than 45 and scoring 70 or lower in the Barthel index was calculated as 62.22% (P = OR/1 + OR. OR = $e^{(b1+b2)}$. R square of Nagelkerke 0.521).

### Clinical improvement

Thirty-one (56.4%) and 22 (40%) of the 55 patients showed a subjective or an objective improvement respectively. Of those who improve objectively, 12 (21%) improved 1 point in the NIHSS, 8 (14.5%) improved 2 points, 1 (1.8%) improved 3 points; and 1 (1.8%) improved 5 points in the Barthel index.

Of the factors studied, there was a significant relation between time elapsed since DC and neurological objective improvement, being a lot shorter in those who improved (199.5 vs 383.3 days, P = 0.002). If we take 85 days as the cut point, the OR of improving is 4.67 (1.05–20.83, P = 0.035). Likewise, a larger bone defect seemed to be related with the improvement, but differences in defect size were not statistically significant between those who improved and those who did not (75.3 vs 65.6 cm², P = 0.1). In relation to the reason for DC (Table 1), every spontaneous intraparenchymal hemorrhage improved, and 12 out of 16 TBI (75%) also improved. Every left sided defect improved, and 11 out of 19 right sided defects (Table 3). There was an improvement in 19 out of 42 (45%) autologous bone flap, 1 out of 7 (14%) PEEK, and 2 out of 6 (33%) methacrylate. These differences were not statistically significant. There was no association between age or previous clinical condition and improvement.

In the multivariate analysis only the time elapsed since the DC (<85 days) remained statistically significant (OR 4.66, 95% CI 1.04–20.66, P = 0.042). The constant of the equation was −0.693, and the b of early surgery was 1.539 (b1); so the probability of improving when operated on the first 85 days was calculated as 70% (P = OR/OR + 1. OR = $e^{(b1)}$. R square of Nagelkerke = 0.104. −2Log (likelihood) = 68.6).

Fig. 1 shows a paradigmatic case of ours: a 66 years old man suffered a moderate TBI during sport practice, and a decompressive craniectomy had to be performed. The patient suffered an infection that needed removal of the replaced bone flap. The patient worsened dramatically without the implant, and improved drastically after the second cranioplasty, as depicted in Fig. 1.

### Discussion

The syndrome of the trephined was first described by Grant et al. in 1939. It was described as a group of vague symptoms like headache, dizziness, fatigue, instability, intolerance to vibration and depression; that appeared in patients who had been craniectomized previously and whom experienced improvement after the cranioplasty. Later on, multiple terms and names were added, like the motor trephined syndrome or the sinking skin flap syndrome.
Table 3 – Relation between the occurrence of clinical objective improvement and the side and type of decompressive craniectomy and between the occurrence of complications and the side of the decompressive craniectomy.

<table>
<thead>
<tr>
<th>Side of DC</th>
<th>Right</th>
<th>Left</th>
<th>Bifrontal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective improvement</td>
<td>No</td>
<td>19</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>11</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>18</td>
<td>7</td>
<td>55</td>
</tr>
<tr>
<td>Complication</td>
<td>No</td>
<td>22</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Yes</td>
<td>8</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>18</td>
<td>7</td>
<td>55</td>
</tr>
</tbody>
</table>

that had in common patients who had been craniectomized and later presented with subjective, objective or both kind of symptoms, that improved after the cranioplasty. In the recent years we have witnessed an increasing number of publications suggesting that cranioplasty itself can produce a neurological improvement irrespectively of whether the patient has presented “de novo” symptoms (like it was originally described), or if he has remained stable without new symptoms.

On the other hand, it is becoming more and more evident that the cranioplasty is a procedure with a higher rate of complications than the rest of scheduled neurosurgical procedures, with reported rates between 10 and 30%.

Our own rate, 18.2%, is in accordance with the rates published so far.

We have prospectively analyzed 55 consecutive patients that went under cranioplasty with the aim of identifying the actual rate of objective improvement after surgery, the percentage of complications associated with this procedure in our environment, and to identify the possible associated factors.

Clinical improvement

Several theories have tried to explain the apparent improvement that some patients show after cranioplasty, and we have sorted them in 3 groups: (a) an improvement in the brain blood perfusion; (b) a normalization of the CSF hydrodynamics and the intracranial pressure; and (c) an improvement in brain metabolism. Although all of them have shown to be right to some extent, none of them

Fig. 1 – A 66 years old man suffered a moderate TBI during sport practice, and had to be operated to evacuate a subdural hemorrhage. The bone flap was not replaced due to intraoperative brain swelling (1: 2 months after decompressive craniectomy.). After 3 months the patient reached a complete recovery, and the bone flap was replaced (this event is previous to the present study) (2: CT scan two days after cranioplasty). After 10 months, he presented with a chronic bone flap infection, so it had to be removed (3: infection of the bone flap). After the removal, the patient progressively worsened, developing a sunken skin flap, progressive contralateral hemiparesis, and in the CT scan a contralateral deviation of the midline was patent (4: Two days after removal of the infected bone. 5: Two months after removal of the bone flap. 6: Patient becomes symptomatic after three months from the removal of the bone flap. Midline deviation is patent.). The patient was kept supine thereafter, and he presented both clinical and radiological improvement (7: CT scan after 2 days of recumbency). When the infection was resolved, a PEEK cranioplasty was implanted (8: CT scan 2 months after the PEEK cranioplasty). The patient made a complete recovery afterwards.
is able to explain why some patients improve and others do not. Some authors have tried to identify the factors that would allow us to predict which patients will benefit the most from surgery. Yamaura et al. were the first to try, and they classified their patients according to the external look of their skin flap in sunk, flat, full, and bulging. They found that those who improved were the ones with a sunken skin flap and suffering moderate neurological deficits. In 1984 Fodstad et al. performed hydrodynamic studies before and after the cranioplasty, and found that elastance (amount of pressure change per volume unit) in the rest position was half of the normal values in those patients defined as trephined syndromes (that is with symptoms before surgery that diminish or vanish after it), and that the elastance turned to normal values after the cranioplasty. In 2004 Kuo et al. reported that patients who improved were the ones operated earlier, and the ones with a better neurological situation. In 2008 Stiver et al. studied the CT scans of 38 patients that had been craniectomized because of a TBI, and were subsequently operated to repair the bone defect. They divided them in those that improved after the cranioplasty (trephined), those that did not improve, or those suffering no neurological deficit, and therefore could not improve. They did not find differences in the admission CT, but did find differences in the CT performed one month after the initial injury. In that CT they identified a higher number of subdural hygromas in the trephined (90 vs 45%). In the CT performed right before the cranioplasty, they also found more CSF disarrangements (hydrocephalus, ex-vacuo dilatation, and edema in the parenchyma underlying the defect) in the trephined. Finally, Lin et al. studied if the brain midline shift measured in the CT scan performed before the cranioplasty could differentiate which patients would improve. They found that those with a previous brain midline shift (between 1 and 12 mm) improved more in their strength and the GCS (Glasgow Coma Scale) score, being this latest statistically significant.

In our group of patients we have found an objective neurological improvement in 40% of them. Since these patients are still in their neurological recovery, improvements noted at a longer period may be due to both the ongoing recovery and the effect of the cranioplasty. For that reason, we decided to include in our analysis only the immediate improvement, so that potential bias was avoided. We have seen that the patients who improved were operated upon significantly earlier (199.5 vs 383.5 days). 85 days was chosen as cut point because it better distinguished between those who improved and those who did not, and showed a tendency to harbor larger bone defects (75.3 vs 65.6 cm³). On the same direction, there was a tendency of being more likely to improve if the underlying pathology was TBI or spontaneous hemorrhage. Patients who improved in our series presented a slightly lower Barthel score before the operation (68 vs 73, P = 0.52), but it was not statistically significant. Therefore, it is unlikely that patients operated upon earlier improved because they were in a worse condition, and thus it was somehow easier to improve. According to our data, it seems that timing of operation is an independent factor of improvement, irrespectively of how bad the condition of the patient was.

There are several important limitations when trying to draw conclusions and to compare with other publications: first, the timing of the improvement measurement, second, what kind or improvement is taken into account and how it is measured, and third, which patients are studied. Referring to what kind of improvement is measured, many publications only look for the motor improvement, or the conscious level, whereas other publications seek any kind of symptoms improvement. We have divided the improvement in subjective and objective, using for the last one validated scales to assess the neurological and functional situation like the NIHSS and Barthel index. It is a limitation of the present study that no neuropsychological test was performed on these patients, and thus some objective improvement might be missed by the scales used. In relation to what patients are included, many authors limit their observations to patients that are operated after a TBI, while other authors include malignant infractions, or even any kind cranioplasty performed after decompression due to ICHT. We have excluded from our analysis only those bone defects caused by neoplastic infiltration. Actually, we have observed that the improvement is even more evident in the patients with a spontaneous hemorrhage, although, probably due to sample size, it did not reach statistical significance.

Complications

The cranioplasty is a relatively simple and straightforward procedure, performed under elective conditions, that nevertheless shows complications rates much higher than the rest of non-emergent neurosurgical procedures. It is especially worrisome the high rate of infections associated with this surgery, and that is why several factors that might play a role have been studied. The bifrontal DC was found to be a risk factor by Gooch et al., who found a complication rate of 67%, while it was 27% in the hemicraniotomies (P<0.05). Our own series did not show an increased risk depending on the type of DC, and neither did the rest of the studies who mentioned it.

Optimum timing of cranioplasty to minimize complications is a controversial issue. Several studies have stated that early surgery increases the risk of infection or complication. However, the definition of early surgery varies greatly among different authors: from Archavits et al., who defined it as less than 7 weeks, to Manson et al. for whom early means less than a year after the DC. There are authors who have not found a relation between timing and complication rate. To add more controversy, Matsuura et al. and Beauchamp et al. found that infections occurred in those operated later (108 vs 74 days and 139 vs 80 days respectively). Our data seems to support that early surgery (less than 85 days after DC) increases the risk of complication (OR 8, 1.69–37.03). The average time to cranioplasty is rather large in our series, but the distribution of times elapsed is highly asymmetrical (Chart 1) with most of its values gathered on its left tail. Nevertheless the time elapsed is still long. This is probably due to the fact that most of the patients are moved to nursing and rehabilitation facilities when they are stable enough, and considered for the cranioplasty procedure later on; and the lack of resources of our social security system restricts the possibility or early operation.

The most popular materials used for cranioplasty nowadays are autologous bone (either cryopreserved at −32 °C to
<table>
<thead>
<tr>
<th>Study and year</th>
<th>N° patients</th>
<th>Design</th>
<th>Factor</th>
<th>Risk/protection</th>
<th>Risk ratio (OR)</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Datti et al., 1985</td>
<td>100</td>
<td>Retrospective</td>
<td>Early surgery (&lt;6 months) in stainless steel implants</td>
<td>Risk</td>
<td>OR 3.07* (P &lt; 0.05)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sinus cavity involved</td>
<td>Risk</td>
<td>21 vs 0% infection rate. P = 0.025</td>
<td></td>
</tr>
<tr>
<td>Manson et al., 1986</td>
<td>42</td>
<td>Retrospective</td>
<td>Early surgery (&lt;1 year)</td>
<td>Risk</td>
<td>OR 11.6* (P = 0.01)</td>
<td></td>
</tr>
<tr>
<td>Moreira et al., 2003</td>
<td>312</td>
<td>Retrospective</td>
<td>Hydroxyapatite (vs cryopreserved bone or PMMA) implants</td>
<td>Risk</td>
<td>OR 1.54 (10.3 vs 7.5%) P &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Matsuno et al., 2006</td>
<td>206</td>
<td>Retrospective</td>
<td>Titanium mesh (vs cryopreserved bone or PMMA) implants</td>
<td>Protection</td>
<td>OR 0.1* (2.6 vs 19.6%) P &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Cheng et al., 2008</td>
<td>75</td>
<td>Retrospective</td>
<td>≥2 surgeries</td>
<td>Risk</td>
<td>OR 6.15 &lt; 0.05</td>
<td></td>
</tr>
<tr>
<td>Gooch et al., 2009</td>
<td>62</td>
<td>Retrospective</td>
<td>Bifrontal craniectomy</td>
<td>Risk</td>
<td>OR 5.53* (67 vs 27%)</td>
<td></td>
</tr>
<tr>
<td>Beauchamp et al., 2010</td>
<td>69</td>
<td>Retrospective</td>
<td>Synthetic material (vs autologous bone)</td>
<td>Risk</td>
<td>OR 4.36 a (41.6 vs 14%)</td>
<td></td>
</tr>
<tr>
<td>Inamasu et al., 2010</td>
<td>70</td>
<td>Retrospective</td>
<td>Cryopreservation of bone flap (vs subcutaneous) in trauma patients (&lt;3 months)</td>
<td>Risk</td>
<td>28.6 vs 0% P = 0.02</td>
<td></td>
</tr>
<tr>
<td>Chang et al., 2010</td>
<td>212</td>
<td>Retrospective</td>
<td>Subgaleal drainage</td>
<td>Protection</td>
<td>OR 0.28 (0.11–0.68) P = 0.015</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>DC for TBI</td>
<td>Protection</td>
<td>OR 0.25 (0.1–0.6) P = 0.005</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>DC for tumor</td>
<td>Protection</td>
<td>OR 0.34 (0.14–0.82) P = 0.016</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Early surgery (&lt;3 months)</td>
<td>Risk</td>
<td>9 vs 20% P = 0.042</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Autologous bone flap</td>
<td>Risk</td>
<td>38 vs 15% P = 0.023</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Subcutaneous abdominal bone preservation</td>
<td>Risk</td>
<td>OR 1.35 (0.53–3.41)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Protection</td>
<td>OR 0.81 (0.4–1.6)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Protection</td>
<td>OR 0.35 (0.09–1.35)</td>
<td></td>
</tr>
<tr>
<td>Yadla et al., 2011</td>
<td>2254</td>
<td>Meta-analysis</td>
<td>Povidone–iodine dries for &gt;5 min</td>
<td>Protection</td>
<td>OR 0.26 (0.08–0.86)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Early surgery (&lt;6 months)</td>
<td>Risk</td>
<td>OR 33.7 P = 0.0037</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Early surgery (&lt;7 weeks) and comorbidities</td>
<td>Risk</td>
<td>OR 18.75 P = 0.073</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Surgical time &gt;200 min</td>
<td>Risk</td>
<td>OR 2.2* (20 vs 10%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Diabetes M.</td>
<td>Risk</td>
<td>OR 6.44* (27.7 vs 5.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Multiple operations</td>
<td>Risk</td>
<td>OR 9.54* (33 vs 4.3%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Early surgery (&lt;2 months)</td>
<td>Risk</td>
<td>OR 2.2 (1.1–4.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DC for TBI</td>
<td>Risk</td>
<td>OR 3.04 (1.2–7.7)</td>
<td></td>
</tr>
<tr>
<td>Schuss et al., 2012</td>
<td>280</td>
<td>Retrospective</td>
<td>VPS</td>
<td>Risk</td>
<td>OR 2.7 (1.3–5.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Subgaleal drainage malfunction</td>
<td>Risk</td>
<td>OR 8.96 (1.84–43.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Longer surgical time</td>
<td>Risk</td>
<td>OR 42.9* (60 vs 3.5%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Risk</td>
<td>5/h infected vs 3.7 h no infected. P = 0.03</td>
<td></td>
</tr>
</tbody>
</table>
–82°C, or stored in the patient subcutaneous abdominal tissue), titanium mesh, acrylic cement (PMMA), hydroxyapatite compounds and PEEK. There is no agreement on which one is better. Autologous bone is cheap and cosmetically perfect, but it is unsettled whether its associated complication risk is good or not. It has been found to be better\cite{22,31,34,37,39,44,46,47,65} or worse\cite{24} than synthetic materials. Titanium mesh\cite{24,28} and PEEK seem to present a better profile of complications than other materials\cite{22}. Our series did not find any differences among materials, but the limited number of patients does not allow drawing any conclusion on that matter.

Surgical time is a well-recognized risk factor. Most of the authors who have studied it have stated that the longer the operation the higher the risk. Lee et al.\cite{29} found that when the surgical time was longer than 200 min, the risk of infection doubled. Huang et al.\cite{43} presented a series where the mean surgical time in those infected was 5 h, while it was 3.7 h in those non-infected (P = 0.03). Lastly, Kim et al.\cite{44} found an OR of suffering an infection of 8.62 (0.96–77.43) in those whose surgery lasted longer than 120 min (Table 4). Multiple surgeries at the cranioplasty site\cite{28,39,46}, and involvement of paranasal sinus cavities\cite{32} have also been recognized as risk factors of presenting a complication, specifically infection.

The implantation of a ventriculo-peritoneal shunt (VPS) and the use of a subgaleal drainage have been advocated to be a risk and protection factors respectively by some authors.\cite{32,40,41,43} We did not find a statistically significant difference between those with a VPS and those without it, and subgaleal drainage is routinely used for at least 24 h in every patient of our series.

There are other factors published, like the proper use of povidone iodine solutions,\cite{35} that had not been so well studied (Table 4). Age was found to be a risk factor by Chang et al.\cite{32} and by our own series; and functional status (Barthel < 70) has never been reported before as a risk factor to the best of our knowledge.

In our study a worse pre-surgical performance status (worse Barthel) and older age have been identified as independent predictors of complication. A shorter time elapsed since the DC has also shown to increase the risk of complications. Despite what other studies have found (Table 4), we have found no relation between the complication rate and the material used, preservation method, underlying pathology or the presence of VPS. The surgical time has not been recorded for this study and that might be a bias that limits the strength of our findings.

### Conclusions

The cranioplasty is a procedure with higher complications rates than the rest of scheduled neurosurgical operations. Older age and worse functional situation (worse score in the Barthel index) are independent risk factors in our series. Other factors that might play a role are the surgical time, the proper use of antiseptic solutions, the presence of VPS, the number of operations, and other medical comorbidities. Early surgery (<85 days) seems to increases the risk in our series as well, but it did not remain as an independent risk factor in the

### Table 4 (Continued)

<table>
<thead>
<tr>
<th>Study and year</th>
<th>Design</th>
<th>N patients</th>
<th>Feature</th>
<th>Risk factor</th>
<th>Risk factor</th>
<th>Risk factor</th>
<th>Risk factor</th>
<th>Risk factor</th>
<th>Risk factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kim et al. 2013</td>
<td>Retrospective</td>
<td>85</td>
<td>Preoperative subgaleal collection</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
<tr>
<td>Wolzot et al. 2013</td>
<td>Retrospective</td>
<td>209</td>
<td>Temporal muscle reaction</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
<tr>
<td>Sundeen et al. 2014</td>
<td>Retrospective</td>
<td>54</td>
<td>Surgical time &gt; 130 min</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
<tr>
<td>Pendas et al. 2014</td>
<td>Prospective</td>
<td>70</td>
<td>Wound disruption</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
<tr>
<td>Pendas et al. 2014</td>
<td>Propective</td>
<td>55</td>
<td>DC for malignant infarction</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
<tr>
<td>Pendas et al. 2014</td>
<td>Propective</td>
<td>70</td>
<td>Longer surgical time</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
<tr>
<td>Pendas et al. 2014</td>
<td>Propective</td>
<td>55</td>
<td>Older ≥ 70</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
<td>Risk</td>
</tr>
</tbody>
</table>

multivariate analysis. The definition of “early” varies greatly among authors. The reason to initially perform the DC and the material used are controversial in the literature and in our series, thus no clear conclusions can be drawn.

On the other hand, cranioplasty produces clinical benefits beyond protection and esthetic improvement. In or series, a 40% objective improvement, and 56% subjective improvement were found. Earlier surgery (<85 days) and larger bone defects seem to increase the likelihood of clinical improvement, irrespectively of the patient’s clinical condition before the surgery.

The recommendation of this group is to perform the cranioplasty as early (<85 days) as it is considered safe, trying to diminish the risk of complication as much as possible. More studies are needed to further identify risk factors of complications, so they can be avoided.

Conflict of interest

The authors do not have any conflict of interest.

REFERENCES


