## **Original Article**

## **Evaluation of Three Different Methods of Cranioplasty: A Comparative Prospective Randomized Study**

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**BACKGROUND:** Multiple materials have been used for cranioplasty with different pros and cons. The current literature is defective in studies comparing titanium mesh, polyetheretherketone (PEEK), and polymethyl methacrylate (PMMA).

**OBJECT:** This prospective randomized study was conducted to compare the outcomes of three cranioplasty techniques; titanium mesh, PEEK, and PMMA, regarding the failure rates, the complications, and the patients' satisfaction.

**METHODS:** A total of 84 cases were included, and they were randomly divided into three groups (28 cases in each group); titanium mesh, PEEK, and PMMA groups. All patients underwent proper preoperative evaluation, including history taking, neurological examination, and routine investigations. The operative time and postoperative complications were recorded. Our primary outcome was implant failure rates, whereas secondary outcomes included implant exposure, surgical site infection, graft resorption, postoperative new-onset seizures, extradural hemorrhage, and patient satisfaction.

**RESULTS:** Age, gender, indication for cranioplasty, and operative time did not show any significant differences between the three groups. The prevalence of implant failure was 10.7%, 3.6%, and 14.3% in the titanium mesh, PEEK and PMMA groups, respectively. Although all complications (apart from extradural hemorrhage) tended to have a higher prevalence in the PMMA group, no significant difference was detected between the three groups regarding these complications. However, this lead to a significant decrease in patients' satisfaction in the PMMA group.

**CONCLUSION:** Titanium mesh, PEEK, and PMMA have a comparable complication profile when used for cranioplasty. However, complication rates showed a slight increase with PMMA, which lead to decreased patient satisfaction.

KEYWORDS: Bone cement, cranioplasty, polyetheretherketone, titanium mesh.

## INTRODUCTION

Cranioplasty is defined as a reconstructive procedure that is used to repair skull defects and restore the skull anatomy. It has many indications including depressed skull fractures, tumors infiltrating calvarial bones, decompressive craniectomy, and inflammatory lesions.<sup>1</sup> Nevertheless, cranioplasty has a high complication rate ranging between 15% and 35%.<sup>2-4</sup> Therefore, optimum reconstruction should be chosen for every patient to achieve an ideal postoperative outcome.<sup>5,6</sup>

The ideal material used for cranioplasty should have the following properties; biocompatibility, low cost, malleability to fit different defect shapes, and resistance to infection. Multiple materials have been used for that purpose with different pros and cons.<sup>7,8</sup> Although autologous bone grafts fit many criteria of the ideal graft, they have a

**Correspondence:** Mahmoud Mohamed Mousa Department of Neurosurgery, Faculty of Medicine, Helwan University, EGYPT Email: nourmousa2008@yahoo.com high resorption rate that may necessitate revision surgery and application of alloplastic material.<sup>9,10</sup> Therefore, bone grafts have been replaced by other materials to decrease resorption rate and donor site morbidity.<sup>11</sup>

Bone cement or polymethyl methacrylate (PMMA) (Teknimed, Biomaterials Innovation, Gentafix 1 ®, France) has proven to be useful in cranioplasty. It was used to fill the spaces between the two bones, acting as a grout.<sup>12</sup> It is malleable, lightweight, strong, and heat resistant, however, it may cause burn injury during the process of its preparation.<sup>11,13</sup> Bone cement has been used alone in cranioplasty, especially for managing relatively small calvarial defects.<sup>14</sup>

Titanium mesh (TiMesh ®, Medtronic, Minneapolis, Minnesota, USA) has been widely used in cranioplasty surgeries. It has good mechanical strength, a low infection rate, and an acceptable cost. It offers an excellent cosmetic outcome when prefabricated using three-dimensional (3-D) computerized tomography (CT).<sup>15</sup> Despite these advantages, some disadvantages have been reported after mesh placement as metal allergy, tissue erosion, implant exposure, and deformity upon application of external

## force.16,17

In the current practice, multiple neurosurgeons prefer polyetheretherketone (PEEK) (Cranial iD ®, Stryker craniomaxillofacial, Kallamazoo, Michigan, USA) as the ideal material for reconstruction, as it is characterized by being inert, biocompatible, and radiolucent. Additionally, it could be applied for complex craniofacial reconstruction as it could be reconstructed using computer-assisted technology.<sup>18,19</sup> On the other hand, being expensive and the increased incidence of epidural effusion are the main disadvantages.<sup>20</sup>

Currently, a great controversy exists between different neurosurgeons regarding the choice of implant material.<sup>11</sup> Although the existing literature is rich in papers comparing only two of the previously mentioned techniques, there is a paucity of studies comparing these three implants (Titanium mesh, PEEK, and bone cement). Hence, we conducted the current study to compare the outcomes of these three techniques used for cranioplasty.

## **METHODS**

The current prospective randomized study was conducted at the Neurosurgery Departments of Helwan University Hospitals, Tanta University Hospitals and Nasser Institute Hospital after obtaining approval from the local ethical committee and Institutional Review Board (IRB) of both Helwan and Tanta universities. The study was conducted over a period of three years, from January 2018 to December 2020.

The sample size was calculated using Power Analysis and Sample Size software program (PASS) version 15.0.5 for windows (2017), with the incidence of implant failure as the primary outcome. Patients were randomly allocated into one of the three groups: Titanium mesh, PEEK, and PMMA groups. The null hypothesis was considered as the absence of a difference between all groups regarding the incidence of postoperative implant failure. To the best of our knowledge, no previous studies have compared the three approaches for the same complication. A sample size of 22 patients in each group was needed to achieve 80% power (1- $\beta$  or the probability of rejecting the null hypothesis when it is false) and detect an effect size ( $f=\sigma m$  $/\sigma$ ) of 0.4 (a moderate effect size) in the proposed study using an F test with a significance level ( $\alpha$  or the probability of rejecting the null hypothesis when it is true) of 5%. Six drop-out patients were expected. Therefore, 28 patients were enrolled in each group.

We included a total of 84 cases aged over 18 years who were diagnosed with cranial defects regardless of the cause (trauma, tumor, infection, or craniectomy). On the other hand, we excluded patients who had previous cranioplasty, metal hypersensitivity, active intracranial infections, bilateral cranial defects, or history of previous radiation. All patients were informed about the study objective, procedure details, advantages, and disadvantages of each technique and a written informed consent was obtained. Before the operation, all the patients were clinically assessed. In addition, routine laboratory and radiological investigations including head CT with bone window were performed for all subjects.

The included cases were randomly allocated into three equal groups (28 cases for each). The first group had titanium mesh cranioplasty, the second one had PEEK cranioplasty, and the last one had PMMA cranioplasty. We waited for at least 8 weeks before performing cranioplasty in cases with decompressive craniectomy giving some time for stabilization of the patient condition and resolution of brain edema.

For all cases, hair shaving and proper scalp preparation were performed. A skin incision was performed taking into consideration that the incision should overlie a healthy bone postoperatively. Dissection was performed through the subcutaneous tissue and subsequent layers until the dura was reached. Care was taken not to injure the dura to decrease the risk of postoperative cerebrospinal fluid (CSF) leak. Hydrogen peroxide was applied to the surgical field to decrease the incidence of infection and bleeding. Debridement of the bony margins was then performed, and the temporalis muscle was dissected in some cases.

The titanium mesh was adjusted by mild compression, and we designed these implants to be larger than the defect by 0.5-1 cm. The mesh was fixed to the surrounding bony edges by titanium screws (Fig. 1). PEEK implants were designed by computer-assisted 3-D technology to exactly match the bony defect (Fig. 2). As regards the bone cement, we covered the skull defect by placing the PMMA and modeling it in situ (Fig. 3). Continuous irrigation with saline was done to protect the brain from the generated heat. After reconstruction, the superficial layers were closed in layers over a subcutaneous drain. The defect size and operative time were recorded for all cases. After surgery, all patients received standard postoperative care. The incision was daily dressed with betadine solution till stitch removal, and a broad-spectrum antibiotic was commenced for all cases.

Regular follow-up visits were scheduled for all cases at 1 week, 2 weeks, 1 month, 3, 6, and 12 months following surgery. In these visits, clinical and radiological assessments of these cases were performed. CT was done at least two times for all cases, the first one directly after surgery and the other one after discharge. Any postoperative complication was identified, managed, and recorded.

The primary outcome of the current study was the rate of implant failure, which was defined as infection, exposure, or any other complication that requires implant removal.<sup>11</sup> Implant exposure was defined as extrusion or exposure of the implant secondary to skin erosion.<sup>21</sup> Secondary outcomes included implant exposure, surgical site infection, graft resorption, postoperative new-onset seizures, extradural hemorrhage, and patient satisfaction. Patient satisfaction was subjectively assessed by the patient himself as follows; completely satisfied, satisfied, fairly satisfied, and unsatisfied.<sup>11,21</sup> Complications were classified into possibly

material-related (infection, fracture, exposure) or material non-related (extradural hematoma, seizures).

#### **Statistical Analysis**

Data collection, tabulation, and analysis were conducted by using the Statistical Package for the Social Sciences (SPSS, IBM, Inc, Chicago; USA) version 26 for windows. Quantitative data were tested for normality using the Kolmogorov-Smirnov test and expressed as mean  $\pm$ standard deviation (SD). Categorical data were expressed as percentage and frequency. For comparing three or more independent groups with quantitative data, one-way analysis of the variance (one-way ANOVA) and Kruskal-Wallis test were used for parametric and non-parametric data, respectively. Post-hoc analysis was conducted by Bonferroni and Dunn's tests for parametric and nonparametric data, respectively. Chi-square test or Fisher's exact test was used for comparing two or more groups of categorical data with Z test and Bonferroni correction for post-hoc analysis. Probability (p < 0.05) was considered statistically significant.



Fig 1: A) Axial magnetic resonance imaging (MRI) T1 weighted images (WI) with contrast showing intensely enhancing mass at left high parietal area with evident dural attachment and enhancement. B) Coronal MRI T1 WI with contrast showing the same lesion. C) 3-D reconstructed CT image showing skull bone erosion and defect at left high parietal area. D) Intraoperative photo showing the mass emerging to the subcutaneous spaces and the planned skin incision for removal of the lesion. E) Intraoperative photo showing complete removal of the lesion with parts of the dura and dural graft exposed underneath the removed pathological bone flap. F) Intraoperative photo showing designed metallic titanium mesh completely covering the bony defect. G) Axial bone window CT image showing the mesh at the site of the defect. H) 3-D reconstructed CT image showing well positioned titanium mesh at the site of the lesion after its complete excision with pathological dura and bone.

### RESULTS

The mean age of the included participants was 39.21, 35.11, and 40.61 years in the titanium, PEEK, and PMMA groups, respectively. Males were more predominant in the three groups as they constituted 60.7%, 67.9%, and 67.9% of the cases in the same groups, respectively. Regarding

systemic comorbidities, diabetes mellitus was present in 21.4%, 14.3%, and 25% of the cases, whereas hypertension was detected in 14.3%, 17.9%, and 10.7% of the cases in the three groups, respectively. On statistical analysis, no significant difference was detected between the three groups regarding any of the previously mentioned parameters (p > 0.05). These data are summarized in **Table 1**.

|                   |        | Titanium group     | PEEK group         | PMMA group         | Р     | P1     | P2     | Р3     |
|-------------------|--------|--------------------|--------------------|--------------------|-------|--------|--------|--------|
| Age (years)       |        | $39.21 \pm 14.088$ | $35.11 \pm 11.583$ | $40.61 \pm 12.547$ | 0.252 | 0.698  | 1      | 0.334  |
| Gender            | Male   | 17 (60.7%)         | 19 (67.9%)         | 19 (67.9%)         | 0.910 | > 0.05 | > 0.05 | > 0.05 |
|                   | Female | 11 (39.3%)         | 9 (32.1%)          | 9 (32.1%)          | 0.810 |        |        | > 0.05 |
| Diabetes mellitus |        | 6 (21.4%)          | 4 (14.3%)          | 7 (25.0%)          | 0.597 | > 0.05 | > 0.05 | > 0.05 |
| Hypertension      |        | 4 (14.3%)          | 5 (17.9%)          | 3 (10.7%)          | 0.924 | > 0.05 | > 0.05 | > 0.05 |

P1: Titanium group & PEEK group. P2: Titanium group & PMMA group. P3: PEEK group & PMMA group.



Fig 2: A) Sagittal MRI T1 WI with contrast showing enhanced frontal dura and a mass invading the bone and scalp layers. B) Coronal MRI T2 WI showing left frontal mass crossing to the other side with invasion of the scalp layers. C) Axial CT bone window image showing frontal bone erosion with extension of lesion to scalp layers. D) Intraoperative photo showing preparing for elevation of bone flap and obvious lesion amalgamated with galeal tissue. E) Intraoperative photo showing dural grafting after removal of pathological dura and bone flap. F) Intraoperative photo showing well positioned PEEK flap fixed with mini plates and screws and covering the bony defect completely. G) Intraoperative photo showing skin incision closure with staples after all layers closure over a subgaleal closed drainage system. H) Coronal CT bone window image showing good closure of the bony defect.



Fig 3: A) Axial MRI T1 WI with contrast showing left sphenoidal wing enhancing mass invading the bone giving en plaque view. B) Sagittal MRI T1 WI with contrast showing the same lesion. C) Intraoperative photo showing dissection and removal of the lesion with the overlying pathological bone. D) Intraoperative photo showing well fitted bone cement "PMMA" at the defective bony area after removal of the lesion. E) Axial CT image "soft tissue window" showing removal of the lesion with well positioned bone cement flap over the site of the lesion. F) Axial CT image "bone window" showing well positioned bone cement over of the site of the lesion after its removal. G) 3-D reconstructed CT image showing the final shape of the PMMA bone cement after its positioning over the site of excised lesion.

The most common indication for surgery was trauma in the three study groups, as traumatic cases constituted 39.3%, 50%, and 39.3% of the cases in the titanium, PEEK, and PMMA groups, respectively. Other indications included meningioma, osteolytic bone tumors, infection, and decompressive craniectomy. Right-sided defects were encountered in 60.7%, 46.4%, and 42.9% of cases in the three groups, respectively, while the remaining cases had

| Table 2: | Indications | and  | operative | data    | of the        | study  | grout | 0   |
|----------|-------------|------|-----------|---------|---------------|--------|-------|-----|
|          |             | **** | operative | ******* | · · · · · · · | Sec. y | 5.000 | × * |

left-sided defects. When it comes to defect size, it had mean values of 62.82 mm, 60.82 mm and 52.86 mm in the study groups, respectively. Operative time had mean values of 119.43, 121.39, and 123.11 minutes in the three groups, respectively. All of the previous parameters showed no statistically significant differences when comparing the three groups (p > 0.05), as illustrated in **Table 2**.

|                                |                       | Titanium group  | PEEK Group      | PMMA group       | Р     | P1     | P2     | P3     |
|--------------------------------|-----------------------|-----------------|-----------------|------------------|-------|--------|--------|--------|
|                                | Trauma                | 11 (39.3%)      | 14 (50.0%)      | 11 (39.3%)       |       |        |        |        |
| suc                            | Meningioma en plaque  | 8 (28.6%)       | 6 (21.4%)       | 7 (25.0%)        |       |        | > 0.05 | > 0.05 |
| icati                          | Osteolytic bone tumor | 4 (14.3%)       | 5 (17.9%)       | 7 (25.0%)        | 0.972 | > 0.05 |        |        |
| Indi                           | Infection             | 3 (10.7%)       | 2 (7.1%)        | 2 (7.1%)         |       |        |        |        |
|                                | DC                    | 2 (7.1%)        | 1 (3.6%)        | 1 (3.6%)         |       |        |        |        |
| Defect                         | Right                 | 17 (60.7%)      | 13 (46.4%)      | 12 (42.9%)       | 0.269 | > 0.05 | > 0.05 | > 0.05 |
| side                           | Left                  | 11 (39.3%)      | 15 (53.6%)      | 16 (57.1%)       | 0.308 | 2 0.05 | 20.05  | ~ 0.03 |
| Defect size (mm)               |                       | $62.82\pm17.8$  | $60.82\pm19.5$  | $52.86 \pm 16.8$ | 0.098 | 1      | 0.126  | 0.307  |
| Total operative time (minutes) |                       | $119.43\pm14.9$ | $121.39\pm14.8$ | $123.11\pm18.1$  | 0.691 | 1      | 1      | 1      |
| Blood loss (ml)                |                       | $184.82\pm77.7$ | $197.32\pm96.6$ | $172.32\pm97.5$  | 0.592 | 1      | 1      | 0.922  |

DC: Decompressive craniectomy. P1: Titanium group & PEEK group. P2: Titanium group & PMMA group. P3: PEEK group & PMMA group.

As regards the complications encountered in the current study, infection was detected in 7.1%, 3.6%, and 10.7% of the cases, while implant exposure was diagnosed in 3.6%, 0%, and 7.1% of the cases in the three groups, respectively. De novo postoperative seizures were reported by 0%, 7.1%, and 10.7% of the cases in the titanium mesh, PEEK, and PMMA groups, respectively, and headache was reported by 10.7%, 3.6%, and 3.6% of the cases in the same groups, respectively. Extradural hemorrhage occurred in only one case in the PEEK group (3.6%).

The prevalence of implant failure was in 10.7%, 3.6%,

and 14.3% in the same groups, respectively. One patient in the PMMA group developed both infection and exposure. Graft resorption occurred only in one case (3.6%) in the PMMA group. Although all of the previous complications (apart from extradural hemorrhage) tended to have a higher prevalence in the PMMA group, no statistically significant difference was detected between the three groups regarding all of the previous complications. However, these increased complication rates had a significant negative impact on patient satisfaction which was significantly better in the PEEK and titanium groups compared to the PMMA group (p = 0.046). These data are summarized in **Table 3**.

| Table 3. Post-o   | norativo comi | nlications and | nationte | caticfaction | in tha | study ( | Trouns |
|-------------------|---------------|----------------|----------|--------------|--------|---------|--------|
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| Table 5. 1 0st-operative compleations and patients satisfaction in the study groups |               |                |            |            |       |        |        |        |  |
|---|---------------|----------------|------------|------------|-------|--------|--------|--------|--|
|   |               | Titanium group | PEEK group | PMMA group | Р     | P1     | P2     | P3     |  |
| Material related complications  |               |                |            |            |       |        |        |        |  |
| Infection   |               | 2 (7.1%)       | 1 (3.6%)   | 3 (10.7%)  | 0.867 | > 0.05 | > 0.05 | > 0.05 |  |
| Exposure  |               | 1 (3.6%)       | 0 (0.0%)   | 2 (7.1%)   | 0.770 | > 0.05 | > 0.05 | > 0.05 |  |
| Graft resorption  |               | 0 (0.0%)       | 0 (0.0%)   | 1 (3.6%)   | 1     | > 0.05 | > 0.05 | > 0.05 |  |
| Failure   |               | 3 (10.7%)      | 1 (3.6%)   | 4 (14.3%)  | 0.520 | > 0.05 | > 0.05 | > 0.05 |  |
| Material non related complication   |               | ons            |            |            |       |        |        |        |  |
| New seizures  |               | 0 (0.0%)       | 2 (7.1%)   | 3 (10.7%)  | 0.362 | > 0.05 | > 0.05 | > 0.05 |  |
| Extradural hemorrhage   |               | 0 (0.0%)       | 1 (3.6%)   | 0 (0.0%)   | 1     | > 0.05 | > 0.05 | > 0.05 |  |
| Headache  |               | 3 (10.7%)      | 1 (3.6%)   | 1 (3.6%)   | 0.611 | > 0.05 | > 0.05 | > 0.05 |  |
| Satisfaction  | Completely    | 7 (25.0%)      | 3 (10.7%)  | 3 (10.7%)  |       |        |        |        |  |
|   | Satisfied     | 17 (60.7%)     | 14 (50.0%) | 10 (35.7%) | 0.046 | > 0.05 | > 0.05 | < 0.05 |  |
|   | Fairly        | 1 (3.6%)       | 6 (21.4%)  | 4 (14.3%)  | 0.040 | ~ 0.05 | ~ 0.05 | < 0.03 |  |
|   | Not satisfied | 3 (10.7%)      | 5 (17.9%)  | 11 (39.3%) |       |        |        |        |  |

P1: Titanium group & PEEK group. P2: Titanium group & PMMA group. P3: PEEK group & PMMA group.

## DISCUSSION

Although cranioplasty seems to be a relatively simple and straightforward surgical procedure, it seems to be associated with multiple postoperative complications.<sup>22</sup> Therefore, the optimum graft should be used to decrease the incidence of such complications.<sup>8,19</sup> Multiple methods have been proposed for the closure of skull defects, including autologous and synthetic materials like titanium, PEEK, and PMMA. To the best of our knowledge, the current literature is defective in studies comparing the previous three techniques, which was a fair motive for us to conduct the present study.

We have selected these three ways of cranial reconstruction as they are common for use among Egyptian neurosurgeons. Of course, the method of manufacturing of each implant differed according to its nature, which would have an impact on material characteristics, making one material superior to the other. This could form some bias as reported, but we tried to decrease this bias as possible in this prospective randomized study. All preoperative criteria between the patients were comparable. In addition, we maintained a complete aseptic technique during the modeling of PMMA to decrease the risk of infection. Although both PEEK and titanium mesh are more recent compared to PMMA, the former two approaches have high cost compared to the latter one, making PMMA more suitable for the economic level of the common Egyptian population if it has a comparable complication profile with the two recent ones.

In our study, the defect size had mean values of 62.82 mm, 60.82 mm, and 52.86 mm in the titanium mesh, PEEK, and PMMA groups, respectively, without any significant difference between the three groups (p = 0.098). Bobinski et al. have reported that defect size had a mean value of 68.8 mm in the cement group,<sup>22</sup> and this is close to our values. In a previous Egyptian study that assessed titanium mesh and bone cement in cranioplasty procedures, 10 cases had cranial defects ranging between 4 cm and 6 cm, 8 cases had defects between 6 cm and 10 cm, in addition to 6 cases who had defect size > 10 cm.<sup>23</sup>

In the current study, the operative time showed no significant difference between the three groups, as it had mean values of 119.43, 121.39, and 123.11 minutes in the titanium, PEEK, and PMMA groups, respectively. This should negate the superiority of any approach over the other regarding the duration of the operation. However, in order to reach conclusive results, more studies including cases with the same cranioplasty indication should be performed to rule out the effect of the concomitant procedure (tumor excision) on that parameter.

Infection was encountered in 7.1%, 3.6%, and 10.7% of the cases in the titanium, PEEK, and PMMA groups, respectively. These infection rates are within the ranges reported by previous studies (0%- 22.2%).<sup>24-27</sup> Although the prevalence of infection was relatively higher with PMMA application in our study, no significant difference was noted between the study groups regarding that perspective.

Previous reports have supported our findings toward increased infection rates with PMMA.28,29 Moreover, a previous Egyptian study has noted high infection rates with bone cement application, as it was encountered in two out of the eight cases undergoing cranioplasty with that approach (25%). In the same study, no cases with titanium mesh developed infection (0%).<sup>23</sup> Hence, if there is a necessity to use bone cement in the operative setting, it should be prepared under complete aseptic conditions, and it is also recommended to use antibiotic-impregnated bone cement. On the other hand, other authors evaluated the safety of bone cement application following retrosigmoid craniectomy. Superficial infections were encountered in 3.2% of cases, while no deep infections were encountered (0%). They have concluded that it is a safe material to be applied for such cases.<sup>30</sup> This was also confirmed in another report.31

Implant exposure was encountered in 3.6%, 0%, and 7.1% of the cases in the titanium, PEEK, and PMMA groups, respectively, with no significant difference in statistical analysis (p = 0.77). Ng et al. have also denied the incidence of implant exposure with PEEK. Nevertheless, the same authors reported much higher exposure rates with titanium mesh as compared to ours (7 out of 12 patients - 58.33%).<sup>32</sup> Thien et al. have also reported no significant difference between titanium mesh and PEEK regarding exposure rates (p = 0.074). However, it was more encountered in the titanium group than in the PEEK group (13.9% versus 4.2%).<sup>21</sup> This might indicate that soft tissue thinning over implant still constitutes a common complication with titanium, and it may appear at a lower incidence with PEEK application. Regarding PMMA exposure rates, a previous study conducted by Kim et al. reported that wound dehiscence and implant exposure was encountered only in one case in the PMMA group (1.03%),<sup>33</sup> which is lower than our findings. Actually, one could agree that titanium mesh is associated with an increased risk of exposure compared to the other two techniques. However, we did not detect any significant difference between the three groups regarding that item. The heterogenicity in the incidence of that complication could differ between studies based on the sample size included and the duration of follow-up.

When it comes to our implant failure as our primary outcome, it occurred in 10.7%, 3.6%, and 14.3% in the titanium, PEEK, and PMMA groups, respectively, with no statistically significant difference when comparing these groups (p = 0.520). Similarly, another study reported no significant difference between titanium mesh and PEEK regarding implant failure (p = 0.129). It was encountered in 25% and 12.5% of cases in the two groups, respectively.<sup>21</sup> Another study reported that implant failure occurred in 8.19% and 12.3% of cases in the PMMA and titanium groups, respectively.<sup>34</sup> Although authors reported incidence rates near to ours, the prevalence of implant failure was higher in the titanium group, which is contradictory to our findings. It should be mentioned that the difference in complication rates, especially infection and exposure, between different studies would eventually lead to a

difference in the implant failure rates reported.

In the current study, no significant difference was noted between the three groups regarding postoperative newonset seizures (p = 0.362). It was reported by 0%, 7.1%, and 10.7% of the cases in the titanium, PEEK, and PMMA groups, respectively. Artificial material may be less fit to the skull deficit resulting in an increased intracranial volume or brain tissue compression, which in turn will lead to the development of postoperative seizures.<sup>35,36</sup> Another study negated any significant difference between titanium mesh and PEEK as regard postoperative new-onset seizures that were encountered in 1.9% and 8.3% of cases in both groups, respectively (p = 0.283).<sup>21</sup> On the other hand, other authors reported no postoperative seizures in any of the included 97 cases who underwent PMMA cranioplasty (0%).<sup>33</sup>

Extradural hemorrhage occurred in only one case in the PEEK group (3.6%), while it was not encountered in the other two groups. Yet, no significant difference was reported on statistical analysis (p = 1). A previous study has reported that epidural hematoma is one of the commonest complications after cranioplasty. The etiology of this postcranioplasty hematoma remains unknown.<sup>37</sup> Thien et al. also reported no significant difference between PEEK and titanium regarding the incidence of extradural hemorrhage (p = 0.455), as it was encountered in 4.2% and 0.9% of cases in the two groups, respectively.21 Moreover, Kim et al. reported that extradural hematoma occurred only in one case (out of 97 cases) who underwent PMMA cranioplasty (1.03%).<sup>33</sup> The incidence of post-cranioplasty hematoma reported by us is near to the incidence rate reported by Thien et al., which confirms our findings. However, the absence of these complications in the other two groups does not mean to generalize the results or to show the inferiority of PEEK against the other two groups, as statistical analysis revealed no statistical difference between the three groups.

Regarding patient satisfaction in the current study, there was a statistically significant difference between the three groups (p = 0.046). Of course, the increased complication rates, despite being insignificant, would have negative consequences on patient satisfaction with the surgical intervention. Likewise, multiple studies have confirmed the superior cosmetic outcomes of both titanium and PEEK in cranioplasty procedures.<sup>18,38,39</sup> Another Egyptian study that compared the outcomes of titanium mesh versus bone cement in 2015 reported that cosmetic outcome was satisfactory for all cases,<sup>23</sup> which contradicts our findings.

To summarize, although bone cement is an old-day technique compared to titanium and PEEK, it has several advantages as it is cheaper compared to the other two materials, making it more popular to use in developing countries like Egypt. Also, it is available and can be easily formed if cranioplasty was not planned (intraoperative surprise when the tumor is found infiltrating the bone or in case of bone flap fall on the floor).<sup>23</sup> Even in larger defects in which the tensile strength of bone cement is questioned, it could be re-enforced with an underlying titanium mesh as reported by Ducic.<sup>14</sup>

Our study has some limitations; it included a relatively small sample size and also lacked long-term follow-up of the included cases. These drawbacks should be properly handled in the upcoming studies.

## CONCLUSION

Based on our findings, it appears that titanium, PEEK, and PMMA have a comparable complication profile when used for cranioplasty. However, complication rates showed slight increase with PMMA, which lead to decreased patient satisfaction in that group. Despite that fact, PMMA should be kept into consideration by every neurosurgeon as a surrogate material for cranioplasty for titanium and PEEK, especially in resource-limited settings.

#### List of abbreviations

3-D: Three-dimensional.
ANOVA: Analysis of the variance.
CSF: Cerebrospinal fluid.
CT: Computerized tomography.
DC: Decompressive craniectomy.
IRB: Institutional review board.
MRI: Magnetic resonance imaging.
PASS: Power analysis and sample size.
PEEK: Polyetheretherketone.
PMMA: Polymethylmethacrylate.
SD: Standard deviation.
SPSS: Statistical Package for the Social Sciences.

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