Analysis of Complications After Cranioplasty with a Customized Three-Dimensional Titanium Mesh Plate

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■ OBJECTIVE: **To report outcomes of cranioplasty (CP) with a customized three-dimensional (3D) titanium mesh plate and identify the relationship between various clinical variables and complications after CP.**

■ METHODS: **Twenty patients who underwent surgery with customized 3D titanium mesh plates and had follow-up for >6 months from January 2015 to December 2017 were enrolled. Complications related to CP were retrospectively reviewed. Patients were divided into 2 groups (no complication group and complication group), and clinical variables related to complications were compared between the 2 groups. Correlation analysis was performed to identify the clinical variable significantly correlated with complications after CP with a customized 3D titanium mesh plate.**

■ RESULTS: **Of 20 patients, 11 developed complications, including extrusion, intracranial infection, severe operative site pain, and wound dehiscence. Among the clinical variables, only the presence of a ventriculoperitoneal shunt was significantly correlated with the overall complication rate (odds ratio = 18.66; 95% confidence interval, 1.56–222.92; $P = 0.021$).**

■ CONCLUSIONS: **A customized 3D titanium mesh plate is associated with a lower risk of intracranial infection, but the rate of postoperative complications, mainly cosmetic problems, such as forehead mesh extrusion and dehiscence, was high at 55%. A ventriculoperitoneal shunt was significantly correlated with the overall complication rate after CP with a customized 3D titanium mesh plate.**

INTRODUCTION

Cranioplasty (CP) is the surgical repair of a skull defect. It is indicated for cosmetic restoration, protection of underlying brain parenchyma, and improving neurologic function.[1-4] A number of artificial materials have been used for CP, such as polymethyl methacrylate, titanium, ceramics, and carbon fiber–reinforced polymer, as well as autologous bone flap. Nevertheless, which material is best for CP remains unclear.[1,5-7]

Among the various artificial materials, titanium has been considered to be the material of choice in moderate-sized to large-sized craniectomy defects because it is biologically inert, strong, lightweight, and inexpensive to produce.[1,8] As advances in technology and imaging have enabled the production of large three-dimensional (3D) custom-made prefabricated plates, 3D customized titanium has been widely used.[6,9] However, CP with titanium is reported to be associated with a risk of complications as high as 34%, and only a few studies addressing complications after CP using large customized 3D titanium, especially with mesh configuration, have been published.[1,2,4,8,10] Therefore, the aim of this study was to report the outcomes after CP with customized 3D titanium mesh plate and identify the relationship between various clinical variables and complications after 3D titanium mesh plate CP.

Key words
- Complication
- Cranioplasty
- Customized 3D titanium
- Extrusion
- Mesh
- Titanium
- Ventriculoperitoneal shunt

Abbreviations and Acronyms
3D: Three-dimensional
CP: Cranioplasty
DC: Decompressive craniectomy
VP: Ventriculoperitoneal

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MATERIALS AND METHODS

Patients and Clinical Variables

Institutional review board approval was obtained for this retrospective study, and the need for informed consent was waived. From January 2015 to December 2017, 87 patients underwent CP at our institution. Among them, 27 patients underwent CP with titanium mesh, but 7 patients were excluded because small flat titanium plates were used owing to the patients' small defective bone flap size. Thus, 20 patients who underwent surgery with customized 3D titanium mesh plates and had >6 months of follow-up after CP were enrolled (Figure 1).

Clinical data of enrolled patients were collected from clinical charts, imaging, and telephone interviews with patients or their family members. The following clinical variables were recorded: sex, age, diabetes mellitus, hypertension, number of days between decompressive craniectomy (DC) and CP, CP operative time, defective bone size, size of customized 3D titanium mesh, depth of forehead skin on axial computed tomography image, and existence of ventriculoperitoneal (VP) shunt. We measured the area of defective bone and customized a 3D titanium mesh plate of the postoperative plain skull true-lateral image using ImageJ (Image Processing and Analysis in JAVA; https://imagej.nih.gov/ij/) (Figure 2).

CP Procedure

All CP surgeries were performed when the cerebral swelling subsided and patients showed no signs of infection. Under general anesthesia, the patient was placed on the operating table with the head supported on a horseshoe-shaped headrest. Prophylactic cephalosporin was given intravenously at the induction of anesthesia. The patient's hair was completely removed with an aseptic medical shaver. Then the scalp was washed with an aqueous solution of chlorhexidine gluconate and left to dry, and povidone-iodine (Betadine, Purdue Frederick, Stamford, Connecticut, USA) solution was applied several times to the patient's whole head and left to dry. After scrubbing, the surgeon donned gown and gloves; disposable cotton drapes with underlying plastic sheet were placed around the previous skin incision, and the aseptic film was attached to it. The previous skin incision was opened, and the dura mater and muscle layer were dissected with great care to avoid brain parenchymal injury. After sufficient dissection, the temporalis muscle that was tensely adherent to the dural layer was cut, and the proximal portion of the temporalis muscle was often left attached to the dural layer. A customized 3D mesh plate was placed in position to ensure its fit and then removed temporarily. Massive irrigation was performed to avoid infection. The 3D titanium mesh was then fixed in position with multiple mini-screws. Multiple dural tack-up sutures were placed to avoid postoperative epidural hematoma. Two wound drains were positioned on the 3D titanium mesh plate, and the wound was closed with tight subcutaneous sutures using 2-0 polyglactin 910 (Vicryl, Johnson & Johnson, Cincinnati, Ohio, USA) sutures and medical stapler. Wound dressing was done in the usual manner. When patients awoke from general anesthesia, a postoperative computed tomography scan was performed to detect any immediate complications related to the surgery.

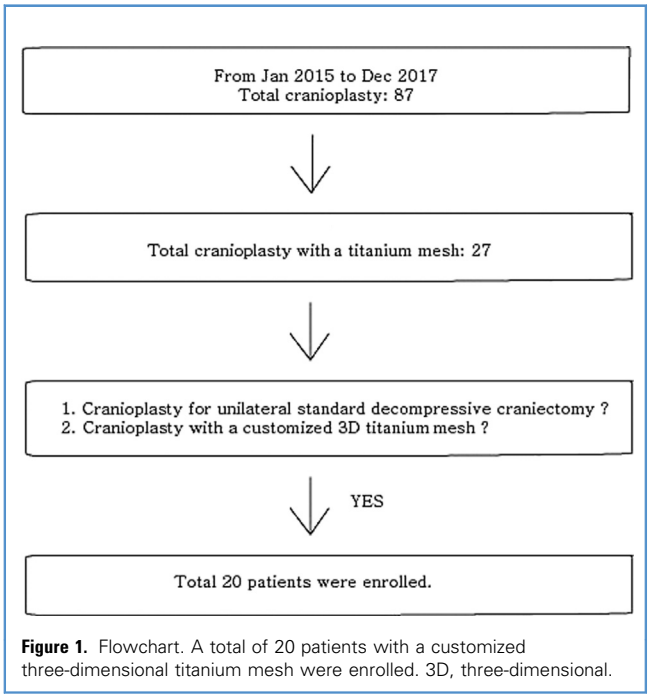

Figure 1. Flowchart. A total of 20 patients with a customized three-dimensional titanium mesh were enrolled. 3D, three-dimensional.

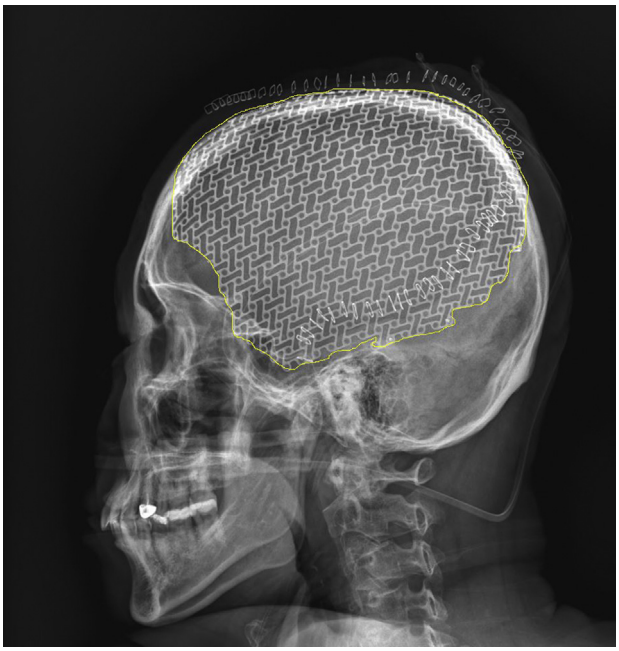

Figure 2. By manually tracing the outline of the customized three-dimensional mesh on the lateral skull plain image, we could measure the surface area of the customized three-dimensional mesh using the ImageJ program.

Statistical Analysis

Group Comparison Analysis. The 20 patients were divided into 2 groups (no complication group and complication group), and the

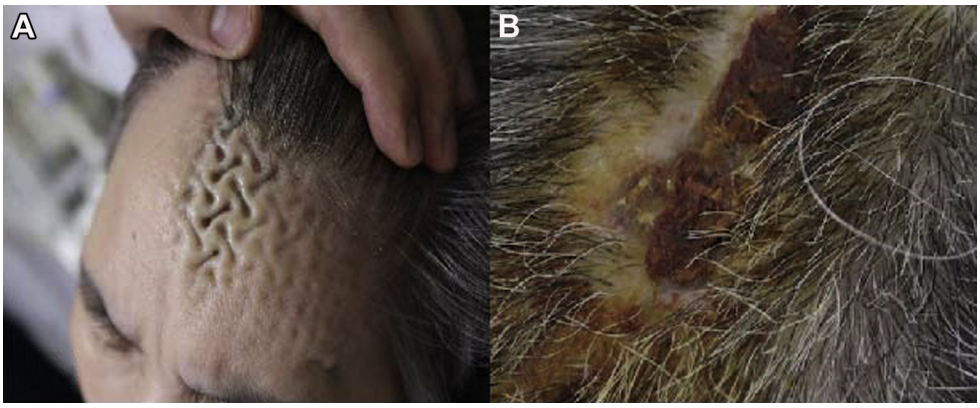

Figure 3. Cosmetic complications after cranioplasty. (**A**) Extrusion of a mesh (severe thinning of the soft tissue and skin, showing the implanted mesh pattern without wound dehiscence or exposure of the titanium mesh). (**B**) Wound dehiscence and exposure of the titanium mesh.

clinical variables were compared between the group using the Mann-Whitney test. Patients who developed any complications, including extrusion, intracranial infection, operative site pain, and wound dehiscence, after CP were included in the complication group. Extrusion refers to a state of severe thinning of the soft tissue showing the implanted mesh pattern without wound dehiscence or exposure of the titanium mesh itself (Figure 3).[9,11] Intracranial infection was defined according to the following criteria: 1) no definite evidence of infection of any other organ except the brain; 2) clinical symptoms, such as fever, neurologic deterioration, and others, consistent with infectious state; and 3) findings such as intracranial abscess, subdural empyema, and cerebritis on brain computed tomography scan.

Subgroup Risk Factor Analysis. To evaluate the relationship between clinical variables and each complication, the complication group was divided into 4 subgroups: extrusion, intracranial infection, pain and tenderness at the operative site, and wound dehiscence and exposure of the titanium mesh. Clinical variables were analyzed using the logistic regression analysis. Each clinical variable was analyzed using univariate logistic regression, and multivariate logistic regression analysis was conducted using forward selection of each clinical variable. IBM SPSS for macOS Version 19.0 (IBM Corporation, Armonk, New York, USA) was used for all statistical tests. A P value <0.05 was considered statistically significant.

RESULTS

Patient demographics and clinical details are presented in Table 1. Five patients underwent DC for trauma, 8 for infection, 3 for subarachnoid hemorrhage, 2 for intracranial hemorrhage, and 2 for acute cerebral infarction. The unilateral standard frontotemporoparietal craniectomy was performed in all cases. The mean age of patients was 53.89 ± 11.76 years (range, 27–81 years). Median number of days between DC and CP was 117 ± 83.5 days (range, 26–1491 days). The mean area of defective bone flaps was 122.3 ± 35.7 cm^2, and mean area of customized 3D titanium mesh plates was 158.2 ± 50.60 cm^2.

Patients who presented with any postoperative complication after CP were included in the overall complication group, which comprised 11 patients who had single or multiple complications, such as extrusion, intracranial infection, operative site pain, and wound dehiscence (Figure 4). Of the 11 patients with complications after CP, only 1 developed intracranial infection; thus, the titanium plate had to be removed to treat infection. Extrusions of the titanium plate were observed in 7 patients; all extrusions were noted in the ipsilateral forehead. We used a visual analog scale as a measurement of pain at the operative site at last follow-up. Of 20 patients, 5 patients had severe pain (visual analog scale score >5) with tenderness at the operative site >1 month postoperatively even though the operative wound was totally healed. No postoperative subdural or epidural

Table 1. Patient Demographics and Clinical Details

Variable	Value
Age, years, mean ± SD	53.89 ± 11.76
Sex, male/female	10/10
Diabetes mellitus, yes/no	2/18
Hypertension, yes/no	6/14
Interval between DC and CP, days, median ± SD	117.00 ± 83.5
Operative time, minutes, mean ± SD	173.26 ± 30.07
Defected bone size, cm^2, mean ± SD	122.30 ± 35.7
3D titanium mesh size, cm^2, mean ± SD	158.02 ± 50.60
Depth of forehead skin, mm, mean ± SD	3.4 ± 1.4
Existence of VP shunt, yes/no	8/12

DC, decompressive craniectomy; CP, cranioplasty; 3D, three-dimensional; VP, ventriculoperitoneal.

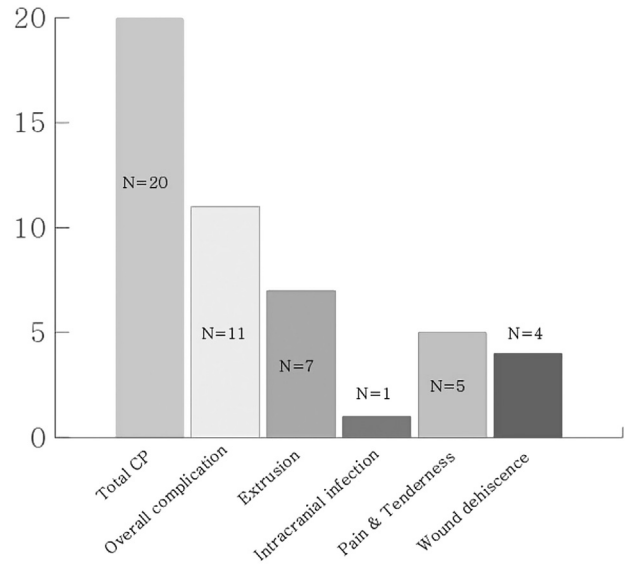

Figure 4. Graph showing the count of each subgroup after cranioplasty with customized three-dimensional titanium mesh. CP, cranioplasty.

hematoma that required an additional procedure for treatment and titanium plate migration was observed in any case.

Group Comparison Analysis

Clinical variables in the complication group and no complication group are compared in Table 2. Median number of days between DC and CP were 99.00 ± 64.8 days (range, 26–714 days) in the complication group and 166.00 ± 159.8 days (range, 54–1491) in the no complication group. The median number of days was greater in the no complication group compared with the complication group, but the difference was not statistically significant (P = 0.295). Defective bone size and 3D titanium mesh size were larger in the complication group compared with the no complication group, but the difference was not statistically significant.

The existence of a VP shunt was the only significant difference between the 2 groups (P = 0.046). All VP shunt systems were located on the contralateral side of the CP, and a CODMAN HAKIM Programmable Valve (Codman Neuro, Raynham, Massachusetts, USA) was used in all VP shunt surgeries (Figure 5). Four patients underwent VP shunt surgery before CP surgery, and 4 patients underwent VP shunt surgery after CP with customized 3D titanium mesh. Of the 4 patients who underwent VP shunt surgery after CP surgery, the mean number of days between CP and VP shunt surgery was 38.2 ± 7.5 days.

Subgroup Risk Factor Analysis

We performed a subgroup risk factor analysis in each complication group (extrusion, intracranial infection, pain and tenderness, and wound dehiscence and exposure) and overall complication group using logistic regression analysis. In the operative site pain and tenderness group, the VP shunt had a higher trend for pain after CP in univariate logistic regression analysis (P = 0.057). In addition, the VP shunt was the only significant predictive variable in the univariate and multivariate logistic regression tests in the overall complication group (odds ratio = 18.66; 95% confidence interval, 1.56–222.92; P = 0.021). No other significant factor related to each complication group and overall complication group was found in the subgroup risk factor analysis.

Table 2. Comparison of Clinical Variables Between No Complication Group and Complication Group

Variable	No Complication Group (n = 9)	Complication Group (n = 11)	P Value
Age, years, mean ± SD	54.0 ± 10.3	53.8± 13.4	0.503
Sex, male/female	4/5	6/5	0.710
Diabetes mellitus, yes/no	No	2/9	0.503
Hypertension, yes/no	2/7	4/7	0.603
Interval between DC and CP, days, median ± SD	166.00 ± 159.8	99.00 ± 64.8	0.295
Operative time, minutes, mean ± SD	177.7 ± 52.0	169.2 ± 35.5	> 0.999
Defected bone size, cm^2, mean ± SD	112.7 ± 43.7	130.8 ± 26.1	0.456
3D titanium mesh size, cm^2, mean ± SD	146.8 ± 63.6	168.1 ± 35.7	0.412
Depth of forehead, mm, mean ± SD	3.5 ± 1.6	3.4 ± 1.3	0.766
Existence of VP shunt, yes/no	1/8	7/4	0.046*

DC, decompressive craniectomy; CP, cranioplasty; 3D, three-dimensional; VP, ventriculoperitoneal.
*Significant value ($P < 0.05$).

DISCUSSION

This study showed that CP using a customized 3D titanium mesh plate resulted in various minor cosmetic complications in up to 50% of patients. Numerous studies have reported the incidence of overall complications of CP with autologous bone flap was comparably high (range, 19.7%–32%).[2,5,7,8,12,13] Among these complications, the primary concerns after CP using autologous bone flap are infection and bone flap resorption.[2,4,14]

Postoperative infection is the most common complication and a serious problem that can result in severe patient morbidity, and a number of reports have documented the incidence of infection following CP (range, 2%–20%).[1,4,7] Studies to determine significant predictive variables for postoperative infection have been limited. Tsang et al.[13] reported that VP shunt at the time of CP was a significant predictive variable for postoperative infection. Several studies also suggested that the presence of neurologic deficit, the location of craniectomy, or the time interval between DC and CP were significantly correlated with postoperative infection.[7,12]

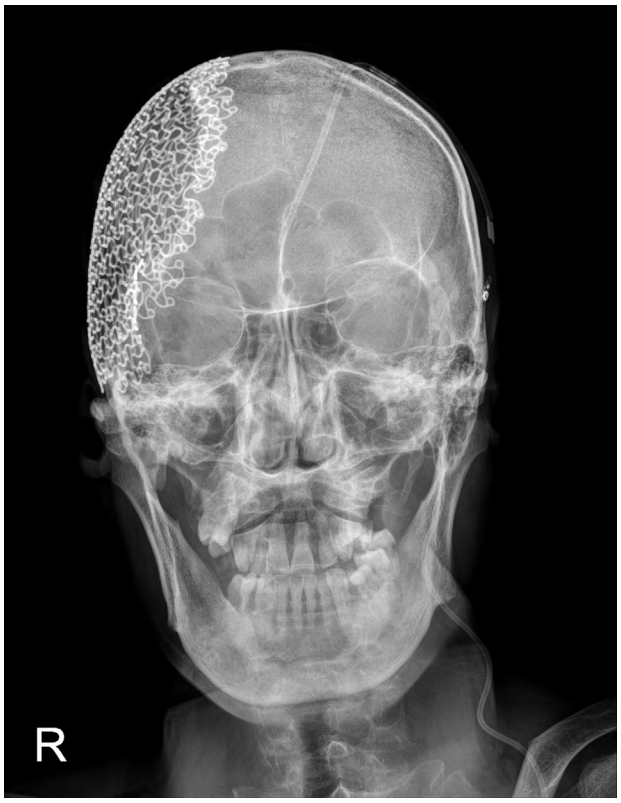

Figure 5. Plain x-ray skull image of patient who had a ventriculoperitoneal shunt with a customized three-dimensional titanium mesh.

Bone flap resorption is also a common and serious problem following CP with an autologous bone flap. The incidence of bone flap resorption has been reported be as high as 34.2% in previous studies.[3,14,15] In a previous correlation analysis to identify the predictive value of bone flap resorption, young age and traumatic brain injury were identified as risk factors in several previous studies,[16,17] and Kim et al.[3] reported that a large bone flap was significantly correlated with bone flap resorption.

The titanium plate has been used as an alternative material for autologous bone flap because of its advantages—that is, low risk of tissue reaction and biologic inertness, especially in patients with a large bone defect.[1,2,4] In line with those findings, only 1 of 20 patients in the present study developed an intracranial infection. However, the risk of minor complications including mainly cosmetic problems, such as extrusion, dehiscence, and exposure of the titanium plate, was relatively high at 55%. Among these cosmetic complications, the most common after CP with a titanium mesh was palpable extrusion of the mesh at the forehead area. Seven patients (35%) presented with an extruded mesh shape on their ipsilateral forehead, and 2 of the patients exhibited serious skin thinning on the mesh plate at the forehead region, indicating a need for a revision surgery soon. Studies investigating extrusion after CP have been limited; however, thinning of the soft tissues in delicate regions, such as the area around the orbital rim, and extrusion in such regions were frequently observed in several previous studies.[5-7] CP with titanium mesh plate was reported to have more tendency in developing extrusion than the other materials, and extrusion could usually occur many years after the CP.[7] Our risk factor analysis did not show any significant predictive value regarding the risk of extrusion after CP, and a more problematic fact is that specific treatment for these extrusions has not yet been established.

A few studies suggested that the presence of a VP shunt was a significant risk factor for postoperative infection after CP and flap depression.[13,18] We also found a significant correlation between the existence of a VP shunt system and the overall complication after CP with a customized 3D titanium mesh plate. We assumed that it may be due to intracranial negative gradient force that was induced by cerebrospinal fluid diversion through a VP shunt. Liao and Kao[19] reported a significant intracranial negative force that was induced by the VP shunt to make the skin of patients who underwent craniectomy become severely depressed. This negative force could pull the skin into the titanium mesh plate continuously, making the occurrence of various complications, such as extrusion, exposure, and severe postoperative pain at the operative site, possible after CP. Therefore, it may be better to use titanium without mesh configuration or other alloplastic materials in a patient who already has a VP shunt or who may need shunting after CP.[5]

This study has several limitations. First, only 20 patients were enrolled, which was a relatively small number. Second, the follow-up period was relatively short. The small sample size and short follow-up time of this study make it difficult to provide generalized conclusions. Finally, our study was a retrospective design and was conducted at a single institution. Clinical studies with larger samples and longer follow-up periods are needed to demonstrate reliable results.

CONCLUSIONS

Although a customized titanium 3D mesh is known to have a low tendency to develop intracranial infection, fits well on the defective bone area, and does not cause any migration of mesh, the rate of postoperative complications including mainly cosmetic problems, such as extrusion, was high at 55%. In addition, the existence of a VP shunt was significantly correlated with overall complications among the various clinical variables.

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