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Original Article

Long-term follow-up for ossification of autologous bone plug and skin sinking after periosteum-preserved burr hole surgery

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Abstract

Background: The demand of a burr hole surgery for chronic subdural hematoma (CSDH) is increasing in the global aging society. Burr hole-derived autologous bone dusts are not associated with extra costs compared with other commonly used synthetic materials. In addition, postoperative calvarium ossification requires periosteum-mediated blood supply, which is lacking after using avascular synthetic materials. Based on these findings, we hypothesized that the combination of the bone plugs and the preserved periosteum during burr hole surgeries for CSDH would induce efficient calvarium ossification.

Methods: We evaluated the long-term effects of bone plugs on the degree of ossification and cosmetic appearance of the skin covering the burr hole sites. We included 8 patients (9 burr holes) who received the autologous bone dust derived from burr holes. As the control group, 9 burr holes that did not receive any burr hole plugs were retrospectively selected. These burr holes were evaluated by computed tomography (CT) scan for the calvarium defect ratios, CT value-based ossification, and the degree of skin sinking.

Results: Ossification was observed in all the bone plugs by the bone density CT scans; they maintained their volume at 12 months after the surgeries. The calvarium defect ratios (volume ratios of the unossified parts in the burr holes) gradually increased during the first 6 months and reached 0.44 at 12 months. The mean CT values also increased from 527 HU to 750 HU for the first 6 months and reached 905 HU at 12 months. The degrees of skin sinking at the burr hole sites with the bone plugs were 1.24 mm whereas those without the bone plugs were 2.69 mm ($P = 0.004$).

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Conclusion: Application of burr hole-derived autologous bone dust is associated with better ossification and objective cosmetic result following burr hole surgery after CSDH.

Key Words: Bone plug, burr hole reconstruction, intramembrane ossification, periosteum, skin sinking

INTRODUCTION

Chronic subdural hematoma (CSDH) is becoming one of the most frequent neurosurgical operations in the world, mainly due to ageing population but also due to the increased use of antithrombotic medications.[4] Regarding a burr hole surgery for CSDH, there are various options to reconstruct the burr holes. In particular, several important factors should be considered such as the prevalence of infectious complications, economical viewpoints, and cosmetic outcomes. Artificial materials such as a hydroxyapatite burr hole button are occasionally used.[6,17] In contrast, autologous bone dusts, byproducts of burr hole surgery, have long been used to surgically repair the burr holes.[1,8,10] In this regard, the ossification effects of fibrin glue-solidified autologous bone dusts have been shown.[10,16] Nevertheless, the long-term effects of this strategy still remain unclear, particularly regarding the degrees of ossification and cosmetic outcomes of the skin above the burr hole sites. In addition, postoperative calvarium ossification is known to require preserved periosteum as the calvarium is remodeled only when the periosteal blood supply is maintained.[14] Moreover, bone plugs can be created from bone dust using a 5 ml syringe without using the fibrin glue.[2] Based on these findings, we recently preserved the periosteum during burr hole surgeries, placed the bone plugs at the site of burr holes, and covered the plugs completely with the periosteum to induce calvarium ossification efficiently. The aim of this study is to elucidate the 1-year follow up for the ossification of the bone plugs and skin sinking with the periosteum-preserving burr hole surgery.

MATERIALS AND METHODS

Patient profiles

This study has been approved by the ethical committee of our institute, and the informed consent was obtained from all the patients included in the study. The burr hole surgery for CSDH performed at the department of neurosurgery in Kindai University Hospital (Osaka-Sayama, Japan) from February 2014 to August 2015. Consecutive eight patients received nine burr hole surgeries, performed by the first author, with the same number of the bone plugs (one patient presented bilateral chronic subdural hematoma) [Table 1]. As the control group, nine burr holes without bone plugs were retrospectively selected from the patients the first author operated before January 2014 with CT scans until 12 months after the surgeries. The following clinical profiles were evaluated: hypertension, diabetes mellitus, hyperlipidosis, smoking, alcohol consumption, and cancer history.

Burr hole surgery

For these patients, a single burr hole surgery was performed as follows [Figure 1]. First, skin incision

Table 1: Patient profiles

	Plug (+)	Plug (-)	*P*
Cases	9	9	
Age (mean)	73.1	78.8	0.6238
Gender (male:female)	5:4	5:4	1
CT profiles (12 months)			
Defect ratios	0.438	0.971	<0.001***
CT values (HU)	905.5	62.1	<0.001***
Skin sinking (mm)	1.245	2.697	0.00426**
Clinical history			
Hypertension	0.333	0.556	0.3566
Diabetes	0.222	0.000	0.1449
Hyperlipidosis	0.222	0.111	0.5388
Smoking	0.111	0.000	0.3173
Alcohol	0.333	0.111	0.2705
Cancer	0.333	0.333	1

Defect ratios: ratio of the unossified part in the burr hole. HU: Hounsfield unit, *P* values were based on Mann–Whitney U test. **: *P*<0.01, ***: *P*<0.001

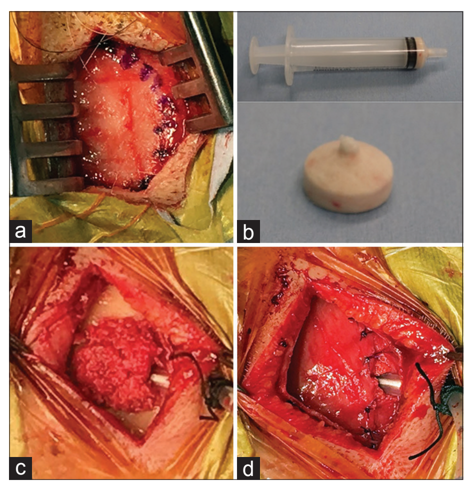

Figure 1: Process of burr hole reconstruction using an autologous bone plug. (a) Periosteum is carefully preserved and undermined under the subgaleal space. Periosteal incision is presented (dot line). (b) The bone plug is created with strong pressure using a 5 ml syringe. (c) The drainage tube is inserted, and then the burr hole is filled with the bone plug. (d) The bone plug is completely covered with the periosteum sutured in place

was made on the stephanion, and the periosteum was carefully preserved [Figure 1a]. Skin was widely undermined below the galea. Then, the periosteum was finely cut in a bow shape and carefully peeled from the skull in the subgaleal space to allow complete suture of periosteum to cover the bone plug at the end of the surgery. Subsequently, a burr hole was made by the cranial perforator (ACRA-CUT, MA), the diameter of the outer drill was 14 mm, and the bone dust was harvested. The bone plugs were created using a 5 ml syringe [Figure 1b] according to a previous study.[2] The dura mater and the outer membrane of the hematoma were cut, and a subdural drainage tube was inserted while avoiding air to enter underneath the subdural space. The bone plugs were placed into the burr hole sites [Figure 1c] and completely covered with periosteum that was sutured in place [Figure 1d]. The drainage tube was gently removed on the next day of the surgery.

CT scan-based evaluation

All the patients underwent CT scans temporally after the surgery [Table 1; Figure 2]. CT images were captured in 2.0-mm slices with multirow high-resolution CT scan systems (Toshiba Aquilion Prime, Tochigi, Japan and GE Discovery 750HD, CT, USA). CT scans were performed on the following day of the surgery as a baseline control [Figure 2a, leftmost]. Consecutive CT scans were performed as routine follow-ups at 1, 3, 6, and 12 months after the surgery [Figure 2a]. The bone density CT scans were performed at the setting of 400 window levels and 2,000 window widths. Measurement of the volume and CT values (Hounsfield unit; HU) of the bone plugs was conducted using Ziostation software (Ziosoft Inc., Tokyo, Japan). Volumetry of the bone plug ossification was conducted as follows. First, the boundary of each bone plug was demarcated by hand at the axial CT images. Then, the Ziostation software calculated its volume three-dimensionally. Based on these data, calvarium defect ratios were calculated. The CT values were also measured based on the average of the region of interest of the bone plug. The degree of skin sinking was measured using the bone density CT scan. The deepest depth from the chord, which was drawn through two points of contact at the edge of skin, was measured [Figure 2a, rightmost]. These data were analyzed by two experienced neurosurgeons.

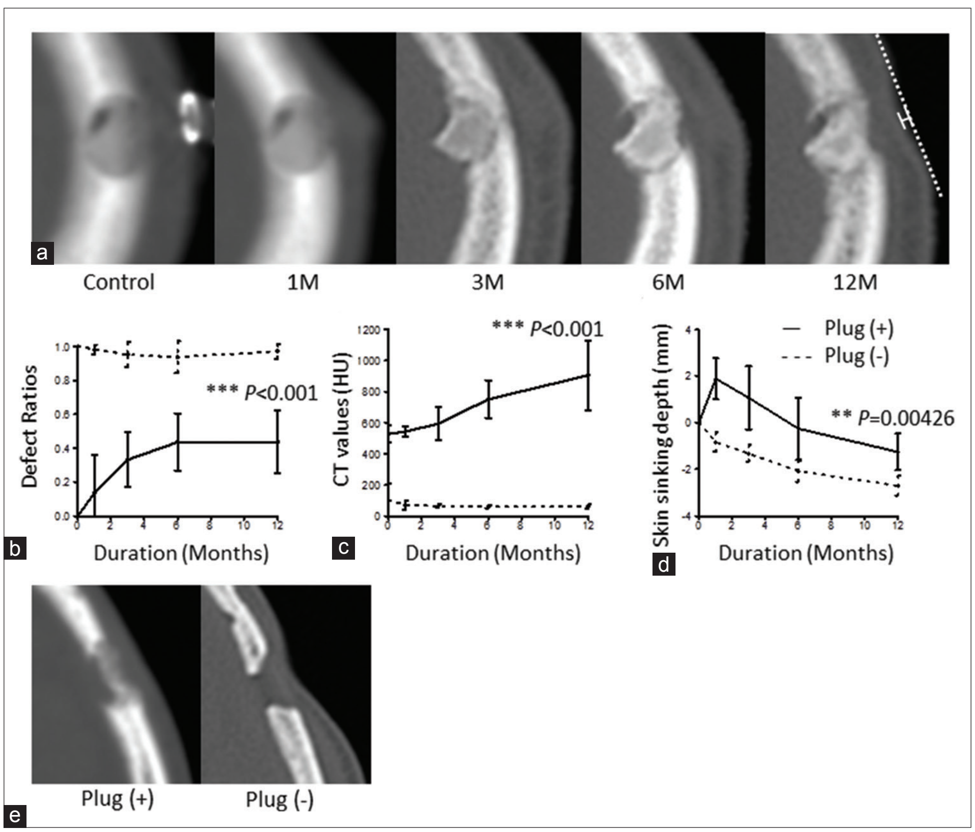

Figure 2: Consecutive changes of the volume and CT values of bone plugs, and the degree of skin sinking at 1 month and 12 months after burr hole surgery. (a) A representative case is presented. Method for measurement of skin sinking on CT scan is shown. A natural curve is drawn through the edges of a skin deposit, and the perpendicular length from the chord is measured. (b) Each volume of the calvarium defect ratios by burr holes is plotted during the postoperative time course (solid line). The defect ratios without bone plugs is plotted in the same way (dashed line). (c) Each CT value is plotted in two groups with (solid line) or without the bone plugs (dashed line). (d) The degree of skin sinking is plotted and compared among the patients with the bone plugs (solid line) and those without the bone plugs (dashed line). Error bars represent standard deviations. (e) Skin sinking with or without the bone plug at 12 months after a surgery. (b-d) *P* values are based on Mann–Whitney U test. **: *P* <0.01, *: *P* <0.001**

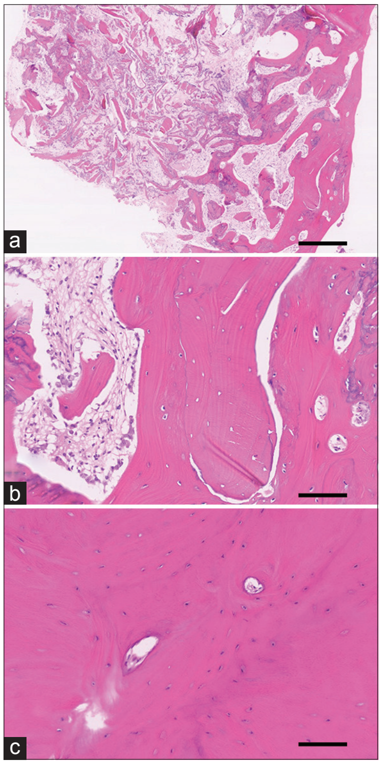

Figure 3: Hematoxylin-eosin staining of the bone plug revealed its re-ossification at 6 months after the implantation. (a) Bone fragments are observed along with fibrous tissue. Mature bone components are partially observed. Original magnification: 40×. Scale bar: 500 μm. (b) Magnified view. Bone spicules and osteocytes are observed. Lining of osteoblasts is also observed. Original magnification: 200×. Scale bar: 100 μm. (c) Intact cortical bone. Osseous lamella and osteocytes but no fibrous components are observed. Original magnification: 200×. Scale bar: 100 μm

Histopathological evaluation

Hematoxylin-eosin (HE) staining was conducted according to a previous study[18] for bone plug extracted from a patient who incidentally underwent the second surgery of recurrent CSDH at 6 months after the first operation [Figure 3a and b]. The intact cortical bone was obtained from a patient who underwent craniotomy and served as a positive control of ossification [Figure 3c].

Statistical analyses

Statistical analyses were performed on R Environment (R Development Core Team, Vienna, Austria) with EZR plugin.[13] Mann–Whitney U test following D'Agostino's K-squared test was performed to compare two-group variables.[11,13] $P < 0.05$ was considered to be statistically significant.

RESULTS

Both groups, with or without the bone plugs, comprised 9 patients (5 males and 4 females) [Table 1]. The mean age of those with the bone plugs were 73.1 years, and those without the bone plugs were 78.8 years. There were no statistically significant differences in patient's characters between the two groups. Ossification was observed in all the 9 bone plugs by the bone density CT scan, and the bone plugs maintained their volume at least up to 12 months. A representative case is presented which shows the chronological changes of the volume and CT values of the bone plugs as well as the degrees of skin sinking [Figure 2a].

The volume of the calvarium defects by burr holes ranged 237–1150 mm^3. The calvarium defect ratios of those with the bone plugs exhibited approximately 0.33 in 3 months after the surgery and 0.44 in 6 months and 12 months [Figure 2b, solid lines]; the defect ratios stabilized after 6 months. The original volume of the bone plugs was evaluated on the following day of the surgery and ranged between 352 mm^3 and 1,150 mm^3, which appeared to depend on the amount of bone dust used. The volume of the bone plugs was as follows: 380–878 mm^3 at 1 month after the surgery, 263–828 mm^3 at 3 months, 258–468 mm^3 at 6 months, and 267–498 mm^3 at 12 months. In contrast, the calvarium defects of the control groups remained unchanged without regeneration.

The CT values on the following day of the surgery ranged between 427 HU and 585 HU [Figure 2c]. The CT values kept increasing during the follow-up periods and stabilized after 6 months. The CT values were as follows: 488–598 HU at 1 month, 440–742 HU at 3 months, 555–924 HU at 6 months, and 503–1120 HU at 12 months. The CT value of the control group remained stable at an average of 62 HU for 12 months.

Skin sinking at the burr hole sites with the bone plugs reverted to the level of normal skin levels at 6 months after the surgery and slightly progressed at 12 months, whereas skin sinking of those without the bone plugs began immediately after the surgery and steadily progressed until 12 months [Figure 2d]. The degrees of skin sinking at 12 months were 1.24±0.78 mm (range: 0.2–2.35 mm) for those with the bone plugs and 2.69±0.43 mm (1.98–3.12 mm) for those without the bone plugs [Figure 2e]. These differences were statistically significant ($P = 0.004$).

HE staining of the bone plug at 6 months after the surgery revealed the lining of osteoblasts, osteocytes, and bone spicules. Fibrous tissues and fibroblasts were also observed, although no inflammatory responses were observed [Figure 3a and b]. The intact cortical bone exhibited osseous lamella around the Haversian canal and sporadic presence of osteocytes [Figure 3c].

DISCUSSION

In this study, we have demonstrated the effectiveness of bone plugs created from burr hole-derived bone dusts to reconstruct calvarium. The use of bone dusts/fibrin glue mixture has been previously reported to induce ossification at the burr hole site as well as the bone gaps created by craniotomy.[10] In this strategy, the fibrin glue is thought to induce chronic inflammation and subsequent neovascularization to promote osteogenesis.[12] However, the fibrin is seldom used only for single burr hole surgeries for CSDH because it increases treatment costs and might induce allergic reactions. In contrast, we demonstrated in this study that the use of bone plugs induces ossification of the burr hole sites even without the fibrin glue [Figure 2]. Another study has compared autologous cortical bone grafts and bone dusts for burr hole reconstruction for craniotomy.[16] In this study, CT values of cortical bone grafts were almost equivalent to those of our bone plugs. Given the time and efforts of the cortical bone graft preparation, these findings suggest that the bone dust is the most useful autologous material for burr hole reconstruction while fibrin glue is unnecessary for this purpose.

We also observed the duration of ossification mediated by the bone plugs. The first step of ossification is resorption of bone graft; the bone plugs without fibrin glue exhibited a significant decrease in volume for the first 3 months. In contrast, regarding the fibrin‑fixed bone dust strategy, the fibrin glue was absorbed for the first 2 months, and the bone dusts were absorbed for the first 3 months, which is almost consistent with the observation of the bone plugs. The difference between these strategies is the second step – osteoblastic activation and bone deposition. Physical fixation of the bone dusts increases the density and interaction of osteogenic components even without the use of fibrin glue, which promotes its resorption and triggers subsequent osteogenesis. Consistently, we observed an increase in CT values during the follow‑up periods and the formation of firmed bone matrix at 6 months after the surgery. Our results (approximately 60% volume retention of bone plugs) are consistent with a previous study based on a rodent model.[3] In addition, HE staining confirmed the osteogenesis of the bone plugs without any inflammatory responses at approximately 6 months. These data suggest the efficient osteoblastic activity of the bone plugs. That is, bone reconstruction requires appropriate materials and pressure to fill the bone gap.

There are two suggested mechanisms of ossification – intramembranous ossification and endochondral ossification.[14] Calvarium is known to be composed of intramembranous ossification‑induced bone alone. Hence, the preservation of periosteum is important for calvarial remodeling. In this regard, our burr hole surgery is designed to carefully collect bone dust and preserve periosteum. Importantly, a bow‑shaped periosteal incision might enable suture at the final closure to completely cover the bone plugs. Thus, the bone dust and periosteum appeared to reconstruct burr hole‑induced calvarium defects efficiently mediated by osteoblastic factors. Previously, the osteogenic potential of calvarial bone dust, bone fragment, and periosteum has been evaluated by measuring three essential osteoblastic factors (collagen, calcium, and alkaline phosphatase) using a rabbit model.[5] This study demonstrated that the bone dusts and, to a lesser degree, the periosteum have been shown to contain these osteogenic components. Furthermore, calvarium‑derived osteoblasts have been shown to induce osteoclasts at higher levels compared with those from long bone.[15] Nevertheless, another study has shown that bone dusts and periosteum had no osteoblastic ability by comparison of the bone dust, periosteum with bone fragments, and full‑thickness cranial bone graft using a rabbit model.[8] Rather, resorption and rejection‑like reactions against bone dust and periosteum were observed. Detailed mechanisms of ossification at the burr hole sites need to be further elucidated.

Current practice dictates that, to prevent skin sinking followed by burr hole surgery, foreign materials such as a hydroxyapatite are widely used to fill and cover burr holes.[7,9] However, there is no report to demonstrate the degree of skin sinking without the use of such materials. Although skin sinking is usually masked and invisible by hair, the skin is extended and pulled into a burr hole even with these materials. In addition, such artificial materials are occasionally problematic, particularly postoperative infection. Our results demonstrated that skin sinking can be prevented with the use of autologous bone plug even without the use of foreign materials. Nevertheless, the present study has some issues in this regard; further follow‑up is required because skin sinking continued even at 12 months. Although we clearly demonstrated that the bone plug technique promotes long‑term reconstruction of burr hole defects as well as patients' cosmetic satisfaction, we need to make an effort for preventing skin sinking in the future.

The present study has several limitations. The biggest limitation is that this technique was applied only for the patients the first author operated, which resulted in a paucity of experimental cases. Thus, we need to accumulate the cases to perform valid statistical analyses. In addition, although we showed 1‑year outcome of this technique in this study, the long‑term outcome also needs to be elucidated in the future.

It is of note that increasing demands for burr hole surgeries for CSDH are inevitable in a global aging society. An autologous bone plug might offer the resolution of not only cosmetic issues relevant to the burr hole surgeries but also prevention for excess usage of foreign materials. In conclusion, the use of autologous bone plug created by bone dusts might be a simple, inexpensive, and cosmetically excellent method to prevent a skin sinking after burr hole surgeries.

CONCLUSION

Application of burr hole-derived autologous bone dust is associated with better ossification and objective cosmetic result following burr hole surgery after CSDH.

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Conflicts of interest
There are no conflicts of interest.

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