Observational Study

Medicine®

OPEN

Treatment outcomes of the simple bone cyst

A comparative study of 2 surgical techniques using artificial bone substitutes

Takashi Higuchi, MD, Norio Yamamoto, MD, PhD, Toshiharu Shirai, MD, PhD, Katsuhiro Hayashi, MD, PhD, Akihiko Takeuchi, MD, PhD*, Hiroaki Kimura, MD, PhD, Shinji Miwa, MD, PhD, Kensaku Abe, MD, Yuta Taniguchi, MD, Hiroyuki Tsuchiya, MD, PhD

Abstract

Simple bone cysts (SBCs) are benign lesions of unknown etiology. Because of its high relapse rate, they occasionally need a long period of treatment and restriction of activities in children and adolescent. Although various treatment modalities with variable differing outcomes have been described in the literature, no consensus has been reached regarding the standard treatment. The purpose of this study was to evaluate the outcome of a minimally invasive technique that uses a ceramic hydroxyapatite cannulated pin (HA pin) for the treatment of SBCs.

Between 1998 and 2015, we have treated 75 patients with SBCs either with continuous decompression by inserting HA pins after curettage and multiple drilling (group 1, n = 39 patients) or with calcium phosphate cement (CPC) filling after curettage (group 2, n = 36 patients). These patients were retrospectively analyzed for recurrence-free survival (RFS) and factors implicated in SBC recurrence.

Seventy-five patients (50 man and 25 females) with a mean age of 17.5 ± 11.6 years and a histopathologically confirmed diagnosis of SBCs were included. The mean follow-up period was 33 ± 25.3 months. RFS were 88% at 1 year and 81% at 5 years. Residual or progressing cysts were observed in 12 patients after the surgery and 10 of them underwent additional surgery. Recurrence rate was significantly higher in patients under the age of 10 years ($P = .01$), in long bone cysts ($P = .01$), and in active phase cysts ($P = .003$) (log-rank test). Multivariate analysis results revealed that age less than 10 years was an independent risk factor of recurrence ($P = .04$). No significant difference in recurrence rate was observed between groups 1 and 2. However, the mean operating time was significantly shorter in group 1. (62.4 ± 25.6 vs 110.5 ± 48.4 minutes in group 2).

Continuous decompression using HA pin is a less invasive surgical technique for the treatment of SBCs compared with CPC filling and has a high healing rate. The relapse rate was still high when the cysts were caused in children aged less than 10 years, located in the long bone, or remained adjacent to the epiphysis.

Level of Evidence: Level 3, Retrospective comparative study

Abbreviations: CPC = calcium phosphate cement, HA pin = hydroxyapatite cannulated pin, MRI = magnetic resonance imaging, RFS = recurrence-free survival, SBCs = simple bone cysts.

Keywords: benign bone tumor, continuous decompression, hydroxyapatite cannulated pin, recurrence, simple bone cyst

1. Introduction

Simple bone cysts (SBCs) are benign bone tumor-like lesions that occur in the diaphyseal part of young people. The cyst wall is covered with a thin sparse membrane of fibrous tissue and the inside has yellow liquid reserves.[1] The predilection age for SBCs is 5 to 10 years and it is the third most frequent occurrence of a benign bone tumor behind osteochondroma and enchondroma. Virchow[2] reported it for the first time in 1867 and its etiology has not yet been elucidated. The current most common cause is believed to be a venous reflux abnormality, theory that Cohen proposed in 1960.[1,3] Various treatments such as the steroid injection method,[4] bone marrow fluid injection method,[4,5] curettage and bone grafting,[6] and decompression/shunt therapy[7,8] have been reported as SBC therapies, but there is no unified treatment strategy due to difficulties in completely controlling local recurrence. Although there is no possibility of metastasis or malignancy, repeating recurrences can cause a problem due to the activity of children during growth and the requirement for multiple surgeries and long-term treatment. Therefore, minimally invasive and more efficient treatments are needed. With the development of the continuous decompression method in 1989, we have improved the recurrence rate through carrying out curettage and drilling from a small opening window, and the placement of a titanium-cannulated screw to reduce pressure and provide a sustained drainage effect. In 1997, we developed and

Editor: Johannes Mayr.

The authors of this work have nothing to disclose.

Department of Orthopaedic Surgery, Graduate School of Medical Science Kanazawa University, Kanazawa, Japan.

** Correspondence: Akihiko Takeuchi, Department of Orthopaedic Surgery, Graduate School of Medical Science Kanazawa University, 13-1 Takaramachi, Kanazawa, Ishikawa 920-8641, Japan (e-mail: a_take@med.kanazawa-u.ac.jp).*

Medicine (2018) 97:18(e0572)

Received: 19 December 2017 / Accepted: 5 April 2018

http://dx.doi.org/10.1097/MD.0000000000010572

Table 1

Specific characteristics of the patients in the 2 groups.

	Group 1	Group 2	*P*
Cases (n)	39	36	
Mean age, y	11.8	23.7	.001*
Gender (n)			
Male	31	19	.03†
Female	8	17	
Cyst site (n)			
Calcaneus	20	4	
Humerus	14	9	
Femur	4	4	
Pelvis and spine	1	13	
Tibia		2	
Talus		2	
Ulna		1	
Cyst phase (n)			
Active	14	13	1.00†
Latent	25	23	
Mean cyst size, mm	45.2	52.2	0.3*
Mean surgical time, min	62.4	110.5	0.001*
Recurrent cysts (n)	9	3	0.12†
RFS (%)			
1-y	84.2	92.8	0.14†
5-y	75.8	87.3	
Mean follow-up, mo	39.5	26.4	0.04*

min = minute, n = number of patients, RFS = recurrence-free survival.
* Mann–Whitney *U* test.
† Fisher exact test.

used a cannulated pin made of hydroxyapatite, which does not need removal, leading to a less invasive treatment for SBCs.[9,10] Although we first attempted to apply the continuous decompression method by inserting a hydroxyapatite cannulated pin (HA pin) for symptomatic SBC treatment, for patients who did not have a typical clinical presentation of SBC or who desired an early recovery, we typically applied calcium phosphate cement (CPC) filling after curettage. In the current study, we investigated the outcome of these 2 methods, the HA pin method and the CPC filling method, and investigated factors associated with SBC recurrence.

2. Methods

Between 1998 and 2015, 75 patients (50 male and 25 female; mean age, 17.5 ± 11.6 years) with SBCs were treated in our hospital with continuous decompression by inserting HA pin (Kobayashi Medical, Tokyo, Japan) after curettage and multiple drilling (group 1, n = 39 patients) or with CPC filling after curettage (group 2, n = 36 patients). The specific characteristics of the patients in the 2 groups were compared using the Mann–Whitney *U* test or the Fisher exact test, and are presented in Table 1. Indication for surgery included symptoms such as pain or activity restriction due to pain or a greater risk of fracture. In patients with symptomatic cyst, the surgical procedures were composed of the following: a minimal fenestration of the cyst wall (approximate diameter, 8 mm in group 1 and at least 20 mm in group 2) was made, followed by curettage of the fibrous tissue. Next, multiple drill holes were made in the medullary cavity and the cyst wall using a Kirschner wire for a connection to healthy bone marrow, followed by insertion of the HA pin in group 1 (Fig. 1) and the appropriate amount of CPC substitute in group 2. Confirmation of the diagnosis was based on a histological study of the specimen surgically removed by curettage. The follow-up period was 33 ± 25.3 months (mean ± standard deviation) for all patients, 39.5 ± 28.0 months for group 1, and 26.4 ± 20.4 months for group 2. In these patients, a retrospective analysis was performed for recurrence-free survival (RFS) and factors implicated in recurrence such as gender, age, cyst sites (long bone or not), cyst phase (active or latent cyst), cyst size [maximum diameter based upon magnetic resonance imaging (MRI)], and cyst wall using a Kaplan–Meier analysis, log-rank test, and Cox proportional hazards analysis. In addition, RFS and surgery time were compared between the 2 surgical methods groups (group 1 and 2) using a log-rank test and Mann–Whitney

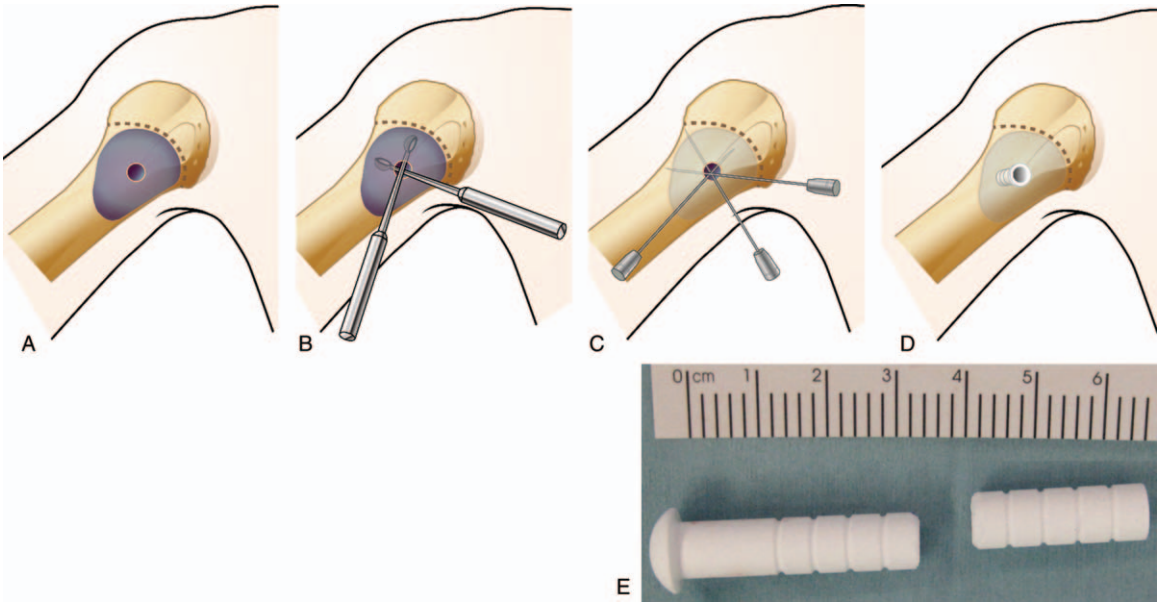

Figure 1. (A) Minimal fenestration of the cyst wall. (B) Curettage of the fibrous tissue. (C) Multiple drill holes were made in the medullary cavity and the cyst wall using a Kirschner wire. (D) Replacement of the hydroxyapatite cannulated (HA) pin. (E) Cannulated hydroxyapatite pin (outside diameter, 8 mm; inside diameter, 3 mm). Easy to cut and adjust the pin length using a scalpel.

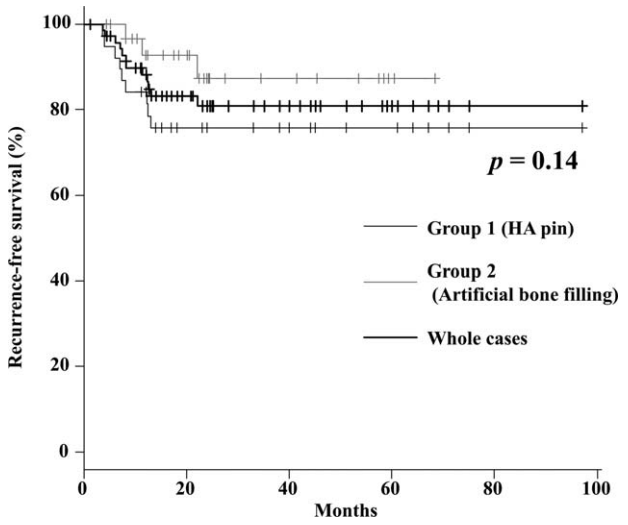

Figure 2. Recurrence-free survival (RFS) in total patients (thick line), group 1 (thin dark line), and group 2 (thin line). There was no significant difference in RFS between groups 1 and 2 with a *P* value of .14 using log-rank test.

U test. Statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan),[11] which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). This was a retrospective clinical case series study and was approved by the local institutional review board. All patients were informed that data of this study would be submitted for publication and gave written consent for participation.

3. Results

Among all 78 patients, 1-year RFS was 88% and 5-year RFS was 81% (Fig. 2). There were 12 patients (7 humerus, 2 femur, and 3 pubis patients) in whom the cysts were classified as a recurrent or nonresponsive cyst or a persistent cyst based upon a modified Neer classification. Among them, 10 patients were treated by an additional operation using CPC filling, 1 patient was treated by 2 surgeries for curettage and CPC filling, and 1 patient was treated conservatively. As a result of univariate analysis, there was no significant difference in RFS when comparing by gender ($P=.44$), cyst size ($P=.31$), and the existence of a cyst wall ($P=.51$). When comparing by age, cyst sites, and cyst phase, the recurrence rate was significantly higher in patients under the age of 10 years ($P=.01$), in long bone cysts ($P=.01$), and in active phase cysts ($P=.003$) (Table 2). Multivariate analysis indicated that an age less than 10 years was an independent risk factor for the recurrence ($P=.04$, hazard ratio 3.52) (Table 3). Comparing the 2 groups, there was no significant difference in RFS between the groups by univariate analysis ($P=.14$, Fig. 2); however, the mean surgery time was significantly shorter in group 1 (62.4 ± 25.6 minutes) than in group 2 (110.5 ± 48.4 minutes) ($P<.001$, Table 1). The mean healing period in group 1, excluding recurrent patients, was 5.5 ± 3.1 months.

4. Case presentations

4.1. Patient 1

Patient 1 was an 8-year-old boy with SBC of the right humerus (Fig. 3A). Because the cyst was large, 2 HA pins were inserted into the cyst cavity after curettage and drilling (B). Eight months after the operation, the cyst had healed (C) and it has not recurred at the final follow-up (6 years after the operation) (D).

Table 2

Univariate predictors of recurrence.

Factors	n	5-y RFS (%)	*P*
Age, y			
≥ 10	49	88.6 (72.0–95.7)	.01
< 10	26	67.8 (45.7–82.4)	
Long bone			
No	42	90.5 (72.7–96.9)	.01
Yes	33	68.0 (47.2–82.0)	
Phase			
Latent	48	91.1 (74.0–97.1)	.003
Active	27	64.0 (42.1–79.4)	
Gender			
Female	25	87.1 (65.0–95.7)	.44
Male	50	77.6 (60.9–87.9)	
Size, mm			
≥30	28	83.4 (61.5–93.4)	.31
<30	20	67.4 (41.2–83.9)	
Cyst wall			
No	16	85.7 (53.9–96.2)	.51
Yes	39	72.2 (52.8–84.7)	
Method			
Group 2	36	87.3 (64.7–95.9)	.14
Group 1	39	75.8 (58.6–86.6)	

n = number of patients, RFS = recurrence-free survival.

4.2. Patient 2

Patient 2 was a 5-year old boy with SBC of the left femur (Fig. 4A). Two HA pins were replaced in the initial operation (B). The cyst gradually shrunk, and 4 months after the operation, the distal area of the cyst had healed and only a small cyst in the proximal area remained (C). At 1 year after the operation, the cyst had enlarged (D) and an additional surgery was performed with curettage and CPC filling (E). At the final follow-up (5 years after the initial operation), a small residual cyst remained at the proximal part of the cyst, though the patient does not have any complaints (F).

5. Discussion

SBC is a benign bone lesion that accounts for approximately 3% of all primary tumors in children.[5] Virchow[2] first reported the disease in 1876, and the etiology has not been fully elucidated. Various hypotheses, such as the tumor origin theory, theory of secondary changes such as tumor and osteomyelitis, and the trauma theory have been proposed.[1] In 1960, Cohen[3] showed that the cystic fluid was the same component as serum and he proposed a venous obstruction theory due to a vascular abnormality. In 1970, Cohen[1] injected a contrast medium into the bone cyst and confirmed that there was no discharge outside

Table 3

Multivariate predictors of recurrence.

Factors	Hazard ratio	*P*
Age (<10 y)	3.52 (1.04–11.94)	.04
Long bone	2.12 (0.48–9.42)	.32
Phase (active)	3.98 (0.91–17.33)	.07

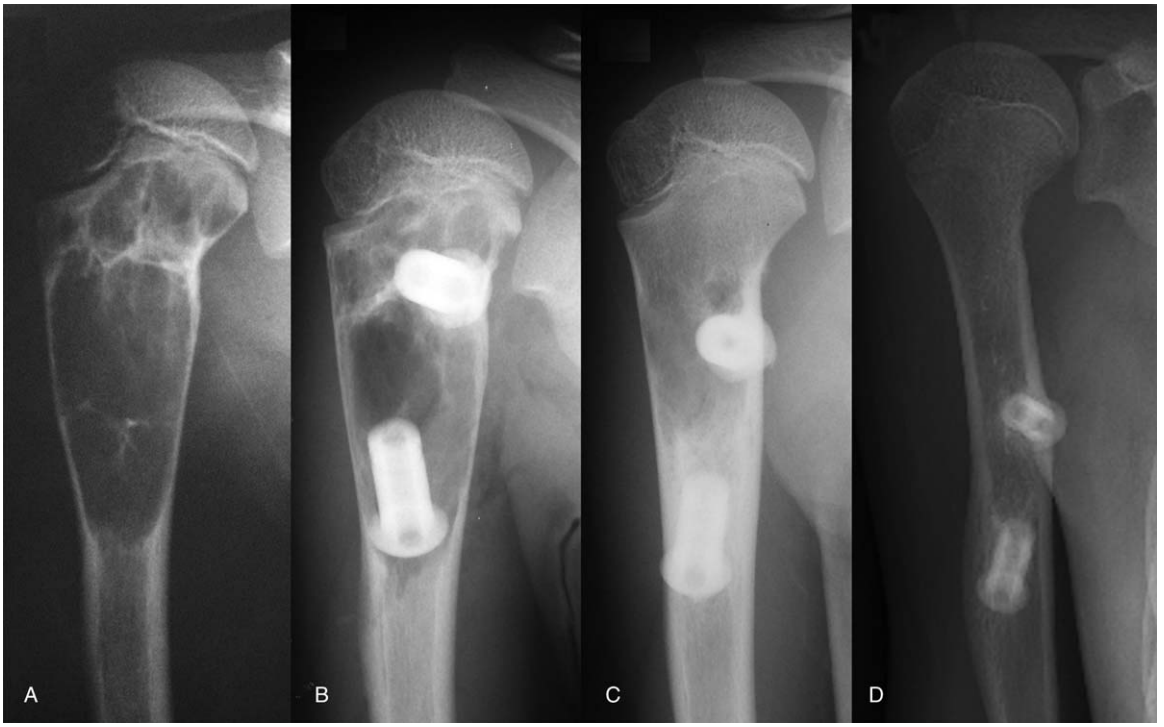

Figure 3. (A) Solitary bone cyst (SBC) of the humerus of an 8-year-old boy. (B) Postoperative radiograph. Two HA pins were placed. (C) The cyst was healing at 8 months after the surgery. (D) Final follow-up. Good remodeling of the cyst was achieved.

the wall under normal pressure, and the fluid stagnated within the cyst for a long time. This result increased the credibility of the venous obstruction theory.[1] Various authors now agree that the obstruction of the venous return and the increase in the resulting intracystic pressure are the main factors influencing the SBC size.[7–10]

Decompression/shunt therapy is a treatment based upon the venous obstruction theory. Kuboyama et al[7] first reported percutaneous bone drilling procedure to open the bone cortex with trephine used for needle biopsy with a drill hole in the cyst wall allow the fluid of the cyst to escape into normal bone marrow. In addition, Chigira et al[8] reported that on a multiple drill holes method to place a penetrated wire, which enabled continuous decompression. Both authors reported good treatment results, but multiple perforations and nail and wire removal were required with this method. We focused on these decompression surgeries and used titanium-cannulated screws for continuous decompression of SBC since 1989. Since 1997, we

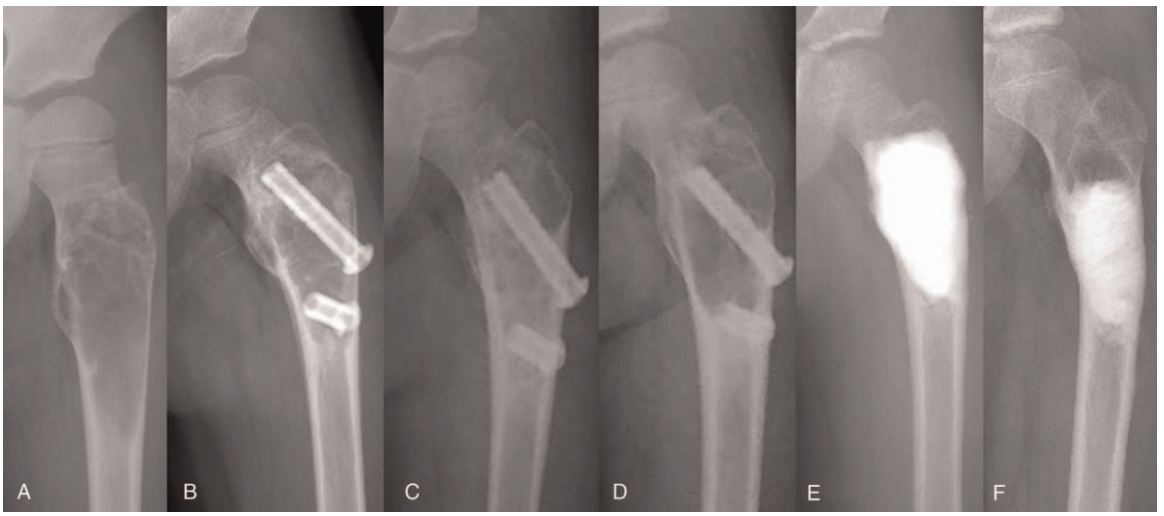

Figure 4. (A) SBC of the proximal femur of a 5-year-old boy. (B) Postoperative radiograph. (C) The cyst shrunk at 4 months after the surgery. (D) Enlargement and recurrence of the cyst was detected at 1 year after surgery. (E) Additional surgery was performed with curettage and calcium phosphate cement filling. (F) Final follow-up. A small residual cyst remained at the proximal area of the cyst.

developed and clinically applied a HA pin, which does not need removal, for the treatment of SBC and have reported satisfactory results compared with the other treatment methods, including observation, injections of steroid, bone marrow, demineralized bone matrix, or curettage and bone graft.[9,10] Advantages of the HA pin method is that use of the fenestration to insert the screw, curettage of the internal cyst wall, and drilling to the normal bone marrow can be performed. Accordingly, a shunt effect between the cyst and the normal bone marrow, and a sustained drainage effect of the screw allow for continuous decompression of the cyst with a single surgery and promotion of new bone formation the cyst. Moreover, it is a minimally invasive procedure, which is done in with a short surgical time and only a small skin incision is needed. In the current study, the operation time using HA pin method was significantly less than that using the curettage and CPC filling method. Furthermore, skin incisions in the HA pin method are small, requiring less than 1 cm per pin, with no delayed wound healing, sustained exudate, or superficial infection, which can occur using the CPC filling method. The HA pin method does require a comparatively later recovery to daily activities, including sports activity. The curettage and CPC filling method allows for early weight bearing. The HA pin method may be advantageous in future bone strength, as the cyst will finally remodel to the initial bone. In SBC of the lower extremity, we usually wait 1 to 4 weeks for full weight bearing, depending on the cyst size, and we permit sports activity after the cyst healed completely, which was 5.5 months on average in the present study.

In this study, the recurrence rate of both methods was 19% and relatively low compared with the past reports.[5,12] The recurrence rate of injection for steroid or bone marrow therapy were reported at 42% and 23%, respectively, with a requirement of several injections.[5] The most common method of curettage and bone grafting has a recurrence rate of 12% to 45%.[12] In the present study, 12 SBCs had a recurrence or a persistent cyst. Jaffe and Lichtenstein[13] reported and defined that the local recurrence of active cysts that abut the growth plate and show an increasing trend of thinning of the cortex was difficult to control compared with that of latent cysts that are apart from the epiphysis. More recently, Haidar et al[14] reported that the recurrence rate significantly increased if the cysts were located less than 2 cm from the growth plate. In the present study, the recurrence rate was also higher in active cysts than in latent cysts.

The recurrence rate in long bone SBCs was also higher than in other locations such as the calcaneus and the pelvis. Recently, the etiology of the calcaneal SBCs was reported to be different from that of the long bone SBCs. Several authors have proposed that calcaneal SBCs are generated from a disturbance in local blood circulation due to a microembolus, cholesterol plaque, or hematoma.[15,16] Takada et al[16] supported this theory using a pathological evaluation of the cyst wall tissue, and found that there were more cholesterol clefts, which are the end product of hematoma and cholesterol plaque in calcaneal SBCs, comparing to long bone SBCs. There were no recurrences of calcaneal SBCs in this study, suggesting that the HA pin method represents an effective minimally invasive treatment of calcaneal SBCs.

Male gender and a younger age have been reported as factors related to recurrence of SBCs.[17] There was no statistical difference in the recurrence rate between genders in the present study, though the recurrence rate in boys tended to be higher. Age was also reported to be a reliable predictor in several reports, with over 10 years of age having a higher rate of cyst healing than those under 10 years old.[10,17] In the present study, < 10 years old was an independent risk factor for the recurrence based upon multivariate analysis.

In SBCs with a high recurrence potential, we try to perform sufficient curettage and drilling to decompress and stimulate osteogenesis in the cyst, and use pleural short pins to prevent pin-hole obstruction by the new bone or contralateral cortex. In SBCs of young patients with an open physes, curettage or drilling might be insufficient due to the risk of epiphyseal injury. Eleven patients in the present study required further surgery due to recurrence or a residual cyst. Additional strategies are necessary to conquer the recurrence of SBCs. Recently, Hou et al[18] performed a novel method to curettage the cyst, followed by ethanol cauterization, insertion of a synthetic calcium sulfate bone-graft substitute in the cyst, and replacement of a cannulated screw, and reported good results with a healing rate of 92%. The number of patients was small, with only 12 patients and 1 recurrence. The HA pin method may be less invasive, as the original method requires screw removal.

The limitation of the present study is that this was a retrospective case–control study and there was a potential selection bias in assigning the patients into the 2 surgical methods. Although there was no statistical difference in the recurrence rate between the 2 methods, the recurrence rate of the CPC bone filling in the present study was comparatively low, at 5.6%. This may be because the indication for CPC filling method in this study was biased. We adapted this method in patients with atypical SBC, which have a higher healing rate, such as older patients or atypical locations such as a trunk SBCs. This fact could lead to a lower recurrence rate in the CPC filling method than the HA pin method.

In conclusion, continuous decompression using HA pin is a less invasive surgical technique for the treatment of SBCs compared with CPC filling and has a high healing rate. The relapse rate was still high when the cysts were caused in children aged less than 10 years, located in the long bone, or remained adjacent to the epiphysis. In order to overcome the limitation of the present study and to conquer the recurrence of SBCs to avoid long-term treatments and the restriction of activities in children, further analyses using large-scale, multicenter, randomized controlled trials are crucial.

Author contributions

Conceptualization: Akihiko Takeuchi, Hiroyuki Tsuchiya.
Data curation: Takashi Higuchi, Kensaku Abe, Yuta Taniguchi.
Formal analysis: Takashi Higuchi, Akihiko Takeuchi.
Investigation: Takashi Higuchi, Akihiko Takeuchi.
Methodology: Norio Yamamoto, Toshiharu Shirai, Katsuhiro Hayashi, Akihiko Takeuchi, Hiroaki Kimura, Shinji Miwa.
Project administration: Hiroyuki Tsuchiya.
Supervision: Akihiko Takeuchi, Hiroyuki Tsuchiya.
Validation: Norio Yamamoto, Hiroyuki Tsuchiya.
Writing – original draft: Takashi Higuchi.
Writing – review & editing: Hiroyuki Tsuchiya.

References

[1] Cohen J. Etiology of simple bone cyst. J Bone Joint Surg Am 1970;52:1493–7.
[2] Virchow R. On the Formation of Bone Cysts. 1876;S-B Akad Wiss, Berlin:369–381.
[3] Cohen J. Simple bone cysts. J Bone Joint Surg Am 1960;42:609–16.
[4] Hashemi-Nejad A, Cole WG. Incomplete healing of simple bone cysts after steroid injections. J Bone Joint Surg Br 1997;79:727–30.

[5] Wright JG, Yandow S, Donaldson S, et al. Simple Bone Cyst Trial GroupA randomized clinical trial comparing intralesional bone marrow and steroid injections for simple bone cysts. J Bone Joint Surg Am 2008;90:722–30.
[6] Sung AD, Anderson ME, Zurakowski D, et al. Unicameral bone cyst: a retrospective study of three surgical treatments. Clin Orthop Relat Res 2008;466:2519–26.
[7] Kuboyama K, Shido T, Harada A, et al. Therapy of solitary unicameral bone cyst with percutaneous trepanation. Rinsho Seikei Geka 1981;16:288–93.
[8] Chigira M, Maehara S, Arita S, et al. The aetiology and treatment of simple bone cysts. J Bone Joint Surg Br 1983;65:633–7.
[9] Tsuchiya H, AbdelWanis ME, Uehara K, et al. Cannulation of simple bone cysts. J Bone Joint Surg Br 2002;84:245–8.
[10] Shirai T, Tsuchiya H, Terauchi R, et al. Treatment of a simple bone cyst using a cannulated hydroxyapatite pin. Medicine (Baltimore) 2015;94: e1027.
[11] Kanda Y. Investigation of the freely-available easy-to-use software "EZR" (Easy R) for medical statistics. Bone Marrow Transplant 2013;48:452–8.
[12] Spence KFJr, Bright RW, Fitzgerald SP, et al. Solitary unicameral bone cyst: treatment with freeze-dried crushed cortical-bone allograft. A review of one hundred and forty-four cases. J Bone Joint Surg Am 1976;58:636–41.
[13] Jaffe HL, Lichtenstein L. Solitary unicameral bone cyst with emphasis on the roentgen picture, the pathologic appearance and the pathogenesis. Arch Surg 1942;44:1004–25.
[14] Haidar SG, Gent ED, Clarke NMP. Distance from the growth plate and its relation to the outcome of unicameral bone cyst treatment. J Child Orthop 2011;5:151–6.
[15] Andermahr J, Jubel A, Prokop A, et al. The calcaneal cyst –pathogenesis and intraosseous vascularization of the calcaneus. FussSprungg 2004;2:219–25.
[16] Takada J, Hoshi M, Oebisu N, et al. A comparative study of clinicopathological features between simple bone cysts of the calcaneus and the long bone. Foot Ankle Int 2014;25:374–82.
[17] Hagmann S, Eichhorn F, Moradi B, et al. Mid- and long-term clinical results of surgical therapy in unicameral bone cysts. BMC Musculoskelet Disord 2011;12:281.
[18] Hou HY, Wu K, Wang CT, et al. Treatment of unicameral bone. J Bone Joint Surg Am 2011;93:92–9.