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Original Article

Grafting for bone defects after curettage of benign bone tumor − Analysis of factors influencing the bone healing

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Abstract

Background: Simple bone cyst often weaken bone properties and predispose to pathological fractures, requiring tumor excision and the filling of bone defects with grafts to prevent complications. The purpose of this study was to evaluate factors potentially affecting the quality and efficiency of graft healing.
Methods: This study retrospectively assessed 84 patients with simple bone cysts who had undergone tumor excision and filling of the bone defects with grafts between 2004 and 2014. Various patient-, tumor- and treatment-related factors that could potentially influence radiologic healing status and time to stable healing were evaluated.
Results: Bone healing was not related to gender and age. Graft type was not significantly correlated with both radiologic healing status or time to stable healing. Only two of all variables evaluated were significantly correlated with the prognosis: (1) Tumors location: patients with tumors located at proximal femur were significantly more likely to achieve complete healing (Neer I) (OR = 3.2; 95%CI, 1.29−8.00; $p = 0.011$). (2) Tumor length: patients with a tumor length less than 6.2 cm, complete healing was nearly five times more likely to occur (OR = 4.84; 95% CI, 1.83−12.84; $p = 0.002$). Degree of graft filling of the bone defects affected the time to stable healing. The average healing times were 4.86 months for filling degree ≥90% and 5.94 months for filling degrees <90%, respectively ($p = 0.009$). Postoperative re-fracture occurred in one case.
Conclusion: Factors influencing the quality of bone healing following intralesional curettage and bone grafting are proximal femur location and tumor length. A greater degree of graft filling can contribute to higher bone healing efficiency.

Keywords: Benign bone tumor; Bone grafts; Bone healing; Bone substitute

1. Introduction

Benign bone tumors or tumor-like lesions often weaken bones and predispose patients to pathological fractures. There are no standard guidelines addressing treatment and follow-up for patients with such tumors. Treatment modalities (steroid injection, surgery, or conservative treatment) for painless benign bone tumors such as a simple bone cyst remain a controversial issue. However, results of a recent systematic review indicated that active treatment provided better results

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than conservative treatment. Although the healing rates were variable, and favorable outcomes were observed.[1]

The goal of the surgery is to prevent from tumor recurrence, and allow the restoration of bone strength. Larger lesions need to be filled with a graft to decrease the risk of pathological fractures.[2] Thus, filling of the bone defects after tumor curettage is currently the most popular approach. The optimum material to fill the bone defects following curettage of bone tumors remains controversial. Types of commonly used materials include cement,[3] autograft,[4] allograft,[5−8] and bone substitutes.[9−13] Nonetheless, the pros and cons of different types of bone grafts applied during the surgery have been demonstrated.

The objective of this study was to assess the parameters that could potentially affect the prognosis after treatment, including factors related to patient, tumor, and treatment. Two major outcomes associated with bone restoration were assessed: the quality (radiographic healing status) and the efficiency (healing time) of final graft incorporation.

2. Methods

2.1. Patient selection

A total of 728 patients with simple bone cyst over limbs were diagnosed at our hospital or referred from other hospitals between January 2004 and January 2014. Of those, patients undergoing surgical treatment were included in this study. In our series, indications for surgery included the following: (1) Patients who were at high risk for a pathological fracture; (2) The presence of pain and disability following a pathological fracture (with a Visual Analog Scale [VAS] score greater than 6 points); (3) Bone malignancy could not be ruled out based on imaging studies.

Only 87 of 728 patients (11.95%) fulfilled the criteria were included for analysis. All patients underwent intralesional curettage procedure followed by bone grafting. Three patients were excluded due to a follow-up of less than 12 months. Finally, 84 patients were enrolled into the study (Fig. 1). There were 51 were males and 33 females, with a mean age of 27.4 (range: 2−82 years). The average follow-up was 19.6 months (range: 12−63 months). The most common location of tumors was the proximal femur in 45 patients (52.6%), followed by the proximal humerus in 20 patients (23.8%). Clinical parameters acquired consisted of age, gender, tumor location, tumor length, and use of graft. Plain films obtained preoperatively were used to evaluate the tumor length.

2.2. Surgical treatment

Surgery involved intralesional curettage through a cortical window. After removal of the fluid, the fibrous membrane lining the cyst wall was curetted. Specimens were sent for histopathological analysis. After confirming the diagnosis of simple bone cysts (SBC), curettage and pulse lavage of the lesion were carried out, followed by packing with allograft or bone substitute (chronOS Strip; DePuy Synthes, West Chester, PA, USA) in a random pattern. Nineteen patients with defects that may predispose to a high risk of fracture were supplemented with fixation devices, including 13 in the proximal femur, 4 in the proximal tibia, and 2 in the proximal humerus.

2.3. Rehabilitation and follow-up

All of the patients who had tumors of the lower limbs were encouraged to begin partial weight bearing in the first postoperative month. Gradual improvement in weight bearing force was observed through X-ray findings during the follow-ups. Passive range-of-motion training immediately after the surgery. Postoperative follow-ups were conducted every 4−6 weeks, depending on the location of tumor. X-ray evaluation continued until the bone graft incorporation reached a stable status. And then, a suggested schedule for follow-up evaluation was at 12 months later.

2.4. Evaluation of degree of bone graft filling

The degrees of graft filling of the bone defects were classified into four categories based on postoperative radiographs. Grade I was defined as a graft with less than 50% filling of the bone defect. Grade II was defined as between 50% and 75% filling; Grade III and Grade IV were 75%−90% and greater than 90% of filling of the bone defect (Fig. 2).

2.5. Radiological evaluation of healing status and healing time

The primary outcome was bone healing assessed by radiographic imaging studies. The quality of bone healing according to radiologic healing status was evaluated on X-ray and modified Neer classification (Table 1) at the last follow-up.[14,15] The efficiency of bone healing was on the basis of time to stable healing. We defined the "time to stable healing" as no X-ray improvement after continuous follow-ups at 3 months. One senior radiologist (Dr. Yu-Chi, Cheng) at the other hospital was responsible to evaluate on patients' serial follow-up imaging findings. Fig. 3 shows an example of radiographic assessment in determining the degree of bone healing for an 8-year-old boy with simple bone cyst.

2.6. Statistical analysis

Frequency and percentage were used to summarize normal variables. Mean and standard deviation (SD) were calculated for continuous variables, including age, tumor length and follow-up duration.

The predicting accuracy of patients' age and tumor length for healing was assessed using receiver operating characteristic (ROC) analysis. The area under the ROC curve (AUC) was used to determine the discriminatory ability of patients' age and tumor length in detecting healing. Based on the AUCs, Youden's index was used to estimate the optimal cut-point that offered the highest sum of sensitivity and specificity for tumor length in predicting healing. For which, patients' age of 10.5 years provided the highest sensitivity (0.85) and specificity

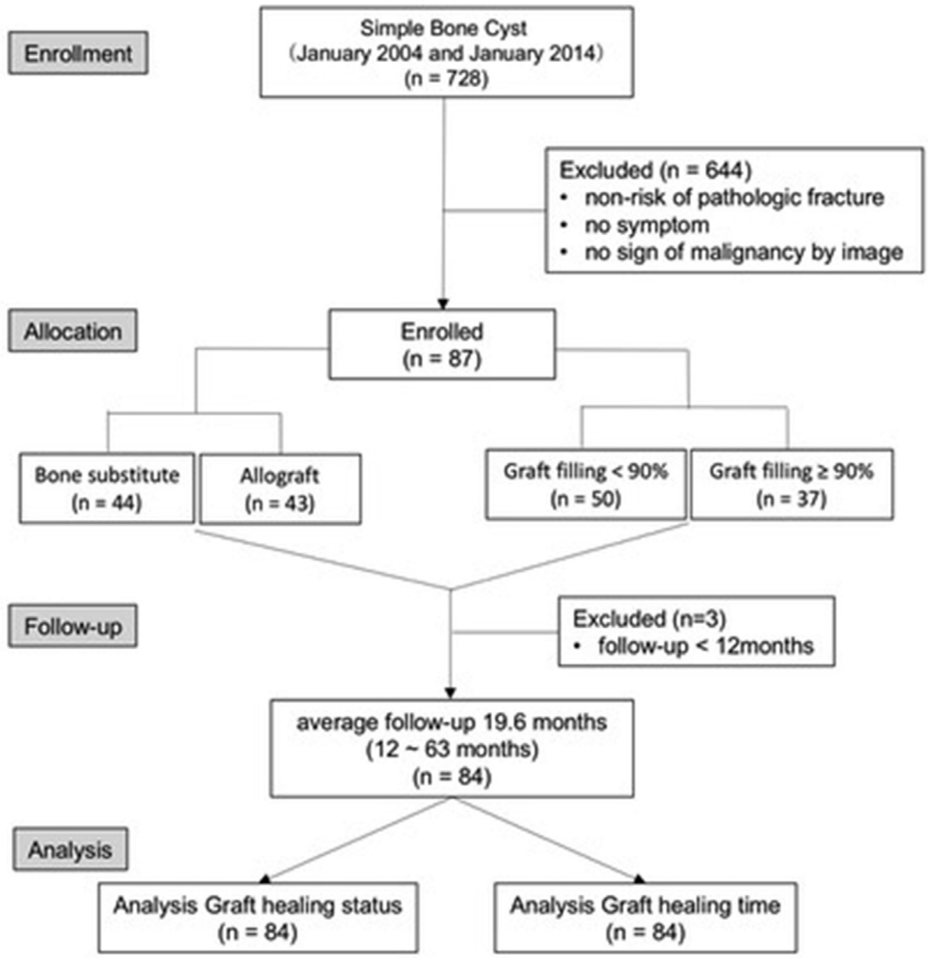

Fig. 1. Study flow chart.

(0.18). Besides, tumor length of 6.2 cm that provided the highest sensitivity of 0.76 and specificity of 0.58 was used to classify groups.

To evaluate factors related to postoperative graft incorporation, the chi-square test and Mann—Whitney U test were performed. All statistical assessments were two-sided, and a *p* value < 0.05 was considered significant. Follow-up results were analyzed by a definitive logistic regression modeling. Statistical analyses were performed using SPSS (Version 23.0; Chicago, IL, USA).

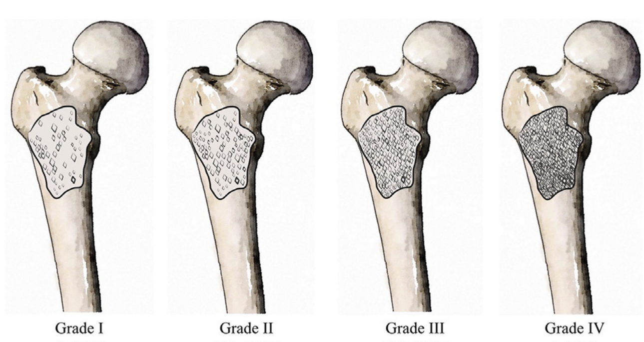

Fig. 2. The degrees of graft filling of the bone defects were classified into four stages.

3. Results

3.1. Quality of bone healing based on radiologic healing status

Treatment outcomes were assessed radiographically using the Neer classification (Table 2). Complete healing of bone defects (Neer classification I) was observed in 51 patients (60.7%) at a mean follow-up of 5.4 months, 25 patients

Table 1
Modified Neer classification of radiologic healing status.

Score	Classification	Description
I	Healed	Cyst filled with new bone, with or without small radiolucent area(s) <1 cm in size
II	Healed with defects	Radiolucent area(s) <50% of the diameter of the bone with enough cortical thickness to prevent fracture
III	Persistent cyst	Radiolucent area >50% of the diameter of the bone and with a thin cortical rim; no increase of the size of the cyst
III	Recurrent cyst	Cyst reappeared in a previously obliterated area or a radiolucent area has increased in size

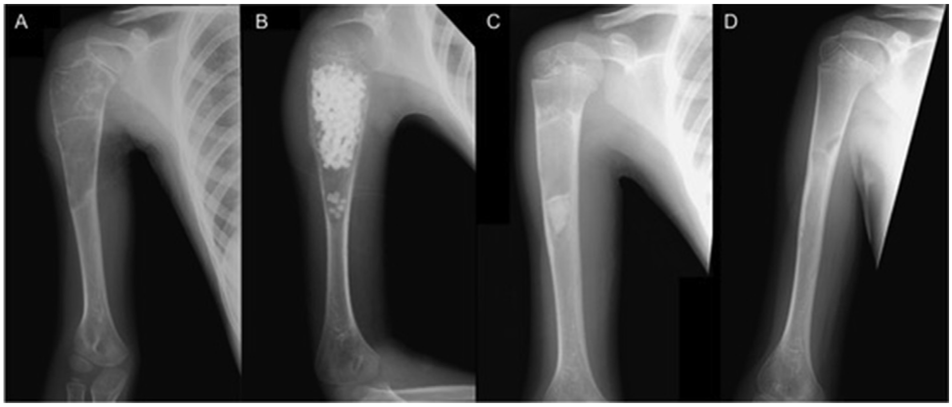

Fig. 3. Assessment of bone healing for an 8-year-old boy with simple bone cyst. A. The X-ray showed an expansile lytic lesion in the right proximal humerus. The status of post surgery: B. Post surgical curettage with an artificial bone grafting. The degree of bone graft filling is grade III. C. At 14 months post surgery: the healing status was Neer classification Score 2. D. At 48 months post surgery: the healing status was Neer classification Score 1.

Table 2
Factors and radiological healing status (Neer score).

Categorical variable comparison	Completed Healed (Neer I) (n = 51)	Non-completed healed (Neer II, III, IV) (n = 33)	OR [95% CI]	*p*
Gender (male)	62.7% (32)	37.3% (19)	1.241 [0.508−3.033]	0.636
Gender (female)	57.6% (19)	42.4% (14)		
Age (<10.5 y/o)	64.3% (9)	35.7% (5)	1.200 [0.364−3.957]	0.764
Age (≥10.5 y/o)	60.0% (42)	40.0% (28)		
Location (proximal humerus)	45.0% (9)	55.0% (11)	0.428 [0.841−6.476]	0.099
Location (proximal femur)	73.3% (33)	26.7% (12)	3.205 [0.125−0.776]	0.011
Tumor length (<6.2 cm)	79.5% (31)	20.5% (8)	4.844 [1.828−12.836]	0.002
Tumor length (≥6.2 cm)	44.4% (20)	55.6% (25)		
Graft (Bone substitute)	64.3% (27)	35.7% (15)	1.350 [0.561−3.250]	0.503
Graft (Allograft)	57.1% (24)	42.9% (18)		
Degree of graft filling (Grade I/II/III)	63.2% (31)	36.7% (18)	1.292 [0.532−3.134]	0.571
Degree of graft filling (IV)	57.1% (20)	42.9% (15)		

(29.8%) had incomplete healing with defects (Neer classification II) and 6 patients (7.1%) had persistent cyst (Neer classification III). Tumor recurrence occurred in 2 patients (2.4%) before achieving a stable healing status.

Table 3
Factors associated with time to stable healing.

	Months	*p*
Gender		
Male	5.35 ± 1.71	0.367
Female	5.72 ± 2.05	
Age		
<10.5 y/o	5.50 ± 2.14	1.000
≥10.5 y/o	5.50 ± 1.80	
Location		
Proximal humerus	5.70 ± 2.13	0.834
Proximal femur	5.40 ± 1.84	
Proximal tibia	5.53 ± 1.61	
Tumor length		
<6.2 cm	5.26 ± 2.09	0.263
≥6.2 cm	5.71 ± 1.60	
Graft		
Bone substitute	5.27 ± 1.55	0.093
Allograft	5.73 ± 2.03	
Degree of graft filling		
Grade I/II/III	5.94 ± 1.68	0.009
Grade IV	4.86 ± 1.92	

Distribution of healing status using the Neer classification at final follow-up was significantly different in tumor location and tumor length. Complete healing was achieved for 79.5% of tumors (n = 31/39) with a length less than 6.2 cm. In contrast, only 44.4% of tumors (n = 20/45) with a length greater than or equal to 6.2 cm achieved a complete healing status ($p = 0.002$). Patient age, gender, graft type (allograft or bone substitute), and the degree of graft filling had no influence on final healing status (Table 2). For tumors located at proximal femur, patients were likely to achieve complete healing (Neer I) (OR = 3.2; 95%CI, 1.29−8.00; $p = 0.011$). On the other hand, for patients with a tumor length less than 6.2 cm, complete healing was nearly five times more likely to occur (OR = 4.84; 95% CI, 1.83−12.84; $p = 0.002$).

3.2. Efficiency of bone healing based on time to stable healing

The efficiency of bone healing was determined by the time required to achieve a stable healing. Factors that could potentially affect the time to final stable healing was evaluated and compared (Table 3). There was no difference with respect to healing time between the groups based on gender, age, tumor location, tumor length, or type of graft (all p values > 0.05). Only "degree of graft filling" was shown to have a significant association, giving the mean healing time of 4.86 ± 1.92 months when the degree of graft filling of the bone defect was grade IV, and 5.94 ± 1.68 months for grade I/II/III ($p = 0.009$).

3.3. Complications

One patient experienced a complication of fracture at the 8th month postoperatively. The tumor with an original length of 11.4 cm was located in the proximal humerus. After curettage, the bone defect was filled with bone substitute at grade I (Fig. 2) and without a fixation device. This patient then received conservative treatment, and fracture union occurred 4 months later without any symptoms.

4. Discussion

Two main concerns associated with benign tumor excision are postoperative recurrence rate and bone strength.[1] Steroid injection is a simple method of treating a simple bone cyst, which can result in a good healing rate (e.g. 77.4% by methylprednisolone acetate[16]); however, studies also reported high failure rates (50%−84%).[17−19] Curettage alone without an allograft or bone substitute may be used, but a higher rate of complications was found for tumors with a volume greater than 60 cm^3.[2] Historically, surgical curettage with bone grafting were the optimal choices to minimize the risk of recurrence. With strict surgical indication mentioned aforementioned, curettage of the bone tumor combined with graft filling of the bone defect has been the main approach applied at our institution.

Both high quality and efficient healing were the goals after intralesional curettage and bone grafting for benign bone tumors. High quality of bone healing means that the bone has healed sufficiently to bear weight and prevent from pathological fractures. High efficiency indicates a stable healing status is achieved within a short period of time so that patients can return to daily activities promptly. One published study declared that most bone defects after excision of benign bone tumors will consolidate without any supplementation;[2] however, this has raised the concerns about the healing quality and healing time.

An autograft is an excellent material to fill the bone defect after tumor excision. The advantages of autografts have been well established. However, insufficiency in the origin of this material to fill the bone defect always limits their usage. Furthermore, increased postoperative mobility of donor site has long been a concern with autografts.[20] One study reported lesser pain, operating time, blood loss and complication in synthetic substitutes compared with iliac crest grafts.[6] Thus, autograft was not used in this study. Alternatively, allografts and bone substitutes are readily available and of unlimited supply for filling large bone defects. However, several disadvantages of allografts have been reported such as disease transmission and a relatively poor incorporation ability.[8] Although the use of a bone substitute is associated with a high cost, these materials are widely used due to their convenience. Furthermore, a recent systematic review[11] demonstrated that the healing outcome were comparable between bone graft and bone substitute following surgical curettage. With the utilization of autograft, allograft or any bone substitution material could result in an approximate healing rate of 90%. Our findings indicated no significant difference to achieve a complete healing status (Neer score I) between two groups (64.3% in the bone substitute group and 57.1% in the allograft group), which was similar to the results reported by Theologis et al. who found that the bone fusion was not influenced by type of bone graft or substitute.[13] In addition, type of graft also did not affect the time to stable healing in the current study.

The relationship between the degree of graft filling of bone defect and bone healing has rarely been discussed in previous studies. We found that the time to reach final incorporation shortened while the degree of graft filling increased; however, it did not reflect the quality of bone healing. The radiologic healing status did not correspondingly increase once the graft was packed more tightly, which might be associated with impaired revascularization due to too tightly packed grafts, as reported by Campanacci et al.[20]

Two factors influencing the radiologic healing status were proximal femur location and tumor length. In our study, patients with a tumor located at proximal femur were significantly more likely to achieve complete bone healing status (Neer score I). It may be associated with the tumor location close to the weight bearing zone and soft tissue-rich environment of proximal femur. Besides, tumor length was negatively correlated with complete bone healing status (Neer score I) and a length < 6.2 cm was 4.84 times more likely to achieve healing complete. Treatment of patients with a large tumor volume or tumor length has been a challenge to orthopedic surgeons. There are two main reasons. First, curettage of low aggressive benign bone tumor such as simple bone cyst is performed through a small bone window. Complete excision may not be easily achieved for large or deep-seated tumor, which consequently could result in a higher local recurrence rate. Second, increased tumor length also correlate with increased risk of preoperative pathological fracture and make the surgery more difficult. Besides, filling of a larger bone defect will increase operation time and treatment cost. Glancy et al.[4] reported a higher "no healing" rate for tumors with large size after curettage and grafting for bone tumors, accompanied by more complications such as stress fracture and bone growth arrest. However, both of proximal femur location and tumor length were not related to the time to achieve a stable healing.

There were some limitations in this study. First, clinical records of patients were retrospectively reviewed. Errors or missing data might be possible. Second, this study analyzed the data of a relatively shorter duration of follow-up. Studies reported that the longer follow up period is needed because longer the follow up period, the higher the rate of recurrence.[21−23] At least two years of follow-up may be more appropriate to report the recurrence rates and compare between the two groups of graft types.[23] Third, there were systemic factors such as comorbidities and bone mineral density that may also influence the blood supply and bone healing were not included for analysis, which may be taken into account source of potential bias when interpreting results.

In conclusion, this study showed that the factors influencing the quality of bone healing following intralesional curettage and bone grafting of simple bone cyst are proximal femur location and tumor length. And, a greater degree of graft filling can contribute to higher bone healing efficiency.

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