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Functional Outcomes of Limb Salvage Surgery in Patients with Giant Cell Tumor of Bone of the Lower Extremities: A Retrospective Study

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ABSTRACT

Giant cell tumor of the bone (GCTB) is a benign, locally aggressive neoplasm that is relatively rare, with a propensity to result in progressive bone destruction, and is associated with a high risk of recurrence. There is no widely held consensus regarding its ideal treatment. Worldwide, there are varying techniques ranging from intralesional curettage to resection of the lesion, supplemented with combinations of numerous adjuncts and fillers, depending on the resected amount and integrity of bone, as well as the preference of the surgeon.

This was a cross-sectional study that included 20 patients who underwent limb salvage surgery for giant cell tumor of the bone of the lower extremities from January 2009 to February 2020 at two tertiary hospitals. The mean follow-up period was 37.3 months (SD=2.84). The extended curettage (EC) group had a mean Musculoskeletal Tumor Rating Scale (MSTS) score of 28.18 (SD=7.51) which is considered as an excellent outcome, while the resection (RS) group had an mean MSTS score of 19.67 (SD=11.02), which is considered as a good outcome. EC resulted to a total of eight complications (47%), while RS had one complication (33%). Prevalence of recurrence was noted to be 11.75% among those who underwent EC, while no recurrence was noted among those in the RS group. Use of bone cement as a filler was noted to have less recurrence as compared with the use of bone grafts, however were both were noted to result in excellent functional outcomes.

Despite the prevalence of complications and recurrence of GCTB of the salvaged extremity in those who underwent EC, there is still report of excellent functionality. It is hence important to disclose all these possible outcomes and to stress the importance of compliance to follow-up for monitoring of these events.

1. Introduction

Giant cell tumor of the bone (GCTB) is a benign but locally aggressive neoplasm comprising approximately 5% of all primary bone tumors [1-6,9,15,18,20]. The natural history of GCTB is progressive bone destruction leading to joint deformity and disability, and despite it rarely causing death, it displays a tendency for local recurrence occurring within two years of the index surgery, and pulmonary metastasis (1.8-9.1% of cases) has also been described [1,2,5,6,14,15,21]. There are documented cases of malignant transformation in less than 1% of GCTs and are hence considered rare [1,5,8].

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There is no widely held consensus regarding the ideal treatment method selection of GCTBs. Options of chemotherapy and radiotherapy are reserved for select cases however evidence shows no clear benefit for its use in these cases [2,14]. Treatment has become mainly surgical and is the universal standard of care due to the association of GTCB with substantial disturbance of local bony architecture especially in periarticular locations [2,4,6,14,15]. In our institution, as well as worldwide, there are advocates of varying surgical techniques ranging from intralesional curettage to wide excision of the lesion, supplemented with cement augmentation and fixation with implants, depending on the amount of bone resected, integrity of the articular surface, and the preference of the surgeon [2].

Regardless of technique, the goal of limb-salvage are eradication of the tumor, preservation of limb function, and prevention of local recurrence and distant metastasis [2,5,14], as some studies show a correlation of the rate of local recurrence varying with the extent of GCT removal [2,3,6,22]. Patients with wide resection of the tumor are noted to have a local recurrence rate approaching 0% [6], but with these leading to higher rates of surgical complications and may lead to functional impairment, necessitating reconstruction [2,3,18]. On the other hand, intralesional curettage despite resulting in less morbidity and functional impairment, regardless of how thoroughly performed, leaves microscopic disease and hence has a reported recurrence rate as high as 60-65% [2,3,14,18,20]. This has led surgeons to enhance surgical procedures with the use of adjuvants such as liquid nitrogen, cement, phenol, hydrogen peroxide, which in some studies, have shown to be useful in decreasing recurrence rates [2,4].

In the Philippines, options for limb-salvage surgery for malignant and aggressive extremity neoplasms after tumor excision are limited as they would often entail the use of bone grafts, not only due to the sheer size of the defects left in the aftermath of the procedure, but also due to the unavailability and unaffordability of tumor prosthesis and implants [4], often resulting to amputation of the involved extremity. In this developing country, there are only a few centers with an active bone bank, and our institution is honored to house one of them, for which a stock of allografts are available for use intraoperatively.

To date, possibly owing to the relative rarity of the disease, there has been no other published work in regards to the functional outcomes of patients in the Philippines diagnosed specifically with GCTBs of the lower extremity who underwent limb-salvage surgery, as well as the complication and recurrence rates following the aforementioned procedure. The researchers would like to provide evidence for this gap in knowledge, as well as to determine the outcomes of the usage of allografts in this population who have access and are able to afford this modality.

2. Materials and Methods

Study Design and Procedure

This was a cross-sectional study investigating patients who underwent limb-salvage surgery of the lower extremity for GCTB from January 2009 to February 2020 at two tertiary hospitals. Limb salvage surgery in this study is defined as resection (RS) or extended curettage (EC) of the GCTB lesion of a Campanacci grading of II or III, with or without the use of local adjuvants, with the goal of eradication of the tumor, preservation of the limb and its function, and prevention of recurrence.

Due to the relative rarity of the disease, convenience sampling of the cases of interest was done. A thorough review of the patient’s electronic hospital records (Enterprise Portal v1.6.1 rev.219), including the operative record for details regarding the surgery was done. All information was collated using a data collection tool.

Functional outcomes, on the other hand, were derived from the surgeon’s clinic charts of the patient’s subsequent follow-up visits postoperatively. These were rated using the Musculoskeletal Tumor Rating Scale (MSTS), a validated questionnaire developed initially by Enneking et al in 1993 and has been in use for over 20 years as a widely recognized tool to evaluate function. This system measures outcomes in seven categories, including motion, pain, stability, deformity, strength, activity, and emotional acceptance, specified to the anatomic location of interest (ie, hip, knee, or ankle) [8]. Each parameter is scored 0-5 and combined for a possible total score of 35. A score of 23 or greater is considered an excellent result; a score of 15-22 is considered a good result; a score of 8-14 is considered a fair result; and lastly, a score of less than 8 is considered a poor result, in terms of functionality [9].

Likewise, the occurrence of any complication or recurrence was noted using these records. The development of progressive lucency at the cement-bone interface in radiographs, or the presence of osteolysis and presence of a soft tissue mass in CT or MR imaging following surgery suggests recurrence of GCTB [6]. A complication on the other hand is defined as any event for which the patient required a specific intervention such as wound complications, infection, implant failure/loosening, fracture, and stiffness of the joint [4].

Approval was first obtained from the Institutional Review Board and Ethics Committee of our institution prior to the commencement of this study.
Eligibility Criteria

Inclusion criteria for the patients to be recruited were as follows:

1. More than 18 years old during time of the diagnosis of GCTB and of limb-salvage surgery;
2. Diagnosed with GCTB of the lower extremity via imaging (radiographs, CT scan, MRI);
3. Classified with GCTB Campanacci grade II or III who underwent limb-salvage surgery, at either St. Luke’s Medical Center-Quezon City or Bonifacio Global City;
4. Has a histopathology result confirming the diagnosis of GCTB;
5. With active follow-up of up to at least 6 months post-operatively;

Exclusion criteria are as follows:

1. Those with open wounds, skin lesions directly overlying the surgical area, and/or active infections (either local or systemic);
2. With pre-surgical conditions or comorbidities other than GCTB rendering the patient unable to ambulate or do range of motion of the lower extremities;
3. With incomplete medical data from either hospital or clinic records;

Study Procedures

Due to the relative rarity of the disease, convenience sampling of the cases of interest was done. After these select cases were listed, identification of the attending surgeons was done, each of which were individually contacted to inform them of the eligibility of their patient/s.

After their confirmation, a thorough review of the patient’s database and electronic hospital records (Enterprise Portal v1.6.1 rev.219) during his/her admission, including the operative record for details surrounding the surgery will also be done. Follow-up data, on the other hand, were obtained from the surgeon’s clinic charts of the patient’s subsequent visits postoperatively to determine information on his/her functional outcomes, which were completed by the investigator using the MSTS questionnaire. All information obtained will be collated using a data collection tool.

Objectives

The general objective of this study aimed to determine the outcomes of limb-salvage surgery in patients diagnosed with GCTB of the lower extremities. The specific objectives were to obtain the following:

Demographic and surgical profile of the selected participants.

Functional outcomes among participants using the Musculoskeletal Tumor Rating Scale (MSTS) score in terms of their motion, pain, stability, deformity, strength, activity, and emotional acceptance. This will be determined according to surgical techniques as well as according to the use of fillers. Each parameter is scored 0-5 and combined for a possible total score of 35. A score of 23 or greater is considered an excellent result; a score of 15-22 is considered a good result; a score of 8-14 is considered a fair result; and lastly, a score of less than 8 is considered a poor result, in terms of functionality [9].

Recurrence and complications among the participants. This will also be determined according to surgical techniques and use of fillers. The development of progressive luency at the cement-bone interface in radiographs, or the presence of osteolysis and presence of a soft tissue mass in CT or MR imaging following surgery suggests recurrence of GCTB [6]. A complication on the other hand is defined as any event for which the patient required a specific intervention such as wound complications, infection, implant failure/loosening, fracture, and stiffness of the joint [14].

Sample size estimation

Sample size was calculated based on the estimation of the population proportion for functional score (MSTS). Assuming that the proportion of post-limb salvage surgery in patients with primary bone tumors with good to excellent results is 90% [9], with a maximum allowable error of 7.5%, and a reliability of 80%, the sample size required is 27.

Statistical Analysis

Statistical analyses were performed using STATA Statistical Software, Version 13, College Station, TX; StataCorp LP. Descriptive statistics involved mean, standard deviation, frequency, percentage, median, and interquartile range. Descriptive statistics on the functional outcomes, and complication occurrence and recurrence was estimated using chi-square test exact binomial with a 95% confidence interval (95% CI). All valid data were included in the analysis. Missing variables was neither imputed nor estimated.

3. Results

We analyzed a total of 20 patients diagnosed radiographically and histologically with giant cell tumor of the bone of the lower extremities that underwent limb salvage surgery in our institution from January 2009 to February 2020. Table 1 illustrates the demographic and surgical profiles of the respondents. It can be noted that the mean age of the respondents was 31.70 years (SD=9.44). Ma-
Majority of the respondents were males (55%), had femoral distal third involvement (40%), and had a Campanacci score of III (55%). There is a mean tumor size of 4.12 cm (SD=2.20) anteroposteriorly, 4.92 cm (SD=2.78) craniocaudally, and 4.92 cm (SD=2.73) transversely. Majority of the respondents underwent EC (85%) along with electrocautery with hydrogen peroxide (20%). The most commonly used filler was bone cement (35.29%). The mean operative time was 4.68 hours (SD=1.87), with a mean intraoperative blood loss of 549.00 milliliters (SD=764.97). The mean duration of hospital stay was 5.25 days (SD=2.84). There was note of shorter duration of operative time (EC 4.28 hrs vs RS 6.94 hrs), less intraoperative blood loss (EC 351.76 mL vs RS 1,666.67 mL), and shorter hospital stay (EC 4.53 days vs RS 9.33 days), in favor of the EC group. The duration of follow-up visit ranged from 6 months to 8 years, with a mean of 37.30 months (SD=30.64). It was also observed that among all the respondents, only 25% (5/20) of the respondents had used denosumab.

Table 2 illustrates the descriptive statistics of the MSTS score according to surgical techniques. It is noted that

| Characteristics                        | Frequency (f) | Percentage (%) | Mean (SD) |
|----------------------------------------|---------------|----------------|-----------|
| **Age (Year)**                         |               |                | 31.70 (9.44) |
| **Sex**                                |               |                |           |
| Male                                   | 11            | 55.00%         |           |
| Female                                 | 9             | 45.00%         |           |
| **Bone Involvement**                   |               |                |           |
| Tibia – Proximal Third                 | 7             | 35.00%         |           |
| Tibia – Distal Third                   | 1             | 5.00%          |           |
| Femur – Proximal Third                 | 3             | 15.00%         |           |
| Femur – Distal Third                   | 8             | 40.00%         |           |
| Foot                                   | 1             | 5.00%          |           |
| **Tumor Size**                         |               |                |           |
| Anteroposterior                        |               |                | 4.12 (2.20) |
| Craniocaudal                           |               |                | 4.92 (2.78) |
| Transverse                             |               |                | 4.92 (2.73) |
| **Campanacci Grade**                   |               |                |           |
| II                                     | 9             | 45.00%         |           |
| III                                    | 11            | 55.00%         |           |
| **Surgical Technique**                 |               |                |           |
| Resection                              | 3             | 15.00%         |           |
| Extended Curettage                     |               |                |           |
| Electrocautery                         | 2             | 10.00%         |           |
| Electrocautery with Phenol             | 2             | 10.00%         |           |
| Electrocautery with Burr               | 2             | 10.00%         |           |
| Electrocautery with Burr and Phenol    | 2             | 10.00%         |           |
| Electrocautery with Hydrogen Peroxide  | 4             | 20.00%         |           |
| Electrocautery with Burr and Hydrogen Peroxide | 3 | 15.00% |           |
| Electrocautery with Hydrogen Peroxide and Ethanol | 2 | 10.00% |           |
| **Use of Fillers**                     |               |                |           |
| Bone Cement                            | 6             | 35.29%         |           |
| Femoral Head Allograft alone           | 1             | 5.88%          |           |
| Hydroxyapatite Crystals alone          | 3             | 17.65%         |           |
| Femoral Head Allograft with Autograft  | 3             | 17.65%         |           |
| Femoral Head Allograft with Bone Cement| 3             | 17.65%         |           |
| Femoral Head Allograft with Bone Cement and DBM | 1 | 5.88% |           |
| **Intraoperative Blood Loss (Milliliters)** |           |                | 549.00 (764.97) |
| Resection                              | 1,666.67 (1,154.70) | | |
| Extended Curettage                     | 351.76 (502.67) | | |
| **Duration of Operation Time (Hours)** |           |                |           |
| Resection                              | 4.68 (1.87)   |                |           |
| Extended Curettage                     | 6.94 (1.42)   |                |           |
| **Duration of Hospital Stay (Days)**    |           |                |           |
| Resection                              | 5.25 (2.84)   |                |           |
| Extended Curettage                     | 9.33 (5.13)   |                |           |
| **Duration of Follow-up (Months)**     |           |                |           |
|                                           | 37.30 (30.64) |                |           |
among the different variants of EC, the use of electrocautery with phenol produced the highest MSTS score of 34 (SD=1.41). Overall, the approaches of EC had a mean score of 28.18 (SD=7.51) which is considered generally as an excellent outcome, while RS had a mean score of 19.67 (SD=11.02), which is generally considered as a good outcome.

The descriptive statistics of the MSTS score according to the use of fillers are presented in Table 3. It is noted that the use of femoral head allografts in general resulted in excellent outcomes (mean 24.37, SD=9.10), similar to the use of bone cement (mean 31.33, SD=5.12), and hydroxyapatite crystals (mean 31.00, SD=2.00).

Table 4 shows the descriptive statistics for the prevalence of complications and recurrence according to surgical technique. As demonstrated, among 17 cases of EC, there was a total of 8 complications (47%), including contractures (2), implant irritation (2), osteoarthritic changes (2), iatrogenic fracture (1), and arthrofibrosis (1). Among the three cases of RS, on the other hand, only 1 complication of postoperative infection (33%) was noted. Recurrence overall was 2 out 20 cases (10%) but segregated to the EC group (11.76% [2/17]).

The descriptive statistics of the prevalence of complications and recurrence according to the use of fillers are presented in Table 5. Five patients among those who utilized femoral head grafts (62.5%) as fillers were noted to develop complications (3/5 developed more than one complication). Likewise, both recurrences noted in this study both had use of femoral head allografts (25%).

4. Discussion

GCTB accounts for only 5% of all primary bone tumors [1,5,6,15,16,18,20] and are known to be locally aggressive benign tumors, and a propensity to be highly recurrent but with a rare metastatic potential [1,5,6,14,15]. Most of these lesions develop in long bones (75%-90%), with majority of cases (50-65%) occurring adjacent to the knee. [2,5,6,9,16,18]. This was similar to our study, which showed the most commonly affected sites being the distal femur (40%) and proximal tibia (35%). Due to its common affliction in these areas, the natural history of GCTB leads to morbidity resulting from the substantial disturbance of the local bony architecture of these periarticular locations [2,3,9,21].

Although some studies show an equal sex distribution, most show a slight predilection among females [2,3,5,6,15,22]. This was in contrast to our study, as it was noted that the majority of our population (55%) comprised of males.

Multiple studies have likewise shown that GCTB may occur in any age group but is observed to peak during the 3rd decade, with 80% of cases occurring between 20-50 years of age [3,5,6,15,20,22]. This is in concordance with our study, showing a mean age of 31.70 years.

The high suspicion for a diagnosis of GCTB begins with a typical radiographic presentation of a lytic bony

| Table 2. Descriptive Statistics of Musculoskeletal Tumor Rating Scale (MSTS) according to Surgical Technique among the Respondents (N = 20) |
|---------------------------------------------------------------|
| **Musculoskeletal Tumor Rating Scale** | **Surgical Technique** | **Electrocautery** | **Electrocautery with Phenol** | **Electrocautery with Burr** | **Electrocautery with Burr and Phenol** | **Electrocautery with Hydrogen Peroxide** | **Electrocautery with Burr and Hydrogen Peroxide** | **Electrocautery with Hydrogen Peroxide and Ethanol** |
| Resection (N=3) | Overall | Electrocautery (N=2) | Electrocautery with Phenol (N=2) | Electrocautery with Burr (N=2) | Electrocautery with Burr and Phenol (N=2) | Electrocautery with Hydrogen Peroxide (N=4) | Electrocautery with Burr and Hydrogen Peroxide (N=3) | Electrocautery with Hydrogen Peroxide and Ethanol (N=2) |
| Overall Score | 19.67 (11.02) | 28.18 (7.51) | 31.00 (0.00) | 34.00 (1.41) | 25.00 (11.31) | 27.00 (8.49) | 29.00 (5.66) | 27.33 (11.59) | 23.50 (13.44) |

Values are presented as mean (standard deviation).

| Table 3. Descriptive Statistics of Musculoskeletal Tumor Rating Scale (MSTS) according to Use of Fillers among the Respondents (N = 17) |
|---------------------------------------------------------------|
| **Musculoskeletal Tumor Rating Scale** | **Use of Fillers (N=17)** | **Bone cement (N=6)** | **Hydroxyapatite crystals (N=3)** | **Overall use of femoral head allografts (N=8)** | **Femoral head allograft alone (N=1)** | **Femoral head allograft with bone cement (N=3)** | **Femoral head allograft with autograft (N=3)** | **Femoral head allograft with bone cement and demineralized bone matrix (N=1)** |
| Overall Score | 31.33 (5.12) | 31.00 (2.00) | 24.37 (9.10) | 35.00 (0.00) | 17.00 (3.60) | 26.67 (10.97) | 29.00 (0.00) |

Values are presented as mean (standard deviation).
A lesion that is well-defined and with non-sclerotic margin and an eccentric, mostly epiphyseal location, extending to the subchondral bone, but may often times present with more aggressive features, ranging from a wide zone of transition with cortical thinning and expansile remodeling to cortical bone destruction. The Campanacci grading was created to classify GCTB based on their radiographic appearance and has been proposed to guide treatment. Type I are considered latent and are represented by small lesions which are well-defined and with an intact cortex, for which there is more room for conservative management. Type II (Figure 1A) are considered active and relatively well-defined, described as typically larger than type I lesions but with an intact periosteum. Type III (Figure 2A) are aggressive lesions, with indistinct borders, extending through the periosteum and surrounding tissues. In our study, 45% of the respondents had grade II and 55% had grade III GCTB lesions. It has been suggested that grade II lesions should be treated with intralesional curettage and grade III lesions with resection and reconstruction. However, this recommendation has not been incorporated into guidelines, as there is lack of correlation between the grade and the aggressiveness of the GCT and does not provide reliable prognostic significance in terms of recurrence and functional outcomes.

### Table 4. Descriptive Statistics of the Prevalence of Complications and Recurrence among the Respondents according to Surgical Technique (N = 20)

| Complications (N=8) | Resection (N=3) | Overall | Electrocautery with Burr (N=2) | Electrocautery with Burr and Phenol (N=2) | Electrocautery with Hydrogen Peroxide (N=4) | Electrocautery with Burr and Hydrogen Peroxide (N=3) | Electrocautery with Hydrogen Peroxide and Ethanol (N=2) |
|---------------------|----------------|---------|-------------------------------|-----------------------------------|------------------------------------------|-------------------------------------------|--------------------------------------------------|
| Contractures 0.00 (0.00%) 2.00 (11.76%) | 1.00 (50.00%) | 1.00 (50.00%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Implant Irritation 0.00 (0.00%) 2.00 (11.76%) | 1.00 (50.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 1.00 (33.33%) | 0.00 (0.00%) |
| Osteoarthritic Changes 0.00 (0.00%) 2.00 (11.76%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 1.00 (25.00%) | 1.00 (33.33%) | 0.00 (0.00%) |
| Infection 1.00 (33.33%) 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Iatrogenic Fracture 0.00 (0.00%) 1.00 (5.88%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 1.00 (50.00%) |
| Atrophicrosis 0.00 (0.00%) 1.00 (5.88%) | 1.00 (50.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Recurrence (N=2) 0.00 (0.00%) 2.00 (11.76%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 1.00 (25.00%) | 0.00 (0.00%) | 1.00 (50.00%) |

Values are presented as frequency (percentage).

### Table 5. Descriptive Statistics of the Prevalence of Complications and Recurrence among the Respondents according to Use of Fillers (N = 17)

| Complications (N=8) | Bone cement (N=6) | Overall use of femoral head allograft (N=8) | Femoral head allograft with bone cement (N=3) | Femoral head allograft with autograft (N=3) | Femoral head allograft with bone cement and demineralized bone matrix (N=1) |
|---------------------|------------------|---------------------------------|---------------------------------|---------------------------------|--------------------------------------------------|
| Contractures 1.00 (12.50%) 2.00 (25.00%) | 1.00 (25.00%) | 1.00 (33.30%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Implant Irritation 0.00 (0.00%) 2.00 (25.00%) | 1.00 (33.30%) | 1.00 (33.30%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Osteoarthritic Changes 0.00 (0.00%) 2.00 (25.00%) | 1.00 (33.30%) | 1.00 (33.30%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Infection 0.00 (0.00%) 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Iatrogenic Fracture 0.00 (0.00%) 1.00 (12.50%) | 1.00 (33.30%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Atrophicrosis 0.00 (0.00%) 1.00 (12.50%) | 1.00 (33.30%) | 0.00 (0.00%) | 0.00 (0.00%) | 0.00 (0.00%) |
| Recurrence (N=2) 0.00 (0.00%) 2.00 (25%) | 0.00 (0.00%) | 1.00 (33.33%) | 1.00 (100.00%) |

Values are presented as frequency (percentage).
Campanacci grade, as well as soft tissue infiltration, and larger size of the lesion does not significantly impact the recurrence of GCTB \[15\].

Figure 1. This demonstrates a case done under extended curettage. Preoperative radiographs (A) and MRI (B) reveal a Campanacci II GCTB of the proximal tibia and patient underwent surgery. Surgical markings (C) were done to map the landmarks, area of the lesion, and the planned incision. Curettage (D) was performed revealing grayish, friable tissue. Extended curettage followed using ethanol (E), hydrogen peroxide (F), electrocautery (G), and use of a highspeed burr (H). Bone grafting (I) was done using autologous iliac bone graft adjacent to the articular surface and morselized femoral head allograft to fill the rest of the defect. Postoperative radiographs (J) show placement of a 4-hole L-plate to the medial aspect of the proximal tibia, augmenting the construct.

Due to the wide range of differential diagnoses that can mimic GCTB in imaging, the diagnosis is ascertained only after a biopsy is obtained. The protocol and goal of the biopsy follows as in any other bone tumor. Only upon histopathologic reading of GCTB has been confirmed may surgical planning and treatment proceed \[2,3,5\]. Surgery is the standard treatment for GCTB, and depending on the involvement of the articulating surfaces, the tumor can be removed either by resection or curettage, with or without adjuvants \[2,4,6,14,15\]. There is still controversy about the surgical management of choice, however the therapeutic goals of surgery remains the same: to achieve a balance between maximizing the removal of the tumor while reducing recurrence rate, preserving function, and preventing occurrence of complications \[9,15\].

Curettage alone has been the opted treatment of GCTB, due to its ability to provide less morbidity and functional impairment, but regardless how thoroughly curettage is performed, it is associated with local recurrence rates as high as 65% \[5,15\]. Wide resection (Figure 3), on the other hand, is associated with decreased risk of local recurrence approaching 0% compared to intralesional curettage \[2,19\]. Despite this however, it is associated with greater surgical morbidity and disability problems leading to poorer functional outcomes \[3,14,22\]. A retrospective cohort study done by Jamshidi et al investigating the outcomes of patients with Campanacci grade III GCTB of the knee who underwent either RS or EC showed that function was significantly better in the EC group in comparison to the RS counterpart \[18\]. This further supports the findings in our study, showing good outcomes in those that underwent RS (MSTS 19.67, SD=11.02) in contrast to those that underwent EC who had excellent outcomes (MSTS score 28.18, SD=7.51). Some studies attribute this to curettage being less invasive as well as being able to preserve the joint adjacent to the tumor \[15,20\]. In contrast, resection results in gradual development of mechanical and structural difficulties in the prostheses of the knee joint, thus affecting the outcomes of these patients in the long term \[9,10,14,18,20\]. A long-term study by Houdek et al investigating the effects of prosthesis on periarticular tumors of the distal femur reports the same findings and found a high risk of revision and reoperation \[11\]. This was likewise reported in the study of Jamishidi that showed significantly more revision surgeries in those that underwent RS \[18\].

Further, evidence shows that 97% of recurrences will occur within two years, with a recurrence after three years being considered exceptional \[2,3,14\]. As mentioned, high local recurrence rate in curettage without local adjuncts was already described in previous studies \[9,15,19\]. Hence, EC (Figure 1 and 2) or the addition of local adjuvants such as cryoablation with liquid nitrogen, alcohol, phenol, ethanol (Figure 1E), zoledronic acid, hydrogen peroxide (Figure 1F), electrocautery (Figure 1G), speed burr drilling (Figure 1H), and bone cement (Figure 2H) and combinations of these in addition to curettage to eradicate additional tumor cells has shown to decrease the recurrence in general to 6-25% \[14\]. This is in concordance with our study, with a recurrence of 11.76% (2/17) among those who underwent EC.

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Figure 2. This demonstrates another case utilizing a different technique of extended curettage. Preoperative radiographs (A), MRI (B), and CT scan (C) reveal a Campanacci III GCTB proximal tibia and patient underwent surgery. Surgical markings (D) were likewise done. Complete exposure (E), and extended curettage proceeded with the use of adjuvants including hydrogen peroxide and electrocautery in 3 cycles. Two femoral heads were secured. One was prepared by removal all surrounding cortical bone and cartilage using a saw to shape it according to the subchondral defect adjacent to the articular surface (G). Plating was then done and patellar tendon was reconstructed and anchored to a post and washer screwed into the tibial shaft; bone cement was then added to augment the fixation (H). Postoperative radiographs (I) show the final construct.

Figure 3. This demonstrates a resection case. Preoperative radiographs (A) and MRI (B) reveal a Campanacci III GCTB of the distal femur and patient underwent surgery. Surgical markings (C) were done to map the landmarks, area of the lesion, and the planned incision. Complete exposure (D) and distal femoral resection were done, revealing a mass measuring 11x10x10cm. Measurements of the femoral shaft and tibial plateau were done and bone cement spacer was shaped accordingly and attached to the end of an intramedullary nail (F). Nail was then secured in place to the femur using a 26mm proximal screw (G). Postoperative radiographs (H) show the implant in place.

In our study, the most common local adjuvant used to extend curettage was hydrogen peroxide alone, comprising 20% of the adjuvants used, and has been as well used in combination with burr and ethanol in 15% and 10% of cases respectively. This may be due to hydrogen peroxide being cheap and easily available, at the same time, being reported as an alternative for phenol with proven in vitro effects against GCT cells [15]. It is noteworthy, however, that hydrogen peroxide use was also seen in the two documented recurrences in our study. Hydrogen peroxide, as demonstrated by Omlor et al, works by inducing apoptosis of cells, and although it has demonstrated a significantly reduced recurrence rate versus in those not treated with hydrogen peroxide and increased recurrence-free survival rate, recurrence can still occur in as high as 22% [15]. In the same study, it was also demonstrated that hydrogen peroxide use versus no hydrogen peroxide use did not significantly influence functional outcomes.

Likewise, electrocautery was also a commonly used local adjuvant and was noted to be used in combination in all 20 cases in our study, but used alone in only 10%. A study investigating the isolated use of electrocautery as
a local adjuvant for benign bone tumors showed a recurrence of 20.8% in giant cell tumors [17].

Other local adjuvants used in this study were phenol, ethanol, and burr. Phenol, although is considered historically as the most prevalent chemical adjunct in the treatment of GCTB for its ability to cause cell lysis and death and is able to decrease recurrence rate to 6-18%, was found to cause serious chemical burns and can be systematically toxic, hence have not been as commonly used [19,21]. Ethanol, on the other hand, is more readily available and less toxic as well [21]. A study by Jones et al reports a recurrence rate of 13.5% following primary curettage of GCTB with adjuvant ethanol [21]. Some authors would recommend the use of a burr to help break ridges of bone in order to obtain adequate exposure of the lesion during curettage and improve the thoroughness of tumor removal [14,16]. A study by Balke et al in 2007 mentions that the use of a high-speed burr decreases residual tumor cells in the area by its thermal effect and the likelihood of recurrence was 4 times higher if burring was not done [19]. Despite this, there are reports of a 12% recurrence rate with the use of burrs in combination with EC [2,3].

As these multiple studies portray, these adjuncts tested alone and in combination were proven to reduce the rate of local recurrence, however there always seems to be a risk of recurrence that may be attributed to residual microscopic disease often under pockets or ridges of bone [3,19]. In addition, due to their heterogenous use, their effectiveness in terms of reducing recurrence has not been proven [15,19]. Hence, recurrence still has to be discussed with patients as possible outcomes of surgery.

In this paper, there were eight cases that utilized femoral head allograft as fillers in defects after curettage was performed. These grafts offer advantages such that it undergoes remodeling and once incorporated, may offer permanent stock and support in a defect [14]. Among these eight cases, the two documented recurrences both had use of these allografts. A study by Sobti et al notes that bone graft reconstruction in addition to curettage alone is only able to afford some local control and may have recurrence rates as high as 50%, and hence is recommended to be used in adjunct to other forms of EC [3]. However, to prevent cartilage destruction, adjuvants to EC such as burring and electrocautery may not be done as aggressively as needed thereby explaining why recurrence might be higher in these cases [19].

On the other hand, the use of polymethylmethacrylate (PMMA) alone was the most common filler used for defects in this study, comprising 35.29%. The advantages of this alternative include its availability, cost, and can offer immediate stability for patients where compliance is of question [16]. It has also been reported that use of PMMA results in local hyperthermia which may induce necrosis of residual disease of up to 3 mm, decreasing recurrence to 10-14% [2,3]. The downside to using bone cement in subchondral regions is that it may damage the adjacent articular cartilage.

A study done by Gao et al investigated functional outcomes in patients treated with bone grafts versus bone cement following curettage in patients with GCT of the long bones. Their study found that MSTS scores were significantly lower than in patients treated with bone graft compared with bone cement. which was contrary to the findings in our study, which reported excellent outcomes for both bone cement and bone allografts. Their study also reported a higher recurrence rate in patients treated with bone grafting. The same findings were found in our study and a study done by Vaishya et al likewise found that recurrence rate was significantly higher in patients treated with bone grafting as compared with patients with PMMA [22]. However, it was recommended that ultimately, extensive curettage be performed extensively with some adjuvant therapy to help in decreasing the incidence of recurrence [22]. In addition, as mentioned in the study of Klenke et al, the selection of bone graft versus cement should always remain individualized [16].

5. Conclusions

There is excellent functional outcome among patients who underwent EC as compared to those who underwent RS as limb salvage surgery for GCTB of the lower extremity. However, there was also note of higher incidence of complications in those who underwent EC over RS. This may indicate that despite the occurrence of complications of the salvaged extremity, this does not necessarily associate with poor outcomes as the patients continue to report good functionality. Nevertheless, it is important to keep in mind that in the face of excellent outcomes, there is still the possibility of recurrence that is associated with EC. Surgeons must hence reiterate the importance of compliance to follow-up to monitor subsequent events. It is recommended that a larger population and a longer follow-up be used in future studies to increase the power and generalizability of the results of this study.

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