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Early outcomes of limb salvage surgery with mega–prosthesis: A single center experience

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ABSTRACT

Objective: To determine the early outcomes of limb salvage surgery with mega prosthesis.

Methods: This retrospective study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC) from 1st January 2017 till 31st January 2020. Data like demographics, histopathology, functional and survival outcomes were retrieved from the Hospital Information System. Musculoskeletal Tumor Society (MSTS) score was used to evaluate the functional outcomes after the surgery. For survival analyses, Kaplan-Meier curve was applied. Prosthesis joint infection, amputation rate, metastasis, mortality rate, and recurrence were also recorded.

Results: This study included 43 patients who underwent limb salvage surgery with endoprosthesis reconstruction at SKMCH&RC. The mean age at the time of diagnosis was (26.5±15.8) years. Patients with distal femoral replacement had the highest MSTS scores (81.45±9.70) while those with proximal humerus replacement has the lowest MSTS scores (56.8±11.2). There was a strong association between site of tumor and MSTS (F=3.30, P=0.017). We also found a correlation between surgical site infection and MSTS scores (r=0.484, P=0.001). Patients with recurrence also had significantly lower MSTS scores (P<0.05). The cumulative survival rate at the end of two-year follow-up was (71.4±17.1)% in proximal femur tumor patients, (88.0±7.8)% in distal femur tumor patients, and (50.0±3.5)% in proximal humerus tumor patients. Besides, patients with Ewing sarcoma had the highest survival rate (97.5±11.0)% while patients with chondrosarcoma had the lowest survival rate (77.8±13.9)%.

Conclusions: Limb salvage surgery with mega-prosthesis can be performed with satisfactory functional and survival outcomes, but further studies are needed to compare it with other limb salvage methods. This study can be used as a reference for future studies.

KEYWORDS: Mega prosthesis; Limb salvage; MSTS score

1. Introduction

Sarcomas are considered as a rare group of neoplasms that arise from the mesenchymal cells. They constitute 1% of all adult neoplasms and 12% of all pediatrics neoplasms[1,2]. Around 80% of the sarcoma arises from soft tissues, and 20% are of bony origin. The World Health Organization 2013 classified the sarcomas depending on their histological and morphological features[2]. Surgery plays an integral part in the management of the sarcoma along with chemotherapy and radiotherapy.

In the past, radical resections like amputation, forequarter/hindquarter amputation, and disarticulations were the choices for the surgical management of cancer depending on the size and extent of

Significance

As the working horse of sarcoma surgery, limb salvage surgery with mega-prosthesis is different from conventional arthroplasty due to the presence of diseased bone and a large segment of bone loss. Our study shows a strong association between site of tumor and MSTS and a correlation between surgical site infection and MSTS scores among patients who undergone limb salvage surgery with mega-prosthesis. Besides, limb salvage surgery with mega-prosthesis can achieve desirably functional and survival outcomes.

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the tumor. However, in the last few decades, limb salvage surgery has gained more popularity due to advancements in diagnostic radiology, neoadjuvant and adjuvant treatments[3,4]. The rationale is resecting the tumor with negative margins and performing the reconstruction to achieve good functional outcomes[5,6].

Limb salvage surgery can achieve good functional outcomes with lower local recurrence rates, higher disease-free survival and overall survival as compared with limb amputations[7,8]. However, reconstructive surgery is associated with some known complications like surgical site infection, implant infection, mechanical failures that require revision surgery, and periprosthetic fracture[9,10].

Sarcoma mostly affects the younger age group, therefore, a long disease-free survival can be expected. In this study, we aim to analyze the functional, surgical, and survival outcomes after limb salvage surgery. Given the rare relative literature, this study can provide a reference for physicians and also help define the potential improvement in the future.

2. Patients and methods

2.1. Study population

This retrospective study was conducted at Shaukat Khanum Memorial Cancer Hospital and Research Centre from 1st January 2017 till 31st January 2020. All the patients who underwent limb salvage surgery with mega-prosthesis were evaluated with a minimum of one year of follow-up. Patients were retrospectively evaluated from a prospectively maintained database using the Hospital Information system.

Inclusive criteria were patients who undergone salvage surgery with mega prosthesis in our institution, with a minimum of 1 year of follow-up. Both patients of upper and lower limb salvage with mega-prosthesis were included. Patients who were presented with recurrent disease at the initial visit were excluded from the study.

2.2. Ethical approval

Ethical approval was sought from the Institutional Review Board (IRB) of SKMCH&RC (IRB # EX-03-03-21-02).

2.3. Preoperative management

On arrival at the hospital, detailed histories of the patients were recorded, and examined in the walk-in clinic. All patients were diagnosed as sarcoma by X-ray (Figure 1), contrast-enhanced magnetic resonance imaging (MRI), computed tomography of the chest, radionuclide bone imaging examination, or histopathological diagnosis preoperatively. Then, decisions on future surgery, neoadjuvant chemotherapy, or radiotherapy were made through multidisciplinary meeting and after patients were examined again by using contrast MRI.

Figure 1. X-ray of distal femur osteosarcoma in a 22-year-old male patient showing mixed density lesion.

2.4. Surgery

For limb preservation surgery, modular mega-prosthesis was used for reconstruction. All surgeries had been performed by a surgeon who had vast experience in sarcoma and implant surgery (minimum 5 years). We used rotating hinge knee modular mega-prosthesis for knee reconstruction, designed for cement fixation of the femoral and tibial components. It has a constrained hinge and also contains a stem that permits axial rotation and distraction within an ultra-high molecular weight polyethylene tibial bearing surface (Figure 2 and Figure 3).

In proximal tibia replacement after tumor resection, a modular rotating hinge knee prosthesis was used for reconstruction. Fixation in diaphysis was done by using cemented stem while distal femur resurfacing was done which was fixed by cement around metaphysis and stem. One of the most important aspects of this proximal tibia replacement is soft tissue reconstruction. The patellar tendon is attached to the implant with heavy sutures or Mersilene tape. The gastrocnemius flap(s) was also used to fill the defect left by the biopsy tract excision and to cover the implant. A split-thickness skin graft was used over the exposed muscle flap at the biopsy track excision site.

For the proximal femur, we used a mega-prosthesis with a dual mobility cup. The femoral and acetabular component was made up of titanium while the head was made up of cobalt chrome alloy. Different sides of the neck were available for modularity and to maintain leg length. Abductors were repaired by using Ethi bond suture and using slots in proximal femur implant.

For proximal humerus, extra-articular resection was done. For replacement, we used a customized implant made of cobalt chrome alloy, and the glenoid was resurfaced. Reconstruction was done by metal-backed polyethylene.

A B

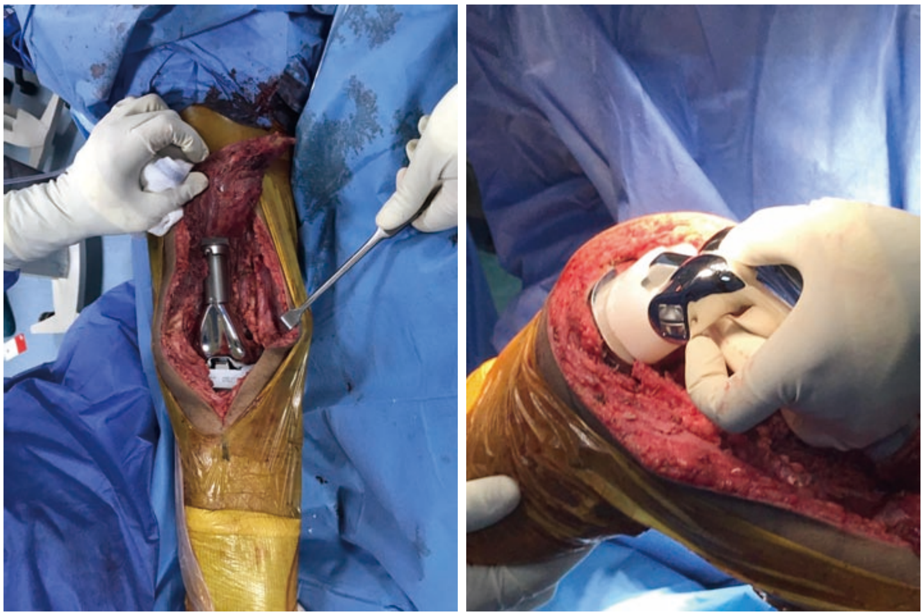

Figure 2. Clinical photograph of the distal femur implant after resection and reconstruction. A: Distal femur implant; B: Distal femoral implant in flexion and the hinge mechanism.

A B

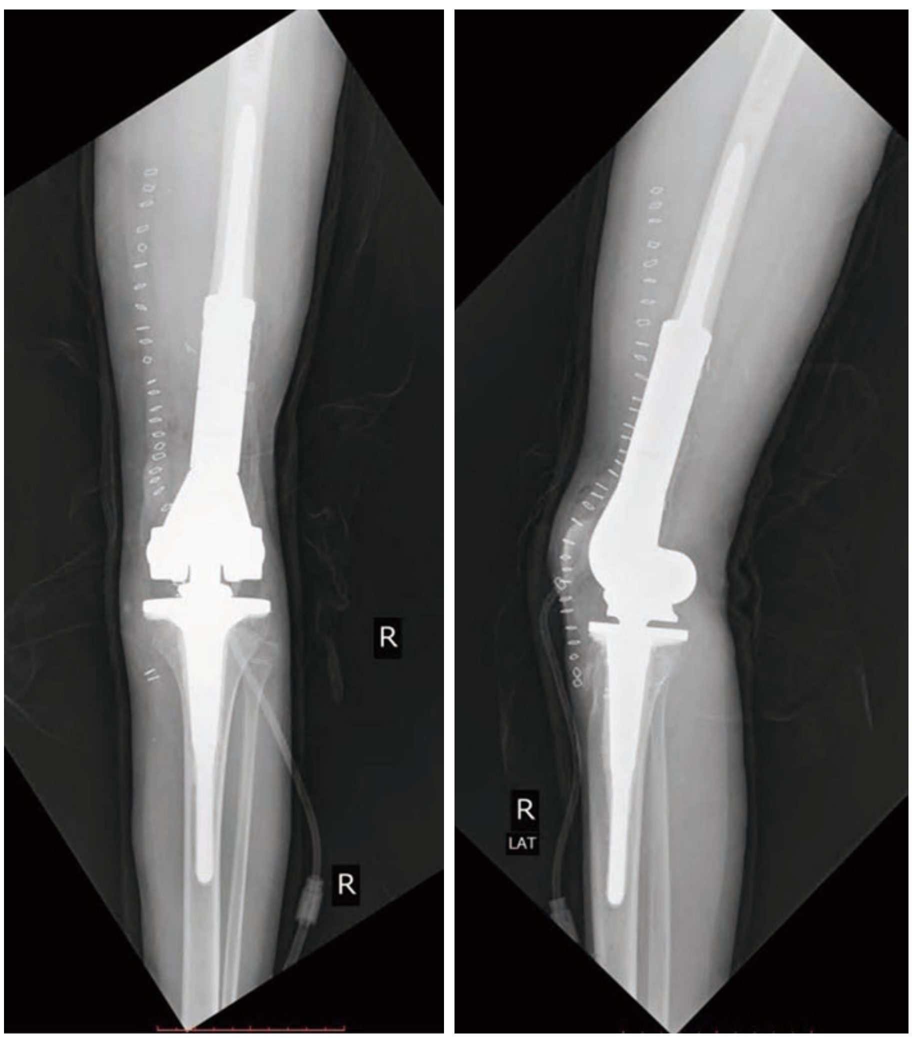

Figure 3. X-ray showing distal femur implant. A: Anteroposterior view of distal femur replacement with the hinge mechanism. B: Lateral view of a distal femoral implant with a tibial tray and stem.

2.5. Post-operative rehabilitation

On the first postoperative day, the rehabilitation of the operated limb started. The patient was kept partial weight-bearing with a gradually increased arc of motion until a range of 0-90 degrees was achieved, which would normally take 3-5 d. Unless full (passive) extension had been achieved, a knee-immobilizer was prescribed to keep the knee extended overnight. The median time to ambulation was 4 (3-6) d. Drain tubes were removed when the drainage was less than 10 mL per hour (to second postoperative day). Four prophylactic perioperative intravenous doses of a broad-spectrum antibiotic were used.

2.6. Data collection

All patients were retrospectively followed up for a period of a minimum of 12 months [(22.3±12.0) months]. Recorded variables included age, gender, surgical details, postoperative complications, functional outcomes, mortality (30 and 90 day), intermediate survival outcomes, implant failure. Implant failure was defined as aseptic loosening, per prosthesis fracture, dislocation, breakage, and amputation due to infection and recurrence.

2.7. Primary and secondary outcomes measurement

The primary outcomes included MSTS score and survival rate of the patients. MSTS score was used to evaluate the functional outcomes after the surgery. It contains six categories: Pain, function, emotional acceptance, hand positioning, manual dexterity, and lifting ability. Each of these categories is assigned a value of 0 to 5 points, and the total summed score is divided by the maximum possible score (30 points) and then multiplied by 100 to obtain the final score[11]. For survival analyses, Kaplan-Meier curve was applied. The Kaplan-Meier survival curve is defined as the probability of surviving in a given length of time considering the time in many small intervals. There are three assumptions used in this analysis. Firstly, we assumed that at any time patients who are censored have the same survival prospects as those who continue to be followed. Secondly, we assumed that the survival probabilities are the same for subjects recruited early and late in the study. Thirdly, we assumed that the event happens at the time specified. For each time interval, survival probability is calculated as the number of subjects surviving divided by the number of patients at risk[12].

Secondary outcomes measurement included prosthesis joint infection, amputation rate, metastasis, mortality rate, and recurrence.

2.8. Statistical analysis

Calculations were performed with Statistical Package for the Social Sciences (SPSS Ver 20) for Windows. Numerial variables were expressed as mean±standard deviation (SD), and paired t-test and Student's t-test were used to determine the difference between two groups. For categorical variables, the number of observations and percentages were reported. Analysis of Variance was applied to determine the association between sites of tumors and MSTS scores, and Person correlation was used to determine the correlation between MSTS scores and surgical site infection. The significant level of this study was set at α=0.05.

3. Results

3.1. Demographic and baseline information

This study included a total of 43 patients who underwent limb salvage surgery with reconstruction. The mean age at the time of diagnosis was (26.5±15.8) years. For gender distribution, 30 patients were males, while 13 patients were females. The most common locations of the tumor were distal femur (n=18, 41.9%), proximal tibia (n=17, 39.5%), proximal femur (n=6, 14.0%) and proximal humerus (n=2, 4.7%). The left side accounted for 51.2% of the lesion locations. Osteosarcoma was the most frequently encountered tumor (n=27, 62.8%) mainly at distal femur (13 cases) and proximal tibia (14 cases), followed by chondrosarcoma (n=9, 20.9%) and Ewing sarcoma (n=5, 11.6%). Furthermore, 1 case of diffuse large B-cell lymphoma (2.3%) and 1 case of plasmocytoma (2.3%) were recorded. Besides, comorbidities were only found in 3 patients, with 1 case of diabetes mellitus and 2 cases of hypertension. Regarding chemotherapy treatment, 4 cases of Ewing, 27 cases of osteosarcoma, 1 case of chondrosarcoma, 1 case of diffuse large B-cell lymphoma, and 1 case of plasmacytoma received the treatment.

3.2. MSTS scores

Postoperative MSTS scores 76.96±3.71 was significantly higher as compared to preoperative MSTS scores 51.78±4.70 (t=2.34, P<0.05). Patients with distal femoral replacement had the highest MSTS scores 81.45±9.70 while proximal humerus had the lowest MSTS scores 56.80±11.20. MSTS scores of proximal femur was 77.41±7.80, and proximal tibia was 74.31±8.90. There was a strong association between site of tumor and MSTS scores (F=3.30, P=0.017).

We also found a correlation between surgical site infection and MSTS scores (r=0.484, P=0.001). Patients with recurrence also had lower MSTS scores (67.4±3.9) as compared to patients who did not have (84.8±4.7), and the difference was also significant (t=2.21, P<0.05). Furthermore, there was no association between surgical site infection and the location of the tumor (P>0.05).

3.3. Survival curve

The survival rate of the patients was analyzed for different types of tumors as well as for the location of tumors by using the Kaplan-Meier survival curve. Patients presented with tumors at proximal humerus had a lower survival rate compared to patients with tumors at proximal tibia which has the highest rate of survival. The cumulative survival rate at mean follow-up of two-year was (71.4±17.1)% in proximal femur tumor patients, (88.0±7.8)% in distal femur tumor patients, and (50.0±3.5)% in proximal humerus tumor patients (Figure 4).

The survival rate of patients was also analyzed by the type of tumor, with Ewing sarcoma had the highest survival rate (97.5±11.0)% while chondrosarcoma had the lowest rate (77.8±13.9)% at the mean follow-up of two years. Osteosarcoma patient had an intermediate survival rate of (92.6±5.0)% (Figure 5).

3.4. Rate of prosthesis joint infection and amputation

Among 4 patients with prosthesis joint infection (9%), 2 patients had early prosthesis joint infection (within 4 weeks) which was settled after debridement and washing out, while 2 patients had late prosthesis joint infection.

One patient got infected after 8 weeks, for which removal of the implant and antibiotic spacer has been conducted. This patient had methicillin-resistant *Staphylococcus aureus* in his culture, for which intravenous vancomycin continued for 6 weeks, and once infection got settled, reconstruction was performed. Another patient had also undergone debridement and cement spacer, and his culture also showed methicillin-resistant *Staphylococcus aureus*. This patient underwent multiple surgeries and ended up with amputation (2.3%).

3.5. Metastasis

Four patients had metastasis, among which one patient of Ewing sarcoma had spinal metastasis while 3 patients of osteosarcoma, chondrosarcoma, and plasmacytoma had pulmonary metastasis. All of the patients who had metastases received palliative chemotherapy.

3.6. Mortality

Thirty-eight patients were alive at the time of the study. Three patients of sarcoma with endoprosthesis reconstruction died during the study duration while 2 patients were lost to follow-up.

There were no 30-days or 90-days mortality observed. One patient died 9 months after the operation due to cardiac arrest. While 1 patient with osteosarcoma died after 6 months due to metastasis. One patient had gastric cancer along with sarcoma, and he died because of metastases of gastric cancer after 4 months. Furthermore, 2 patients had lost to follow-up.

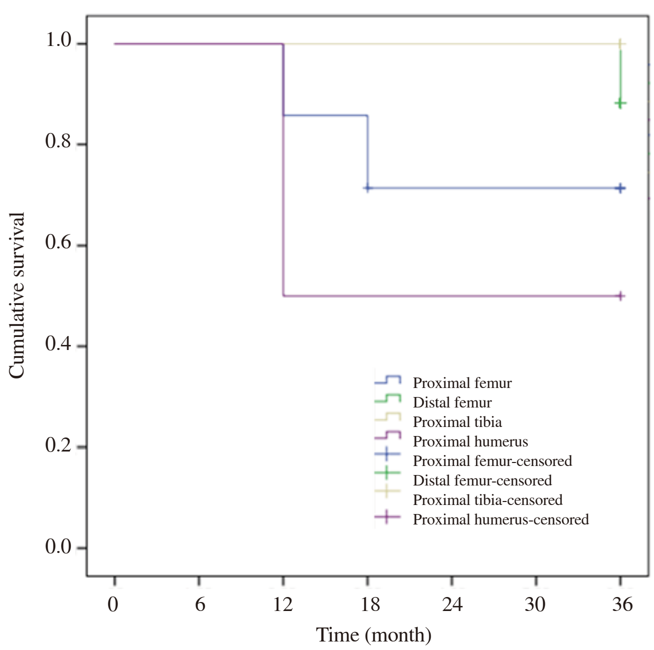

Figure 4. Kaplan-Meier survival curve for different locations of tumor.

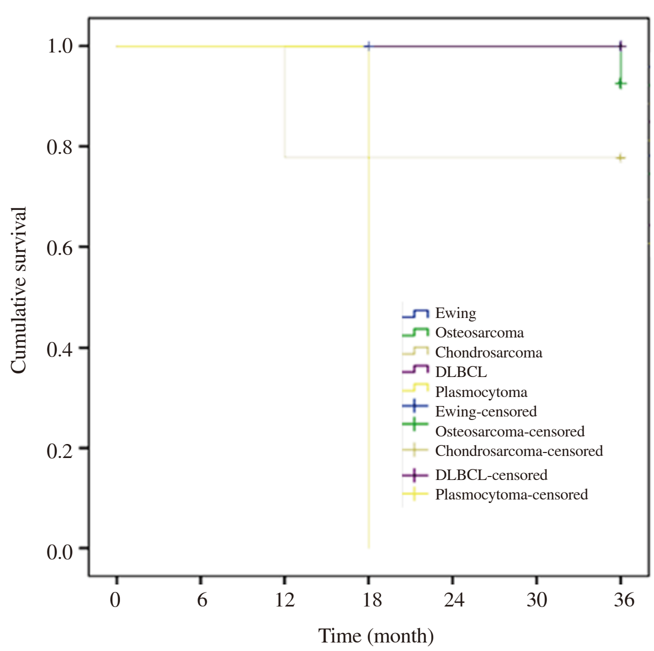

Figure 5. Kaplan-Meier survival curve for different types of tumor. DLBCL: Diffuse large B-cell lymphoma.

3.7. Recurrence

Local recurrence was observed in 3 patients (6.45%) during the study duration. Recurrence was detected in 1 patient with plasmacytoma who underwent proximal femur reconstruction. Two patients of chondrosarcoma had recurrence with one at the distal humerus and the other one at the proximal femur. The patient had a recurrence at the proximal femur underwent surgery for excision and replacement, while other patients underwent palliative radiation.

None of the patients had a periprosthetic fracture. Complications like Trendelenburg's gait (n=1), dislocation of the hip joint (n=1), foot drop (n=2), and abductor lurch (n=1) were recorded.

4. Discussion

Nowadays, endoprosthesis is widely used for reconstruction following resection of the tumors. Despite the development and advancement in the designs and material of endoprosthesis, limb salvage surgery is still a very demanding procedure. Hence, it should be performed by experienced surgeons[13,14]. Our hospital is a dedicated and specialized center for cancer care in Pakistan. We receive patients from all over Pakistan and neighboring countries. We retrospectively analyzed the record of patients who underwent limb salvage surgery using endoprosthesis to determine the functional and short-term survival outcomes.

The main objective of limb salvage surgery is to maintain the functional capacity of the affected limbs. A study reported that more than half of the patients achieved MSTS scores of 90% or more[15]. In our study, 45% of the patients achieved a 90% scores. Most of the patients after surgery returned to work with good functional capacity. These results from our study reflected the point that limb salvage surgery resulted in better functional outcomes and less recurrence rates. The patients of this study group mostly belonged to the young age group, therefore, good functional outcomes are crucial in their upcoming life.

A study by Goryn *et al*. showed the local recurrence rate was 17.7% after 5 years of follow-up[16]. Nerubay *et al*., Mankin *et al*., and Joen *et al*. reported their local recurrence rates were 21.09%, 20%, and 30% after total femur resection[5,17,18]. Our local recurrence rate is lower because patients were followed for an average of (23.3±12.0) months. Local recurrence also results in low MSTS scores.

The main complication of our study is infection. There were 4 cases of surgical site infection, in which 2 (4.1%) patients have a superficial infection while 2 patients have a deep infection (4.1%). The infection rate was higher compared to arthroplasty in the normal population which is less than 3%[19]. Tang *et al*. in their studies of mega prosthesis in tumor patients also found infection is the main complication with infection rate as high as 10.8%[20]. The rate of surgical site infection was higher in tumor patients due to immunosuppression caused by chemotherapeutic agents and malnutrition.

In our study, we observed lower MSTS scores in patients with infection which had also been shown in several other studies. The lower MSTS scores in infected patients was mainly due to prolonged hospital stay, multiple admission, and stiffness associated with periprosthetic infection. Several measures had been taken to contain the infection, for example, use of meticulous surgical techniques, reduction of dead space, avoiding the use of synthetic grafts, and using flap for wound coverage[21].

There is also a matter of debate in tumor society to go for biological reconstruction or use mechanical reconstruction through the mega prosthesis. Our study had shown a promising result of mechanical reconstruction with an average MSTS scores of 76.4%. Biological reconstruction involved the use of autologous/allogeneic bone grafting and inactivated autograft replantation; frequently used inactivating methods involve alcohol, liquid nitrogen, pasteurization, and microwave[22,23]. Complications following biological reconstruction are not negligible, including infection, fracture, bone nonunion, and limb length discrepancy. The presence of allograft is the main difficulty in our society while treatment of bone with inactivating method has still in the initial phase of the trial. Mechanical reconstructive methods rely on prostheses to fill bone defects; Advantages of such procedures include ideal resection margin and early postoperative ambulatory exercise. However, with prolonged follow-up, the risk of prosthesis-related complications such as prosthesis loosening, fracture, and infection will increase[24]. In our study, we had observed a strong association between the site of tumor and MSTS scores. Patients having distal femur resection with endoprosthesis have the highest MSTS scores while prostheses in the upper limb have a lower MSTS scores. Maclean *et al*. had also shown lower MSTS scores in upper limb patients because skillful activities are not possible after endoprosthesis reconstruction[25]. In our study, we had also observed that MSTS scores are higher for distal femur as compared to proximal tibia which has been also showing in a study by Zhang *et al*., which showed better functional outcomes in the distal femur as compared to proximal tibia[26]. Stiffness and repair of extensor mechanism may be the factors that result in the decrease in functional outcomes in the proximal tibia as compared to the distal femur. More clinical trials are needed to evaluate these factors[27].

In our study, we used cemented mega prosthesis in all patients. There is also a debate regarding the use of cemented or uncemented prostheses in the tumor as most patients are young, so many authors urge to use the uncemented prosthesis and biological fixation. Many authors have shown the better result of the uncemented prosthesis as compared to the cemented prosthesis[28], but many studies had shown more loosening in uncemented prosthesis which may be due to the use of postoperative radiation and chemotherapy which hinders biological fixation and results in poor functional outcomes. Sharma *et al*. also showed good results with the use of cemented mega prosthesis[29]. It is recommended that surgeons should use familiar implants and use the proper surgical technique for the long-term survival of implant and good functional outcome[30].

In our study, we saw a survival rate of 88.37% around 2 years of follow-up with only 3 cases of mortality. It is comparable to another study which showed survival of 79% in 3 years which declined to 71% in 5 years. We also need long-term follow-up to check the survival of patients and further complication[31].

In our study, we observed metastasis in 4 (9.3%) patients, but a long-term follow-up is needed to find the actual metastatic rate. Yain *et al.* in their study found 60 percent of metastasis in osteosarcoma during treatment, and in long-term follow-up the metastatic rate may increases, so that closed surveillance is required[32].

This is one of the few studies addressing the surgical and survival outcomes after limb salvage surgery using endoprosthesis. These are initial experiences from our institute. The limitation of the study is the small number of patients and only two years of follow-up after the completion of treatment. Thus, long-term surgical complications and the rate of local recurrence cannot be determined from this study and a control experiment should be conducted to further verify the efficiency of the surgery. However, this study can be used as a reference point for future studies.

Limb salvage surgery is a safe procedure to be performed. With the advancements in the management of the disease, limbs salvage surgery is becoming more common. However, sometimes due to the advanced nature of the disease, limb salvage is not possible to conduct. Although there are complications associated with the procedure, it is associated with better functional outcomes. A follow-up study is needed to assess the long-term surgical, functional and oncological outcomes of our patients.

Conflict of interest statement

The authors report no conflict of interest.

Authors' contributions

M.B.: Corresponding author and manuscript writing; S.R.U.L.A.J.: Data analysis; I.R.: Research supervision; O.S., W.J.: Data collecion.

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