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Original Article

Complications after Limb Salvage Surgeries for Musculoskeletal Malignancies: 10-Year Experience of the Main Sarcoma Center in Bulgaria

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Abstract

Introduction: Limb salvage surgery is currently the most frequently used treatment option in Bulgaria for individuals with musculoskeletal malignancies. Clinical data about complications from these procedures is limited in the country, with only a few studies currently available.

Aim: The aim of our study is to analyze complication rates and patterns in Bulgarian patients treated with limb salvage surgery for musculoskeletal malignancies.

Materials and methods: Our series consist of a retrospective review of 43 patients with musculoskeletal malignancies, who underwent limb salvage surgeries at Boycho Boychev University Orthopedic Hospital in Sofia, Bulgaria, over a period of 10 years. For staging, we used the AJCC and Enneking's staging systems for malignant musculoskeletal tumors. Functionality was assessed with the MSTS system. Assessment of complications was done with a modified Clavien-Dindo classification for surgical complications and Henderson's classification of failure of limb salvage after reconstructive surgery.

Results: The mean follow-up time for the series is 40 months (range 12 to 120 months). At the current follow-up, the overall survival rate for the series is 72%. The overall complication rate for the series is 72% and the surgical revision rate is 46.5%. Of the encountered complications, 84% were classified as grade IIIb using the Clavien-Dindo classification.

Conclusion: Bulgarian patients treated with limb salvage for musculoskeletal malignancies have high complication rates, with no clear prevalence between mechanical and non-mechanical complication patterns. Many of the encountered complications are severe and require additional surgical management.

Keywords

joint prostheses, limb salvage, neoplasm recurrence, sarcoma, postoperative complications

INTRODUCTION

Limb salvage surgeries (LSS) are currently considered the gold standard for the treatment of bone and soft tissue sarcomas, as more than 80% of patients can be treated with this surgical method.[1] Complications that are general for LSS include local recurrence, wound infections and dehiscence, neurovascular injuries, and problems with the soft-tissue

coverage.[2-4] The implementation of biological reconstruction with allo- and autografts is associated with complications such as nonunion or delayed union, graft fractures, and infection.[3,5] Mechanical complications such as failure of the expanding mechanism in pediatric patients, aseptic loosening, stress shielding and periprosthetic fractures, and deep infection are the main concerns in patients with endoprosthetic reconstructions.[3]

In most cases, the complications associated with LSS are severe and require some form of surgical treatment, which will lower the quality of life of these patients. Overall complications rates range from 23 to 46 % in recent studies.[3-7]

AIM

The aim of our study was to analyze complication rates and patterns in Bulgarian patients treated with LSS for malignant bone and soft tissue sarcoma.

MATERIALS AND METHODS

A total of 43 patients (22 women and 21 men) with malignant bone and soft tissue sarcoma, who underwent LSS at Boycho Boychev University Orthopedic Hospital in Sofia, Bulgaria, over a period of 10 years, were included in the study. The mean age of the cohort is 29 years (from 13 to 79). Histological diagnosis included bone and soft-tissue Ewing's sarcoma (17 patients), high-grade osteosarcoma (16 patients), high-grade chondrosarcoma (6 patients), leiomyosarcoma (1 patient), malignant giant-cell tumor of bone (1 patient), and metastases from renal-cell carcinoma (2 patients).

Of the 43 patients, 32 underwent LSS with endoprosthetic reconstruction. Sixteen reconstructions were replacements of the distal femur (50%). Reconstructions of the proximal femur were 8 (25%). A total of 3 patients (9.3%) had reconstructions of the tibia, 2 of which were distal and 1 proximal. Five patients (15.7%) had humeral reconstruction, two of whom received a total humerus replacement, and the other three received a proximal humerus replacement. The mean resection length for lower extremity reconstructions in our series was 20.7 centimeters (range, 10 to 46 cm) and for upper extremity reconstructions 21.6 cm (from 14 to 32 cm). Endoprosthetic reconstruction was carried out with MUTARS endoprostheses (WITTENSTEIN intens GmbH, Igersheim, Germany) and the Bulgarian made Implant G (ET IMPLANT D.G, Etropole, Bulgaria) individual monoblok tumor endoprostheses. A total of 25 patients received a MUTARS-type endoprosthesis, 6 of which were expandable-type MUTARS Xpand; another 7 patients received an individual Implant G endoprosthesis.

Segmental resection and reconstruction with an intercalary frozen allograft were done in 2 cases. One of them had a 13-cm segmental resection of the tibial diaphysis and the other had a 20-cm segmental resection of the femoral diaphysis. Wide surgical excision or resection without any reconstruction was done in the other 9 cases.

All patients were managed by our multidisciplinary oncologic committee. The retrospective information we analyzed included patient age and gender, tumor type, tumor location and size, tumor stage, surgical resection length, tumor necrosis percentage, metastases, postoperative complications, and functionality. For staging, we used the American Joint Committee on Cancer (AJCC) system for bone and soft tissue sarcoma and the Enneking staging system for malignant musculoskeletal tumors.[8] Functionality was assessed with the musculoskeletal tumor society score (MSTS) system, which measures 3 general criteria (pain, emotional acceptance, and function) and 3 specific ones for the upper and lower extremity. Each of these criteria are rated from 0 to 5 with a maximum score of 30 indicating a good functional outcome.

Assessment of complications was done with the Clavien-Dindo's classification for surgical complications. The original 5 grade system is well known and is based on the therapy needed to treat a certain complication. We used a modified Clavien-Dindo classification for postoperative complication in orthopedic surgery presented by Willhuber et al.[9] Additionally, patients were evaluated with Henderson et al.'s classification of failure of limb salvage after reconstructive surgery. This system categorizes complications into mechanical, non-mechanical, and pediatric with 6 specific types for endoprosthetic and allograft reconstructions.

Patient information was acquired through our institution's medical records. Full patient consent was taken for all diagnostic and therapeutic procedures that were described in the current study. All measures were taken to guarantee patient anonymity according to the ethical norms of our institution.

RESULTS

The mean follow-up time for the series was 40 months (range, 12 to 120 months). Staging with the AJCC system concluded that 21 (48.8%) patients were stage 2b, 12 patients (27.9%) were stage 4a or 4b, 9 patients (20.9%) were stage 2a, and 1 patient (2.3%) was stage 3. Staging was also carried out with the Enneking's staging system where 29 patients were stage 2b (67.4%), 12 stage 3, and 2 patients were stage 2a. A total of 11 patients (25.5%) had distant metastases, most commonly in the lungs. Evaluation of postoperative tumor necrosis revealed that 28.5% of patients had total tumor necrosis, 53.5% of patients had a tumor necrosis of 50%–90% and a total of 5 patients had tumor necrosis below 50%. Twelve patients died due to disease complications. At the current follow-up, the overall survival rate for the series was 72%.

A total of 73 surgical interventions were conducted, 34 (46.5%) of them being secondary revision surgeries. The

overall complication rate was 72%, as 31 patients had one or more complications during the follow-up period, which were split in two groups of mechanical and non-mechanical complications. Mechanical complications were encountered in 16 patients (51%), the most common of them being soft-tissue failure such as wound dehiscence and muscle contracture in a total of 5 patients. The rest were peripheral nerve injury in 1 patient, aseptic loosening in 4 patients and structural failure of the reconstruction in 6 patients. Nine of the 16 patients required surgical management of their complications and the rest were successfully treated by conservative means. Non-mechanical complications were noted in the other 15 patients (49%), 13 of whom had local recurrence of the tumor. Eight of them were patients with endoprosthetic reconstruction, 4 had wide surgical resection/excision without reconstruction and 1 patient had resection and biological reconstruction. Deep infection was observed in 2 (8%) patients, both with endoprosthetic reconstruction. All patients in this group required revisional surgery.

Classification of the encountered complications with a modified Clavien-Dindo system for complications in orthopedic surgery revealed that 84% of patients were classified as grade IIIb – requiring surgical treatment in the operating theater with regional or general anesthesia. The other 16% were classified as grade II – requiring pharmacological intervention for at least 72 hours or active observation **(Table 1)**.

Complications in patients with endoprosthetic and allograft reconstructions were classified with Henderson et al.'s classification of failure of limb salvage after reconstructive surgery. Of the 32 patients that received a tumor endoprosthesis, 25 had one or more complications **(Table 2)**.

Over half of these patients (60%) had a mechanical category problem, with soft-tissue failures being the most common. Local recurrence (32%) was the prevalent complications from the non-mechanical category. We also encountered 2 deep infections in this group, as both cases were marked as a late complication. Both of our patients with intercalary allograft reconstructions had complications that were classified with Henderson et al. classification as mechanical type 3A structural failure – plate and screws breakage leading to reconstruction instability. They received surgical treatment, with one of them having, one year later, a local recurrence treated with radical surgery.

Henderson et al.'s classification was not implementable for the 9 patients that were treated with wide surgical excision/resection without reconstruction. Four of them had local recurrence which was treated surgically. The other 5 patients had no complications.

The mean MSTS score for our study was 61.5%. Patients with endoprosthetic reconstruction had a mean MSTS score of 55.3%. Those of them that received a MUTARS-type implant had a mean MSTS score of 58%, and those with the Implant G individual endoprosthesis had an MSTS score of 52%. The patient group that had no reconstructive surgery had a mean MSTS score of 66%.

Table 1. Summary of the encountered complications classified with a modified Clavien-Dindo system

Grade	Type of complication (n)	Total number of patients n (%)
I	-	-
II	Wound dehiscence (2) Aseptic loosening (1) Muscle contracture (1) Peripheral nerve injury (1)	5 (16%)
III IIIb	Wound dehiscence (2) Structural failure of reconstruction (6) Aseptic loosening (3) Local recurrence (13) Deep infection (2)	26 (84%)
IV	-	-
V	-	-

Table 2. Classification of complications encountered in patients with endoprosthetic reconstruction

Category	Type of complication (n)	Total number of patients n (%)
Mechanical	**Type 1** - soft-tissue failures: **A** - functional: muscle contracture (1), peripheral nerve injury (1) **B** - coverage: wound dehiscence (4)	6 (24%)
	Type 2 - aseptic loosening: **A** - early: ≤2 years after surgery (1) **B** - late: ≥2 years after surgery (3)	4 (16%)
	Type 3 - structural failures **A** - implant: implant wear (3), expanding mechanism malfunction (2)	5 (20%)
Non-mechanical	**Type 4** - infections **A** - early: ≤2 years after surgery (2)	2 (8%)
	Type 5 - tumor progression/recurrence **A** - soft-tissue progression (7) **B** - bony progression (1)	8 (32%)
Pediatric	**Type 6** - pediatric complications	-

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DISCUSSION

Our findings show that the overall complication rate in Bulgarian patients who received LSS was 72%, with a re-operation rate of 46.5%, which is significantly higher than the rate reported by other authors. Gharehdaghi et al. report a complication rate of 45.5% with a 42% re-operation rate in their study of 40 patients with a follow-up of 24 months.[5] Similar results were reported by Kaneuchi et al., where the overall complication rate was 46%, but the re-operation rate was 31%.[3] Zou et al. observed complications in 16 of their 45 patients with LSS for bone sarcoma.[6] Pala et al. report a 23.5% overall implant failure rate in their patients with MUTARS endoprostheses.[7] Furthermore, 81% of the patients with complications in our series were classified as Clavien-Dindo grade IIIb requiring surgical management. Compared to a similar study like that of Ankalkoti et al., in which of 41 patients, 9 (21.94%) were classified as Clavien-Dindo grade III and 5 (12.19%) as grade IIIb, our results are significantly higher.[10]

Mechanical complications were present in 51% of our patients. Soft tissue failure, most notably wound dehiscence, was the most common complication type and was observed in 4 patients. With an incidence between 30% to 43%, occurrence of wound complications depends on several risk factors such as tumor size, radiotherapy dose, duration of surgery, wound closure method, patient comorbidity, and anatomical localization.[11,12] In our study, all patients that had this type of complications had a tumor diameter of at least 8 cm or more, with a localization in the proximal and distal thigh. Aseptic loosening is another mechanical complication that we encountered in 16% of our patients, which is comparable to other studies with the same type of endoprosthesis.[7,13] Usually, a late complication with a reported incidence of 2% to 48%, aseptic loosening is associated with younger and more active patients, cemented fixation, larger bone resection and shorter and smaller in diameter endoprosthetic stems.[3,7,13,14] We encountered loosening of the prosthetic stem in the distal femur in 2 patients with a MUTARS-type endoprosthesis and 1 with an Implant G individual knee endoprosthesis. The other case of aseptic loosening was in the distal tibia again in a patient with a MUTARS implant. Cementless fixation was used in 3 cases, as the case with loosened stem of the Implant G endoprosthesis which required cemented fixation. Patient age in our study did not seem to play a significant role as all the patients with aseptic loosening had reached skeletal maturity and did not take part in active sports. Resection length also varied ranging from 14 cm to 21 cm and didn't demonstrate influence in those cases. Prosthetic stem diameter varied as the smallest one was 12 mm in one case, and between 14 mm and 17 mm in the other 3 cases. Stem length in all 3 cases with a MUTARS implant was 120 mm, which is most likely the reason for aseptic loosening to occur, as there are several studies that suggest higher rates of this complication when shorter prosthetic stems are used. As for the case with the Implant G endoprosthesis, the diameter of the stem was 14 mm and the length was 350 mm, as the femoral component is monoblok.

Implant structural failures were observed in 20% of our patients. Three of the cases were implant wear-related, as all of them had a Bulgarian-made endoprosthesis. The components that were damaged were the polyethylene inner of a hip endoprosthesis and the polyethylene sleeves that are part of the locking mechanism of a knee endoprosthesis, leading to joint instability. We did not encounter any wear-related issues in our MUTARS patients. However, we did encounter a failure of the expanding mechanism in two of our cases with an expanding endoprosthesis type MUTARS Xpand. This specific complication occurred one year after initial surgery in both cases and was treated with surgical replacement of the faulty mechanism. In our opinion, this complication developed because of poor patient compliance and misuse of the external impulse transmitter responsible for the non-invasive elongation of the endoprosthesis. Although the incidence of expanding mechanism failure is 6.1% in current literature, its occurrence ultimately leads to worse functional result for the patients mainly because of the additional surgeries and muscle contractures that follow.[15,16] We didn't encounter any prosthetic or periprosthetic fractures in our study.

Structural failure, more precisely failure of fixation (Henderson type 3A) was present in both of our cases with allograft reconstruction. In a recent study by Wisanuyotin et al., structural failure was the most common complication in 8 of their 57 allograft reconstructions, with 1 case of fixation failure.[17] In their rare case of a medullary osteogenic sarcoma of the pelvis, Öztürk et al. report a structural failure consisting of a constraint ring failure and cup malposition leading to the need of revision surgery.[18]

Non-mechanical complications were present in 49% of patients in our series. Local recurrence was the most severe complication in this group, as well as the most common complication in the series (32% of all patients). The overall rates of local recurrence after LSS are between 2% and 10% in recent studies.[3,6] There is an increased risk of local recurrence in the presence of factors such as positive surgical margins, an unsatisfactory local response to preoperative chemotherapy, and, sometimes, the site of the biopsy. Additionally, the experience of the surgical team performing the biopsy and LSS, as well as the presence of undetected or "missed" skip metastases should also be considered as a risk factor. Of the patients that received an endoprosthetic reconstruction, 8 had local recurrence, 7 of which were soft tissue, and 1 had a bony recurrence. Patients with LSS without reconstructions had a total of 5 recurrences, 4 of them being soft-tissue and 1 was bony recurrence. Two of the cases with local recurrence underwent radical surgical treatment in the form of amputation and disarticulation. All cases were managed by the same surgical team, as all of them had an open biopsy. We could not find any link between primary tumor localization and the incidence of local recurrence. There were no skip metastases present in any of the said cases as well. Post-chemotherapy tumor ne-

crosis was between 5% and 15%, indicating a strong possibility of local recurrence in 4 cases. In the other 11 cases, tumor necrosis was between 70 and 100%.

Deep infection is the other severe non-mechanical complication that we encountered in 2 patients (8%). In both cases, the infection developed less than a year after initial surgery, as one of the cases was diagnosed 6 months after surgery and the other 8 months after surgery. Microbiological testing of multiple joint aspirate revealed growth of *Acinetobacter baumanii* in one patient and *Staphylococcus epidermidis* in the other. One patient had a MUTARS endoprosthesis and the other had an individual Implant G endoprosthesis. Surgical treatment involved debridement, lavage, and removal of the dacron sleeve that we use for soft-tissue reattachment. Control of the infection was established as both patients are currently receiving multimodal antibiotic treatment. Reported literature infection rates range from 9% to 20%.[13,19] Patients with sarcomas tend to have a higher infection rate compared to those with secondary malignant bone and soft-tissue tumors.[13,19] The early deep infections that we encountered were most likely caused by an infected dacron sleeve, which we implement in all patients with endoprosthetic reconstruction. We had success with the revision surgery without component removal and replacement, as currently the gold standard for management of these complications is a two-stage revision.[7,13,19]

Study limitations

The study's retrospective nature and the lack of data regarding the condition of surgical margins are our primary limiting factors.

CONCLUSIONS

Bulgarian patients treated with limb salvage for musculoskeletal malignancies have high complication rates, with no clear prevalence between mechanical and non-mechanical complication patterns. Many of the encountered complications are severe and require additional surgical management.

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Conflict of Interest

Authors declare no conflict of interest.

Author contributions

Both Y.I. and K.P. contributed equally to the diagnosis, staging, treatment, and follow-up of all patients included in the current study.

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Осложнения после операций по сохранению конечностей при злокачественных новообразованиях опорно-двигательного аппарата: 10-летний опыт Главного центра сарком в Болгарии

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Резюме

Введение: Операция по сохранению конечностей в настоящее время является наиболее часто используемым методом лечения в Болгарии для лиц со злокачественными новообразованиями опорно-двигательного аппарата. Клинические данные об осложнениях этих процедур в стране ограничены, и в настоящее время доступно лишь несколько исследований.

Цель: Целью нашего исследования является анализ частоты и характера осложнений у болгарских пациентов, перенёсших операцию по сохранению конечностей по поводу злокачественных новообразований опорно-двигательного аппарата.

Материалы и методы: Наша серия представляет собой ретроспективный обзор 43 пациентов со злокачественными новообразованиями опорно-двигательного аппарата, перенёсших операции по сохранению конечностей в ортопедической клинике УМБАЛ „Бойчо Бойчев" в Софии, Болгария, в течение 10 лет. Для определения стадии мы использовали системы AJCC и Enneking для злокачественных опухолей опорно-двигательного аппарата. Функциональность оценивалась с помощью системы MSTS. Оценка осложнений проводилась с использованием модифицированной классификации хирургических осложнений Clavien-Dindo и классификации Henderson по неспособности сохранить конечность после реконструктивной хирургии.

Результаты: Среднее время наблюдения в этой серии составило 40 месяцев (диапазон от 12 до 120 месяцев). При текущем наблюдении общая выживаемость в этой серии составляет 72%. Общая частота осложнений в этой серии составляет 72%, а частота хирургических ревизий – 46.5%. Из встретившихся осложнений 84% были отнесены к степени IIIb по классификации Clavien-Dindo.

Заключение: Болгарские пациенты, прооперированные по сохранению конечностей по поводу злокачественных новообразований опорно-двигательного аппарата, имеют высокий уровень осложнений, без чёткого преобладания механических или немеханических осложнений. Многие из встречающихся осложнений являются тяжёлыми и требуют дополнительного хирургического лечения.

Ключевые слова

протезы суставов, сохранение конечности, рецидив новообразования, саркома, послеоперационные осложнения