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Role of Amputation in Improving the Quality of Life, Mobility, and Pain Outcomes in Children with Metastatic Osteosarcoma

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Abstract

Background: Few studies have analyzed the benefit of limb amputations in children with metastatic osteosarcoma and limited lifespan.

Objective: We studied outcomes of limb amputations in children with metastatic osteosarcoma.

Design: We performed a retrospective review of patients who underwent limb amputations (January 1995–June 2015) and died within 1 year of surgery.

Setting/subjects: We studied 12 osteosarcoma patients at a single institution.

Measurements: Data on mobility, pain, and emotional and psychological wellbeing were retrieved from medical records from 1 month before surgery to 6 months after surgery.

Results: Of 12 patients (seven females, five males; median age at surgery 13 years [range 7–20 years]) meeting study criteria, three and nine had primary osteosarcoma in upper and lower limbs, respectively. Mobility improved post-amputation in eight bedridden/wheelchair-bound patients. Post-amputation, emotional and psychological wellbeing improved for nine patients, three patients had persistent psychological and/or emotional symptoms, and no patient experienced signs of regret. Daily mean pain scores were significantly lower at one week (median 3 [range 0–6]; p=0.03) and three months (median 0 [range 0–8]; p=0.02) post-surgery than at one-week pre-surgery (median 5.5 [range 0–10]). Morphine consumption (mg/kg/day) showed a trend toward

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higher values at one week (median 0.2 [range 0–7.6]; p=0.6) and three months (median 0.2 [range 0–0.5]; p=0.3) post-surgery than at one-week pre-surgery (median 0.1 [range 0–0.5]).

Conclusions: Patients undergoing limb amputations had reduced pain and improved mobility and emotional and psychological wellbeing. Amputations are likely to benefit children with limited life expectancy.

Keywords

limb amputation; metastatic osteosarcoma; mobility; pain; emotional and psychological wellbeing; end of life

Introduction

Historically, patients with bone and soft tissue sarcomas of the lower extremity have mainly been treated by limb amputation. An early study of 430 cases of osteogenic sarcoma reported higher 5-year survival rates (~23%) for patients undergoing amputations than those receiving other therapies.[1] With the advent of neoadjuvant chemotherapy in the 1970s, the popularity of limb-sparing surgery (LSS) grew, and it is now used in up to 90% of children with osteosarcoma.[2] Currently, forequarter amputations, hemipelvectomies, and knee, shoulder, or hip disarticulations are rarely performed as primary procedures for extremity sarcomas.[3] Major limb amputations can potentially decrease the quality of life of patients because of prolonged recovery, interference with bodily functions, high associated morbidity and/or mortality, possibility of disability, and long-term psychological distress.[3] A large meta-analyses by Li et al. suggested that patients with osteosarcoma having LSS had significantly better 5-year survival rates and lower rates of metastases than those undergoing limb amputations.[4] Consistent with this, a meta-analysis by Han et al. revealed significantly lower 5-year survival rates in amputees than those receiving LSS; also, Musculoskeletal Tumor Society (MSTS) scores, which indicate functional outcomes, were significantly lower for amputees than those receiving LSS.[5]

In line with the increasing appeal of LSS, evidence supports that limb amputations play an important role in some patients, especially those for whom survival is not the main concern. A study found that severely ill or debilitated patients with metastatic musculoskeletal disease were likely to opt for major limb amputation.[6] In these patients who had low chances of survival, amputations improved the ability to carry on daily activities, significantly alleviated pain, improved emotional, sexual, and social lives, and increased the overall quality of life.[6]

From a palliative perspective, studies on outcomes of patients with metastatic musculoskeletal cancer undergoing amputations are lacking, and analyses on children are scarcer. It remains unclear whether amputations are beneficial for patients in whom mortality rates will not reduce after surgery. Herein, we studied the effect of limb amputations in children with metastatic osteosarcoma having a limited life expectancy by assessing mobility, pain, and psychological and emotional well-being in this patient population.

Methods

This retrospective study was approved by the Institutional Review Board of St. Jude Children's Research Hospital (St. Jude). Informed consent was waived. The study included patients with metastatic osteosarcoma who underwent limb amputation between January 1, 1995, and June 1, 2015, with focus on analyzing outcomes of patients who died within a year of amputation, as the impact was likely the greatest for patients with limited life expectancy. Medical records of patients from the institutional database were studied for the outcome categories of function (mobility), pain, and emotional and psychological wellbeing.

Mobility Data

Qualitative data on patients' mobility before and after limb amputation were collected from physical therapy notes. Considering 0 as the month of surgery, data on mobility were summarized from –1 month to 0, 0–3 months, and 3–6 months. Mobility was assessed as poor to good, using the following categories: bedridden, wheelchair, crutches/walker, prosthesis, and normal. For patients who died before six months of amputation, data were still collected if mobility was noted between three and six months.

Emotional and Psychological Wellbeing Data

Data on emotional and psychological wellbeing were collected through progress notes within 30 days before and after surgery. Quotes that helped answer questions related to a patient's emotional, psychological, and physical symptoms were extracted from records. "Improvement" was defined as comments in medical records of decreased or improved physical, emotional, or psychological symptoms. "Regret" was defined by representable quotes by the patient's family and staff that surgery was beneficial. If representable quotes did not meet the criteria for "improvement" or "regret," then no conclusion was drawn.

Pain Measurement Data

Data on pain were collected through daily pain scores (PS) documented in nursing notes and pain/surgery services notes. Data were collected on mean PS and total dose of opioids and adjuvant analgesics calculated as the daily morphine equivalent (MED) dosage in mg/kg/day. Adjuvant medication data were collected for gabapentinoids, tricyclic antidepressants, and nonsteroidal anti-inflammatory drugs. Data on pain was collected one week before amputation and then one week, one month, three months, and six months after amputation, within a one-day range (before and after) of the specific date.

Statistical Analyses

The Wilcoxon signed-rank test was used to determine whether there was a significant difference in the distribution of PS between –1 week and +1 week or +3 months; there were few PS at one month and six months. This test was also used to determine whether there was a significant difference in the distribution of opioid consumption between –1 week and +1 week or +3 months; there were few data values for opioid consumption at one month and six months. All calculations were done using R 3.3.1 (R Core Team). All tests were two sided. For exploratory analyses, a raw P-value less than 0.05 was considered statistically significant.

Results

Between January 1995 and June 2015, 46 patients had a limb amputation. Median survival after surgery was six months (range 3–13 months). Twelve of 46 patients had a diagnosis of osteosarcoma and died within 1 year of surgery and contributed to the study analyses. Median age at amputation was 13 years (range 7–20 years). Primary tumor location was the lower extremity for nine (75%) patients and the upper extremity for three (25%) patients. Of the 12 patients, six (50%) underwent surgery for intractable pain, five (42%) for disease progression, and one (9%) for infection. Only four (33%) patients received a combination of chemotherapy and radiation post-operatively, whereas eight (67%) patients received chemotherapy alone. There were five disarticulations of the hip, one disarticulation of the shoulder, three above-knee amputations, two interthoracoscapular amputations, and one abdominopelvic amputation (Table 1).

Mobility

Of 12 patients, 11 (92%) were wheelchair bound or bedridden before surgery. Data could not be collected for 1 patient who died 15 days after surgery. In eight (67%) patients, mobility was substantially improved as they progressed from being bedridden or wheelchair bound to ambulating independently with a prosthesis and/or crutches. Three months after surgery, five of these eight patients remained self-ambulating with a prosthesis or crutches or mobility was normal. Mobility improved in only one of three patients with primary osteosarcoma in an upper limb. Mobility decreased in four (33%) patients by six months because of disease progression or the need for re-hospitalization; two of these four patients died shortly after surgery (Table 2).

Emotional and Psychological Wellbeing

Representable quotes by family and staff indicated that the emotional and psychological wellbeing improved for nine (75%) of 12 patients and there was no evidence of regret for the amputation. Furthermore, three (25%) of 12 patients exhibited persistent psychological and/or emotional symptoms after the surgery without any signs of regret. The following are representable comments that demonstrate the impact of the emotional and psychological wellbeing for one patient before and after the operation:

Emotional and Psychological Wellbeing Pre-operatively:

> “***’s pain related to his leg appears to be getting worse. Mother states that he has been in significant distress at home; he seems more anxious than usual and has been hesitant to walk around because of the fear of worsening pain. He is tearful today in clinic and states that he feels increasingly secluded from his friends.”

Emotional and Psychological Wellbeing Post-operatively:

> “He has been doing well emotionally. There doesn’t seem to be any anxiety or sadness related to loss of limb.” “Since the hemipelvectomy, ***’s overall quality of life seems to have improved.”

Other Representative Quotes—In regards to relating to other amputees: “*** spoke with several other St. Jude peers before her surgery; they discussed their amputation experience all morning. *** seemed in better spirits in the afternoon.”

In regards to using a prosthesis: “*** had a somewhat reserved excitement over his prosthesis. He states that he looks forward to physical rehabilitation every week and has been getting around the house better with his new prosthesis.”

In regards to their outlook after surgery: “They had recently met with the surgeons and mom said that she is feeling good. *** states that she is nervous but is also happy because she feels that she will have less anxiety about her cancer afterwards.” “She is excited about not having to ask her mom for help so much when she walks again.”

Pain

Daily mean PS were significantly lower at one week (median 3 [range 0–6]; p=0.03) and three months (median 0 [range 0–8]; p=0.02) post-surgery than at one-week pre-surgery (median 5.5 [range 0–10]). However, there was no significant difference when pre-surgery PS were compared with PS six months after surgery (Table 3). Opioid doses as MED (mg/kg/day) showed a trend toward higher values at one week (median 0.2 [range 0–7.6]; p=0.6) and three months (median 0.2 [range 0–0.5]; p=0.3) post-surgery than at one-week pre-surgery (median 0.1 [range 0–0.5]); these differences were not statistically significant (Table 4).

Discussion

Our study reports outcomes in the areas of mobility, pain, and emotional and psychological wellbeing in children with metastatic osteosarcoma. Although several studies have focused on these outcome categories in adults, there are few studies in the pediatric population. The closest related study on mobility and performance status was done in children undergoing limb amputation for soft tissue sarcomas.[3] Other studies have compared outcomes of children undergoing LSS or amputation, described different modalities used for incurable advanced or metastatic sarcoma, and reported the incidence of phantom limb pain post-amputation.[2–4, 7, 8]

In our study, two third of patients progressed from a sedentary lifestyle to ambulating independently by three months post-amputation. These observations are consistent with those from studies on adult sarcoma patients undergoing amputation. An observational study by Davies et al. at an amputee rehabilitation center showed that all patients younger than 50 years regained functional mobility within a year of amputation.[9] van Houdt et al. reported similar findings in sarcoma patients undergoing amputation and concluded that younger patients were more likely to benefit from amputations than older patients in terms of survival and mobility.[10] In contrast, a study found a trend toward increased physical disability, using the Toronto Extremity Salvage Score (TESS), in adult patients undergoing an amputation versus those receiving LSS.[11] The study concluded that amputees experienced severe limitations in normal functioning in their family, work, and social environments. Interestingly, our patients demonstrated an improvement in physical disability after the amputation. Also, this improvement in functionality occurred during the most meaningful period of life for some patients succumbing to their metastatic disease. Most of our patients had a progressive decline in mobility before amputation and within a few months regained their ability to ambulate.

Representable quotes from patient charts in our study suggested that amputation had a mostly positive effect on emotional and psychological well-being of children. There is always the concern that an amputation may cause psychological distress, but most of our patients could identify with other amputees, looked forward to learning how to use their prosthetics, and acquired a new positive outlook and independence that they did not have before surgery. Merimsky et al. reported that the quality of life of patients with musculoskeletal cancer is directly related to the degree of local disease control.[3, 6] Robert et al. found that in long-term survivors of osteosarcoma, limb functionality was the single most important factor affecting the quality of life.[12] In our patients, despite the burden of metastatic disease, the emotional and psychological well-being appeared to improve after amputation for at least 9 patients.

A case study by Pacenta et al. underscored the challenges of controlling osteosarcoma-related local pain in a 17-year-old patient who decided to not undergo surgery.[13] The patient had bilateral pulmonary metastases and a femur pathological fracture, which caused breakthrough pain despite administering opioids, gabapentin, and naproxen. The pain was well controlled by using a continuous peripheral nerve block, but the patient remained immobile until his death after 88 days.[13] In comparison, pain was controlled in our 12 patients by using oral opioids, although there was a trend in increased opioid consumption after surgery. Anghelescu et al. found that the mean duration of postoperative neuropathic pain was 6.5 weeks after surgery for patients with extremity osteosarcoma, which could explain continued opioid use over time in our patients.[14] Our study did not investigate phantom limb pain; nevertheless, a previous study showed great improvement in outcomes of amputees with phantom limb pain, with little recurrence after 1 year of surgery.[15]

The role of amputation in pediatric patients with metastatic osteosarcoma in our study correlates well with positive findings from several studies on adults with osteosarcoma and/or other bone tumors.[16–21] A study by Malawer et al. reported palliative amputations in 11 patients (average age 54 years) with advanced cancers such as melanoma, sarcoma, and carcinoma. Demographics of these patients were similar to those of our pediatric patients, and both sets of patients had almost identical median postoperative survival as well as comparable outcomes in pain, quality of life, and ambulation postoperatively.[22] A study done by Daigeler et al. expressed a consistent view with ours that amputations in a palliative setting were of benefit to only selected patients who were considerably impaired due to complications such as intractable pain, paralysis/sensory disorders, and excessive fungating tumor growth.[23]

Given that palliative surgery remains a poorly defined modality of care in cancer patients, it is important to understand the factors that may influence the surgeon’s decision to perform major procedures such as amputations. In our patients, amputations were performed for reasons other than primarily prolonging survival. A prospective study by Miner et al.

identified goals and expectations between surgeons and their patients with incurable cancers. Most patients and surgeons agreed that the goal of surgical intervention should be to alleviate a significant symptom or chief complaint even when prolongation of survival was not expected.[24] These goals correlate well with a study by McCahill et al. that surveyed members of the Society of Surgical Oncology and found that symptom and pain relief was the most important factor in palliative surgery and increased survival was the least important.[25] Of note, Sallonow and Feuer stressed on the importance of using a multidisciplinary approach to decide whether to perform an amputation in specific subsets of patients, given the potential benefits of the operation.[26] Children in particular need to overcome several psychological and emotional barriers before they undergo such invasive procedures.

Our study has some limitations, most notably the retrospective study design and the small sample size. Additionally, it was difficult to acquire a full dataset of pain measurements and opioid use because some medical records did not have pain measurements or drug dosages at every post-operative clinic follow-up. Our patients only lived until up to a year after surgery and we could not identify long-term outcomes. We could not standardize the variability among patients, and therefore it remains unknown whether a particular factor caused a difference in measurements.

In conclusion, our findings suggest that limb amputation in children with metastatic sarcoma and limited life expectancy may be beneficial to alleviate symptoms of local disease and improve mobility, pain, and psychological and emotional wellbeing. These findings are critical to improve patient outcomes by helping clinicians more readily discuss the role of amputation in this patient population. Further research should include prospective investigations based on comprehensive measures of mobility, pain, and emotional and psychological wellbeing and quality of life.

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Table 1.

Tumor location, amputation procedure, and treatment for children with metastatic osteosarcoma

Gender	Age at diagnosis (years)	Age at procedure (years)	Osteosarcoma location	Procedure	Treatment
M	20	20	Ilium	Abdominopelvic amputation	Surgery, chemotherapy, radiation
F	9	9	Distal femur	Hip disarticulation	Surgery, chemotherapy
F	10	10	Humerus	Interthoracoscapular amputation	Surgery, chemotherapy, radiation
F	18	18	Femur	Hip disarticulation	Surgery, chemotherapy
F	8	9	Humerus	Shoulder disarticulation	Surgery, chemotherapy
M	9	10	Humerus	Interthoracoscapular amputation	Surgery, chemotherapy
F	6	7	Distal femur	Hip disarticulation	Surgery, chemotherapy, radiation
F	13	14	Proximal tibia	Hip disarticulation	Surgery, chemotherapy
M	17	17	Proximal tibia	Above knee amputation	Surgery, chemotherapy, radiation
F	19	19	Proximal femur	Hip disarticulation	Surgery, chemotherapy
M	15	17	Distal Femur	Above knee amputation	Surgery, chemotherapy
M	11	13	Distal femur	Above knee amputation	Surgery, chemotherapy

Table 2.

Mobility of patients before and after amputation

Procedure to death (months)	Mobility (–1 month)	Mobility (+3 months)	Mobility (+6 months)
5	Wheelchair	Wheelchair	
1	Wheelchair		
10	Wheelchair	Wheelchair	Bedridden
13	Wheelchair	Bilateral crutches	Prosthesis
13	Wheelchair	Walker	Walker
6	Normal	Normal	Normal
5	Wheelchair	Crutches	Prosthesis
3	Wheelchair	Prosthesis and crutches	
8	Wheelchair	Bilateral crutches	Wheelchair
3	Wheelchair	Bilateral crutches	Wheelchair
8	Bedridden	Bilateral crutches	Prosthesis
6	Wheelchair	Prosthesis	Bedridden

Table 3.

Mean pain scores before and after amputation

Mean pain score	N	Mean ± SD	Median (range)	Raw P
–1 week	12	5.4 ± 2.9	5.5 (0–10)	
+1 week	12	2.9 ± 2	3 (0–6.3)	0.03
+1 month	6	2.3 ± 2.1	2.5 (0–5)	
+3 months	10	1.7 ± 2.7	0 (0–8)	0.02
+6 months	3	1.7 ± 2.9	0 (0–5)	

N, number of entries; SD, standard deviation

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Table 4.

Mean morphine equivalent (mg/kg/day) use before and after amputation

Mean opioid consumption	N	Mean ± SD	Median (range)	Raw P
–1 week	12	0.2 ± 0.2	0.1 (0–0.5)	
+1 week	8	1.1 ± 2.6	0.2 (0–7.6)	0.6
+1 month	4	0.3 ± 0.3	0.2 (0.1–0.7)	
+3 months	8	0.2 ± 0.1	0.2 (0–0.5)	0.3
+6 months	2	0.1 ± 0.1	0.1 (0.1–0.2)	

N, number of entries; SD, standard deviation