

Surgical palliation for malignant disease requiring locoregional control

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Background: Surgical palliation of cancer is best defined as procedures performed with non-curative intent to improve quality of life or control symptoms of advanced malignancy. Soft tissue involvement of advanced malignancies may produce symptoms such as pain, bleeding, or odor that significantly reduce quality of life. Literature on outcomes of palliative resection of soft tissue malignancy for local or regional control is lacking.

Methods: Soft tissue resections performed with palliative intent for locoregional control were identified from a prospectively maintained palliative surgery database at a tertiary care center from January 2004 to July 2013. Tumor type, presenting symptom, procedure performed, and symptom recurrence were recorded. Patients were followed for at least 60 days or until death.

Results: Thirty-one patients who underwent palliative soft tissue resection for local control were identified. Primary tumor types included melanoma (n=9, 29.0%), squamous cell carcinoma (n=9, 29.0%), sarcoma (n=5, 16.1%), breast (n=3, 9.7%), and other (n=5, 16.1%). Eighteen of 31 patients (58.1%) underwent resection for pain, two (6.5%) for bleeding, and eleven (35.5%) for local control or other symptoms. Procedures were performed on the trunk (n=17, 54.8%), extremities (n=7, 22.6%), head/neck (n=5, 16.1%), or multiple areas (n=2, 6.5%). Eleven of 31 patients (35.5%) underwent axillary, inguinal, or neck lymph node dissection, seventeen (54.8%) radical resection, and three (9.7%) wound excision. Split-thickness skin graft was performed in 6 of 17 radical resections (35.3%). Five patients (16.1%) had symptom recurrence at the site of the initial palliative procedure, of whom four (12.9%) underwent a second palliative procedure. Seven patients (22.6%) had new disease-related symptoms develop during follow-up. Thirty-day morbidity was 29.0%; mortality was 3.2%, which was associated with progression of disease.

Conclusions: Palliative surgery for local control of advanced soft tissue malignancy can provide durable symptom relief and improved quality of life. These procedures positively impact patients regardless of primary tumor type or tumor extent. Careful patient selection is important in order to maximize benefit of surgical palliation and minimize morbidity and mortality.

Keywords: Palliative surgery; soft tissue malignancy; treatment outcome

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Introduction

Soft tissue lesions associated with advanced malignancy may represent either locoregional progression of soft tissue tumors or distant metastatic disease of visceral cancers. Examples of soft tissue tumors causing symptomatic

lesions include cutaneous melanoma, squamous cell carcinoma, and soft tissue sarcoma. Visceral cancers with described cutaneous metastases include liver, lung, kidney, and gynecologic primaries (1). These lesions are often symptomatic, with lesion-related complaints of pain, odor, ulceration and bleeding, and/or disfiguring appearance.

Although such patients are ultimately unable to be cured of their disease, treatment of soft tissue lesions is important in order to achieve local control of disease, relieve symptoms, and improve quality of life (2).

Radiotherapy is a well-established, commonly used palliative treatment modality for advanced malignancy (3). Routine fractionated dosing, lower dosages often administered over the course of several weeks, used in neoadjuvant or adjuvant settings provides better long-term tumor control but with greater toxicity to the patient. Hypofractionation, giving the same dose of radiation over a reduced number of treatments, has allowed for shorter courses of therapy with reduced side effects to the patient. As long-term control of malignancy is less important, this approach to radiotherapy has been used with good results for symptoms of incurable cancer (4). Several reports have demonstrated the efficacy of targeted radiation for various primary tumor types that have metastasized to the soft tissues (5-9).

Palliative surgery is best defined as procedures that are performed without curative intent in order to treat the symptoms of advanced malignancy. Palliative operations can afford patients symptom relief with low treatment toxicity (10). Soft tissue lesions of advanced malignancy are ideal therapeutic targets for palliative surgery, as soft tissue excisions are often short-stay procedures with few surgery-related major complications. While palliative radiotherapy is well-described in the literature, reports regarding palliative excision of soft tissue lesions are lacking. The objective of this study was to evaluate the efficacy and utility of palliative soft tissue excision for soft tissue lesions caused by a variety of primary tumors.

Methods

The medical records of all patients who were diagnosed with advanced malignancy with soft tissue involvement and who had undergone soft tissue excision with palliative intent from January 1, 2004 through July 1, 2013 were identified from a prospectively maintained surgical oncology database. Patient information including demographics, pre-operative functional status assessment, and laboratory studies were collected. In addition, procedure information such as primary tumor type, indication for operation, site and extent of excision, need for complex wound coverage, and post-operative complications were obtained from the medical record. Surgical complications occurring within 30 days of the operation were graded using a surgical secondary events grading system, as described elsewhere,

in which grade 1 complications required local or bedside care; grade 2 complications required invasive monitoring or intravenous medication; grade 3 complications required an operation, interventional radiology procedure, intubation, or therapeutic endoscopy; grade 4 complications resulted in a persistent disability or required major organ resection; and grade 5 complications resulted in death (11). Assessment of patient satisfaction using the question, "Was it worth it?" has been a standard component of post-operative assessment in our practice (12). Symptom resolution, as documented in the patients' records, was also captured.

All patients meeting inclusion criteria were identified and followed up for a minimum of 60 days or until death. Data were analyzed using SAS statistical software, version 5.0 (SAS Institute, Inc., Cary, North Carolina, USA). Data were expressed as percentages in the case of categorical variables. Frequencies were compared by the χ^2 test. All reported P values were two-tailed and for all tests values less than 0.05 were considered significant. This study was approved by the institutional review board at Rhode Island Hospital.

Results

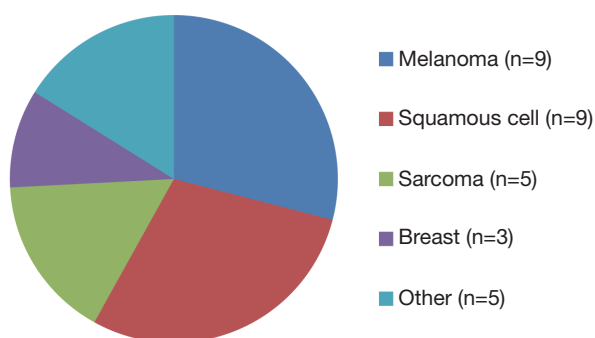
Between January 2004 and July 2013, 31 patients who underwent palliative soft tissue resection for advanced malignancy were identified. The mean age of the patients was 70 (range, 23-95) years, with 19 patients (61.3%) over the age of 65, and 48.4% were male (*Table 1*). Twenty patients (65.5%) had a National Cancer Institute (NCI) fatigue score of greater than or equal to one while only five (16.1%) had an Eastern Cooperative Oncology Group (ECOG) level of greater than or equal to two. One-fifth (19.4%) reported significant (greater than ten pounds) unintentional weight loss within 6 months pre-operatively. Approximately one-third of patients had pre-operative hypoalbuminemia while one-third of patients were anemic.

Primary tumor types varied widely, including melanoma (n=9, 29.0%), squamous cell carcinoma (n=9, 29.0%), sarcoma (n=5, 16.1%), breast (n=3, 9.7%), and other (n=5, 16.1%), comprised of lung, liver, appendix, vulvar, and penile (*Figure 1*). Indications for soft tissue excision were the following: for symptoms such as pain (18 of 31, 58.1%) or bleeding (2 of 31, 6.5%), or for local control (11 of 31, 35.5%) (*Table 2*). Procedures were performed on the trunk (n=17, 54.8%), extremities (n=7, 22.6%), head/neck (n=5, 16.1%), or multiple areas (n=2, 6.5%) (*Table 3*). Regarding extent of surgery, 17 of 31 patients (54.8%) underwent radical resection, 11 of 31 (35.5%) underwent axillary,

Table 1 Patient demographics

Characteristic	Proportion
Total patients	n=31
Age >65 years	61.3%
Male sex	48.4%
NCI fatigue score ≥ 1	64.5%
ECOG level ≥ 2	16.1%
Hypoalbuminemia	35.5%
Hemoglobin <10.0	32.2%
Significant pre-operative weight loss	19.4%

NCI, National Cancer Institute; ECOG, Eastern Cooperative Oncology Group.

**Figure 1** Primary tumor types.**Table 2** Indication for operation

Indication	n (%)
Pain	18 (58.1)
Bleeding	2 (6.5)
Local control	11 (35.5)

Table 3 Site of operation

Site	n (%)
Trunk	17 (54.8)
Extremities	7 (22.6)
Head/Neck	5 (16.1)
Multiple areas	2 (6.5)

inguinal, or neck lymph node dissection, and 3 (9.7%) underwent wound excision (*Table 4*). Wound excisions averaged 90 (median 48, range, 2-500) cm². Split-thickness

Table 4 Extent of resection

Extent	n (%)
Wound excision	3 (9.7)
Lymph node dissection	11 (35.5)
Radical resection	17 (54.8)
Skin graft or flap reconstruction	8 of 17 (47.1)

skin graft or flap procedure was performed in 8 of 17 radical resections (47.1%) to provide adequate wound coverage.

Post-operative 30-day morbidity was 29.0%. Minor complications (grades 1-2, n=6) consisted of wound complications, and major complications (grades 3-4, n=2) were comprised of pneumonia after sternal wound debridement and fluid collection requiring percutaneous drainage after buttock resection. One patient (3.2%) died within 30 days of the procedure, from progression of disease. Symptom recurrence at the site of initial palliative procedure was experienced by five patients (16.1%), of whom four (12.9%) underwent a second palliative excision. Average time to site recurrence was 334 (range, 21-1,099) days. Seven patients (22.6%) developed new disease-related symptoms at sites different from the original palliative soft tissue excision during follow-up, consisting of local recurrence (n=1), regional recurrence (n=3), distant disease (n=2), and perforated viscus from malignant obstruction (n=1).

Symptom improvement was explicitly documented in 25 of 31 (80.6%) patients' records; this was indicated in various ways, including decreased need for narcotic pain medication, relief from bulky disease, or prevention of subsequent bleeding events. All patients who experienced symptom relief did so within 30 days of surgery. Six patients did not have documented symptom improvement, all of whom experienced post-operative complications. Twenty-eight of 31 (90.3%) of patients expressed their satisfaction with their palliative procedure, stating that the procedure had been "worth it".

Discussion

Soft tissue lesions secondary to advanced malignancy often cause significant symptoms, including pain, bleeding, or odor, which can severely impact a cancer patient's quality of life. Although various treatment modalities are available, rapid and effective control of these lesions while minimizing patient toxicity remains a challenging clinical situation.

Palliative surgery may represent an ideal treatment modality for soft tissue lesions, as it provides short-stay hospital treatment with low major morbidity in selected patients. In this study, patient-reported outcomes were excellent, with 90% stating that undergoing the procedure had been “worth it,” and objective symptom improvement was documented in approximately 80% of patients. These outcomes are consistent with previous literature on palliative surgery (10,12). Patient satisfaction following palliative soft tissue excision is likely a reflection of careful patient selection and counseling, utilizing clinical tools such as the palliative triangle (13,14). The three patients who did not state that the procedure had been “worth it” had had new lesions develop during follow-up; while they were satisfied with the results of the original procedure, the perceived benefit was diminished by the development of new soft tissue lesions. Pre-operative conversations specifying the goals of treatment among the operating surgeon, the patient, and the patient’s family have been shown to improve outcomes following palliative surgery, with lower morbidity and mortality and higher patient satisfaction. Indeed, this may represent the most appropriate way to assess outcomes following palliative surgery (13).

This study demonstrates the efficacy of palliative excision for soft tissue lesions of advanced malignancy. The patient population described here represents a wide variety of tumor types, with soft tissue and visceral primaries. Despite the heterogeneous tumors, cutaneous metastases have been found to behave rather similarly across primary tumor types (15). Palliative excisions were performed to varying extents throughout the body, with some needing complex wound coverage. This study further illustrates the safety of palliative soft tissue excision. Taken as a group, these patients experienced 30-day major morbidity and mortality rates of 6.5% and 3.2%, respectively. Admittedly, 30-day morbidity and mortality are suboptimal measures of palliative surgery outcomes, as the goals of treatment are to maximize quality of life benefit while minimizing treatment toxicity (10). However, such measures are objective data that can be used to evaluate the potential negative outcomes of surgery and to provide a context within which to assess the impact and potential value of the procedure. These data also may be useful both to guide the surgeon counseling the patient with advanced malignancy as well as to inform the patient as active decisions regarding palliative intervention are considered.

Radiation therapy is an effective modality for palliation of malignant soft tissue lesions. Barnes *et al.* evaluated

28 patients with non-melanoma skin cancer who received up to three fractionated doses over 3 weeks (16). The majority of lesions involved the head and neck. Ninety percent completed the treatments, with an overall partial or complete response rate of 71%. Seegenschmiedt *et al.* performed a retrospective review spanning 18 years of all melanoma patients at their institution, identifying 121 patients with late-stage melanoma (17). Eleven patients had primary or recurrent lesions that were deemed unsuitable for surgical excision, 57 had in-transit or lymph node metastasis, and 53 had distant organ metastasis. Of the 110 patients with in-transit, lymph node, or distant metastases, 36 patients (32.7%) had a partial response and 34 patients (30.9%) had a complete response. Meanwhile, 23 patients (20.9%) experienced progression of disease despite radiotherapy. A more recent retrospective review of melanoma patients undergoing palliative radiotherapy by Kirova *et al.* showed a similar response rate, with associated symptom relief from bony and brain metastases (18). Unfortunately, these studies did not comment on the durability of symptom relief.

More recent treatment modalities for soft tissue malignancy include isolated limb chemoperfusion, electrochemotherapy, and local immunotherapy (2). Isolated limb perfusion has been extensively studied for soft tissue melanoma and sarcoma. The target limb is isolated from the systemic circulation using a cardiac bypass circuit, with heated chemotherapy infusion that is washed out before restoring systemic circulation. Disadvantages include potential complications of limb perfusion such as compartment syndrome and its inherent cost (19). Electrochemotherapy uses electrical impulses to make cell membranes more permeable, facilitating greater uptake of chemotherapeutic agents into cancer cells. This modality is effective in reducing tumor size, allowing wide local excision. However, the patient may require general anesthesia for discomfort from the electrical impulses and is at risk of experiencing side effects from cytotoxic agents (20). Local immunotherapy consists of direct injection of agents such as interleukin-2 or imiquimod into the lesion. Reported response rates have been favorable for both agents (21,22). All of the above palliative treatments described above are most favorable for smaller, more limited metastatic lesions.

The advantages of surgical excision over other treatment modalities include: (I) its relatively low cost compared to other treatments that require expensive chemotherapeutic agents, multiple treatments, or need for specialized

equipment; (II) essentially immediate therapeutic results as opposed to needing several weeks to appreciate a significant response to treatment; (III) often single treatment session with relatively few indications for reoperation; and (IV) potential to effectively treat relatively large soft tissue lesions not amenable to other treatments. There are disadvantages to surgical resection, including potential wound complications, which are amplified when complex wound coverage using skin grafts or flaps is needed, and infectious complications. However, as demonstrated in our series, these resections are able to be performed in highly selected patients with low risk of major complications. We believe that the presence of regional or distal metastatic disease does not preclude surgical excision of metastatic primary or recurrent soft tissue malignancies. Surgical management is able to effectively control a variety of symptoms related to soft tissue malignancies, specifically pain, discomfort, or bleeding from high-grade or bulky disease.

Conclusions

Palliative surgical excision of symptomatic soft tissue lesions from soft tissue or visceral primary tumors can be performed with acceptable post-operative morbidity and mortality and, more importantly, excellent patient satisfaction and resolution of symptoms. Patient selection remains paramount to maximize treatment efficacy while minimizing its toxicity.

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