Local Recurrence of Extremity Soft Tissue Sarcoma

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KEYWORDS

• Sarcoma • Recurrence • Metastasis • Radiation • Amputation • Limb salvage
• Isolated limb infusion • Hyperthermic isolated limb perfusion

KEY POINTS

- Multimodality management of recurrent extremity soft tissue sarcoma is dependent upon prior therapy and includes surgery, irradiation, brachytherapy and systemic chemotherapy.
- Amputation may provide local control and palliation of symptoms for recurrent extremity soft tissue sarcoma.
- Regional therapy in the form of hyperthermic isolated limb perfusion or isolated limb infusion has a role in the management of recurrent extremity soft tissue sarcoma to provide local control as a limb-salvage therapy treatment option.

INTRODUCTION

Soft tissue sarcomas (STSs) are a heterogeneous group of malignancies with distinct clinical and pathologic features, all characterized by mesodermal differentiation.[1] STS is relatively rare, accounting for only 1% of adult malignancies with an estimated 11,900 people diagnosed annually and approximately 4870 deaths in the United States.[2] More than 50 different subtypes have been identified with undifferentiated pleomorphic sarcoma, gastrointestinal stromal tumors, liposarcoma, leiomyosarcoma, synovial sarcoma, and malignant peripheral nerve sheath tumors being the most common.[3] These tumors may arise from the extremity, head or neck, truncal region, retroperitoneum or chest wall, as well as, other locations. The anatomic location of these tumors is important because it influences treatment and outcome. Several prognostic factors, such as tumor stage, size, grade, and anatomic location, have

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been demonstrated to have an impact on overall survival in the management of primary extremity STS.[4–6] Similarly, margin of resection, low-grade histology, and the use of radiotherapy are important factors in achieving local disease control.[7–9]

Treatment involves a multidisciplinary effort by those specializing in the management of sarcoma. Surgery is the standard treatment of primary extremity STS. The objective of surgical resection is to obtain negative margins but this may be difficult in situations of abutment or involvement of critical neurovascular structures. In these situations, radiation therapy (RT) may be administered as either neoadjuvant therapy or in the adjuvant setting. Neoadjuvant RT is recommended in situations in which a microscopic positive margin is anticipated. The disadvantage of neoadjuvant RT is that it does result in an increased risk of wound healing complications. Positive margins after surgical resection are associated with an increased risk of local recurrence.[10,11] Re-resection to negative margins is preferred but may not be possible, especially in situations of critical nerve or vascular involvement, or when resection may result in loss of function or significant impairment of the involved extremity. Postoperative RT is recommended and has been demonstrated to improve the local control of patients with positive surgical margins.[12,13] Postoperative RT, although associated with a lower risk of short-term wound complications, is associated with higher rates of long-term treatment-related effects, possibly related to the higher dosages of radiation.[14]

The role of systemic chemotherapy in the management of primary extremity STS varies among institutions. The relative indications of systemic chemotherapy include high-grade tumors larger than 5 cm or intermediate-grade tumors larger than 10 cm, especially in younger patients. The use of chemotherapy in the treatment of primary extremity STS is controversial and has yielded inconsistent results. In a randomized controlled trial of preoperative chemotherapy followed by surgery compared with surgical resection alone of subjects with high-risk tumors, there was no difference in 5-year disease-free survival or overall survival.[15] In smaller tumors in a retrospective cohort of subjects receiving neoadjuvant chemotherapy in high-grade extremity sarcomas, Grobmyer and colleagues[16] demonstrated an improvement in disease-specific survival for tumors larger than 10 cm receiving neoadjuvant chemotherapy but not in smaller tumors. Generally accepted indications for adjuvant chemotherapy include synovial sarcoma and pediatric rhabdomyosarcoma, as well as situations of local recurrence and metastatic disease. Single-agent and anthracycline-based regimens are generally accepted and frequently used in situations of locally advanced, unresectable, or metastatic STS.[17–20]

Despite appropriate aggressive multimodality therapy, local recurrence is not uncommon, affecting up to 7% to 24%.[11,21,22] Management of recurrent STS is a challenge because often patients have undergone neoadjuvant therapy before surgical resection. Local recurrence for those who may not have undergone preoperative therapy may be associated with a better prognosis than for those treated with a combined multimodality initial approach.[23] Little is known about the effect of local recurrence on overall outcome. It is generally thought that local recurrence of STS is associated with a poor prognosis and has a negative impact on distant metastasis and survival.[24]

Historically, local recurrences of extremity sarcomas were managed with amputation.[25] Amputation offers definitive local control but often at the expense of patient function, with potential for significant morbidity and a negative impact on overall quality of life. Furthermore, amputation does not have an impact on distant metastasis or overall outcome.[26–28] For this reason many suggest that attempts to surgically manage local recurrence a second time should be more aggressive than the initial treatment approach. Re-resection of extremity STS recurrence is a treatment option,