Original Article

Diagnosis And Surgical Management Of Soft Tissue Sarcoma

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Abstract

Background: All patients should be managed by a multidisciplinary team with expertise in STS. The differential diagnosis of STS of the extremities includes ruling out desmoids and other malignant and benign lesions previously discussed. An essential element of the workup is a history and physical examination (H&P). Laboratory tests have a limited role. Adequate and high-quality imaging studies are crucial to good clinical management of patients, because the presence of metastatic disease may change the management of the primary lesion and the overall approach to the patient‘s disease management. Imaging studies should also provide details about tumor size and contiguity to nearby visceral structures and neurovascular landmarks. The propensities to spread to various locations vary among the subtypes of sarcoma. Therefore, imaging should be individualized based on the subtype of sarcoma. MRI with or without CT is indicated for all lesions with a reasonable chance of being malignant. MRI is preferred for extremity sarcomas, whereas CT is preferred for retroperitoneal sarcomas. CT angiogram may be useful in patients for whom MRI is not feasible. Plain radiograph of the primary lesion is optional. Given the risk for hematogenous spread from a high-grade sarcoma to the lungs, imaging of the chest is essential for accurate staging. Amputation was once considered the standard treatment to achieve local control in patients with extremity sarcomas. In recent years, technical advances in reconstructive surgical procedures, implementation of multimodality therapy, and improved selection of patients for adjuvant therapy have minimized the functional deficits in patients who might otherwise require amputation. Because surgery is the standard primary treatment for most sarcomas, the panel has included a separate section on principles of sarcoma surgery. If a patient cannot be surgically treated according to these principles, preoperative RT or chemotherapy should be considered as alternate treatment options. The biopsy site should be excised en bloc with the definitive surgical specimen. Dissection should be through grossly normal tissue planes uncontaminated by the tumor. If it is close to or displaces major vessels or nerves, these do not need to be resected if the adventitia or perineurium is removed and the underlying neurovascular structures are not involved with gross tumor. Radical excision or entire anatomic compartment resection is not routinely necessary. Limb-sparing surgery is recommended for most patients with extremity STS to achieve local tumor control with minimal morbidity. Evaluation for post- operative rehabilitation is recommended for all patients with extremity sarcoma. If indicated, rehabilitation should be continued until maximum function is achieved.

Keywords: Soft Tissue Sarcoma

INTRODUCTION

Soft-tissue sarcoma (STS) is a diverse group of rare cancers that arise from pathological transformations in the mesenchyme, which is the mesodermal portion of the embryo that develops into connective and skeletal tissues. These rare cancers account for nearly 1% of all adult malignancies. ***(1)***

While the exact cause of carcinogenesis has remained elusive and these cancers can arise from any body part, most STSs are diagnosed in the extremities (59.5%), followed by the trunk (17.9%). At the time of initial diagnosis, distant metastases are rarely present, but blood is the most common route for the disease to spread, most frequently to the lungs. ***(2)***

According to the World Health Organization classification, over one hundred distinct histological subtypes have been categorized. Given this diversity, the appropriate course of treatment could be guided by a better understanding of the disease pathobiology at the molecular level. The most common histologic subtypes in adults include liposarcoma (LPS), angiosarcoma, leiomyosarcoma (LMS), rhabdomyosarcoma (RMS), Ewing‘s sarcoma (ES), and synovial sarcoma (SS). ***(3).***

Liposarcoma:

LPSs are mesenchymal-derived cancers that originate from adipose precursors, named so because of the resemblance they bear to fat cells when examined under microscopy. These tumors are typically large and bulky, with extensions that branch off from the confines of the main tumor mass. LPS is the most common STS subtype, comprising 20% of all adult STS. They most frequently occur in adults over age 40 years, and the 5-year survival rates range from 56% to 100% depending upon tumor histology. ***(2).***

Evaluation and Workup:

All patients should be managed by a multidisciplinary team with expertise in STS. The differential diagnosis of STS of the extremities includes ruling out desmoids and other malignant and benign lesions previously discussed. An essential element of the workup is a history and physical examination (H&P). Laboratory tests have a limited role. ***(4)***

Adequate and high-quality imaging studies are crucial to good clinical management of patients, because the presence of metastatic disease may change the management of the primary lesion and the overall approach to the patient‘s disease management. Imaging studies should also provide details about tumor size and contiguity to nearby visceral structures and neurovascular landmarks. The propensities to spread to various locations vary among the subtypes of sarcoma. Therefore, imaging should be individualized based on the subtype of sarcoma.

(5) MRI with or without CT is indicated for all lesions with a reasonable chance of being malignant. MRI is preferred for extremity sarcomas, whereas CT is preferred for retroperitoneal sarcomas. CT angiogram may be useful in patients for whom MRI is not feasible. Plain radiograph of the primary lesion is optional. Given the risk for hematogenous spread from a high-grade sarcoma to the lungs, imaging of the chest is essential for accurate staging. ***(6)***

Abdominal/pelvic CT should be considered for myxoid round cell liposarcoma, leiomyosarcoma, epithelioid sarcoma, or angiosarcoma, and MRI of the total spine should be considered for myxoid round cell liposarcomas because of the higher risk for metastasis to spine compared with other STS. ***(7)***

Central nervous system imaging should be considered for patients with alveolar soft part sarcomas and angiosarcomas because alveolar soft part sarcomas have a relatively increased propensity to metastasize to the brain, especially in patients with stage IV disease in the presence of pulmonary metastases. ***(4)***

PET scan may be useful for prognostication and grading, and to assess response to chemotherapy. Tumor metabolism data acquired by PET will be useful in accurate grading and prognostication in sarcoma. Recent reports in literature have shown the value of PET in evaluating response to preoperative chemotherapy in patients with high-grade extremity STS and for predicting outcome in patients with liposarcoma. ***(8)***

Pathology of STS:

Biopsy:

A pretreatment biopsy is highly preferred for diagnosing and grading sarcomas and should be performed by an experienced surgeon or radiologist. Biopsy can be accomplished by core needle or open incisional techniques. Although fine needle aspiration (FNA) is a convenient technique, it can be difficult to make an accurate primary diagnosis with FNA alone. FNA may be acceptable in select institutions with clinical and pathologic expertise. Endoscopic or needle biopsy may be indicated for deep thoracic, abdominal, or pelvic sarcomas. ***(5)***

Principles of Pathologic Assessment:

Pathologists with sarcoma expertise should review the pathologic assessment of biopsies and resected specimens, especially for initial histopathologic classification. Margins must be thoroughly evaluated in these specimens. Morphologic assessment based on microscopic examination of histologic sections remains the gold standard of sarcoma diagnosis. ***(7)***

Differential diagnosis of a soft tissue mass includes malignant lesions (i.e., primary, or metastatic carcinoma, melanoma, or lymphoma), desmoids, and benign lesions (i.e., lipomas, lymphangiomas, leiomyomas, and neuromas). Because identifying a histopathologic type of sarcoma is often difficult, several ancillary techniques, such as conventional cytogenetics, immunohistochemistry, and molecular genetic testing, are useful to support the morphologic diagnosis. Pathologists should have access to optimal cytogenetic and molecular diagnostic techniques. Results of appropriate ancillary studies used as an adjunct to morphologic diagnosis should be included in the pathology report. ***(5)***

The report should include specific details about the primary diagnosis (using standardized classification according to the WHO classification); organ; sarcoma site, depth, size, and histologic grade; presence or absence of necrosis; status of excision margins and lymph nodes; TNM stage; and additional features of the tumor, such as mitotic rate, presence or absence of vascular invasion, and the type and extent of inflammatory infiltration. The size at presentation depends on the location tumors in the proximal extremities and retroperitoneum are often large, whereas distal extremity tumors are often small. ***(7)***

Molecular Diagnosis of STS:

Molecular genetic testing has emerged as a particularly useful ancillary test because many STS subtypes are associated with characteristic genetic aberrations, including single base-pair substitutions, deletions, amplifications, and translocations. STS can be divided into 2 major genetic groups:

1. Sarcomas with specific genetic alterations, such as chromosomal translocations or point mutations, and usually simple karyotypes,
2. Sarcomas with nonspecific genetic alterations and complex unbalanced karyotypes. ***(7)***

STS with recurrent chromosomal translocations can be classified into subtypes depending on the presence of fusion gene transcripts (e.g., EWS- ATF1 in clear cell sarcoma, TLS-CHOP in myxoid or round cell liposarcoma, SYT-SSX [SYT-SSX1 or SYT-SSX2] in synovial sarcoma, and PAX-FKHR [PAX3-FKHR or PAX7-FKHR] in alveolar rhabdomyosarcoma). The fusion

genes resulting from chromosomal translocations can provide useful diagnostic and prognostic information. ***(7)***

Common techniques used in molecular diagnosis include conventional cytogenetic analysis, fluorescence in-situ hybridization, and polymerase chain reaction (PCR) based methods. Several studies revealed that PCR–based molecular analysis is a useful adjunct and more sensitive than conventional cytogenetics for the diagnosis of certain STS subtypes, including alveolar rhabdomyosarcoma, synovial sarcoma, and myxoid liposarcoma, which have variation in fusion gene partners. ***(6)***

The molecular heterogeneity of fusion transcripts has been suggested to predict prognosis in certain sarcoma subtypes. In patients with alveolar rhabdomyosarcoma presenting with metastatic disease, PAX7-FKHR was associated with a favorable prognosis compared with PAX3-FKHR. In those with synovial sarcoma, the prognostic impact of fusion gene transcripts SYT-SSX1 and SYT-SSX2 is less clear, with conflicting results in many large studies. In myxoid liposarcoma, the variability of fusion transcript has no effect on clinical outcome. ***(5)***

Although molecular genetic testing appears promising, it involves highly complex techniques, and the methods are not absolutely sensitive or provide specific results. In addition, technical limitations associated with molecular testing suggest that molecular evaluation be considered only as an ancillary technique. Molecular test results should therefore only be interpreted in the context of the morphologic features of a sarcoma. ***(7)***

Staging:

The American Joint Committee on Cancer (AJCC) STS staging system has historically used a 4-grade system, but within the STS staging groups this effectively functioned as a 2-tiered system (G1/G2 [low] and G3/G4 [high]). The 2 most widely used systems, the French Federation of Cancer Centers Sarcoma Group (FNCLCC) and National Cancer Institute system, are 3-tiered grading systems. The latter is based on the evaluation of tumor histology, location, and amount of tumor necrosis, whereas the former is based on tumor differentiation, mitosis count, and tumor necrosis. ***(2)***

Surgical Management of Soft Tissue Sarcoma

Amputation was once considered the standard treatment to achieve local control in patients with extremity sarcomas. In recent years, technical advances in reconstructive surgical procedures, implementation of multimodality therapy, and improved selection of patients for adjuvant therapy have minimized the functional deficits in patients who might otherwise require amputation. ***(9)***

Principles of Surgery:

Because surgery is the standard primary treatment for most sarcomas, the panel has included a separate section on principles of sarcoma surgery. If a patient cannot be surgically treated according to these principles, preoperative RT or chemotherapy should be considered as alternate treatment options. ***(10)***

Because the risk for failure in the surgical bed can be high, many clinicians choose to augment surgery with RT and chemotherapy, either pre- or postoperatively. When appropriate, the guidelines incorporate those therapies that are supported by clinical trial data or extensive clinical experience. ***(11)***

Sarcoma Surgery:

The biopsy site should be excised en bloc with the definitive surgical specimen. Dissection should be through grossly normal tissue planes uncontaminated by the tumor. If it is close to or displaces major vessels or nerves, these do not need to be resected if the adventitia or perineurium is removed and the underlying neurovascular structures are not involved with gross tumor. Radical excision or entire anatomic compartment resection is not routinely necessary. ***(2)***

If resections with microscopically or grossly positive margins are anticipated, surgical clips should be left in place to identify high-risk areas for recurrence, particularly for retroperitoneal or intra-abdominal sarcomas, to help guide future RT. If closed suction drainage is used, the drains should exit the skin close to the surgical incision edge (in case reresection or RT is indicated). ***(10)***

Limb-sparing surgery is recommended for most patients with extremity STS to achieve local tumor control with minimal morbidity. Evaluation for post- operative rehabilitation is recommended for all patients with extremity sarcoma. If indicated, rehabilitation should be continued until maximum function is achieved. ***(12)***

Resection Margins:

Resection with appropriately negative margins is recommended, although negative but closer margins may be effective in patients undergoing RT. Close margins may be necessary to preserve uninvolved critical neurovascular structures. Microscopically positive surgical margins are associated with a higher rate of local recurrence and lower rate of disease-free survival in patients with extremity sarcomas. ***(9)***

Both the surgeon and pathologist should document surgical margins in evaluating a resected specimen. If surgical margins are positive on final pathology, re-resection to obtain negative margins should strongly be considered if it will not have a significant impact on functionality. Adjuvant RT should be considered after resections with close soft tissue margins (< 1 cm) or a microscopically positive margin on bone, major blood vessels, or nerve. ***(11)***

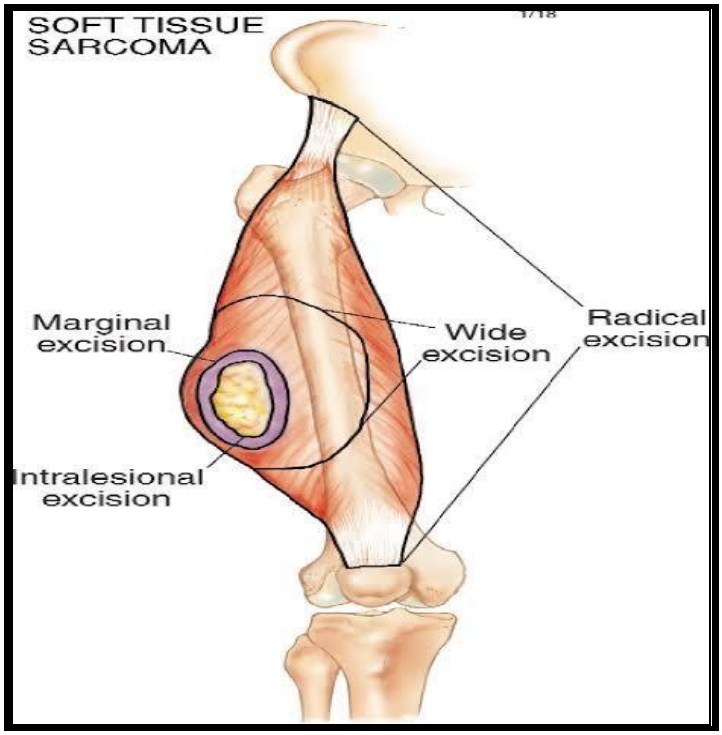

Figure (1): Various types of limb sparing surgery *(13)*

Amputation for Extremity Sarcoma:

Before considering amputation, patients should be evaluated by a surgeon with expertise in the treatment of STS. Amputation should be considered for patient preference, or if the gross total resection of the tumor is expected to render the limb nonfunctional. ***(10)***

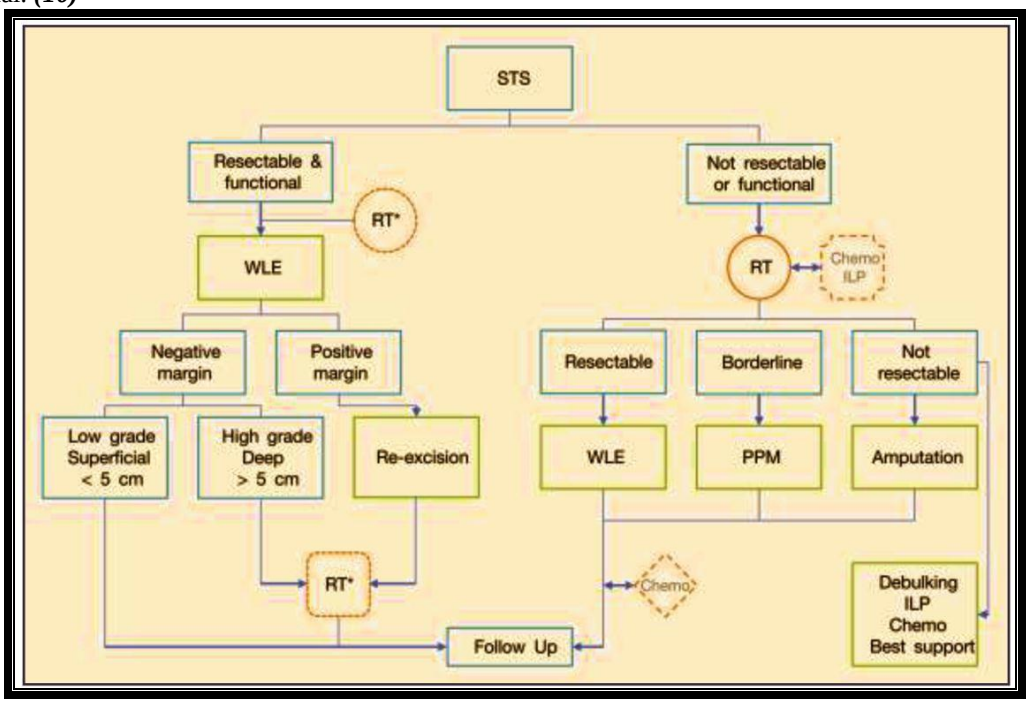

Figure (2): Algorithm for management of localized soft tissue sarcoma (STS).

*Radiotherapy is given either pre-operatively or post-operatively in resectable STS that are high-grade, deep, or large. Chemotherapy may be used pre-operatively in chemo-sensitive STS sub-types that are difficult to resect. Isolated limb perfusion is also a pre-operative treatment option for limb STS that are difficult to resect. Post-operative chemotherapy may be offered in selected high-grade STS. RT, radiotherapy; WLE, wide local excision; Chemo, chemotherapy; ILP, isolated limb perfusion; PPM, planned positive margin. ***(11)***

Guidelines for RT:

External-beam radiation therapy (XRT) can be administered as primary therapy, preoperatively, or postoperatively in STS. Advances in RT technology, such as brachytherapy, intensity-modulated radiation therapy (IMRT), and intraoperative radiation therapy (IORT), have led to improved treatment outcomes in patients with STS. ***(8)***

Brachytherapy involves the direct application of radioactive seeds into the tumor bed through catheters placed during surgery. The main advantage of IMRT is its ability to more closely contour the high-dose radiation volume to the tumor while minimizing the volume of high-dose radiation to the surrounding tissues. IORT delivers radiation during surgery and is performed using different techniques, such as electron beam radiation or brachytherapy. ***(10)***

Preoperative RT:

Preoperative RT has several advantages. First, the treatment volume is smaller because the need to cover the operative field is not present. Second, it may reduce seeding during surgical manipulation of the tumor. The tumor may or may not regress with preoperative RT, but the pseudocapsule may thicken and become acellular, easing resection, and decreasing the risk for recurrence. ***(14)***

However, the main disadvantage of preoperative RT is its effect on wound healing. A higher acute wound healing complication rate has been observed when primary closure is used. Therefore, involvement of a plastic surgeon may be necessary to reduce wound complications when preoperative radiation is contemplated. ***(8)***

After preoperative radiation, a 3- to 6-week interval is necessary before resection to allow acute radiation reactions to subside and decrease the risk for wound complications. Very long intervals between resection and postoperative radiation are not recommended because of the development of late fibrosis. ***(11)***

Postoperative RT:

Postoperative RT has been shown to improve local control in patients with high-grade extremity STS with positive surgical margins. However, treatment decisions regarding the use of post-operative RT should be individualized and not solely based on the finding of marginnegative reresection. When surgical resection is the initial therapy, postoperative RT choices include brachytherapy, IORT, or XRT. When XRT is used, sophisticated treatment planning with IMRT and/or proton therapy can be used to improve therapeutic effect. ***(12)***

Most institutions include the entire operative bed within that radiation field. Total doses of RT should always be determined through normal tissue tolerance. RT is not a substitute for suboptimal surgical resection, and re-resection may be necessary. If the patient has not previously undergone RT, control of microscopic residual disease would be attempted with postoperative RT if re-resection is not feasible. ***(10)***

Brachytherapy alone has been used as an adjuvant treatment. Radiation delivered at 45 to 50 Gy at low-dose rate to the tumor bed has been shown to reduce recurrence without a significant effect on wound healing. However, brachytherapy-alone techniques require special expertise and significant experience. The panel recommends 45 Gy low dose-rate brachytherapy for patients with negative margins. ***(14)***

Low dose-rate brachytherapy (16–20 Gy) or a high dose-rate equivalent is recommended for patients with positive margins followed by XRT. XRT is delivered to the target volume to a total dose of 50 Gy (45 Gy for retroperitoneal or intra-abdominal sarcomas) after surgical healing is complete (3–8 weeks). ***(14)***

Recent reports suggest that IORT provides excellent local control to STS of the extremity. However, because IORT has not been proven superior, the guidelines recommend IORT (10–16 Gy) followed by a 50Gy dose of XRT. If no IORT or brachytherapy was used in the immediate operative or postoperative period, XRT is delivered to the target volume of a 50-Gy total dose (45 Gy for retroperitoneal or intra-abdominal sarcomas) after surgical healing is complete. An XRT boost should be used based on the margin status. For negative margins, an additional 10 to 16 Gy is recommended to the original tumor bed. For microscopically positive margins, an additional 16 to 20 Gy is recommended, and for grossly positive margins, an additional 20 to 26 Gy is suggested. ***(14)***

Surgical management of soft tissue sarcoma:

Based on the initial workup, the patients are assigned to 1 of the following categories:

- **Stage I.**
- **Stage II–III.**
- **Stage IV.**
- **Recurrent disease.** ***(11)***

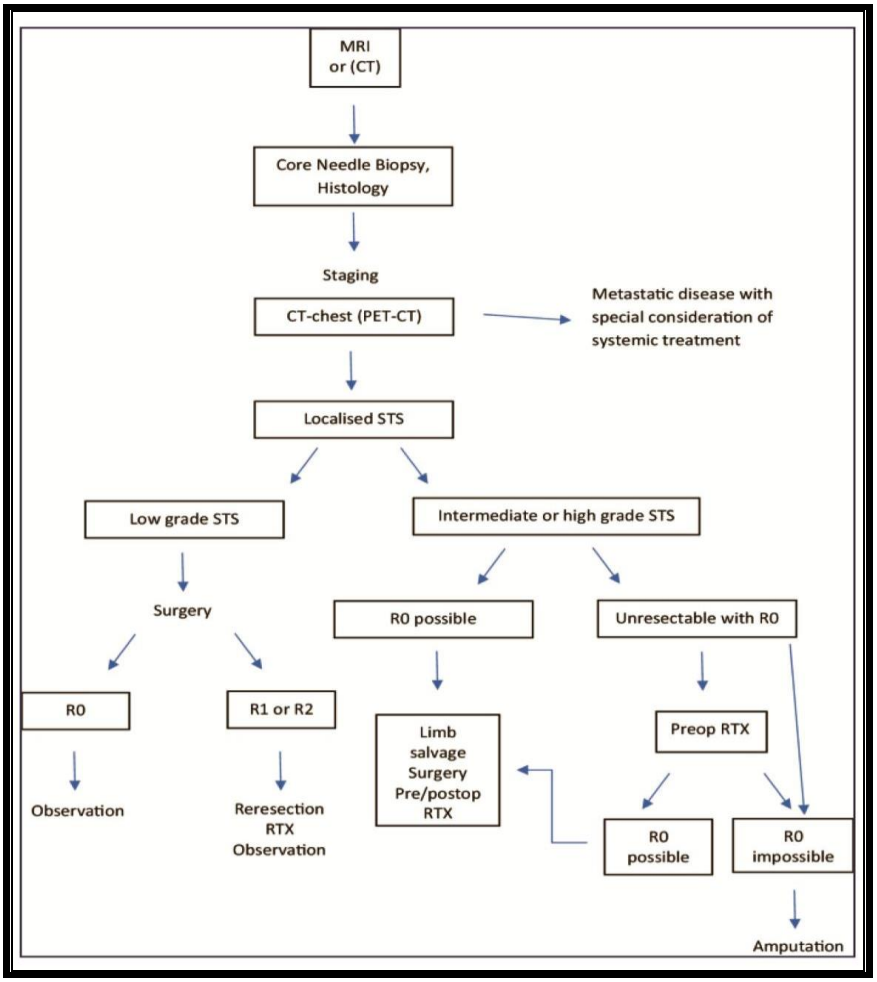

Figure (3): Algorithm for the treatment of soft tissue sarcoma (STS) of the extremities. CT: computed tomography, RTX: radiation therapy. ***(10)***

Stage I:

Surgery is the primary treatment for low-grade stage I tumors and is considered definitive if margins are greater than 1 cm or the fascia plane is intact. Retrospective studies have shown a local control rate of 90% or more for surgery alone. Long-term results of a prospective trials showed that selected patients with primary T1 STS of the extremity and trunk can be treated with surgery alone (R0 resection) with acceptable local control and excellent long-term survival. In the surgery alone arm, the cumulative incidence rates of local recurrence at 5 and 10 years were 7.9% and 10.6%, respectively, in patients who underwent R0 resection, and the 5- and 10-year sarcoma-specific death rates were 3.2%. ***(10)***

The panel recommends surgery alone as the primary treatment for low-grade stage I tumors (T1a– 2b, N0, M0). If the final surgical margins are 1.0 cm or less, postoperative RT is included with a category 2B recommendation for T1a–b tumors and a category 1 recommendation for

T2a–b tumors. RT may not be necessary in patients with small lesions (≤ 5 cm), because these tumors are less frequently associated with local recurrence. ***(14)***

Stage II–III:

Large high-grade extremity sarcomas (> 8–10 cm) at high risk for local recurrences and metastases should be considered for preoperative therapy. Preoperative chemotherapy or chemoradiation is used in many centers for downstaging large high-grade tumors to enable effective surgical resection, especially in the case of chemosensitive histologies.

(11) Concurrent chemoradiation with doxorubicin-based regimens has been shown to improve local control rates in patients with STS, although acute reactions must be considered. Available evidence, although underpowered, suggests that anthracycline-based postoperative chemotherapy would improve disease-free survival in selected patients who are at high risk for recurrence but otherwise have good performance status. ***(10)***

Treatment options for stage II or III high-grade tumors should be decided by a multidisciplinary team, based on the performance status; comorbid factors, including age, tumor location, and histologic subtype of the tumor; and institutional experience. Resectable Tumors: Surgery followed by RT with or without adjuvant chemotherapy or surgery alone (for small tumors that can be resected with wider surgical margins) is the primary treatment for resectable high-grade sarcomas with acceptable functional outcomes. ***(11)***

The guidelines have also included preoperative RT, chemotherapy, or chemoradiation before surgery as alternative options for patients with resectable tumors with acceptable functional outcomes and for potentially resectable tumors with associated concerns for adverse functional outcomes. The panel included preoperative chemotherapy or chemoradiation for resectable disease with acceptable functional outcomes with a category 2B recommendation. ***(10)***

Postoperative RT boost for residual gross disease or microscopically positive margins or adjuvant chemotherapy alone can be considered for patients who have undergone preoperative RT or chemoradiation, whereas postoperative RT with or without adjuvant chemotherapy is recommended for those who underwent preoperative chemotherapy. ***(14)***

Because limited and conflicting data are available for adjuvant chemotherapy in patients with stage II or III disease, adjuvant chemotherapy for stage II or III tumors is included as a category 2B recommendation for all patients with resectable tumors, irrespective of the functional outcomes. Unresectable tumors can be treated primarily with preoperative RT, chemoradiation, or chemotherapy. Tumors that become resectable after preoperative treatment can be treated with surgery. ***(11)***

Definitive RT (7000–8000 cGy) can be considered for select patients with unresectable tumors after preoperative treatment. Observation is an option for asymptomatic patients whose tumors are not believed to be amenable to local control with definitive radiation. For symptomatic patients, the panel recommends moving directly to a palliative approach, defined broadly as chemotherapy, palliative surgery, or best supportive care. ***(12)***

Stage IV (Metastatic Disease):

Single agents (doxorubicin, ifosfamide, or dacarbazine) or anthracycline-based combination regimens (doxorubicin or epirubicin with ifosfamide and/or dacarbazine) have been widely used to treat metastatic disease. Liposomal anthracyclines were found to be active as first-line treatment for advanced sarcomas with a better toxicity profile than doxorubicin. ***(15)***

Other chemotherapeutic agents have also been tested in clinical trials. Combined gemcitabine and docetaxel was found to be highly active in patients with predominantly uterine leiomyosarcomas who experienced no response to or for medical reasons could not tolerate ifosfamide plus doxorubicin. ***(15)***

Isolated limb perfusion (ILP) has been used in Europe as a limbsparing treatment for unresectable intermediate or high-grade extremity STS. In European clinical trials, melphalan in combination with tumor necrosis factor-α (TNF-α) resulted in better response rates and limbsalvage rates than ILP with melphalan alone. Recombinant TNF-α–1A and melphalan has been approved in Europe for ILP in patients with locally advanced high-grade STS of the extremities. ***(10)***

Patients with limited metastasis confined to a single organ and limited tumor bulk or regional lymph node involvement should undergo primary tumor management. Another option is to consider regional node dissection for nodal involvement with or without RT or metastasectomy with or without chemotherapy with or without RT. The guidelines do not specify rules governing metastasectomy, which remains controversial for many cancers, including sarcoma. ***(12)***

Several variables influence the decision to use metastasectomy, including the disease-free interval from original diagnosis to detection of the metastases, the patient‘s performance status, and the amount of prior therapy. Thoracotomy and video-assisted thoracic surgery should be used selectively depending on the clinical presentation of metastatic disease. In addition, patients can also undergo radiofrequency ablation or embolization procedures as an alternate method for control of metastatic lesions. In the guidelines, a subsequent distinction is made between asymptomatic and symptomatic patients for those who present with disseminated disease. One reasonable management option for asymptomatic patients is to offer close observation with a ―watchful waiting‖ strategy, especially for patients who had a very long disease-free interval and have only a minimal burden of metastases (e.g., subcentimeter pulmonary nodules). ***(11)***

Alternatively, patients can also be treated with palliative approaches, such as palliative RT, chemotherapy, or palliative surgery. Palliative RT involves expedient treatment with sufficient dose to halt tumor growth or cause tumor regression. The outcome of this approach depends on the rapidity of growth and the status of systemic disease. ***(10)***

In addition, the guidelines have included ablation procedures (e.g., radiofrequency ablation or cryotherapy), embolization procedures, or stereotactic radiosurgery/radiotherapy as options for symptomatic patients with disseminated metastases. The guidelines are intentionally nonspecific about this group of options, because many different factors impact this decision (e.g., patient performance status, patient preferences, specific clinical problems from the metastases, treatment availability) and specific details are best left to clinical judgment. ***(14)***

Surveillance:

Surveillance is deemed important to detect recurrences that might still be potentially curable. However, limited data are available in the literature on effective surveillance strategies. The guidelines outline a prudent follow-up schedule that avoids excessive testing. ***(12)***

Higher-grade and larger tumors have a higher risk for dissemination; therefore, the surveillance recommendations for patients with these tumors are somewhat more intensive, particularly for the first 3 years after resection. Periodic imaging (MRI, CT, or ultrasound) of the primary site should be performed based on the estimated risk for locoregional recurrence. ***(11)***

However, when the area can be easily followed by physical examination, imaging may not be required. After 10 years, the likelihood of developing a recurrence is small and follow-up should be individualized. ***(2)***

Stage I tumors are routinely followed with H&P every 3 to 6 months for 2 to 3 years, then annually. Chest imaging should also be considered every 6 to 12 months. For stage II through IV disease, H&P and chest imaging should be performed every 3 to 6 months for 2 to 3 years, then every 6 months for the next 2 years, and then annually. ***(12)***

Because these patients‘ risk never returns to zero, long-term followup is indicated, including consideration of MRI or CT scanning. No study has ever proved that the use of more sensitive CT scans in routine surveillance would improve clinical

outcomes. According to the reported data from MD Anderson Cancer Center, routine use of chest CT adds little clinical benefit when risk for pulmonary metastases is low. ***(10)***
However, in certain subsets of patients for whom chest radiographs are difficult to interpret because of anatomic considerations (e.g., scarring, emphysema), chest CT surveillance may be indicated. ***(11)***

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