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REVIEW

Recent Advances in Retroperitoneal Sarcoma: Diagnosis, Surgery, Radiotherapy, Systemic Therapy, and Recurrence Management

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Abstract

Introduction: Retroperitoneal sarcomas (RPS) are rare malignant mesenchymal tumors that present at large size, near critical organs and major vessels, and comprise diverse histological subtypes, making diagnosis and management challenging. This review summarizes evidence on RPS diagnosis, pathology, treatment, recurrence, and future directions. **Methods:** A narrative literature review was conducted using PubMed and contemporary evidence sources, focusing on publications from 2020 onward. Guidelines, consensus statements, randomized trials, systematic reviews, meta-analyses, and observational studies on RPS diagnosis, pathology, treatment, surveillance, and recurrence were reviewed. **Results:** Contrast-enhanced computed tomography remains the primary imaging modality, while magnetic resonance imaging is used selectively. Image-guided core needle biopsy is recommended to establish histology and guide treatment. For localized disease, surgery at experienced sarcoma centers remains the main potentially curative treatment, guided by histology and multidisciplinary decision-making. Following the STRASS trial, preoperative radiotherapy is not routinely recommended but may benefit selected patients with well-differentiated or low-grade dedifferentiated liposarcoma. Systemic therapy has a limited role in localized disease but is being investigated in neoadjuvant and advanced or metastatic settings using histology-directed approaches. Long-term surveillance is essential because recurrence is common; recurrent disease requires individualized assessment and may involve repeat surgery, radiotherapy, systemic therapy, or combined approaches. **Conclusions:** RPS management has evolved toward a histology-driven, multidisciplinary approach. Surgery remains the cornerstone, while radiotherapy and systemic therapy should be selected according to histology, tumor biology, recurrence risk, disease extent, and patient characteristics. International collaboration, prospective trials, molecular characterization, and biomarker-driven strategies are needed to improve outcomes and personalize treatment.

Keywords: Retroperitoneal sarcoma, soft tissue sarcoma, liposarcoma, leiomyosarcoma, surgery, radiotherapy

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Introduction

Retroperitoneal sarcomas (RPS) are rare malignant mesenchymal tumors arising in the retroperitoneal space and account for a small proportion of adult soft tissue sarcomas. Their deep anatomical location, often large size at presentation, and close relationship to vital organs and major vascular structures make diagnosis and treatment particularly challenging. Liposarcoma and leiomyosarcoma are the predominant histological subtypes, although other entities, including solitary fibrous tumor, malignant peripheral nerve sheath tumor, and undifferentiated pleomorphic sarcoma, may also arise in the retroperitoneum. The anatomical location of RPS is a major determinant of outcome because complete resection can be technically challenging and local recurrence remains common despite apparently complete surgery [1, 2].

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Over the past decade, management of RPS has increasingly shifted from a surgery-centered approach toward histology-specific, multidisciplinary decision-making. Current consensus recommendations emphasize referral to specialized, high-volume sarcoma centers, where imaging, biopsy, pathological review, surgical planning, and consideration of radiotherapy or systemic therapy can be integrated into individualized treatment strategies. This approach has become particularly important following the STRASS trial and subsequent analyses, which have challenged the routine use of preoperative radiotherapy and highlighted the importance of selecting patients according to histological subtype, expected patterns of recurrence, and individual risk rather than applying a uniform treatment strategy [3–5].

Diagnostic Evaluation

The diagnostic evaluation of suspected RPS begins with high-quality cross-sectional imaging, with contrast-enhanced computed tomography (CT) of the abdomen and pelvis generally serving as the primary imaging modality. CT provides information on tumor size, anatomical origin, relationship to adjacent organs and major vessels, and potential resectability. Magnetic resonance imaging (MRI) has a complementary role in selected patients, particularly when further soft-tissue characterization is required, pelvic extension is suspected, or vascular, neural, or other complex anatomical involvement needs clarification. Certain imaging characteristics may suggest a particular histological subtype, such as the presence of macroscopic fat in well-differentiated liposarcoma or a predominantly solid and heterogeneous appearance in dedifferentiated liposarcoma and leiomyosarcoma. However, imaging findings alone are generally insufficient to establish a definitive diagnosis, and histological confirmation is required in most patients [1, 6, 7].

Image-guided core needle biopsy is recommended for most patients before definitive treatment. Preoperative tissue diagnosis allows accurate histological classification, facilitates multidisciplinary treatment planning, and may prevent inappropriate surgery for non-sarcomatous lesions or other retroperitoneal mimics. Available evidence indicates that preoperative core needle biopsy does not adversely affect oncological outcomes when appropriately performed, supporting its use when technically feasible [5, 8]. Biopsy should be planned in collaboration with the treating sarcoma team, with the biopsy tract positioned so that it can be safely incorporated into the subsequent surgical field and with unnecessary tissue-plane violation avoided.

Pathological classification of RPS has also become increasingly precise with advances in immunohistochemistry and molecular diagnostics. In particular, MDM2 and CDK4 amplification testing is important in the evaluation of suspected well-differentiated and dedifferentiated liposarcoma, while molecular and immunohistochemical findings can help distinguish other histological subtypes with overlapping morphological features [1, 9, 10]. Accurate pathological classification is clinically important because the major RPS subtypes differ substantially in their biological behavior. Liposarcoma, particularly well-differentiated and dedifferentiated subtypes, has a greater propensity for local recurrence, whereas leiomyosarcoma is more commonly associated with hematogenous metastatic spread. Consequently, histological diagnosis directly informs prognostic assessment, surgical planning, surveillance strategies, and consideration of radiotherapy or systemic treatment [1, 9, 10].

Surgical Management

Surgery remains the cornerstone of treatment for localized RPS, with the primary goal of achieving complete macroscopic resection while minimizing unnecessary morbidity. Because RPS frequently surrounds or displaces adjacent organs and major vessels, resection often requires en bloc removal of involved organs or structures when necessary to achieve an adequate oncological resection. The interpretation of surgical margins is also influenced by tumor biology and anatomical constraints, and achieving a complete macroscopic resection remains a key determinant of local control. Current evidence emphasizes that surgery should be performed at experienced, high-volume sarcoma centers by multidisciplinary teams with expertise in retroperitoneal surgery [5, 11, 12].

The optimal extent of resection remains an important area of debate and should be individualized according to histological subtype, tumor location, extent of involvement, and expected pattern of recurrence. For retroperitoneal liposarcoma, particularly large well-differentiated and dedifferentiated tumors, extended or compartmental resection may improve local control in selected patients. In contrast, leiomyosarcoma has a greater propensity for hematogenous dissemination, and extensive multivisceral resection should be considered carefully when it is unlikely to provide meaningful oncological benefit. Thus, contemporary surgical management increasingly favors a histology-specific approach rather than a uniform operative strategy for all RPS [13, 14].

Multivisceral and vascular resections may be required in selected patients and can be performed safely in experienced centers. However, these procedures are associated with greater technical complexity and perioperative morbidity and should be undertaken in institutions with appropriate vascular, urologic, hepatobiliary, and reconstructive expertise. Centralization of care is consistently associated with improved surgical outcomes, including higher rates of complete resection and lower perioperative morbidity, and may contribute to improved long-term survival [5, 12, 15].

Surgery may also provide meaningful disease control in selected patients with recurrent RPS. The decision to perform repeat resection should consider the site and extent of recurrence, disease-free interval, rate of tumor progression, feasibility of complete resection, anticipated morbidity, previous treatments, and patient performance status. Repeat surgery may be particularly valuable for patients with predominantly localized, slowly progressive recurrent liposarcoma, whereas its role is more limited

in patients with rapidly progressive or widely metastatic disease. Accordingly, management of recurrent RPS should be individualized through multidisciplinary assessment rather than based on an assumption that repeat surgery is appropriate for all patients [13, 16].

Radiotherapy

Radiotherapy remains one of the most debated components of RPS management. The landmark STRASS randomized trial compared preoperative radiotherapy followed by surgery with surgery alone and found no significant improvement in abdominal recurrence-free survival with the addition of radiotherapy. Consequently, routine preoperative radiotherapy is not recommended for all patients with resectable RPS [3, 17].

Subsequent analyses, however, have suggested that the effect of radiotherapy may vary according to histological subtype and patterns of recurrence. In particular, exploratory analyses have raised the possibility of a benefit from preoperative radiotherapy in selected patients with well-differentiated or low-grade dedifferentiated liposarcoma, which has a predominantly local pattern of failure. Conversely, no clear benefit has been demonstrated for leiomyosarcoma, which more commonly recurs at distant sites. These findings support a selective rather than routine approach to preoperative radiotherapy, with treatment decisions based on histology, estimated local recurrence risk, tumor location, resectability, and the anticipated morbidity of local recurrence [3, 17].

When radiotherapy is considered, preoperative administration is generally preferred over postoperative treatment because the target volume is better defined before surgery and the small bowel may be displaced from the treatment field. Nevertheless, the potential benefits must be weighed against treatment-related toxicity, particularly gastrointestinal toxicity. Radiotherapy should therefore be discussed within a multidisciplinary sarcoma team, particularly for patients with a high risk of local recurrence in whom the expected benefit is considered to outweigh the potential risks [5, 17].

Radiotherapy

Despite the negative primary outcome of the STRASS trial, subsequent analyses and interpretation of subgroup findings have suggested that selected patients with liposarcoma, particularly those with well-differentiated or low-grade dedifferentiated disease, may derive a local control benefit from preoperative radiotherapy. Some subsequent systematic reviews and meta-analyses have also reported lower rates of local recurrence with radiotherapy, although these findings are limited by substantial heterogeneity and the predominance of nonrandomized studies. Current evidence therefore supports a selective rather than routine approach to radiotherapy, particularly in histological subtypes and clinical settings associated with a high risk of local recurrence [4, 18, 19].

Advances in radiation technology have improved the feasibility of delivering highly conformal treatment while limiting radiation exposure to adjacent organs. Intensity-modulated radiotherapy (IMRT), volumetric-modulated arc therapy (VMAT), and image-guided radiotherapy can improve dose distribution and may reduce exposure of the bowel and kidneys. Proton therapy may offer additional dosimetric advantages in selected patients, although evidence of a clinically meaningful benefit remains limited. Postoperative radiotherapy has also been investigated in retrospective studies, with some suggesting improved local control; however, the available evidence is insufficient to support its routine use. Because the retroperitoneum contains radiosensitive abdominal organs, radiotherapy planning should be individualized and performed within a multidisciplinary sarcoma team [4, 20, 21].

In patients with unresectable RPS or those who are medically unsuitable for surgery, definitive radiotherapy may be considered in carefully selected cases. Particle therapy, including carbon-ion radiotherapy, is of particular interest because its physical and biological properties may allow delivery of high biologically effective doses while limiting radiation exposure to surrounding normal tissues. However, the available evidence is primarily derived from retrospective single-center studies and should therefore be interpreted cautiously. One retrospective series of 76 patients with unresectable RPS treated with definitive carbon-ion radiotherapy reported 3- and 5-year local control rates of 79.0% and 72.0%, respectively, with grade ≥3 late adverse events occurring in 5.2% of patients. A dose of 70.4 Gy was delivered in 16 fractions over 4 weeks, with respiratory gating and active pencil-beam scanning used in more recent patients [22]. Although these findings are encouraging, carbon-ion radiotherapy remains an investigational approach, and prospective studies are required to establish its efficacy, safety, and appropriate patient selection.

Systemic and Medical Management

Systemic therapy has a more limited role in RPS than in many other solid malignancies, particularly in localized resectable disease. Routine adjuvant chemotherapy is not established as standard treatment for most patients with primary RPS. Treatment decisions should instead be individualized according to histological subtype, tumor grade, growth kinetics, metastatic risk, and patient fitness rather than applied uniformly across all RPS subtypes [23–25].

Neoadjuvant chemotherapy has attracted increasing interest, particularly for high-risk tumors and histological subtypes with greater chemosensitivity. Contemporary studies, including the STRASS2 trial, are evaluating whether histology-directed neoadjuvant chemotherapy can reduce the risk of distant recurrence and improve outcomes in patients with high-risk primary RPS. The rationale is strongest for tumors with a substantial risk of occult metastatic disease or those in which tumor response may influence subsequent surgical management. Nevertheless, this approach remains investigational, and there is currently insufficient evidence to recommend neoadjuvant chemotherapy routinely for unselected

patients with localized RPS [4, 23, 24].

For advanced or metastatic disease, systemic treatment is generally selected according to histological subtype and prior therapy. Anthracycline-based regimens remain commonly used for advanced soft tissue sarcoma, while other cytotoxic and targeted agents may be considered according to tumor subtype and clinical circumstances. In liposarcoma, agents such as trabectedin and eribulin have demonstrated activity in selected patients, whereas pazopanib is used in some non-lipogenic soft tissue sarcomas. Treatment selection should therefore reflect the biological characteristics of the individual tumor rather than treating RPS as a single disease entity.

Targeted therapies and immunotherapy remain areas of active investigation. Immune checkpoint inhibitors have not demonstrated consistent efficacy across all sarcoma subtypes, and available evidence in RPS remains limited. Certain molecularly defined tumors may ultimately benefit from biomarker-driven therapies, but most targeted and immunotherapeutic approaches should currently be considered within clinical trials or selected salvage settings rather than as routine standard treatment [26–28]. Increasing understanding of the molecular characteristics of liposarcoma, leiomyosarcoma, and other RPS subtypes may facilitate the development of more precise treatment strategies in the future.

Recurrence and Surveillance

Recurrence remains a major clinical challenge in patients with RPS. The predominant pattern of recurrence varies according to histological subtype: local recurrence is particularly common in liposarcoma, whereas distant metastases are more frequent in leiomyosarcoma and other high-grade subtypes. Recurrence may occur several years after apparently complete resection; therefore, prolonged surveillance is warranted. The risk of recurrence is influenced by histological subtype, tumor grade and size, completeness of resection, and whether the disease is primary or recurrent at presentation [2, 16, 29].

Postoperative surveillance relies primarily on serial cross-sectional imaging. Evidence supporting specific surveillance schedules remains limited, and current recommendations are largely based on expert consensus and retrospective data. In clinical practice, imaging is commonly performed every 3–6 months during the first 2–3 years after surgery, followed by progressively longer intervals according to histological subtype and individual recurrence risk. Longer-term and, in selected patients, annual surveillance beyond 5 years may be appropriate because late recurrence remains possible. Chest imaging should also be incorporated, particularly in patients with high-grade tumors or histological subtypes associated with a substantial risk of pulmonary metastasis [12, 29].

Management of recurrent RPS should be individualized through multidisciplinary assessment. Repeat surgery may provide meaningful disease control in selected patients with localized, technically resectable, and relatively slow-growing recurrence, particularly when complete resection can be achieved with acceptable morbidity. For unresectable or metastatic recurrence, treatment options include systemic therapy, radiotherapy, and, in selected cases, local ablative procedures or palliative surgery. The pattern, extent, and tempo of recurrence, together with the patient's performance status and previous treatments, should guide therapeutic decisions rather than the time elapsed since the initial operation alone.

Future Directions

Future advances in RPS management are likely to focus on histology-specific treatment algorithms, improved molecular classification, and more effective integration of surgery with systemic therapy and radiotherapy. Increasing evidence suggests that an all-comers approach is insufficient for this biologically heterogeneous group of tumors. Important research priorities include identifying liposarcoma subgroups most likely to benefit from radiotherapy, determining which patients may benefit from neoadjuvant systemic therapy, improving prediction of local and distant recurrence, and incorporating molecular biomarkers and radiomic features into individualized treatment planning [13, 16].

Prospective multicenter studies and international collaborative trials will be particularly important because the rarity of RPS makes adequately powered single-center studies difficult. Greater integration of molecular profiling with clinical and imaging data may also facilitate risk stratification and the development of biomarker-driven therapies.

In conclusion, RPS remains a challenging malignancy in which outcomes depend substantially on accurate diagnosis, histology-specific treatment selection, and multidisciplinary management at experienced sarcoma centers. Surgery remains the cornerstone of treatment for localized disease, although the extent of resection should be individualized according to tumor subtype, anatomy, and expected patterns of recurrence. Radiotherapy has no established role as a routine treatment for all patients but may provide benefit in selected patients with a high risk of local recurrence, particularly those with specific liposarcoma subtypes. Systemic therapy remains an evolving component of management and is best considered according to histology, disease extent, and individual risk, with several approaches still under investigation.

Because both local and distant recurrence may occur late, structured long-term surveillance and individualized salvage strategies remain essential. Future progress will depend on prospective clinical trials, international collaboration, molecular characterization, and biomarker-driven approaches that can further refine patient selection and move RPS management toward increasingly precise and individualized care.

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• The authors declare no conflict of interest.

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