

Cancer Association of South Africa (CANSA)



Fact Sheet on Retroperitoneal Sarcoma

Introduction

Sarcoma is a rare type of cancer that develops in the connective tissues, Connective tissues include: muscle, bone, nerves, cartilage, tendons, blood vessels including fatty and fibrous tissues.

Soft tissue sarcomas are a group of rare tumours that together make up only 1 percent of all adult cancers. Although these tumours can occur anywhere in the body, about 20 percent (0.2 percent of all cancers) develop in the back of the abdomen, next to the kidneys, in a relatively “hidden” location known as the retroperitoneum. Here, retroperitoneal sarcomas grow slowly over time and, in fact, once detected, are typically 20 to 30 centimetres, quite possibly the largest tumours in the human body. But aside from their visually shocking giant size, retroperitoneal sarcomas are among the most challenging cancers to treat.

Retroperitoneal SARCOMA

Retroperitoneal Sarcoma (RPS)

Retroperitoneal sarcomas occur in the retroperitoneum. The retroperitoneum is an area behind the peritoneum. The peritoneum is the lining of the abdominal space that covers all of the abdominal organs.

The retroperitoneum is deep in the abdomen and pelvis, behind the abdominal lining, where organs such as the major blood vessels, kidneys, pancreas and bladder are located.

The main types of sarcoma that occur in the retroperitoneum are:

- Liposarcoma – sarcoma of fatty tissue
- Leiomyosarcoma – sarcoma of involuntary muscle
- Other less common types of sarcoma that can occur in the retroperitoneum include:
 - solitary fibrous tumour
 - pleomorphic sarcoma
 - malignant nerve sheath tumour
 - synovial sarcoma
 - Ewing’s sarcoma

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Incidence of Retroperitoneal Sarcoma in South Africa

The South African National Cancer Registry (2017) does not provide any information regarding the incidence of Retroperitoneal Sarcoma.

Signs and Symptoms of Retroperitoneal Sarcoma

Often, Retroperitoneal Sarcoma (RPS) manifests with vague, indolent symptoms that present a diagnostic challenge or is discovered incidentally on imaging.

Diagnosis and Grading of Retroperitoneal Sarcoma

Retroperitoneal Sarcoma (RPS) manifests with vague, indolent symptoms that present a diagnostic challenge or is discovered incidentally on imaging. Adequate, detailed imaging of the retroperitoneum with good visualization of the tumour and its relationship with adjacent organs and their potential involvement is critical. Contrast-enhanced CT of the abdomen and pelvis is often sufficient for the diagnosis of RPS. This imaging modality also provides a good indication of the nature of the tumour and is ideal for biopsy planning. A CT scan of the chest is then sufficient to complete staging in most cases. Magnetic resonance imaging can be used in patients with allergies to intravenous contrast as well as in cases in which an assessment of spinal/vertebral foramina, nerves, and/or posterior muscles involvement is necessary.

Mcaddy, N.C., Hallin, M., Strauss, D., Smith, M., Hayes, A., Yusuf, S., Moskovic, E., Fotiadis, N., van Houdt, W., Jones, R.L., Gronchi, A., Thway, K. & Messiou, C. 2019.

BACKGROUND: Initial grading of retroperitoneal leiomyosarcoma (LMS) is performed by core biopsy (CB) however, discrepancy between grade of tumour at initial CB and surgical excision is recognised, raising concerns about the accuracy of CB for directing neoadjuvant therapy. The histological grading system used for staging LMS consists of 3 components: tumour differentiation, mitotic index and proportion of necrosis. We postulate that assessment of necrosis by histopathology alone is inadequate, resulting in under-grading of LMS. We propose and assess a combined grading system that incorporates CT scan findings into pre-surgical grading.

METHODS: Retrospective, blinded review of CT, CB histology and final surgical histology of patients with retroperitoneal LMS was undertaken. A modified grading system, c_T H-Grade, was derived by replacing the CB necrosis score with a CT-derived necrosis score. The sensitivity and specificity of c_T H-Grade, the standard histopathology scoring, H-grade were compared. Inter-observer variability in assessment of CT necrosis was also assessed.

RESULTS: 53 patients fulfilled criteria for inclusion. CT was more sensitive at detection of necrosis than CB histology alone with sensitivity of 100% vs 53%. The use of c_T HGrade resulted in increased detection of high-grade tumours with c_T H-grade having sensitivities of 80% and 35% for Grade 2 and 3 tumours respectively vs 53% and 15% with H-Grade. Assessment of reader agreement demonstrated Kappa scores of 0.8.

CONCLUSION: Histology from CB under-grades LMS due to undersampling of tumour necrosis. CT is more sensitive in assessing necrosis and its incorporation into a modified CT-histopathology grading system (c_T H-Grade) improves accuracy of grading with significant implications for patient management.

Treatment of Retroperitoneal Sarcoma

Complete surgical resection with negative margins remains the cornerstone of treatment of nonmetastatic Retroperitoneal Sarcoma (RPS) and is the only chance for cure. In order to achieve negative margins, multivisceral *en bloc* resection is often necessary.

Radiation therapy (RT) has long been an important tool in the multimodal treatment of this disease. There has been great debate, however, over the use of radiation therapy.

Villano, A.M., Zeymo, A., Nigam, A., Chan, K.S., Shara, N., Unger, K.R. & Al-Refaie, W.B. 2020.

Background: Given the rarity of retroperitoneal soft tissue sarcoma, few studies have assessed if radical excision of retroperitoneal soft tissue sarcoma with adjacent organs improves survival outcomes. This propensity score-matched study aimed to evaluate the impact of radical excision versus resection of tumor alone.

Methods: The National Cancer Database 2004 to 2015 was used to assess short- and long-term outcomes of resection of tumor alone versus radical excision (tumor plus ≥ 1 adjacent organs) via 1:1 propensity-matched analyses. Subgroup analyses included low-grade, high-grade, liposarcoma, leiomyosarcoma, adjacent organ involvement alone, localized tumors alone, and high-volume hospitals (≥ 10 resections/y). Multivariable logistic regression models identified factors associated with radical excision.

Results: Comparison of propensity-matched groups (N = 1,139/group) revealed no significant differences in 30-day mortality, 90-day mortality, or overall survival (for all, $P > .580$). For all subgroup analyses comparing resection of tumor alone with radical excision, including localized tumors without organ invasion (N = 208/group), there were no identified differences in short- or long-term survival. Although it yielded lower R2 resection rates ($P = .007$), radical excision was associated with greater mean length of stay ($P < .001$).

Conclusion: Radical excision was not associated with improved retroperitoneal soft tissue sarcoma survival irrespective of grade, histology, hospital volume, or adjacent organ involvement. Resection of ostensibly involved adjacent viscera may increase morbidity without survival benefit. These results inform ongoing discussion regarding histology-tailored, situation-specific extent of retroperitoneal soft tissue sarcoma resections.

Bonvalot, S., Gronchi, A., Le Péchoux, C., Swallow, C.J., Strauss, D., Meeus, P., van Coevorden, F., Stoldt, S., Stoeckle, E., Rutkowski, P., Rastrelli, M., Raut, C.P., Hompes, D., De Paoli, A., Sangalli, C., Honoré, C., Chung, P., Miah, A., Blay, J.Y., Fiore, M., Stelmes, J.J., Dei Tos, A.P., Baldini, E.H., Litière, S., Marreaud, S., Gelderblom, H. & Haas, R.L. 2020.

Background: Unlike for extremity sarcomas, the efficacy of radiotherapy for retroperitoneal sarcoma is not established. The aim of this study was to evaluate the impact of preoperative radiotherapy plus surgery versus surgery alone on abdominal recurrence-free survival.

Methods: EORTC-62092 is an open-label, randomised, phase 3 study done in 31 research institutions, hospitals, and cancer centres in 13 countries in Europe and North America. Adults (aged ≥ 18 years) with histologically documented, localised, primary retroperitoneal sarcoma that was operable and suitable for radiotherapy, who had not been previously treated and had a WHO performance status and American Society of Anesthesiologists score of 2 or lower, were centrally randomly assigned (1:1), using an interactive web response system and a minimisation algorithm, to receive either surgery alone or preoperative radiotherapy followed by surgery. Randomisation was stratified by hospital and performance status. Radiotherapy was delivered as 50.4 Gy (in 28 daily fractions of 1.8 Gy) in either 3D conformal radiotherapy or intensity modulated radiotherapy, and the objective of surgery was a macroscopically complete resection of the tumour mass with en-bloc organ resection as necessary. The primary endpoint was abdominal recurrence-free survival, as assessed by the investigator, and was analysed in the intention-to-treat population. Safety was analysed in all patients who started their allocated treatment. This trial is registered with ClinicalTrials.gov, [NCT01344018](https://clinicaltrials.gov/ct2/show/study/NCT01344018).

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Findings: Between Jan 18, 2012 and April 10, 2017, 266 patients were enrolled, of whom 133 were randomly assigned to each group. The median follow-up was 43.1 months (IQR 28.8-59.2). 128 (96%) patients from the surgery alone group had surgery, and 119 (89%) patients in the radiotherapy and surgery group had both radiotherapy and surgery. Median abdominal recurrence-free survival was 4.5 years (95% CI 3.9 to not estimable) in the radiotherapy plus surgery group and 5.0 years (3.4 to not estimable) in the surgery only group (hazard ratio 1.01, 95% CI 0.71-1.44; log rank p=0.95). The most common grade 3-4 adverse events were lymphopenia (98 [77%] of 127 patients in the radiotherapy plus surgery group vs one [1%] of 128 patients in the surgery alone group), anaemia (15 [12%] vs ten [8%]), and hypoalbuminaemia (15 [12%] vs five [4%]). Serious adverse events were reported in 30 (24%) of 127 patients in the radiotherapy plus surgery group, and in 13 (10%) of 128 patients in the surgery alone group. One (1%) of 127 patients in the radiotherapy plus surgery group died due to treatment-related serious adverse events (gastropleural fistula), and no patients in the surgery alone group died due to treatment-related serious adverse events.

Interpretation: Preoperative radiotherapy should not be considered as standard of care treatment for retroperitoneal sarcoma.

Funding: European Organisation for Research and Treatment of Cancer, and European Clinical Trials in Rare Sarcomas.

Willis, F., Schimmack, S., Uhl, M., Haefner, M.F., Mechtersheimer, G., Hinz, U., Schmidt, T., Debus, J., Fröhling, S. & Schneider, M. 2020 .

Introduction: In retroperitoneal soft tissue sarcoma (STS) local recurrence (LR) rates remain high despite more aggressive surgical approaches. Since wide resection margins cannot be achieved in all patients, application of intraoperative radiation therapy (IORT) has been frequently discussed. Still, the significance of IORT in multimodal treatment of retroperitoneal STS remains unclear.

Material and methods: Patients undergoing resection of primary or recurrent retroperitoneal STS at the University of Heidelberg Department of General, Visceral and Transplantation Surgery were retrospectively analyzed. Univariate Kaplan-Meier and multivariate Cox regression analyses were performed to identify predictors of LR-free survival and to investigate the impact of IORT and high cumulative radiation doses. Analyses with propensity-score matched subgroups for IORT and cumulative radiation dose were performed to control for selection bias. Subgroup analyses for patients with retroperitoneal liposarcoma were likewise performed.

Results: 272 patients were identified. Recurrent tumors, histology of dedifferentiated liposarcoma or unclassified sarcoma and microscopically incomplete resection were associated with decreased LR-free survival. In liposarcoma, only recurrent and dedifferentiated tumors were confirmed as poor prognostic factors concerning LR. IORT and cumulative radiation doses exceeding 60 Gy did not influence LR rates (estimated 5-year LR-free survival: IORT: 39%, non-IORT: 46%; p = 0.79).

Conclusion: In this retrospective evaluation, additional application of IORT does not significantly influence oncological outcome in retroperitoneal soft tissue sarcoma. Randomized trials are needed to clarify the benefit of IORT.

Herzberg, J., Niehaus, K., Holl-Ulrich, K., Honarpisheh, H., Guraya, S.Y. & Strate, T. 2019.

“Retroperitoneal liposarcomas are a heterogeneous group of mesenchymal tumours that have a wide spectrum of histological subtypes and vague clinical presentations. Herein, we present the case of a 75-year-old man with anorexia, weight loss of 7 kg, and a growing abdominal circumference within a span of 6 weeks. Computed tomography of the abdomen and pelvis showed a large mass that filled almost the entire abdominal cavity. After consultation with a multidisciplinary tumour board, en bloc resection of the tumour was performed. In addition, the left kidney and a part of the left diaphragm were removed. The tumour measured 35 × 29 × 20.5 cm and weighed 11.6 kg. The histological report confirmed low-grade dedifferentiated liposarcoma with scarce atypical adipocytes, lipoblasts containing spindle cell, pleomorphic, and chondroid components. The patient had uneventful recovery and remained stable during the follow-up

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period. We report this case to highlight the need for customized surgical oncological measures in the treatment of solid abdominal tumours due to locoregional invasion that usually necessitates en bloc resection.”

Recurrence of Retroperitoneal Sarcoma

Retroperitoneal sarcoma can reappear in the same area after the treatment for a previous tumour; this is called a local recurrence. It can also come back near the site of the first tumour or spread through to the abdomen. If the sarcoma does reappear, it is important to get treated as quickly as possible. It is useful to check for recurrences through self-examination: as the treating physician what to look for.

The sarcoma can also spread to another part of the body. This is called metastasis. In retroperitoneal sarcoma patients, ‘metastases may appear in the lungs, which is why a chest x-ray is usually taken at follow-up appointments.

Treatment for secondary sarcoma may involve surgery, radiotherapy or chemotherapy as appropriate. Treatment is usually assessed on an individual basis.

Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG). 2018.

Introduction: Retroperitoneal sarcoma (RPS) is a rare disease accounting for 0.1%–0.2% of all malignancies. Management of RPS is complex and requires multidisciplinary, tailored treatment strategies at all stages, but especially in the context of metastatic or multifocal recurrent disease. Due to the rarity and heterogeneity of this family of diseases, the literature to guide management is limited.

Methods: The Trans-Atlantic Retroperitoneal Sarcoma Working Group (TARPSWG) is an international collaboration of sarcoma experts from all disciplines convened in an effort to overcome these limitations. The TARPSWG has compiled the available evidence surrounding metastatic and multifocally recurrent RPS along with expert opinion in an iterative process to generate a consensus document regarding the complex management of this disease. The objective of this document is to guide sarcoma specialists from all disciplines in the diagnosis and treatment of multifocal recurrent or metastatic RPS.

Results: All aspects of patient assessment, diagnostic processes, local and systemic treatments, and palliation are reviewed in this document, and consensus recommendations provided accordingly. Recommendations were guided by available evidence, in conjunction with expert opinion where evidence was lacking.

Conclusions: This consensus document combines the available literature regarding the management of multifocally recurrent or metastatic RPS with the practical expertise of high-volume sarcoma centers from multiple countries. It is designed as a tool for decision making in the complex multidisciplinary management of this condition and is expected to standardize management across centers, thereby ensuring that patients receive the highest quality care.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments

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- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The [South African National Clinical Trials Register](#) provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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Retroperitoneal Sarcoma

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