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ORIGINAL ARTICLE – BONE AND SOFT TISSUE SARCOMAS

Management of Primary Retroperitoneal Sarcoma (RPS) in the Adult: A Consensus Approach From the Trans-Atlantic RPS Working Group

Trans-Atlantic RPS Working Group

ABSTRACT

Background. Retroperitoneal soft tissue sarcomas (RPS) are rare tumors that include several well-defined histologic subtypes. Although surgery is the mainstay of curative therapy, no universally accepted recommendations concerning the best management have been developed to date. Optimization of the initial approach is critical for maximizing patient outcomes.

Methods. An RPS Trans-Atlantic Working Group was established in 2013. The primary aim was to evaluate the current evidence critically and to develop a consensus document on the approach to this difficult disease. The outcome applies to primary RPS that is nonvisceral in origin. The evaluation included sarcomas of major veins (inferior vena cava, renal vein, ovarian/testicular vein), undifferentiated pleomorphic sarcoma of the psoas, and ureteric leiomyosarcoma (LMS). It excluded desmoid, lipoma and angiomyolipoma, gastrointestinal stromal tumors, visceral sarcomas such as those arising from the gut or its mesentery, uterine LMS, prostatic sarcoma, paratesticular/spermatic cord sarcoma, Ewing's sarcoma, alveolar/embryonal rhabdomyosarcoma, primitive peripheral neuro-ectodermal tumor, sarcoma arising from teratoma, carcinosarcoma, sarcomatoid carcinoma, clear cell sarcoma, radiation-induced sarcoma, paraganglioma, and malignant pheochromocytoma.

Results. Management of RPS was evaluated from diagnosis to follow-up, and a level of evidence was attributed to each statement. This rare and complex malignancy is best managed by an experienced multidisciplinary team in a specialized referral center. The best chance of cure is at the time of primary presentation, and an individualized management plan should be made based on the statements included in this article.

Conclusions. International collaboration is critical for adding to the current knowledge. A prospective registry will be set up.

Correspondence to: Alessandro Gronchi
Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy, e-mail: alessandro.gronchi@istitutotumori.mi.it

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Trans-Atlantic RPS Working Group

Sylvie Bonvalot, Department of Surgery, Institute Gustave Roussy, Villejuif, France
Alessandro Gronchi, Department of Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
Peter Hohenberger, Department of Surgical Oncology and Thoracic Surgery, University Hospital of Mannheim, Mannheim, Germany
Saskia Litiere, Department of Biostatistics, European Organization for Research and Treatment of Cancer (EORTC) Head Quarters, Bruxelles, Belgium
Raphael E. Pollock, Department of Surgery, Division of Surgical Oncology, Ohio State University Medical Center, Columbia, USA
Chandrajit P. Raut, Department of Surgery, Division of Surgical Oncology, Brigham and Women's Hospital, Harvard Medical School, Boston, USA
Piotr Rutkowski, Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland
Dirk Strauss, Department of Surgery, Royal Marsden Hospital, NHS Foundation Trust, London, UK
Carol J. Swallow, Department of Surgery, University of Toronto, Toronto, Canada
Frits Van Coevorden, Department of Surgical Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands

INTRODUCTION

Retroperitoneal sarcomas (RPS) are rare tumors, with an expected incidence of 0.5 to 1 new cases per 100.000 inhabitants per year.[1] Surgery is the mainstay of curative therapy, and local control is critical for outcome.[2–13]

Nevertheless, anatomic constraints in the retroperitoneum limit the ability to achieve wide resection margins. As a consequence, local recurrences of RPS are more frequent than recurrences of extremity sarcoma and comprise the leading cause of death, especially in cases of low- to intermediate-grade tumors (e.g., liposarcoma, the histopathologic subtype of approximately one-half of sarcomas arising at this site).[2–16] Other treatment methods such as radiation therapy (RT) and chemotherapy (CT) are either currently being evaluated prospectively (RT)[17] or have proved to be of limited value (CT).[18,19] Indeed, neither method is routinely used, and surgery remains the primary approach.

An RPS trans-Atlantic working group was established in 2013.[20,21] Invitations were sent to major RPS referral European and North American Institutions, actively participating to the Connective Tissue Oncology Society. Centers that accepted the invitation were included in the working group. The primary aim of the working group was to evaluate the current evidence critically and to develop a consensus document on the approach to this difficult disease. A multicenter retrospective review, currently ongoing, and a prospective registry, under preparation, also were planned.

METHODS: TERMS OF REFERENCE

The RPS trans-Atlantic working group developed guidelines based on existing data from retrospective analyses of prospectively maintained data sets by single and multi-institutions and, where possible, prospective trials. The working group met initially during the 2013 American Society of Clinical Oncology Annual Meeting in Chicago, Illinois, and the 2013 Connective Tissue Oncology Society Annual Meeting in New York City. The group formally convened during the 2013 European Society of Medical Oncology (ESMO) meeting to update the ESMO guidelines for sarcoma and gastrointestinal stromal tumor.

The following statements apply to primary RPS that is nonvisceral in origin:

- Included are sarcomas of major veins (inferior vena cava, renal vein, ovarian/testicular vein), undifferentiated pleomorphic sarcoma of the psoas, and ureteric leiomyosarcoma (LMS).
- Excluded are benign entities such as desmoid, lipoma, and angiomyolipoma.
- Excluded are gastrointestinal stromal tumors, visceral sarcomas such as those arising from the gut or its mesentery, uterine LMS, prostatic sarcoma, and paratesticular/spermatic cord sarcoma.
- Excluded are Ewing's sarcoma, alveolar/embryonal rhabdomyosarcoma, primitive peripheral neuro-ectodermal tumor, sarcoma arising from teratoma, carcinosarcoma, sarcomatoid carcinoma, clear cell sarcoma, and radiation-induced sarcoma.
- Excluded are paraganglioma and malignant pheochromocytoma.

The excluded entities also are rare tumors, and patients generally benefit from pretreatment pathologic diagnosis as well as multidisciplinary discussion and decision making at a center specializing in the management of soft tissue sarcomas.

In evaluating the newly identified undiagnosed retroperitoneal (RP) mass, a wide spectrum of possible diagnoses must be considered. In particular, metastatic adenocarcinoma, lymphoma, germ cell tumor, and paraganglioma should be ruled out.

RESULTS: STATEMENTS OF PRINCIPLE AND RECOMMENDED PRACTICE

Principles of recommended practice from diagnosis to follow-up evaluation are summarized in 26 statements. Each statement has been attributed a level of evidence according to the scale reported in Table 1.[22]

1. As a rare and complex malignancy, RPS is best managed by an experienced multidisciplinary team in a specialized reference center (IVA).[23–26]

Staging and Preoperative Assessment

2. The optimal management of RPS is facilitated by pretreatment diagnosis and staging.[25,26]

   2a. Thorough review of cross-sectional imaging by a specialized sarcoma tumor board is required (IVA).

   2b. The standard method for staging is contrast tomography (CT) scan of the chest/abdomen/pelvis with IV contrast. Magnetic resonance imaging (MRI) is an option for patients with IV CT contrast allergy or other contraindication, Li-Fraumeni syndrome, or pelvic tumors and for assessing the extent of tumor to specific sites (i.e., vertebral foramina, sciatic notch) that is not clear on the CT scan (VA).

   2c. Functional assessment of the contralateral kidney typically is necessary for planning treatment of

TABLE 1 Level of evidence (LOE) and grade of recommendation (GOR) adapted from the Infectious Diseases Society of American-United States Public Health Service Grading System

I	Evidence from at least one large randomized–control trial of good methodologic quality (low potential for bias) or meta-analyses of well-conducted randomized trials without heterogeneity
II	Small or large randomized trials with a suspicion of bias (lower methodologic quality) or meta-analyses of such trials or those with demonstrated heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case–control studies
V	Studies without control group, case reports, experts opinions
A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (e.g., adverse events, costs), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

the ipsilateral RPS. This may be achieved using CT with IV contrast or differential renal scanning (VA).

2d. Bone scan, head CT, brain MRI, and positron emission tomography (PET) scanning usually are NOT required (VD).

3. Image-guided percutaneous coaxial core needle biopsy (14 or 16 gauge) is strongly recommended (Fig. 1) unless the imaging is pathognomonic (e.g., heterogeneous dedifferentiated/well-differentiated liposarcoma) and no preoperative treatment is planned (IVA).[25–28]

   3a. Multiple needle cores should be obtained to allow for histologic and molecular subtyping (VA).

   3b. Repeat core biopsy with more aggressive sampling may be required (VB).

   3c. Sampling of the more solid, dedifferentiated tumor component represented by well-perfused areas in contrast-enhanced CT or contrast-enhanced MRI is encouraged (IVA).[29] If [18F]Fluorodeoxyglucose ([18F]FDG)-PET is available, hot spots with high standard uptake value (SUV) are the target areas of biopsy (IVA).[29]

   3d. Risk of needle track seeding is minimal and should not be a reason to avoid a biopsy (IVA).[27,28]

4. Fine-needle aspiration (FNA)/cytology rarely yields diagnostic information, causes delay in treatment, and should be avoided (VE).
5. Laparotomy and open biopsy of suspected RPS should be avoided. This practice exposes the peritoneal cavity to contamination by sarcoma, distorts subsequent planes of dissection, may not provide diagnostic tissue due to lack of three-dimensional image guidance, and may put vital neurovascular structures at risk (VE).
6. Laparoscopic biopsy of suspected RPS carries the same risks as open biopsy (VE).

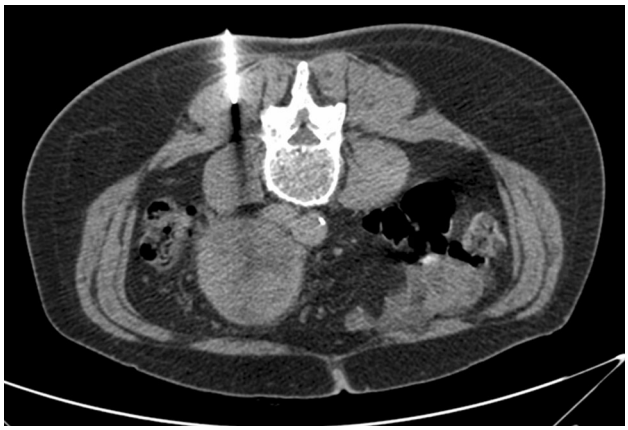

FIG. 1 Contrast enhanced Computed Tomography scan of a right retroperitoneal mass in a 56-year old man: precutaneous 16 gauge core needle biopsy to establish preoperative histologic diagnosis and plan the approach at the multidisciplinary Sarcoma conference

7. If at open or laparoscopic exploration for suspected adnexal mass, no abnormalities of the uterus, fallopian tubes, or ovaries are found but an RP mass is detected, it is recommended that nothing further be done at that time. The patient should undergo subsequent dedicated imaging. If appropriate imaging studies are already available at the time of exploration, open core needle biopsy can be considered but should be performed in a way that minimizes the risk of peritoneal contamination and maximizes the chance of obtaining lesional tissue. Frozen sections should not be taken because decisions should be based only on final pathology. If doubt exists as to these conditions, no biopsy should be performed intraoperatively (VA).
8. If at open or laparoscopic hernia repair or during any other abdominal procedure an RP mass is detected, it is recommended that nothing further be done to assess or explore the mass at that time. The patient should undergo subsequent dedicated imaging. If appropriate

imaging studies are already available at the time of exploration, open core needle biopsy can be considered but should be performed in a way that minimizes the risk of peritoneal contamination and maximizes the chance of obtaining lesional tissue. If there is doubt as to these conditions, no biopsy should be performed intraoperatively (VA).

Primary Surgical Approach

9. The best chance of resection with curative intent is at the time of primary presentation. The individual management plan should be determined after discussion at a multidisciplinary sarcoma case conference with presentation of both imaging and pathologic findings (IIIA).[2–13]
   - 9a. This applies equally to well-differentiated retroperitoneal liposarcoma and to the large radiographically "benign" lipomatous mass (VA).[13]
   - 9b. The multidisciplinary team that makes management decisions should include a surgeon with specialized training in resection of RPS (VA).
10. Biologic behavior, response to treatment, and clinical outcomes vary by histologic subtype of RPS. The management plan, including the plan for resection, should be developed in recognition of this (IIIA).[30,31]
11. Because RPS can grow to a very large size without causing symptoms, patients may present late with symptoms of mass effect (e.g., malnutrition, shortness of breath, debility). Performance status should be assessed as part of the development of an individual management plan, and nutritional support, physiotherapy, and the like may be required in concert with preoperative planning (VB).
12. Complete gross resection is the cornerstone of management (IIIA).[2–13]
    - 12a. In the case of primary RPS, surgery should be aimed at achieving macroscopically complete resection, with a single specimen encompassing the tumor and involved contiguous organs, and at minimizing microscopically positive margins. This is best achieved by resecting the tumor en bloc with adherent structures even if not overtly infiltrated (IIIA)[32] (Fig. 2).
    - 12b. In primary RPS, preservation of specific organs (e.g., kidney, duodenum, bladder) should be considered on an individualized basis and mandates specific expertise in the disease for appropriate decisions to be made given the overall tumor extent/expected biology and given the individual patient's characteristics (VA). Judgment must be used in deciding which neurovascular structures to sacrifice, with the potential for local control weighed against the potential for long-term dysfunction. Judgment must similarly be exercised in determining appropriateness of en bloc resection of liver and pancreas (VA).
    - 12c. Resection of RPS requires technical expertise in multiple sites throughout the abdominal and pelvic cavity, including the handling of large vessels. Single organ or site expertise is not sufficient (VA).
    - 12d. The ability to orchestrate a team of complementary surgical experts is critical to successful management of RPS patients (VA).
    - 12e. Surgical expertise in RPS resection requires specific anatomic knowledge of the retroperitoneal space to minimize the risk of intra- and perioperative morbidity. Examples include retroperitoneal autonomic and somatic nerves, the lymphatic system, paravertebral vessels, and organs of the gastrointestinal tract. The required expertise also includes experience with additional procedures such as full-thickness thoracoabdominal wall resection and reconstruction, diaphragmatic resection and reconstruction, major vascular resection and reconstruction, and bone resection. These abilities, which may accrue from the participation of multidisciplinary surgical teams, can make it possible to achieve macroscopically complete tumor resection in the majority of patients. Members of the surgical team must be familiar with the functional consequences of major neurovascular ablation (VA).
    - 12f. In cases of loco-regional recurrences, surgery still may reproduce what is done for primary RPS if the first operation consisted of a simple excision. Otherwise, it should be aimed simply at achieving macroscopic complete resection, including surrounding organs only when overtly infiltrated (IVA).[13]
13. Grossly incomplete resection of RPS is of questionable benefit and potentially harmful, and can be regarded only as potentially palliative for carefully selected patients. Grossly incomplete resection is to be avoided by informed imaging review, thoughtful planning, and referral to another center if appropriate (IIIA).[2–13]
14. Complete resection of large RPS may involve a long and complex operative procedure. Anesthesiologists and nurses experienced with such procedures, including vascular resection and reconstruction, are essential to a successful operative outcome (VA).

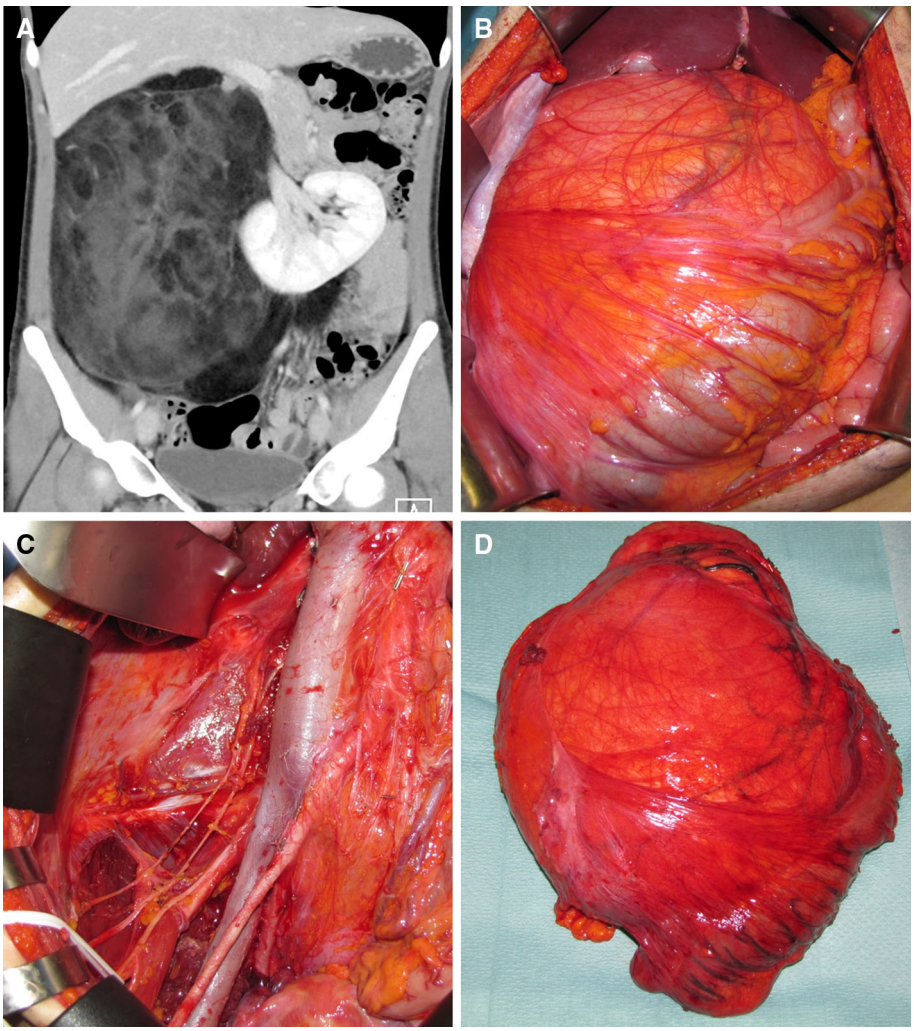

FIG. 2 Dedifferentiated liposarcoma in a 44-year-old woman. **a** Contrast-enhanced computed tomography scan of right retroperitoneal mass. **b** Tumor at laparotomy. **c** Surgical field after tumor removal. **d** Surgical specimen. The tumor is covered by the right kidney and colon (and psoas muscle in the back, not shown)

14a. The approach to intra- and postoperative management (including warming techniques, transfusions, anticoagulation, analgesia, nutrition, physiotherapy, and so forth) should be standardized and agreed upon by relevant stakeholders (VA).

14b. Extended peritoneal stripping and retroperitoneal space exposure, together with long operative times, can result in significant fluid shifts and requirement for fluid resuscitation, including colloids (VA).

14c. An advanced postoperative monitoring environment usually is appropriate (VA).

14d. Serious life-threatening complications can develop immediately or in a delayed manner after resection of RPS. Postoperative care should be undertaken by an experienced team of physicians and nurses (VA).

15. Liposarcoma (LPS) is the most common histologic subtype of RPS. The principal site of RP LPS recurrence is intraabdominal/loco-regional in the erstwhile retroperitoneum (IIIA).[2–13,30,31] Strategies to reduce intraabdominal recurrence should be pursued.

16. Intraoperatively, low-grade LPS appears grossly similar to normal fat, and frozen section evaluation of marginal or "suspicious" tissue usually is not helpful. The extent of resection in LPS should be guided by asymmetry shown on preoperative imaging, knowledge of functional anatomy, and experience with patterns of recurrence. Complete resection of all RP fatty tissue at risk for harboring tumor is ideal (IIIA).[11–13,32]

17. In general, use of intraoperative frozen sections is unlikely to be helpful or to alter the extent of a well-planned and carefully executed resection. Thus, the operative plan should be crafted based on other sources of data. The approach should be imaging based, deliberate, and not "exploratory," avoiding dissection in marginal tumor planes. Frozen section analysis may be of assistance in particular circumstances, for instance, in cases of vascular LMS or to assess neural margins of excision (VA).

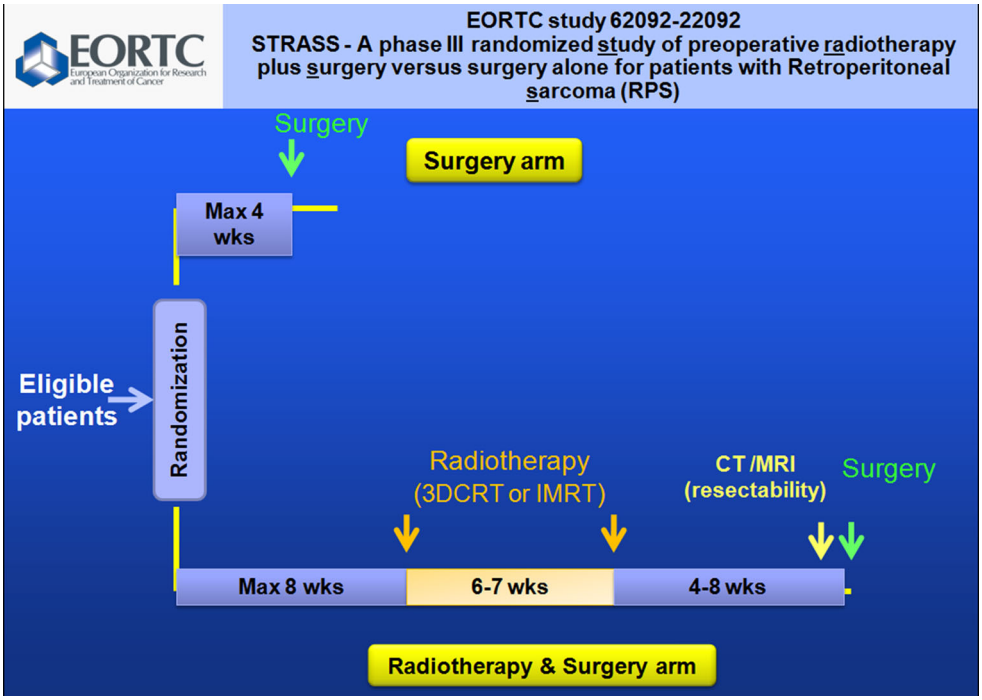

FIG. 3 Preoperative radiotherapy prospective randomized trial (EORTC 62092–STRASS): study design

Adjuvant/Neoadjuvant Therapies

18. Although no randomized trials of neoadjuvant therapy versus resection alone for RPS have been reported to date, neoadjuvant therapy in the form of chemotherapy, chemotherapy combined with deep-wave hyperthermia, external beam radiation, or combined radiation and chemotherapy is safe for well-selected patients and may be considered after careful review by a multidisciplinary sarcoma tumor board (IVC).[33–42] This is particularly relevant in the case of technically unresectable/borderline resectable RPS that could potentially be rendered resectable by downsizing, and also for chemo-sensitive histologies such as synovial sarcoma,[43] LMS of the inferior vena cava, and the like (VC). The sensitivity of solitary fibrous tumor to X-ray therapy (XRT) also should be considered (IVB).[44]
19. Intraoperative radiation therapy (IORT, with electron beam) is of no study-proven value. Although it may be considered for margins considered at risk, the field often is too large for its practical application (IVE).[45–50]
20. Postoperative/adjuvant external beam radiation after complete gross resection is of no study-proven value and is associated with significant short- and long-term toxicities. A therapeutic XRT dose can be achieved for the minority of patients after resection [51,52] (IVE).
21. At this writing, an international cooperative trial (STRASS) is examining the potential benefit of preoperative XRT in RPS (Fig. 3).[17]
22. Brachytherapy is of no study-proven value and may be associated with significant short- and long-term complications (IVE).[53–55]
23. Postoperative/adjuvant chemotherapy after complete gross resection is of no study-proven value (IE).[18,19]

Follow-up Evaluation

24. Risk of recurrence after grossly complete resection of RPS does not plateau, even after 15 to 20 years. Patients should be followed indefinitely (IIIA).[2–16]
    - 24a. The median time to recurrence of high-grade RPS is less than 5 years after definitive treatment (IIIA).[2–16]
    - 24b. Recurrence shown on imaging may antedate symptomatic recurrence by months to years. Follow-up assessment should include clinical evaluation and cross-sectional imaging (VA).
    - 24c. The interval between follow-up evaluations is not evidence based but should likely be shorter initially (e.g., 3–6 months). After 5 years, annual follow-up evaluation is appropriate (VB).
25. Every effort should be made to enter eligible patients into international collaborative prospective trials or registries (VA).
26. Evaluations of long-term function and quality of life after therapy for RPS are lacking. Ideally, quality of life should be assessed both pre- and postoperatively (VA).

CONCLUSION

Given the rarity of RPS, international collaboration is critical for adding to the current knowledge. Besides surgeons, medical and radiation oncologists will be invited to join the working group. Participating centers will contribute individual data to carry out a comprehensive retrospective multicentric analysis of prognostic factors and outcomes of primary RPS as well as post-relapse outcomes. This analysis will be the subject of a future publication. Moreover, this international collaboration will be facilitated by entry of all RPS patients into a prospective registry. Other centers willing to join this initiative will be most welcome. This registry will include standardized guideline definitions of imaging for diagnosis, the extent of surgical resection, and the administration of complementary therapies, allowing us to compare our results openly in the near future.

Conflict of interest There are no conflicts of interest.

REFERENCES

1. Cormier JN, Gronchi A, Pollock RE. Soft tissue sarcomas. In: Brunicardi F, Andersen D, Billiar T, Dunn D, Hunter J, Matthews J, Pollock RE (eds) Schwartz's principles of surgery. New York: McGraw-Hill; 2014.
2. Lewis JJ, Leung D, Woodruff JM. Retroperitoneal soft-tissue sarcoma: analysis of 500 patients treated and followed at a single institution. *Ann Surg.* 1998;228:355–65.
3. Stoeckle E, Coindre JM, Bonvalot S, et al. Prognostic factors in retroperitoneal sarcoma: a multivariate analysis of a series of 165 patients of the French Cancer Center Federation Sarcoma Group. *Cancer.* 2001;92:359–68.
4. Gronchi A, Casali PG, Fiore M, et al. Retroperitoneal soft tissue sarcomas: patterns of recurrence in 167 patients treated at a single institution. *Cancer.* 2004;100:2448–55.
5. Hassan I, Park SZ, Donohue JH, et al. Operative management of primary retroperitoneal sarcomas: a reappraisal of an institutional experience. *Ann Surg.* 2004; 239:244–50.
6. van Dalen T, Plooij JM, van Coevorden F, et al. Long-term prognosis of primary retroperitoneal soft tissue sarcoma. *Eur J Surg Oncol.* 2007;33:234–8.
7. Lehnert T, Cardona S, Hinz U, et al. Primary and locally recurrent retroperitoneal soft-tissue sarcoma: local control and survival. *Eur J Surg Oncol.* 2009;35:986–93.
8. Anaya DA, Lahat G, Liu J, et al. Multifocality in retroperitoneal sarcoma: a prognostic factor critical to surgical decision making. *Ann Surg.* 2009;249:137–42.
9. Strauss DC, Hayes AJ, Thway K, et al. Surgical management of primary retroperitoneal sarcoma. *Br J Surg.* 2010;101: 520–3.
10. Bonvalot S, Rivoire M, Castaing M, et al. Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. *J Clin Oncol.* 2009;27:31–7.
11. Gronchi A, Lo Vullo S, Fiore M, et al. Aggressive surgical policies in a retrospectively reviewed single-institution case series of retroperitoneal soft tissue sarcoma patients. *J Clin Oncol.* 2009;27:24–30.
12. Bonvalot S, Miceli R, Berselli M, et al. Aggressive surgery in retroperitoneal soft tissue sarcoma carried out at high-volume centers is safe and is associated with improved local control. *Ann Surg Oncol.* 2010;17:1507–14.
13. Gronchi A, Miceli R, Colombo C, et al. Frontline extended surgery is associated with improved survival in retroperitoneal low-intermediate grade soft tissue sarcomas. *Ann Oncol.* 2012;23:1067–73.
14. Singer S, Antonescu CR, Riedel E, et al. Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. *Ann Surg.* 2003;238:358–70.
15. Dalal KM, Kattan MW, Antonescu CR, et al. Subtype-specific prognostic nomogram for patients with primary liposarcoma of the retroperitoneum, extremity, or trunk. *Ann Surg.* 2006;244: 381–91.
16. Canter RJ, Qin LX, Ferrone CR, et al. Why do patients with low-grade soft tissue sarcoma die? Ann Surg Oncol. 2008;15: 3550–60.
17. http://clinicaltrials.gov/ct2/show/NCT01344018. Accessed 14 Feb 2014.
18. Pervaiz N, Colterjohn N, Farrokhyar F, et al. A systematic meta-analysis of randomized controlled trials of adjuvant chemotherapy for localized resectable soft-tissue sarcoma. *Cancer.* 2008;113:573–81.
19. Woll PJ, Reichardt P, Le Cesne A, et al. Adjuvant chemotherapy with doxorubicin, ifosfamide, and lenograstim for resected soft-tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial. *Lancet Oncol.* 2012;13:1045–54.
20. Gronchi A, Pollock RE. Surgery in retroperitoneal soft tissue sarcoma: a call for a consensus between Europe and North America. *Ann Surg Oncol.* 2011;18: 2107–10.
21. Gronchi A, Pollock RE. Quality of local treatment or biology of the tumor: which are the trump cards for loco-regional control of retroperitoneal sarcoma? *Ann Surg Oncol.* 2013;20:2111–13.
22. Dykewicz CA. Summary of the guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *Clin Infect Dis.* 2001;33:139–44.
23. Gutierrez JC, Perez EA, et al. Should soft tissue sarcomas be treated at high-volume centers? An analysis of 4,205 patients. *Ann Surg.* 2007;245:952–8.
24. Heudel PE, Cousin P, Lurkin A, et al. Territorial inequalities in management and conformity to clinical guidelines for sarcoma patients: an exhaustive population-based cohort analysis in the Rhône-Alpes region. *Int J Clin Oncol.* 2014;19:744–52.
25. von Mehren M, Benjamin RS, Bui MM, et al. Soft tissue sarcoma, version 2.2012: featured updates to the NCCN guidelines. *J Natl Compr Cancer Netw.* 2012;10:951–60.
26. ESMO/European Sarcoma Network Working Group. Soft tissue and visceral sarcomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol.* 2012;23(Suppl 7):vii92–9.
27. Miah AB, Hannay J, Benson C, et al. Optimal management of primary retroperitoneal sarcoma: an update. *Expert Rev Anticancer Ther.* 2014;14:565–79.
28. Strauss DC, Hayes AJ, Thomas JM. Preoperative core needle biopsy is safe and does not affect oncological outcome in retroperitoneal sarcoma. Poster HH, p. 112, CTOS 17th Annual Meeting, November 2012.
29. Lahat G, Madewell JE, Anaya DA, et al. Computed tomography scan-driven selection of treatment for retroperitoneal liposarcoma histologic subtypes. *Cancer.* 2009;115:1081–90.
30. Gronchi A, Miceli R, Shurell E, et al. Outcome prediction in primary resected retroperitoneal soft tissue sarcoma: histology-specific overall survival and disease-free survival nomograms built on major sarcoma center data sets. J Clin Oncol. 2013;31:1649–55.

31. Toulmonde M, Bonvalot S, Méeus P, et al. Retroperitoneal sarcomas: patterns of care at diagnosis, prognostic factors, and focus on main histological subtypes: a multicenter analysis of the French Sarcoma Group. *Ann Oncol.* 2014;25:735–42.
32. Bonvalot S, Raut CP, Pollock RE, et al. Technical considerations in surgery for retroperitoneal sarcomas: position paper from E-Surge, a master class in sarcoma surgery, and EORTC-STBSG. *Ann Surg Oncol.* 2012;19:2981–91.
33. Pisters PW, O'Sullivan B. Retroperitoneal sarcomas: combined modality treatment approaches. *Curr Opin Oncol.* 2002;14:400–5.
34. Gilbeau L, Kantor G, Stoeckle E, et al. Surgical resection and radiotherapy for primary retroperitoneal soft tissue sarcoma. *Radiother Oncol.* 2002;65:137–43.
35. Pawlik TM, Pisters PW, Mikula L, et al. Long-term results of two prospective trials of preoperative external beam radiotherapy for localized intermediate- or high-grade retroperitoneal soft tissue sarcoma. *Ann Surg Oncol.* 2006;13:508–17.
36. Feng M, Murphy J, Griffith KA, et al. Long-term outcomes after radiotherapy for retroperitoneal and deep truncal sarcoma. *Int J Radiat Oncol Biol Phys.* 2007;69:103–10.
37. Ballo MT, Zagars GK, Pollock RE, et al. Retroperitoneal soft tissue sarcoma: an analysis of radiation and surgical treatment. *Int J Radiat Oncol Biol Phys.* 2007;67:158–63.
38. Paryani NN, Zlotecki RA, Swanson EL, et al. Multimodality local therapy for retroperitoneal sarcoma. *Int J Radiat Oncol Biol Phys.* 2012;82:1128–34.
39. Smith MJ, Ridgway PF, Catton CN, et al. Combined management of retroperitoneal sarcoma with dose intensification radiotherapy and resection: long-term results of a prospective trial. *Radiother Oncol.* 2014. doi:10.1016/j.radonc.2013.10.041.
40. Pisters PW, Ballo MT, Fenstermacher MJ, et al. Phase I trial of preoperative concurrent doxorubicin and radiation therapy, surgical resection, and intraoperative electron-beam radiation therapy for patients with localized retroperitoneal sarcoma. *J Clin Oncol.* 2003;21:3092–7.
41. Gronchi A, De Paoli A, Dani C, et al. Preoperative chemo-radiation therapy for localized retroperitoneal sarcoma: a phase I-II study from the Italian Sarcoma Group. *Eur J Cancer.* 2014;50:784–92.
42. Angele MK, Albertsmeier M, Prix NJ, et al. Effectiveness of regional hyperthermia with chemotherapy for high-risk retroperitoneal and abdominal soft-tissue sarcoma after complete surgical resection: a randomized phase-III multicenter study. *Ann Surg.* (in press).
43. Canter RJ, Qin LX, Maki RG, et al. A synovial sarcoma-specific preoperative nomogram supports a survival benefit to ifosfamide-based chemotherapy and improves risk stratification for patients. *Clin Cancer Res.* 2008;14:8191–7.
44. Saynak M, Bayir-Angin G, Kocak Z, et al. Recurrent solitary fibrous tumor of the pleura: significant response to radiotherapy. *Med Oncol.* 2010;27:45–8.
45. Radaelli S, Stacchiotti S, Casali PG, et al. Emerging therapies for adult soft tissue sarcoma. *Expert Rev Anticancer Ther.* 2014;14:689–704.
46. Alektiar KM, Hu K, Anderson L, et al. High-dose-rate intraoperative radiation therapy (HDR-IORT) for retroperitoneal sarcomas. *Int J Radiat Oncol Biol Phys.* 2000;47:157–63.
47. Gieschen HL, Spiro IJ, Suit HD, et al. Long-term results of intraoperative electron beam radiotherapy for primary and recurrent retroperitoneal soft tissue sarcoma. *Int J Radiat Oncol Biol Phys.* 2001;50:127–31.
48. Yoon SS, Chen YL, Kirsch DG, et al. Proton-beam, intensity-modulated, and/or intraoperative electron radiation therapy combined with aggressive anterior surgical resection for retroperitoneal sarcomas. *Ann Surg Oncol.* 2010;17:1515–29.
49. McBride SM, Raut CP, Lapidus M, et al. Loco-regional recurrence after pre-operative radiation therapy for retroperitoneal sarcoma: adverse impact of multifocal disease and potential implications of dose escalation. *Ann Surg Oncol.* 2013;20:2140–7.
50. Roeder F, Schulz-Ertner D, Nikoghosyan AV, et al. A clinical phase I/II trial to investigate preoperative dose-escalated intensity-modulated radiation therapy (IMRT) and intraoperative radiation therapy (IORT) in patients with retroperitoneal soft tissue sarcoma. *BMC Cancer.* 2012;12:287.
51. Le Péchoux C, Musat E, Baey C, et al. Should adjuvant radiotherapy be administered in addition to front-line aggressive surgery (FAS) in patients with primary retroperitoneal sarcoma? *Ann Oncol.* 2013;24:832–7.
52. Paryani NN1, Zlotecki RA, Swanson EL, et al. Multimodality local therapy for retroperitoneal sarcoma. *Int J Radiat Oncol Biol Phys.* 2012;82:1128–34.
53. Mohindra P, Neuman HB, Kozak KR. The role of radiation in retroperitoneal sarcomas. *Curr Treat Options Oncol.* 2013;14:425–41.
54. Smith MJ, Ridgway PF, Catton CN, et al. Combined management of retroperitoneal sarcoma with dose intensification radiotherapy and resection: long-term results of a prospective trial. *Radiother Oncol.* 2014;110:165–71.
55. Dziewirski W1, Rutkowski P, Nowecki ZI, et al. Surgery combined with intraoperative brachytherapy in the treatment of retroperitoneal sarcomas. *Ann Surg Oncol.* 2006;13:245–52.