Surgical Management of Retroperitoneal Sarcoma

Subjects: Surgery

Contributor: Dana A. Dominguez, Sagus Sampath, Mark Agulnik, Yu Liang, Bao Nguyen, Vijay Trisal, Laleh G. Melstrom, Aaron G. Lewis, Isaac Benjamin Paz, Randall F. Roberts, William W. Tseng

Surgery is the cornerstone of treatment for retroperitoneal sarcoma (RPS). Surgery should be performed by a surgical oncologist with sub-specialization in this disease and in the context of a multidisciplinary team of sarcoma specialists. For primary RPS, the goal of surgery is to achieve the complete en bloc resection of the tumor along with involved organs and structures to maximize the clearance of the disease. The extent of resection also needs to consider the risk of complications.

Keywords: retroperitoneal sarcoma ; liposarcoma ; leiomyosarcoma

1. Preoperative Planning

The surgeries performed for RPS are major undertakings that involve planning and preparation, even before arriving at the operating room. RPS operations often last many hours, can involve the concurrent resection of multiple organs/structures and, overall, may be associated with significant blood loss, risk of complications and even intra- or postoperative death. The RPS patient, often anxious to “get it out”, should be counseled appropriately about the potential extent of surgery and subsequent impact on quality of life. While preoperative imaging is useful to anticipate important details of resection, the true extent of surgery may only be realized intraoperatively.

Any pre-existing co-morbidities should undergo medical evaluation in anticipation of major surgery. Those with borderline or pre-existing renal insufficiency may need further investigation (e.g., split renal perfusion scan) to determine the tolerance of an ipsilateral nephrectomy. Those with significant cardiopulmonary disease should undergo updated evaluation (e.g., echocardiogram) and, if needed, intervention to improve organ function as much as possible. Patients with diminished reserve may not tolerate a major RPS operation and data from preoperative medical evaluation can impact decision-making for RPS surgery. Importantly, for all RPS patients, careful screening for malnutrition should be carried out and protein-caloric intake improved to help optimize the outcome for surgery [1][2][3].

Depending on individual and institutional practice, the surgeon may find it useful to obtain outpatient consultations with other surgical services as part of the preoperative planning for RPS surgery. This may include the vascular surgeon if major vessel resection and reconstruction are likely, or the urologist, for intraoperative stent placement or possible extended bladder resection. As RPS surgery can go beyond the typical “abdominal case”, advanced discussion with the anesthesiologist is often helpful to anticipate potential intraoperative needs (e.g., blood products) and the appropriate level of venous access and hemodynamic monitoring.

2. Surgical Approach

The standard incision most commonly used is a wide midline laparotomy, as this permits the most access to the tumor and the great vessels (aorta, inferior vena cava or IVC, and iliac vessels). Lateral extension of the incision to provide access to the side of the tumor may be added or an entirely different incision (e.g., lateral thoracoabdominal) may also be appropriate, depending on each case and the surgeon preference. The key to any incision in RPS surgery is that it needs to provide optimal, safe exposure to the tumor and surrounding organs and critical structures.

The goal of RPS surgery is to achieve the complete en bloc resection of the tumor along with involved adjacent organs and structures to maximize clearance of the disease. The type of resection can be defined as R0 (complete resection with negative microscopic margins), R1 (complete resection with positive microscopic margins) or R2 (incomplete resection). In primary disease, the piecemeal, partial removal (debulking/R2 resection) or rupture of the tumor should be strongly avoided, as this has been demonstrated to have a detrimental effect on oncologic outcomes. Multiple large cohorts examining prognostic factors for OS have demonstrated significant hazard ratios from 1.70–2.20 for an R2 resection when controlling for other predictive factors [4][5][6]. In fact, in some studies, patients who had an R2 resection had equivalent

outcomes to patients who underwent biopsy alone, adding the risk of surgical morbidity, without any added benefit [7][8][9]. Regrettably, inadvertent incomplete resection is sometimes carried out by a non-specialist surgeon for liposarcoma when the obvious high grade or dedifferentiated component of the tumor is removed while the surrounding lipomatous low grade or well differentiated disease is left behind. A non-specialist may also perform lymph node dissection, which is completely unnecessary in RPS and can expose the patient to undue risk (e.g., chylous leak).

At minimum, complete gross resection should be achieved in each case. Microscopic negative margins (R0) can be strived for; however, this is frequently difficult if not overtly impossible to achieve [10]. Within the restricted abdominal space, the large size of RPS tumors would hypothetically necessitate the removal of all abutted organs, structures and even surfaces (e.g., posterior retroperitoneum). Accurate pathologic margin assessment of all “inked” surfaces on the resection specimen is also not practical, particularly for larger tumors. If R0 resection is truly achieved, this is likely associated with an improved outcome [11]; however, the data to support this is likely biased (e.g., smaller tumors). The consensus among most sarcoma specialists is that in describing RPS surgery, it is more appropriate to distinguish between R2 (gross disease left behind) and R0/R1 resection.

The obvious tumor involvement of organs and structures, ideally anticipated during preoperative planning (e.g., imaging review), does necessitate concomitant resection. In recent, large series reported by single and multi-institutional sarcoma centers, resection of one or more organs is carried out in 58–87% of all cases of primary RPS [12][13]. Most commonly, ipsilateral nephrectomy and partial colectomy are performed in more than half (55–57%) of all cases. With appropriate planning and available support (e.g., vascular surgeon), resection of involved major vessels (e.g., IVC) can be performed; however, the frequency of this is less common (10–15%). An additional, laterality-specific organ resection may be needed depending on the patient case. For left sided tumors, distal pancreatectomy and splenectomy may be required [14]; for right sided tumors, pancreaticoduodenectomy (Whipple) can be considered, but is in fact rarely carried out (1.4% of cases) [15].

To maximize the clearance of the disease, sarcoma specialists in Italy and France have described an extended or compartmental approach to resection [6][16]. The fundamental concept is that even without obvious tumor involvement, adjacent organs, structures and even surfaces (e.g., psoas fascia) should be resected en bloc with the tumor in an effort to obtain circumferential “soft tissue margins”. This is analogous to obtaining wide soft tissue margins in high grade, extremity sarcoma but adapted to the retroperitoneum. When first introduced, this approach generated controversy [17][18] and to date, extended or compartmental resection in primary RPS is not universally accepted across sarcoma centers, particularly in the United States. In concept, in an appropriately selected patient, when technically feasible and safe, extended resection should be applied to strive for an R0 resection; in daily practice, extended resection may have a more limited application to liposarcoma and after consideration of the entirety of each patient’s situation (e.g., co-morbidities, expected oncologic outcome).

For organ abutment without obvious tumor involvement, the decision to resect should consider the “expendability” of the organ and risk for complications. One kidney or a portion of colon is well tolerated in most patients. By comparison, in a recent review of major vascular resection RPS, sarcoma specialists have advocated for the dissection of tumor-abutted vessels if feasible, as opposed to resection [19]. Aligned with this, even for extended or compartmental resection, component procedures that are potentially morbid (e.g., major vascular resection or Whipple) are carried out only for overt invasion [20].

Several studies have investigated the frequency of microscopic infiltration in resected organs in an attempt to help guide surgical decision making [21][22]. These data are inherently biased in that only resected tissue is available for study and the level of pathologic assessment is not standardized. Histologic organ invasion is common, but not universal across all resected organs and the frequencies of involvement vary by organ, the histologic type of RPS and from study to study. As such, the decision to resect abutted organs and structures is arguably still controversial and, clinically, one must consider potential morbidity while maintaining oncologic principles (e.g., no gross violation of tumor integrity) with the goal of at least a complete en bloc resection.

A histology-based approach to RPS surgery in primary disease has recently gained increased recognition among sarcoma specialists [10][23][24][25]. This surgical approach considers the anticipated origin and local extent of the tumor based on an intimate understanding of histologic type. For example, in the retroperitoneum, a (right sided) leiomyosarcoma may arise from the IVC and a malignant peripheral nerve sheath tumor from the nerve root. As such, the maximum clearance of disease is focused on these key areas while achieving minimum complete gross resection elsewhere. In fact, frozen section analysis of these key “margins” (e.g., IVC in leiomyosarcoma) may be beneficial. For liposarcoma, the need to further clear “at risk” adjacent fat remains controversial and may support an extended resection. A histology-based

approach in retroperitoneal liposarcoma must incorporate differences (e.g., local invasiveness) in tumors that are entirely well differentiated versus those with a dedifferentiated component. A lipoma-like well differentiated liposarcoma next to the duodenum and head of pancreas, as an example, is very different from a grade 3 dedifferentiated liposarcoma, even when controlled for tumor size. For all retroperitoneal liposarcoma, there is also the possibility of multifocal disease–defined as the synchronous presence of two or more tumors–which although rare, can occur in primary disease [26][27]. Importantly, with histology based RPS surgery, the surgical approach (e.g., need for extended resection) is also dependent on the potential patterns of future recurrence. Extended resection may not be necessary for leiomyosarcoma which has a much greater risk of distant than local recurrence or for a solitary fibrous tumor which has a minimal risk for either event [25].

Beyond primary disease, the surgical management of locally recurrent RPS is less well-defined. In this patient population, negative prognostic factors include a higher number of organs resected at the initial surgery, age at second surgery, multifocality at second surgery, high grade, incomplete resection and dedifferentiated liposarcoma histology [28]. Local recurrence is an especially challenging issue for retroperitoneal liposarcoma. In this histologic type, data from a single high volume sarcoma center suggests that a growth rate of greater than one centimeter per month can be considered to identify patients that may not benefit from resection [29]; however, this “rule” is not universally accepted. In liposarcoma, the issue of local recurrence is further complicated by second, even third and beyond recurrences, as well as late recurrence after a prolonged disease-free interval. While there exists some skepticism about the benefit of surgery in locally recurrent RPS [30], there is also data to support surgery in select patients, even after multiple recurrences [31][32]. The decision to operate on recurrent disease is complex and in daily practice should be discussed among a multidisciplinary team of RPS specialists and consider other treatment modalities.

3. Morbidity of Surgery

The operations performed for RPS are often challenging and overall, the morbidity can be substantial. In a large multi-institutional series of patients with primary disease, the frequency of severe complications, defined as Clavien-Dindo grade 3 or higher, was 16.4% [33]. Reoperation was required in 10.5% of patients and within 30 days of surgery, 1.8% died. Not surprisingly, resections that involved major vessels or pancreaticoduodenectomy had the highest association with severe complications. In this series, the frequency of any grade complication was not reported. In other single and multi-institutional series from sarcoma specialist centers, these data range from 27–34% with a recent outlier of 82.9% [34][35][36].

As discussed, concomitant multiorgan resection occurs often in RPS surgery and the risk of complications can be additive with each component of the operation. As an example, an RPS patient who undergoes concomitant distal pancreatectomy/splenectomy or left colectomy may develop a leak that could jeopardize an iliac artery reconstruction. Clinically, the totality of complications can also be subtle (e.g., additional massive third-spacing in a post-nephrectomy patient) and compounded by pre-existing co-morbidities and malnutrition, when present. As a result, there is increasing recognition of the need for better tools to account for these situations, such as the “comprehensive complication index” [36][37][38]. The uniqueness and complexity of RPS surgery again highlights the need for management by a specialist.

4. Outcomes after Surgery

Despite aggressive surgery with en bloc multiorgan resection, LR in primary RPS remains high. Reported LR rates from specialist centers vary up to 49% at 5 years [6][12][13][39][40][41][42][43]. These rates were not significantly improved, even in cohorts reporting the highest rates of complete resection (>90%) [12][39]. Multiple studies have identified factors associated with increased LR risk, including histologic type, grade, receipt of radiation therapy and completeness of resection [10]. Extended or compartmental resection with the liberalized en bloc resection of adjacent organs/structures is associated with lower reported rates of LR [6][16]. In the single center study from Italy, a significant decrease in LR (49.3 vs. 27.8%, $p < 0.0001$) was found when comparing patient outcomes before and after the implementation of this surgical approach [16]. Similarly, in a multi-institutional study from France, patients who underwent extended resection had a 3.3-fold decrease in LR versus those who underwent standard (but complete) resection [6].

In contrast to LR, rates of distant metastasis (DM) in primary RPS have remained fairly constant, ranging from 12–22% in the largest cohorts [10]. The histologic type is the key distinctive factor determining the pattern of recurrence, specifically the risk for LR versus DM. In a large multi-center study of 1007 RPS patients, after complete resection by a specialist, those with well-differentiated liposarcoma had an 8-year LR rate of 22%, without any patient with DM. By comparison, patients with leiomyosarcoma had an 8-year LR rate of 10% but had the highest rate of DM among all histologic types:

50% at 8 years [10][12]. Patients with dedifferentiated liposarcoma had outcomes “in the middle” with LR rates of 36–43% and DM rates of 8–31% [10][12].

Over the last several decades, reported data show improved overall survival (OS) in patients with primary RPS. As an example, in the 1990s, the Dutch Sarcoma Group reported a 5-year OS rate of 39% [42], whereas more recent single and multi-institutional cohorts have reported 5-year OS rates of 67–69% [12][13]. One recent study specifically examined trends in OS over a 15-year period among 10 sarcoma centers [44]. When three periods of time were compared, the authors found an improvement in OS from 61.2% (earliest) to 71.9% (most recent). The study also noted significantly lower 90-day postoperative mortality over the time periods, concluding that the improved survival for patients undergoing resection for primary RPS was likely due to better patient selection, quality of surgery and better perioperative management [44].

References

1. Kirov, K.M.; Xu, H.P.; Crenn, P.; Goater, P.; Tzanis, D.; Bouhadiba, M.T.; Abdelhafidh, K.; Kirova, Y.M.; Bonvalot, S. Role of Nutritional Status in the Early Postoperative Prognosis of Patients Operated for Retroperitoneal Liposarcoma (RLS): A Single Center Experience. Eur. J. Surg. Oncol. 2019, 45, 261–267.
2. Previtali, P.; Fiore, M.; Colombo, J.; Arendar, I.; Fumagalli, L.; Pizzocri, M.; Colombo, C.; Rampello, N.N.; Mariani, L.; Gronchi, A.; et al. Malnutrition and Perioperative Nutritional Support in Retroperitoneal Sarcoma Patients: Results from a Prospective Study. Ann. Surg. Oncol. 2020, 27, 2025–2032.
3. Casirati, A.; Baia, M.; Vandoni, G.; Della Valle, S.; Greco, G.; Morosi, C.; Fiore, M.; Gronchi, A.; Gavazzi, C. Risk of Misclassification during Diagnosis of Malnutrition in Retroperitoneal Sarcoma Patients. Clin. Nutr. ESPEN 2022, 49, 459–465.
4. Gronchi, A.; Miceli, R.; Shurell, E.; Eilber, F.C.; Eilber, F.R.; Anaya, D.A.; Kattan, M.W.; Honoré, C.; Lev, D.C.; Colombo, C.; 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, 1649–1655.
5. Squires, M.H.; Ethun, C.G.; Donahue, E.E.; Benbow, J.H.; Anderson, C.J.; Jagosky, M.H.; Salo, J.C.; Hill, J.S.; Ahrens, W.; Prabhu, R.S.; et al. A Multi-Institutional Validation Study of Prognostic Nomograms for Retroperitoneal Sarcoma. J. Surg. Oncol. 2021, 124, 829–837.
6. Bonvalot, S.; Rivoire, M.; Castaing, M.; Stoeckle, E.; Le Cesne, A.; Blay, J.Y.; Laplanche, A. Primary Retroperitoneal Sarcomas: A Multivariate Analysis of Surgical Factors Associated with Local Control. J. Clin. Oncol. 2009, 27, 31–37.
7. Abdelfatah, E.; Guzzetta, A.A.; Nagarajan, N.; Wolfgang, C.L.; Pawlik, T.M.; Choti, M.A.; Schulick, R.; Montgomery, E.A.; Meyer, C.; Thornton, K.; et al. Long-Term Outcomes in Treatment of Retroperitoneal Sarcomas: A 15 Year Single-Institution Evaluation of Prognostic Features. J. Surg. Oncol. 2016, 114, 56–64.
8. Lewis, J.J.; Leung, D.; Woodruff, J.M.; Brennan, M.F. Retroperitoneal Soft-Tissue Sarcoma: Analysis of 500 Patients Treated and Followed at a Single Institution. Ann. Surg. 1998, 228, 355–365.
9. Toulmonde, M.; Bonvalot, S.; Méeus, P.; Stoeckle, E.; Riou, O.; Isambert, N.; Bompas, E.; Jafari, M.; Delcambre-Lair, C.; Saada, E.; 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.
10. Rust, D.J.; Kato, T.; Yoon, S.S. Treatment for Local Control of Retroperitoneal and Pelvis Sarcomas: A Review of the Literature. Surg. Oncol. 2022, 43, 101814.
11. Stahl, J.M.; Corso, C.D.; Park, H.S.; An, Y.; Rutter, C.E.; Han, D.; Roberts, K.B. The Effect of Microscopic Margin Status on Survival in Adult Retroperitoneal Soft Tissue Sarcomas. Eur. J. Surg. Oncol. 2017, 43, 168–174.
12. Gronchi, A.; Strauss, D.C.; Miceli, R.; Bonvalot, S.; Swallow, C.J.; Hohenberger, P.; Van Coevorden, F.; Rutkowski, P.; Callegaro, D.; Hayes, A.J.; et al. Variability in Patterns of Recurrence After Resection of Primary Retroperitoneal Sarcoma (RPS): A Report on 1007 Patients From the Multi-Institutional Collaborative RPS Working Group. Ann. Surg. 2016, 263, 1002–1009.
13. Tan, M.C.B.; Brennan, M.F.; Kuk, D.; Agaram, N.P.; Antonescu, C.R.; Qin, L.X.; Moraco, N.; Crago, A.M.; Singer, S. Histology-Based Classification Predicts Pattern of Recurrence and Improves Risk Stratification in Primary Retroperitoneal Sarcoma. Ann. Surg. 2016, 263, 593–600.
14. Bagaria, S.P.; Swallow, C.; Suraweera, H.; Raut, C.P.; Fairweather, M.; Cananzi, F.; Quagliuolo, V.; Grignani, G.; Hompes, D.; Ford, S.J.; et al. Morbidity and Outcomes After Distal Pancreatectomy for Primary Retroperitoneal Sarcoma: An Analysis by the Trans-Atlantic Australasian Retroperitoneal Sarcoma Working Group. Ann. Surg. Oncol. 2021, 28, 6882–6889.

15. Tseng, W.W.; Tsao-Wei, D.D.; Callegaro, D.; Grignani, G.; D'Ambrosio, L.; Bonvalot, S.; Ethun, C.G.; Cardona, K.; Mullen, J.T.; Canter, R.J.; et al. Pancreaticoduodenectomy in the Surgical Management of Primary Retroperitoneal Sarcoma. Eur. J. Surg. Oncol. 2018, 44, 810–815.
16. Gronchi, A.; Lo Vullo, S.; Fiore, M.; Mussi, C.; Stacchiotti, S.; Collini, P.; Lozza, L.; Pennacchioli, E.; Mariani, L.; Casali, P.G. Aggressive Surgical Policies in a Retrospectively Reviewed Single-Institution Case Series of Retroperitoneal Soft Tissue Sarcoma Patients. J. Clin. Oncol. 2009, 27, 24–30.
17. Pisters, P.W.T. Resection of Some—But Not All—Clinically Uninvolved Adjacent Viscera as Part of Surgery for Retroperitoneal Soft Tissue Sarcomas. J. Clin. Oncol. 2009, 27, 6–8.
18. Crago, A.M. Extended Surgical Resection and Histology in Retroperitoneal Sarcoma. Ann. Surg. Oncol. 2015, 22, 1401–1403.
19. Cananzi, F.C.M.; Ruspi, L.; Fiore, M.; Sicoli, F.; Quagliuolo, V.; Gronchi, A. Major Vascular Resection in Retroperitoneal Sarcoma Surgery. Surgery 2021, 170, 848–856.
20. Bonvalot, S.; Raut, C.P.; Pollock, R.E.; Rutkowski, P.; Strauss, D.C.; Hayes, A.J.; Van Coevorden, F.; Fiore, M.; Stoeckle, E.; Hohenberger, P.; 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, 2981–2991.
21. Fairweather, M.; Wang, J.; Jo, V.Y.; Baldini, E.H.; Bertagnolli, M.M.; Raut, C.P. Incidence and Adverse Prognostic Implications of Histopathologic Organ Invasion in Primary Retroperitoneal Sarcoma. J. Am. Coll. Surg. 2017, 224, 876–883.
22. Tyler, R.; Lee, M.; Ierodiakonou, V.; Hodson, J.; Taniere, P.; Almond, M.; Ford, S.; Desai, A. Prognostic Implications of Histological Organ Involvement in Retroperitoneal Sarcoma. BJS Open. 2021, 5, zrab080.
23. Alford, S.; Choong, P.; Chander, S.; Henderson, M.; Chu, J.; Powell, G.; Williams, S.; Ngan, S. Value of PET Scan in Patients with Retroperitoneal Sarcoma Treated with Preoperative Radiotherapy. Eur. J. Surg. Oncol. 2012, 38, 176–180.
24. Delisle, M.; Gyorki, D.; Bonvalot, S.; Nessim, C. Landmark Series: A Review of Landmark Studies in the Treatment of Primary Localized Retroperitoneal Sarcoma. Ann. Surg. Oncol. 2022, 29, 7297–7311.
25. Bonvalot, S.; Roland, C.; Raut, C.; Le Péchoux, C.; Tzanis, D.; Frezza, A.M.; Gronchi, A. Histology-Tailored Multidisciplinary Management of Primary Retroperitoneal Sarcomas. Eur. J. Surg. Oncol. 2022.
26. Tseng, W.W.; Madewell, J.E.; Wei, W.; Somaiah, N.; Lazar, A.J.; Ghadimi, M.P.; Hoffman, A.; Pisters, P.W.T.; Lev, D.C.; Pollock, R.E. Locoregional Disease Patterns in Well-Differentiated and Dedifferentiated Retroperitoneal Liposarcoma: Implications for the Extent of Resection? Ann. Surg. Oncol. 2014, 21, 2136–2143.
27. Tseng, W.W.; Swallow, C.J.; Strauss, D.C.; Raut, C.P.; Gronchi, A. ASO Author Reflections: Management of Locally Recurrent Retroperitoneal Sarcoma: The Balance Is Tipped Towards Biology. Ann. Surg. Oncol. 2022, 29, 7349–7350.
28. Raut, C.P.; Callegaro, D.; Miceli, R.; Barretta, F.; Rutkowski, P.; Blay, J.Y.; Lahat, G.; Strauss, D.C.; Gonzalez, R.; Ahuja, N.; et al. Predicting Survival in Patients Undergoing Resection for Locally Recurrent Retroperitoneal Sarcoma: A Study and Novel Nomogram from TARPSWG. Clin. Cancer Res. 2019, 25, 2664–2671.
29. Park, J.O.; Qin, L.X.; Prete, F.P.; Antonescu, C.; Brennan, M.F.; Singer, S. Predicting Outcome by Growth Rate of Locally Recurrent Retroperitoneal Liposarcoma: "The One Centimeter per Month Rule". Ann. Surg. 2009, 250, 977.
30. Hamilton, T.D.; Cannell, A.J.; Kim, M.; Catton, C.N.; Blackstein, M.E.; Dickson, B.C.; Gladdy, R.A.; Swallow, C.J. Results of Resection for Recurrent or Residual Retroperitoneal Sarcoma After Failed Primary Treatment. Ann. Surg. Oncol. 2017, 24, 211–218.
31. Willis, F.; Musa, J.; Schimmack, S.; Hinz, U.; Mechtersheimer, G.; Uhl, M.; Schmidt, T.; Fröhling, S.; Büchler, M.W.; Schneider, M. Outcome after Surgical Resection of Multiple Recurrent Retroperitoneal Soft Tissue Sarcoma. Eur. J. Surg. Oncol. 2021, 47, 2189–2200.
32. Grobmyer, S.R.; Wilson, J.P.; Apel, B.; Knapik, J.; Bell, W.C.; Kim, T.; Bland, K.I.; Copeland, E.M.; Hochwald, S.N.; Heslin, M.J. Recurrent Retroperitoneal Sarcoma: Impact of Biology and Therapy on Outcomes. J. Am. Coll. Surg. 2010, 210, 602–608.
33. Macneill, A.J.; Gronchi, A.; Miceli, R.; Bonvalot, S.; Swallow, C.J.; Hohenberger, P.; Van Coevorden, F.; Rutkowski, P.; Callegaro, D.; Hayes, A.J.; et al. Postoperative Morbidity After Radical Resection of Primary Retroperitoneal Sarcoma: A Report From the Transatlantic RPS Working Group. Ann. Surg. 2018, 267, 959–964.
34. Meric, F.; Milas, M.; Hunt, K.K.; Hess, K.R.; Pisters, P.W.T.; Hildebrandt, G.; Patel, S.R.; Benjamin, R.S.; Plager, C.; Papadopolous, N.E.J.; et al. Impact of Neoadjuvant Chemotherapy on Postoperative Morbidity in Soft Tissue Sarcomas. J. Clin. Oncol. 2000, 18, 3378–3383.

35. Bonvalot, S.; Gronchi, A.; Le Péchoux, C.; Swallow, C.J.; Strauss, D.; Meeus, P.; van Coevorden, F.; Stoldt, S.; Stoeckle, E.; Rutkowski, P.; et al. Preoperative Radiotherapy plus Surgery versus Surgery Alone for Patients with Primary Retroperitoneal Sarcoma (EORTC-62092: STRASS): A Multicentre, Open-Label, Randomised, Phase 3 Trial. Lancet Oncol. 2020, 21, 1366–1377.
36. Tirotta, F.; Parente, A.; Hodson, J.; Desai, A.; Almond, L.M.; Ford, S.J. Cumulative Burden of Postoperative Complications in Patients Undergoing Surgery for Primary Retroperitoneal Sarcoma. Ann. Surg. Oncol. 2021, 28, 7939–7949.
37. Tirotta, F.; Parente, A.; Richardson, T.; Almonib, A.; Evenden, C.; Max Almond, L.; Desai, A.; Hodson, J.; Ford, S.J. Comparison of Comprehensive Complication Index and Clavien-Dindo Classification in Patients with Retroperitoneal Sarcoma. J. Surg. Oncol. 2021, 124, 1166–1172.
38. Ruspi, L.; Cananzi, F.C.M.; Aymerito, F.; Sicoli, F.; Samà, L.; Vanni, E.; Quagliuolo, V. Measuring the Impact of Complications after Surgery for Retroperitoneal Sarcoma: Is Comprehensive Complication Index Better than Clavien-Dindo Classification? Eur. J. Surg. Oncol. 2022, 48, 978–984.
39. Gronchi, A.; Miceli, R.; Colombo, C.; Stacchiotti, S.; Collini, P.; Mariani, L.; Sangalli, C.; Radaelli, S.; Sanfilippo, R.; Fiore, M.; et al. Frontline Extended Surgery Is Associated with Improved Survival in Retroperitoneal Low- to Intermediate-Grade Soft Tissue Sarcomas. Ann. Oncol. 2012, 23, 1067–1073.
40. Pierie, J.P.E.N.; Betensky, R.A.; Choudry, U.; Willett, C.G.; Souba, W.W.; Ott, M.J. Outcomes in a Series of 103 Retroperitoneal Sarcomas. Eur. J. Surg. Oncol. (EJSO) 2006, 32, 1235–1241.
41. Hassan, I.; Park, S.Z.; Donohue, J.H.; Nagorney, D.M.; Kay, P.A.; Nasciemento, A.G.; Schleck, C.D.; Ilstrup, D.M. Operative Management of Primary Retroperitoneal Sarcomas: A Reappraisal of an Institutional Experience. Ann. Surg. 2004, 239, 244–250.
42. van Dalen, T.; Plooij, J.M.; van Coevorden, F.; van Geel, A.N.; Hoekstra, H.J.; Albus-Lutter, C.; Slootweg, P.J.; Hennipman, A.; for the Dutch Soft Tissue Sarcoma Group. Long-Term Prognosis of Primary Retroperitoneal Soft Tissue Sarcoma. Eur. J. Surg. Oncol. (EJSO) 2007, 33, 234–238.
43. Chouliaras, K.; Senehi, R.; Ethun, C.G.; Poultsides, G.; Tran, T.; Grignol, V.; Gamblin, T.C.; Roggin, K.K.; Tseng, J.; Fields, R.C.; et al. Recurrence Patterns after Resection of Retroperitoneal Sarcomas: An Eight-Institution Study from the US Sarcoma Collaborative. J. Surg. Oncol. 2019, 120, 340–347.
44. Callegaro, D.; Raut, C.P.; Ng, D.; Strauss, D.C.; Honoré, C.; Stoeckle, E.; Bonvalot, S.; Haas, R.L.; Vassos, N.; Conti, L.; et al. Has the Outcome for Patients Who Undergo Resection of Primary Retroperitoneal Sarcoma Changed Over Time? A Study of Time Trends During the Past 15 Years. Ann. Surg. Oncol. 2021, 28, 1700–1709.