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ORIGINAL ARTICLE – SARCOMA

Severe Postoperative Complications are Associated with Impaired Survival in Primary but not in Recurrent Retroperitoneal Sarcoma

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ABSTRACT

Background. Retroperitoneal sarcoma (RPS) surgery entails multivisceral resection, which may cause postoperative complications. We assessed the effects of complications on survival to identify their predisposing factors in primary (PRPS) and recurrent (RRPS) RPS.

Methods. We retrospectively analyzed our institutional database. Severe postoperative complications (SC) were defined as Clavien-Dindo classification ≥ 3. Predisposing factors for complications were investigated, as was their effect on long-term outcomes.

Results. In total, 154 RPS resections (78 PRPS and 76 RRPS) performed between January 2008 and December 2018 were included. Neoadjuvant chemotherapy and multifocal tumors were more common in RRPS than PRPS (34.2% vs. 11.3%, $P = 0.001$ and 42.1% vs. 10.3%, $P < 0.001$, respectively). Although surgical extent in RRPS was limited compared with PRPS (weighted organ score 1 vs. 2, $P = 0.01$; transfusion requirement 23.6% vs. 35.8%, $P = 0.04$), SC and mortality rates were comparable. SC rates were 30.1% and 35.5% for PRPS and RRPS, respectively. NACT rate tended to be higher in PRPS patients with SC (20.8% vs. 7.4%, $P = 0.09$), whereas weighted organ score and transfusion requirement were increased in RRPS patients with SC (2 vs. 1, $P = 0.01$; 40.7% vs. 14.3%, $P = 0.009$, respectively). PRPS patients with SC had decreased overall survival (35 months, 95% confidence interval [CI] 12.2–57.7) compared with those without SC (90 months, 95% CI 71.4–108.5, $P = 0.01$).

Conclusions. Postoperative complications are associated with impaired outcomes in PRPS but not in RRPS. The negative effects of complications on outcomes should be factored to perioperative management.

Retroperitoneal sarcomas (RPS) are a rare and heterogeneous group of mesenchymal tumors.[1] They usually present as large masses and, due to their location in the retroperitoneum, are in contact with various major structures, such as the kidneys, colon, duodenum, and major vessels. A macroscopically complete resection is the only curative modality for RPS, whereas other modalities, such as chemotherapy and radiation, are adjuncts to resection.[2,3] However, despite its importance, the extent of a proper surgical resection for the treatment of RPS is highly debated. Although resection of adjacent organs in epithelial-derived tumors is indicated only when they are directly invaded by the tumor, the pseudo-capsule is not a real biological barrier for mesenchymal tumors in RPS, and even adjacent, normal-appearing organs can be involved by the tumor. This led to a plea for extended resection, also termed "compartmental resection," in which all organs adjacent to the tumor are resected en bloc, and that approach has been supported by retrospective data on

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outcomes.[4,5] Although recently presented histological data showed that microinvasion is somewhat less ubiquitous than initially perceived and that it is probably histological subtype-dependent, multivisceral resection is receiving more acceptance and becoming more widely practiced.[6,7] Given that surgical extent is associated with postoperative complications, however, concerns were raised that compartmental resection will result in higher postoperative morbidity. This was refuted by the reported rates of severe postoperative complications (SC) and postoperative mortality as being in the range of 16–18% and 1.8–3%, respectively, which is comparable to other RPS series.[8,9]

A multitude of studies associated SC with impaired long-term oncological outcomes in various tumors types.[10–13] This association may reflect an aggressive tumor biology, which affects the technical aspects of the resection, or alternatively, it may be related to the immunomodulatory effects of the complications.[14] The effects of SC on outcomes in RPS are not well-defined, and they are of specific interest, because the surgical extent in RPS may not be completely dictated by tumor characteristics, but rather from the surgeon's choice to resect the tumor together with its surrounding healthy tissue.

Recurrent RPS (RRPS) is a common clinical problem in sarcoma referral centers.[15] While there are specific histological subtypes than tend to recur locally, there are many patients operated in nonspecialized centers with incomplete or inadequate resection of the primary lesion who are referred to these centers after the primary surgery.[16–18] The purpose of this study was to investigate and compare the effects of SC on survival in both primary RPS (PRPS) and RRPS in a single center.

PATIENTS AND METHODS

Patients and Treatment

Patients who underwent surgery for PRPS and RRPS in our institution between January 2008 and December 2018 were identified from a prospectively maintained institutional database (n = 154). Visceral sarcomas (i.e., gastrointestinal tract or genitourinary tract), gastrointestinal stromal tumors, and desmoid tumors were excluded from this study. PRPS are treated by extended resection in our institution, whereas resection of adjacent organs is performed when they are grossly invaded in RRPS. Resection was classified as macroscopically complete (R0 or R1) or incomplete (R2). Tumor grade was determined according to the FNCLCC grading system.[19] Preoperative treatment (neoadjuvant chemotherapy [NACT] and radiotherapy [RT]) were provided after multidisciplinary tumor board discussion. Surgical extent was evaluated both by the total number of organs resected, as well as by the weighted organ score, which better reflects the surgical burden and risk for postoperative complications.[9] Patients were operated 4–6 weeks after completion of preoperative treatment. Adverse events were classified according to the Clavien-Dindo (CD) classification, and SC were classified as CD ≥ 3 .[20] Patients were prospectively followed by computerized tomographic (CT) scan of chest and abdomen every 4 months for the first 2 years, then every 6 months for the following 3 years, and yearly thereafter. The study was approved by the institutional review board (TLV-19-238).

Statistical Analysis

Median and interquartile range extremes were used to describe continuous variables, whereas categorical variables were expressed as absolute and relative frequency, and they were compared by means of Wilcoxon rank-sum test or Fisher's exact test, respectively. Overall survival (OS) was defined as the time between surgery and death from any cause, Progression-free survival (PFS) in PRPS and RRPS operated in our institution was defined as the time from surgery to first relapse (either local or systemic) by imaging in R0/1 cases or progression on imaging in R2 cases. RRPS cases referred to our institution within 3 months from the primary operation were defined as RRPS for the purposes of this analysis (n = 8). Patients who died within 30 days from the operation were excluded from the survival analysis. Time was censored at the date of last follow-up for surviving patients. Survival curves were estimated with the Kaplan–Meier method and compared by the log-rank test. Multivariable analysis for OS was performed by the Cox proportional hazards regression model. Logistic regression was performed to assess risk factors associated with SC. All statistical analyses were performed with SPSS for Windows version 25 (SPSS, Munich, Germany). A P value < 0.05 was considered significant.

RESULTS

Patient and Tumor Characteristics

During the study period, we operated on 154 patients with RPS, including 78 with PRPS and 76 with RRPS. Patient and tumor characteristics are described in Table 1. Neoadjuvant chemotherapy and multifocality rates were significantly increased in RRPS versus PRPS (34.2% vs. 11.3%, $P = 0.001$ and 42.1% vs. 10.3%, $P < 0.001$, respectively). Tumor size was smaller in the RRPS group (12 vs. 20 cm, $P < 0.001$). High-grade tumors were more abundant in PRPS than in RRPS (60.3% vs. 38.7%,

TABLE 1 Patients and tumor characteristics in patients with primary (PRPS) and recurrent retroperitoneal sarcoma (RRPS)

	All patients (n = 154)	Primary (n = 78)	Recurrent (n = 76)	P
Age, median (IQR)	65 (54–72)	64 (56–72)	66 (56–70)	0.48
Gender F/M, n (%)	78/82 (48.8/51.2)	44/34 (56.4/43.6)	33/43 (43.4/56.6)	0.11
Charlson comorbidity index, median (IQR)	4 (3–5)	4 (3–6)	5 (3–5)	0.14
Neoadjuvant chemotherapy, n (%)	35 (22.7)	9 (11.3)	26 (34.2)	0.001
Pre-operative radiation, n (%)	11 (7.1)	3 (3.8)	8 (10.5)	0.11
Size (cm), median (IQR)	14 (8-22)	20 (17-28)	12 (8-17)	< 0.001
Multifocality, n (%)	40 (26)	8 (10.3)	32 (42.1)	< 0.001
Histotype, n (%)				0.33
WDLPS	58 (37.7)	27 (34.6)	31 (40.8)	
DDLPS	56 (36.4)	34 (43.6)	22 (28.9)	
LMS	23 (14.9)	9 (11.5)	14 (18.4)	
MPNST	3 (1.9)	2 (2.6)	1 (1.3)	
Other	14 (9.1)	6 (7.7)	8 (10.5)	
Grade, n (%)				0.006
1	56 (36.6)	26 (33.3)	30 (40)	
2	21 (13.7)	5 (6.4)	16 (21.3)	
3	76 (49.7)	47 (60.3)	29 (38.7)	

IQR interquartile range; *WDLPS* well differentiated liposarcoma; *DDLPS* dedifferentiated liposarcoma; *LMS* leiomyosarcoma; *MPNST* malignant peripheral nerve sheath tumor

P = 0.006), probably reflecting the tendency of those tumors to recur systemically. Age, sex, patient comorbidities (as assessed by the Charlson comorbidity index, CCI), preoperative radiation, and histologic subtype did not differ between the groups.

Surgical Procedures and Postoperative Complications

Table 2 describes the intraoperative data. The extent of surgery in the RRPS group was limited in comparison to that in the PRPS group. The number of organs resected tended to be lower in the former compared to the latter (1 vs. 2, respectively, P = 0.11), whereas the weighted organ score and the transfusion requirement were significantly lower in the RRPS group (1 vs. 2, P = 0.02 and 23.6% vs. 35.8%, P = 0.04, respectively). The portion of patients with vascular resection and length of hospital stay did not differ between the groups (Table 2). The most common multivisceral resection was nephrectomy and colectomy, which was performed in 42.5% in the PRPS group. Although the surgical extent was more limited in the RRPS group compared with the PRPS group, the rate of severe postoperative complications and 30-day mortality did not differ between the groups (35.5% vs. 30.1%, P = 0.53 and 3.9% vs. 6.4%, P = 0.49, respectively) (Table 3). Supplementary Table 1 shows the incidence of different risk factors among patients with SC versus those without, in both the PRPS and RRPS cohorts. In the PRPS group, both

TABLE 2 Data on surgical procedures

Variable	All patients (n = 154)	Primary RPS (n = 78)	Recurrent RPS (n = 76)	P
No. of organs resected, median (IQR)	1.5 (1–3)	2 (1–3)	1 (0–2)	0.11
Weighted organ score, median (IQR)	1 (1–3)	2 (1–3)	1 (0-2)	0.02
Vascular resection n, (%)	15 (9.7)	9 (11.5)	6 (7.8)	0.41
Transfusion n, (%)	46 (29.8)	28 (35.8)	18 (23.6)	0.04
R				0.11
0–1	133 (86.3)	71 (91)	62 (81.5)	
2	11 (7.1)	3 (3.8)	8 (10.5)	
LOS, median (IQR)	13.5 (8–24)	13 (11–28)	15 (13–25)	0.3

RPS retroperitoneal sarcoma; *IQR* interquartile range; *LOS* length of stay

TABLE 3 Postoperative complications

Variable	All patients (n = 154)	Primary RPS (n = 78)	Recurrent RPS (n = 76)	P
30-day mortality	8 (5.2)	5 (6.4)	3 (3.9)	0.49
Reoperation	20 (13.6)	11 (14.7)	9 (11.8)	0.7
Postoperative bleeding	14 (9.2)	9 (11.5)	5 (6.7)	0.27
Anastomotic leak	15 (9.8)	7 (9)	8 (10.7)	0.72
Severe morbidity (CD $\geq$ 3)	51 (31.5)	24 (30.1)	27 (35.5)	0.53

n (%) for all values

RPS retroperitoneal sarcoma; *CD* Clavien-Dindo

NACT and higher CCI tended to be associated with SC (7% vs. 20.8%, P = 0.09; 4 vs. 5, P = 0.23), albeit non-significantly. In RRPS, the weighted organ score and transfusion requirements were significantly associated with SC (2 vs. 1, P = 0.01; 40.7% vs. 14.3%, P = 0.009). Both risk factor remained significant after multivariate analysis (odds ratio [OR] = 1.48, 95% confidence interval [CI] 1.04–2.12, P = 0.014; OR = 4.16, 95% CI 1.33–13.02, respectively).

Effects of Severe Postoperative Complications on Long-term Outcomes

We compared long-term oncological outcomes between PRPS and RRPS patients with and without SC. After a median follow-up of 26 months, the PRPS patients with SC had a median OS of 35 months (95% CI 12.2–57.7) versus 90 (95% CI 71.4–108.5) for those without SC (P = 0.01; Fig. 1a). The same effect was seen for PFS: patients with SC had a median PFS of 21.7 months (95% CI 13.2–30.4) versus 51.5 months (95% CI 37.1–65.8) for those without SC (P = 0.03). However, RRPS patients with SC had a median OS of 69 months (95% CI 40–97) compared with 45 months (95% CI 20.9–69.1) for patients without SC (P = 0.2). Similarly, the median PFS was comparable for patients with and without SC (12 [3.7–20.3] vs. 14 [5.1–22.9] months, P = 0.69). The multivariate analysis revealed that age (hazard ratio [HR] = 1.05, P = 0.04), tumor grade (HR = 4.17, P = 0.006) and SC (HR = 3.34, P = 0.04) were predictors of reduced OS in PRPS, whereas tumor grade (HR = 3.06, P = 0.001) was the only predictor of reduced OS in RRPS (Table 4).

DISCUSSION

The association between complications and impaired oncological prognosis for various other tumor types, which is well reported.[10,12,13] A reasonable explanation for long-term effects of postoperative complications is that these tumors are associated with a more aggressive biology that dictates an extended surgery. However, recent data point to the importance of the perioperative period for cancer recurrence and to the ability of surgical complications to modulate the immune response system.[14] We observed that SC negatively affect prognosis even after accounting for biological risk factors, such as tumor grade. This stands in contrast to a multicenter report on RPS outcomes that did not report any negative effect of complications on long-term outcomes.[9] In the same report, the SC rate was 16.4% versus 30.1% in our series. It is possible that the number of adverse events unfolds the association of SC with survival, because the HR for OS was increased with SC (HR = 1.23), but a level of statistical significance was not reached in that report (P = 0.2).[9] We assume that surgical extent was not the reason for increased complication rate in our patients, because the rate of combined nephrectomy and colectomy (approximately 40%) and vascular resection is comparable (approximately 10%). However, patient age was higher in our series (median age of 65 vs. 58 years), and age was demonstrated as being responsible for increased surgical morbidity in a number of surgical series.[8,9,21] Interestingly, the median age in the series reported by Pasquali et al. was 63, close to the median age of our series (65), and the SC rate was comparable.[22] In addition, patients in our cohort had significant comorbidities, as assessed by a median CCI of 4, but a direct comparison to the MacNeill study is not possible, because data on comorbidities were not provided.[9]

We also sought to determine risk factors for SC. The only risk factor that tended to be associated with SC in PRPS was NACT, whereas both the weighted organ score and transfusion requirement were risk factors in RRPS. The possibility that NACT may be associated with a worse postoperative course should be balanced versus its potential benefit in the treatment of RPS, which further highlights the need to establish its role in the management of RPS.[23] However, it should be noted that because the overall use of NACT in our series is low, it is possible that these patients represent a subgroup with adverse prognostic factors, such as the inability to achieve a complete

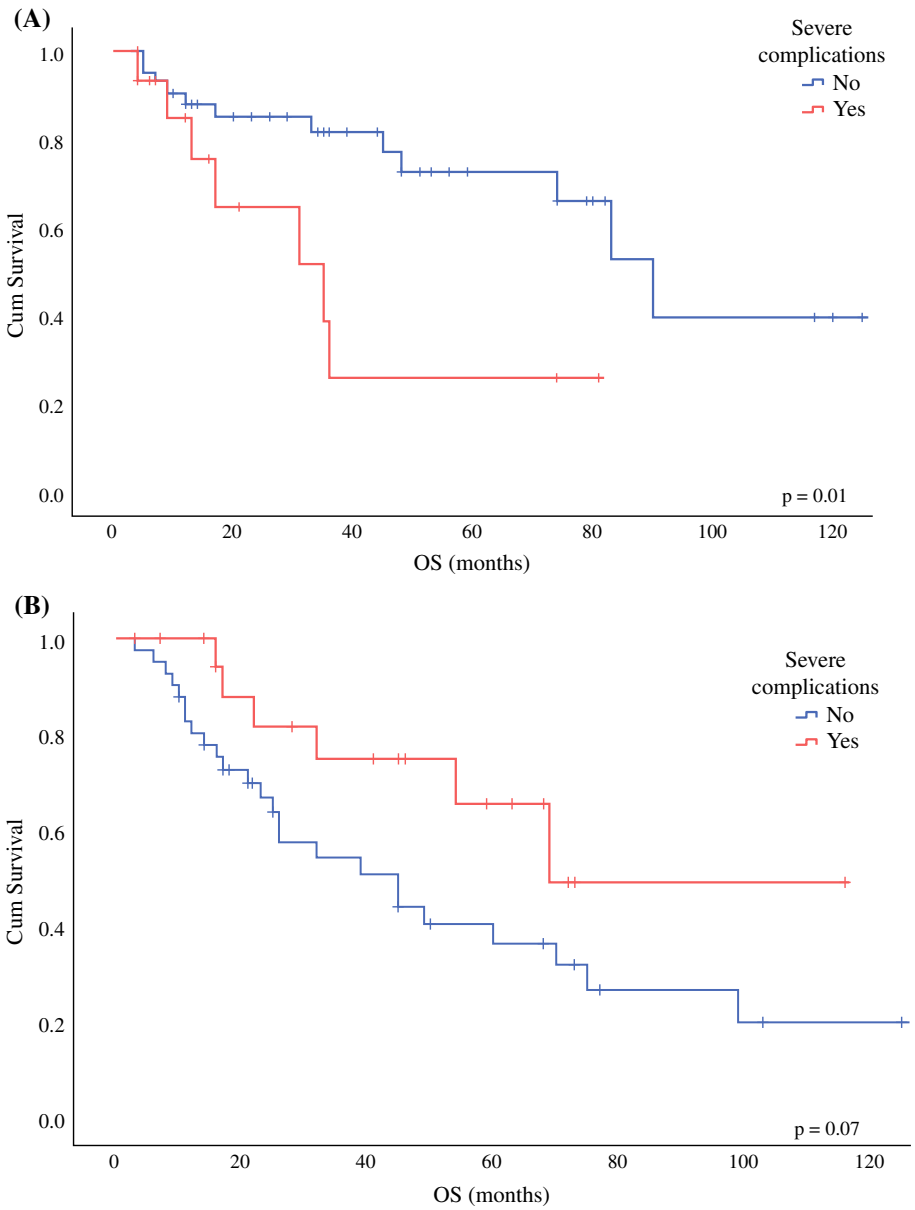

FIG. 1 Overall and cumulative survival of patients with primary and recurrent retroperitoneal sarcoma (RPS) according to the occurrence of severe postoperative complications (SC). **a** Primary RPS. **b** Recurrent RPS. *P* by log-rank test

resection without NACT. Although it is tempting to implicate surgical extent in the occurrence of SC, in our series it was associated with SC only in the RRPS group and not in the PRPS group.[9] Further research is needed to evaluate the role of an individualized marker for the assessment of the physiological stress exerted by surgery and it relation to complications.[24,25] Indeed, surgical extent does not always dictate outcomes, because clinical experience shows that different patients respond differently to the same procedure. Alternatively, as surgical extent was associated with SC in the larger TARPS report, a reasonable attitude to minimize complications and their detrimental outcomes, would be to limit surgical extent. This approach can be based on novel intraoperative technologies to assess adjacent organ histological invasion, such as fluorescence imaging.[26] This approach could limit the resection of uninvolved organs and consequently the occurrence of SC.

We found that weighted organ score was the parameter that demonstrated the increased surgical extent in PRPS and the parameter associated with SC in RRPS, and not the mere number of organs resected. Our data support the notion that number of organs resected by itself is an inaccurate measure of surgical extent as compared to the weighted organ score, which is derived from the presumed effects of resection. These findings substantiate the use of the score, developed by MacNeill et al.[9]

Patients with recurrent RPS underwent a more limited resection than those with primary RPS, as judged by the number of organs resected and their weighted score. This is

TABLE 4 Multivariate analysis of factors associated with overall survival

Variable	Primary RPS			Recurrent RPS		
	HR	95% CI	*P*	HR	95% CI	*P*
Age	1.05	1.00–1.11	0.04	0.98	0.94–1.01	0.33
Size	1.01	0.97–1.05	0.57	0.99	0.94–1.03	0.93
Grade	4.17	1.49–11.63	0.006	3.06	1.54–6.09	0.001
R status	3.11	1.08–8.9	0.03	1.01	0.54–1.9	0.95
Multifocality	2.43	0.4–14.87	0.33	1.56	0.63–3.6	0.34
Severe complications	3.34	1.03–10.82	0.04	1.25	0.35–4.45	0.72

RPS retroperitoneal sarcoma; *HR* hazard ratio; *CI* confidence interval

in concordance with data published on RRPS from other specialized sarcoma centers.[15] Despite the limited surgical extent, the rates of postoperative mortality, reoperation, and SC were not significantly different from those of patients with PRPS. We hypothesized that this is due to the baseline status of the RRPS patients, as manifested by increased preoperative chemotherapy rate, and tumor multifocality. Long-term oncologic outcomes in this group were related to tumor biology characteristics, such as tumor grade and multifocality, and not to the postoperative course. In light of the morbidity associated with surgical resection in RRPS, it is prudent to balance that parameter against the potential oncologic benefit associated with resection.[15]

Our study has several limitations that bear mention. As a retrospective study, there is a possibility of inaccurate documentation of mild postoperative complications, such as bowel ileus or superficial wound infection. In addition, the selection criteria for patients with RRPS may represent a subgroup with improved prognosis, i.e., patients who did not have distant metastases and were generally fit for surgery despite tumor load and previous chemotherapy. Moreover, our findings on the impairment of long-term outcomes by SC were not reported by a large multi-institutional study, which may point to the limitations of our relatively small cohort that can be affected by even a small number of events.[9] Alternatively, patient characteristics differ between the two studies, as discussed above.

CONCLUSIONS

Our data revealed that postoperative surgical complications may affect long-term outcomes in patients with PRPS, whereas tumor characteristics play a more prominent role in outcomes in patients with RRPS. The effects of complications on outcomes may represent a novel factor to be included in the perioperative management of patients with RPS, by either judicious use of preoperative modalities or novel technologies to limit uninvolved organ resection.

DISCLOSURE The authors declare no competing interests regarding this manuscript.

REFERENCES

1. Schaefer IM, Fletcher CDM. Recent advances in the diagnosis of soft tissue tumours. *Pathology.* 2018;50(1):37–48.
2. Constantinidou A, Jones RL. Systemic therapy in retroperitoneal sarcoma management. *J Surg Oncol.* 2018;117(1):87–92.
3. Haas RL, Baldini EH, Chung PW, van Coevorden F, DeLaney TF. Radiation therapy in retroperitoneal sarcoma management. *J Surg Oncol.* 2018;117(1):93–8.
4. 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(1):31–7.
5. 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(1):24–30.
6. Fairweather M, Wang J, Jo VY, Baldini EH, Bertagnolli MM, Raut CP. Incidence and adverse prognostic implications of histopathologic organ invasion in primary retroperitoneal Sarcoma. *J Am Coll Surg.* 2017;224(5):876–83.
7. Fairweather M, Wang J, Jo VY, Baldini EH, Bertagnolli MM, Raut CP. Surgical management of primary retroperitoneal sarcomas: rationale for selective organ resection. *Ann Surg Oncol.* 2018;25(1):98–106.
8. 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(6):1507–14.
9. MacNeill AJ, Gronchi A, Miceli R, et al. Postoperative Morbidity after radical resection of primary retroperitoneal sarcoma: a report from the transatlantic RPS working group. *Ann Surg.* 2018;267(5):959–64.
10. Artinyan A, Orcutt ST, Anaya DA, Richardson P, Chen GJ, Berger DH. Infectious postoperative complications decrease long-term survival in patients undergoing curative surgery for colorectal cancer: a study of 12,075 patients. *Ann Surg.* 2015;261(3):497–505.
11. Nathan H, Yin H, Wong SL. Postoperative complications and long-term survival after complex cancer resection. *Ann Surg Oncol.* 2017;24(3):638–44.
12. Saeki H, Tsutsumi S, Tajiri H, et al. Prognostic significance of postoperative complications after curative resection for patients with esophageal squamous cell carcinoma. *Ann Surg.* 2017;265(3):527–33.
13. Hayashi T, Yoshikawa T, Aoyama T, et al. Impact of infectious complications on gastric cancer recurrence. *Gastric Cancer.* 2015;18(2):368–74.

14. Hiller JG, Perry NJ, Poulogiannis G, Riedel B, Sloan EK. Perioperative events influence cancer recurrence risk after surgery. *Nat Rev Clin Oncol.* 2018;15(4):205–18.
15. Raut CP, Callegaro D, Miceli R, 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(8):2664–71.
16. Gronchi A, Strauss DC, Miceli R, 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(5):1002–9.
17. Nizri E, Fiore M, Colombo C, et al. Completion surgery of residual disease after primary inadequate surgery of retroperitoneal sarcomas can salvage a selected subgroup of patients: a propensity score analysis. *J Surg Oncol.* 2019;119(3):318–23.
18. Blay JY, Honore C, Stoeckle E, et al. Surgery in reference centers improves survival of sarcoma patients: a nationwide study. *Ann Oncol.* 2019;30(8):1407.
19. Coindre JM. Grading of soft tissue sarcomas: review and update. *Arch* Pathol *Lab Med.* Oct 2006;130(10):1448–53.
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205–13.
21. Smith HG, Panchalingam D, Hannay JA, et al. Outcome following resection of retroperitoneal sarcoma. *Br J Surg.* 2015;102(13):1698–709.
22. Pasquali S, Vohra R, Tsimopoulou I, Vijayan D, Gourevitch D, Desai A. Outcomes following extended surgery for retroperitoneal sarcomas: results from a UK Referral Centre. *Ann Surg Oncol.* 2015;22(11):3550–6.
23. van Houdt WJ, Raut CP, Bonvalot S, Swallow CJ, Haas R, Gronchi A. New research strategies in retroperitoneal sarcoma. The case of TARPSWG, STRASS and RESAR: making progress through collaboration. *Curr Opin Oncol.* 2019;31(4):310–6.
24. Labgaa I, Joliat GR, Kefleyesus A, et al. Is postoperative decrease of serum albumin an early predictor of complications after major abdominal surgery? A prospective cohort study in a European centre. *BMJ Open.* 2017;7(4):e013966.
25. Mantziari S, Hubner M, Coti-Bertrand P, Pralong F, Demartines N, Schafer M. A novel approach to major surgery: tracking its pathophysiologic footprints. *World J Surg.* 2015;39(11):2641–51.
26. Nicoli F, Saleh DB, Baljer B, et al. Intraoperative near-infrared fluorescence (NIR) imaging with indocyanine green (ICG) can identify bone and soft tissue sarcomas which may provide guidance for oncological resection. *Ann Surg.* Mar 27 2020.