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ORIGINAL ARTICLE – SARCOMA

Significant Predictors of Postoperative Morbidity After Radical Resection of Retroperitoneal Sarcoma in a Tertiary Center

Claudia Di Prata, MD[1,2], Benjamin Renouf, MSc[3], Dimitri Tzanis, MD, PhD[1], Toufik Bouhadiba, MD[1], Sarah Watson, MD, PhD[4], Sophie El Zein, MD[5], Sylvie Helfre, MD[6], Nayla Nicolas, MD[7], Julie Perlbarg-Samson, MD[8], Olivier Brenet, MD[9], and Sylvie Bonvalot, MD, PhD[1]

[1]Department of Surgical Oncology, Institute Curie, Paris, France; [2]Department of Surgical, Oncological, and Gastroenterological Sciences, University of Padua, Padua, Italy; [3]Department of Hospital Research Direction, Institute Curie, Paris, France; [4]Department of Medical Oncology, Institute Curie, Paris, France; [5]Department of Biopathology, Institute Curie, Paris, France; [6]Department of Radiotherapy, Institute Curie, Paris, France; [7]Department of Radiology, Institute Curie, Paris, France; [8]Department of Medical Information, Institute Curie, Paris, France; [9]Department of Anesthesiology, Institute Curie, Paris, France

ABSTRACT

Background. The safety of multivisceral resection of retroperitoneal sarcoma is an issue. Previous reports have investigated its associations with the pattern of resection and factors recognized mostly per operatively.

Methods. All consecutive RPS resections from May 2015 to April 2022 were studied retrospectively with respect to adverse events. Two univariate and multivariate logistic regression analyses were performed to investigate the associations between severe adverse events and factors recognized pre- and per operatively. Associations of adverse events with overall survival (OS) and local recurrence (LR) were investigated.

Results. A total of 265 surgical interventions corresponding to 251 patients were recorded (38 RPS surgeries/year). Severe postoperative adverse events (Clavien–Dindo ≥ 3) occurred in 50 patients (18.9%), 15 (5.6%) patients underwent an iterative laparotomy, and 6 patients (2.3%) died within 90 days. On multivariate analysis including all parameters known preoperatively, male sex, performance status, dedifferentiated liposarcoma histology, and low serum albumin level were found to be significant predictors of major complications, whereas the timing of surgery and preoperative treatment were not. On univariate analysis including all per operative parameters, transfusion requirement, operative time, number of digestive anastomoses, and pancreas and/or major arterial resection were found to entail higher operative risk. On multivariate analysis, only transfusion requirement was significant. There was no impact of postoperative adverse events on OS or LR.

Conclusions. The recognition of preoperative parameters that impact safety could mitigate the extent of the surgery, specifically the resection of adherent organs not overtly invaded. For the best decision, this surgery should be performed in referral centers.

Retroperitoneal sarcomas (RPS) are rare cancers with an annual incidence of 0.76 new cases per 100,000 people.[1] To date, the only potentially curative treatment is surgery through complete en bloc gross excision.[2] After the STRASS trial and STREXIT study, it was suggested that preoperative radiotherapy could impact local control of liposarcoma (LPS), whereas chemotherapy is still under evaluation for high-grade LPS and leiomyosarcoma (LMS).[3,4] Centralization in a high-volume sarcoma center and surgery performed by a specialized surgeon achieve better outcomes.[5,6] The surgical approach recommended for primary RPS in the consensus manuscript by the Transatlantic Australasian Retroperitoneal Sarcoma Working Group (TARPSWG) consists of a macroscopically complete resection with a single specimen encompassing the tumor and involved contiguous organs, best achieved by resecting the tumor en bloc with

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S. Bonvalot, MD, PhD
e-mail: sylvie.bonvalot@curie.fr

adherent organs, even if not overtly infiltrated.[2,7] This "compartmental" surgery has been associated with up to threefold reductions in local recurrence rates in retrospective cohort studies and better overall survival compared with historical data.[8–10] However, optimization of surgical treatment by extending resection is prioritized when the local recurrence rate is high or is the main cause of death, specifically in primary LPS.[11,12] Conversely, en bloc resection of only the tumor and organs that are infiltrated is recommended for primary tumors exhibiting distinct borders or at predominant metastatic risk, such as LMS.[11,12] For the patients selected for resection of recurrence, the decision is based on the nature of the previous operation, histologic type, and tumor biology.[13] The potential morbidity of such frequent multivisceral resection is an issue, and "theoretical" indications for each individual organ resection, particularly when not overtly infiltrated, must be balanced with all preoperative parameters and patterns of resection that could affect risk. In three retrospective studies concerning the post-radical resection era of primaries and local recurrences, severe postoperative adverse events occurred in 16–18% of patients, and the 90-day mortality rates of primary and recurrence cases were 3–4 and 0.4%, respectively.[14–16] In these studies, logistic regression analyses were performed to investigate the associations between adverse events and clinicopathological characteristics, but they mostly included per operative parameters with a weighted resected organ score that considered the pattern of resection. However, preoperative characteristics were limited to age, tumor size, and preoperative treatments. Additionally, technical difficulties between primary and relapsed tumors can be different; primary tumors are generally larger when diagnosed, while relapsed tumors are exposed to loss of original tissue planes and adhesions from prior surgery or therapy.[16] The objective of this study was to compare the morbidity of primary RPS and recurrences or persistence after incomplete surgery, and to investigate the associations between adverse events and both pre- and per operative characteristics. A nomogram was built to help inform patients about the morbidity risk according to significant preoperative parameters.

PATIENTS AND METHODS

All patients with RPS who underwent surgery at the Institute Curie between 1 May 2015 and 30 April 2022 were identified from the Department of Surgery operating schedule. Eligibility criteria included histological diagnosis of RPS confirmed by a sarcoma expert pathologist and primary or recurrent disease without visceral metastasis at diagnosis. Patients with desmoid fibromatosis, gynecologic sarcomas, or gastrointestinal stromal tumors were excluded. When a patient was operated on multiple times, each intervention was considered a separate item. The following data were extracted from the institutional database: patient demographics (age, sex), symptoms at diagnosis, performance status (PS) according to the Eastern Cooperative Oncology Group (ECOG),[17] anesthesiologic risk according to the American Society of Anesthesiologists,[18] diabetes (according to the American Diabetes Association),[19] cardiovascular disease (CVD) (medical history of myocardial infarction, angioplasty, and coronary stenting or drug-requiring hypertension),[20] obesity (BMI $\geq$ 30),[21] previous other cancers, and tobacco consumption. We recorded albumin serum levels prior to surgery and defined a low serum albumin level (SAL) as less than 3.5 g/dl.[22] We classified three tumor groups: primary tumors (P), persistence after previous incomplete piecemeal resection of a primary tumor, and recurrence (R) after macroscopically complete previous surgery. Tumor size, histology, and grading according to French grading,[23] as well as surgical details, were recorded, in addition to the following: setting of surgery (elective or emergency), length of surgery, blood transfusion requirement, number and type of resected organs, and reconstruction. Appendectomy, ovariectomy, and cholecystectomy were not considered. Completeness of resection was classified as macroscopically complete (R0/1) or incomplete (R2). Adverse events were reported according to the Clavien–Dindo classification within 30 days of surgery.[24] Only complications graded > 2 were considered for the study. Complications requiring surgical, endoscopic, or radiologic intervention were graded 3 (3A without general anesthesia, 3B requiring general anesthesia). Life-threatening complications were graded 4 (4A single and 4B multiple organ failure). Postoperative death (grade 5) was recorded up to 90 days after surgery. If a patient had multiple complications, we recorded the highest grade. The length of hospital stay (LOS) and readmission rate were recorded. Associations of adverse events with patient and tumor characteristics and treatments were investigated in univariate and multivariate analyses (MVA). The oncologic endpoints were overall survival (OS) and local recurrence-free survival (LRFS). Associations among adverse events, OS, and LRFS were investigated in an MVA. Each patient provided informed consent for the operation and clinical data acquisition. The institutional review board of our hospital approved this retrospective study.

Statistical Analyses

Comparisons between the P and R groups were performed using the chi-squared test, Fisher's exact test, and Yates's continuity correction. Wilcoxon's rank test was used to compare medians. A *p*-value of < 0.05 was considered statistically significant. Two univariate and multivariate logistic regression analyses were performed to investigate associations between adverse events and clinicopathologic characteristics. The first one included all parameters known preoperatively [age at surgery, gender, ASA, ECOG, diabetes, CVD, SAL, tobacco, obesity, previous cancer, symptoms, tumor side and size, histology (DD LPS versus others), grade, preoperative treatments]. The second included all per operative parameters (pattern of surgery, number of digestive anastomoses, pancreas and/or major arterial resection, transfusion requirement, use of amine, operative time, omentoplasty). Overall survival (OS) was defined as the time between surgery and death from any cause. Local recurrence-free survival (LRFS) was defined as the time between surgery and recurrence in the operative field. OS and LRFS were estimated using the Kaplan–Meier method. Associations between adverse events and OS and LRFS were investigated with multivariate Cox models, adjusting for patient and disease characteristics. Death times of patients with Clavien–Dindo grade 5 were censored. For the nomogram, the variables were selected by applying a backward procedure in the multivariable logistic regression model with significant parameters known preoperatively: patient age, sex, ECOG, SAL, and histology. Missing data were excluded from the analyses. Statistical analyses were performed with R software (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Over a 7-year span, 265 surgical interventions corresponding to 251 patients were recorded (38 RPS surgeries/year). Patient and tumor characteristics are summarized in Table 1. Patients in the P group were significantly older (p = 0.013), had larger tumors (median P size = 25 cm versus R = 10 cm, $p < 10^{-10}$) with more frequent symptoms ($p < 10^{-5}$), had a higher rate of grade 3 (P n = 37, 19.5% versus R n = 1, 1.9%, p = 0.013), and received less preoperative chemotherapy (P n = 13, 6.8% versus R n = 11, 20.4%, p = 0.007) and less preoperative radiotherapy (P n = 12, 6.3% versus R n = 14, 25.9%, $p = 10^{-4}$). No patients received postoperative RT or CT. Patients with tumor persistence after macroscopically incomplete surgery had similar patient and tumor characteristics except that they were operated on when the tumor size was similar to recurrence (12 cm). A total of 45 (17%) patients had a low SAL (< 3.5g/dl) with a median of 3.1 g/dl in this group [interquartile range (IQR) 2.7–3.3 g/dl], and the rate of malnourished patients (< 3.5 g/dl) was not significantly different between P (n = 36, 18.9%) and R (n = 7, 13%) (p = 0.45). In the P group, 10 patients (5.2% of 190 patients) had multifocal disease (synchronous sarcomatosis) discovered intraoperatively.

Surgical details are summarized in Table 2. The median operative time was 240 min (IQR 195–300 min). All surgeries were conducted in an elective setting, except 5 (1.9% of 265) (preoperative tumor rupture, P n = 4 and occlusion, R n = 1). The median number of organs resected en bloc with the tumor was higher in the P group (P n = 2 versus R n = 1, $p < 10^{-5}$). The most commonly resected organs were the kidney (n = 173, 65.3%) and colon or rectum (n = 159, 60%). These two organs were more frequently resected in the P group ($p < 10^{-12}$, $p < 10^{-4}$), whereas the small intestine was more frequently resected in the R group (p = 0.005). The combination of kidney and colon was the most common multivisceral resection, performed in n = 128 (48.3%) patients. A total of 166 (62.6%) of 265 patients had a digestive anastomosis, more frequently in the P group (p = 0.014), and 92 patients (35%) required transfusion [mean unit of packed red blood cells n = 2 (IQR 2–4)], more frequently in the P group (P n = 76, 40% versus R n = 12, 22%, p = 0.02). Eight patients (3%) had a temporary digestive derivation (7 P, 1 R) because of malnutrition (n = 6), concomitant ulcerative colitis (n = 1), or ultralow rectal resection (n = 1). Patients with low SAL received significantly more temporary digestive derivation [n = 6 (13.3%) of 45 malnourished patients versus n = 2 (1.16%) of 173 with a normal SAL; p = 0.01]. Ten patients (3.8%) had a major arterial resection, more frequently in patients in the R group (n = 5, 9.3% versus n = 5, 2.6% in P, p = 0.045). A total of 22 patients (8.3%) received mesh for parietal muscle or diaphragm resections, 11 (4.2%) received a biliodigestive reconstruction, and 5 (1.9%) received a urinary reconstruction. Complete resection (R0/1) was achieved in 97.4% of cases.

Severe postoperative adverse events (Clavien–Dindo ≥ 3) occurred in 50 patients (18.9%) (Tables 2, 3) without a significant difference between P and R. Of these patients, 6 (2.3%) died within 90 days. Death was due to a surgical complication: n = 2 (0.8%): hemorrhage due to pancreatic fistula (n = 2, 0.8%, one of the two died after mesenteric infarcts following embolization of the mesenteric superior arteria by coils that migrated); and due to a medical complication n = 4 (1.5%) (pneumonia n = 3, 1.1% and venous thromboembolism n = 1, 0.4%). In total, 25 patients (9.4%) underwent reoperations: 15 (5.6%) had an iterative laparotomy, and 5 (1.9%) had superficial reoperations (Table 3), and 25 patients were not reoperated on (9.4%). Of them, 7 (2.6%) had renal failure requiring temporary dialysis, 8 (3%) had pneumonia/respiratory failure, 3 (1.1%) had reversible cardiogenic shock, and 1 (0.4%) had venous thromboembolism.

On univariate logistic analysis including all preoperative parameters (Table 4, left panel), the probability of suffering a severe postoperative adverse event increased significantly with age (cutoff: 72 years old) (OR 2.42, p = 0.013), male sex (HR 2.04, p = 0.026), PS (OR 2.92, p = 0.027), low SAL (OR 3.43, p = 0.001), and histology [de-differentiated (DD) LPS versus others] (OR 2.36, p = 0.011). None of the other factors were significant, including the timing of surgery (P versus R), tumor size, and administration of preoperative

TABLE 1 Patient and tumor characteristics

		Primary		Recurrence		*p*-value	Persistence		Total	
		N	(%: *N*/190)	*N*	(%: *N*/54)		*N*	(%: *N*/21)	*N*	(%: *N*/265)
Patient characteristics										
Sex	Male	85	(44.7)	23	(42.6)		13	(61.9)	121	(45.7)
	Female	105	(55.3)	31	(57.4)	0.78	8	(38.1)	144	(54.3)
Age (years)	Median	63	(53–70)	57.5	(47.3–66.8)	0.013	60	(57–65)	61	(50–69)
	< 75	159	(83.7)	53	(98.1)		20	(95.2)	232	(87.5)
	≥ 75	31	(16.3)	1	(1.9)	0.055	1	(4.8)	33	(12.5)
ASA	1	34	(17.9)	8	(14.8)	0.6	5	(23.8)	47	(17.7)
	2	119	(62.6)	34	(63.0)	0.96	14	(66.7)	167	(63)
	3	37	(19.5)	12	(22.2)	0.66	2	(9.5)	51	(19.2)
ECOG	0	153	(80.5)	39	(72.2)		15	(71.4)	207	(78.1)
	1	13	(6.8)	5	(9.3)	0.66	3	(14.3)	21	(7.9)
Diabetes	YES	13	(6.8)	5	(9.3)	0.76	2	(9.5)	20	(7.5)
CVD	YES	60	(31.6)	12	(22.2)	0.18	6	(28.6)	78	(29.4)
Albumin serum level	≥ 3.5 g/dl	124	(65.3)	34	(63)		15	(71.4)	173	(65.3)
	< 3.5 g/dl	36	(18.9)	7	(13)	0.45	2	(9.5)	45	(17)
Median (g/dl) (All patients)		4	(3.5–4.3)	4.3	(3.9–4.5)	0.024	4.2	(4.0–4.5)	41	(3.5–3.44)
Median (g/dl) (Patients with ≥ 3.5 g/dl)		4.2	(3.8–4.4)	4.35	(4.2–4.5)	0.02	4.3	(4.15–4.55)	4.2	(3.9–4.5)
Median (g/dl) (Patients with < 3.5 g/dl)		3.05	(2.78–3.3)	3.2	(3.0–3.3)	0.42	3.3	(3.25–3.35)	3.1	(2.7–3.3)
Tobacco	YES	46	(24.2)	13	(24)	0.27	3	(14.3)	62	(32.5)
Obesity	YES	24	(12.6)	8	(14.8)	0.84	4	(19)	36	(13.6)
Other cancers	YES	34	(17.9)	9	(16.7)	0.83	0	(0)	43	(16.2)
Symptoms	YES	75	(39.5)	4	(7.4)	$< 10^{-5}$	5	(23.8)	84	(32.1)
Tumor characteristics										
Side	Left	92	(48.4)	29	(53.7)		12	(57.1)	133	(50.2)
	Right	98	(51.6)	25	(46.3)	0.45	9	(42.9)	132	(49.8)
Histological size (cm)	Median	25	(16–34)	10	(7–15.8)	$< 10^{-10}$	12	(9–21)	20	(11–30)
	< 30 cm	117	(61.6)	50	(92.6)		19	(90.5)	186	(70.5)
	≥ 30 cm	72	(37.9)	4	(7.4)	$<10^{-4}$	2	(9.5)	78	(29.5)
Histology	WD LPS	32	(16.8)	20	(37)	0.0014	5	(23.8)	57	(21.5)
	DD LPS	111	(58.4)	23	(42.6)	0.039	8	(38.1)	142	(53.6)
	LMS	30	(15.8)	6	(11.1)	0.39	5	(23.8)	41	(15.5)
	SFT	6	(3.2)	1	(1.9)	1	1	(4.8)	8	(3)
	UPS	4	(2.1)	0	(0)	0.57	0	0	4	(1.5)
	Others	7	(3.7)	4	(7.4)	0.27	2	(9.5)	13	(4.9)
French grading	1	36	(18.9)	19	(35.2)	$< 10^{-5}$	3	(14.3)	58	(21.9)
	2	83	(43.7)	9	(16.7)	0.028	4	(19)	96	(36.2)
	3	37	(19.5)	1	(1.9)	0.013	4	(19)	42	(15.8)

DD LPS de-differentiated liposarcoma, *ASA* American Society of Anesthesiologists score,

PS (*ECOG*), performance status according to the Eastern Cooperative Oncology Group, *CVD* cardiovascular disease, *WD LPS* well-differentiated liposarcoma, *DD LPS* de-differentiated liposarcoma, *LMS* leiomyosarcoma, *SFT* solitary fibrous tumor, *UPS* undifferentiated pleomorphic sarcoma

treatments. On multivariate logistic analysis (Table 4, right panel), male sex, PS, histology, and SAL remained significant. The nomogram predicting morbidity risk according to preoperative parameters is shown in Fig. 1. On univariate logistic analysis including per operative parameters (Table 5, left panel), the probability of suffering a severe postoperative adverse event increased significantly with transfusion requirement (OR 2.65, $p = 0.002$), operative time (OR 2.98,

TABLE 2 Surgical details

		Primary		Recurrence		p-value	persistence		Total	
		N	(%: $N = 190$)	N	(%: $N = 54$)			(%: $N = 21$)	N	(%: $N = 265$)
Preoperative treatment										
Preoperative CT	[Yes]	13	(6.8)	11	(20.4)	0.007	4	(19)	28	(10.6)
Preoperative RT	[Yes]	12	(6.3)	14	(25.9)	10^{-4}	6	(28.6)	32	(12.1)
Surgery										
Number of resected organs	Median	2	(1–2)	1	(0–2)	$< 10^{-5}$	2	(1–2)	2	(1–2)
Resection										
	Kidney	148	(77.9)	12	(22.2)	$< 10^{-12}$	13	(61.9)	173	(65.3)
	Colon	124	(65.3)	18	(33.3)	$< 10^{-4}$	17	(81)	159	(60)
	Colon + kidney	109	(57.4)	7	(13)	$< 10^{-9}$	12	(57.1)	128	(48.3)
	Psoas	32	(16.8)	9	(16.7)	1	6	(28.6)	47	(17.7)
	Small bowel	3	(1.6)	6	(11.1)	0.005	6	(28.6)	15	(5.7)
	IVC/iliac vein	23	(12.1)	10	(18.5)	0.32	3	(14.3)	36	(13.6)
	Major nerve	7	(3.7)	4	(7.4)	0.27	1	(4.8)	12	(4.5)
	Major artery	5	(2.6)	5	(9.3)	0.045	0	0	10	(3.8)
	Bladder	6	(3.2)	2	(3.7)	1	1	(4.8)	9	(3.4)
	Stomach	5	(2.6)	3	(5.6)	0.38	1	(4.8)	9	(3.4)
	Pancreas (tail + spleen)	18	(9.5)	5	(9.3)	0.96	4	(19)	27	(10.2)
	Pancreas (head)	1	(0.5)	2	(3.7)	0.12	0	(0)	3	(1.1)
	Pancreas (total pancreatectomy)	1	(0.5)	1	(1.9)	0.39	0	(0)	2	(0.8)
Digestive anastomosis	[Yes]	123	64.7	25	46.3	0.014	18	85.7	166	62.6
	[No]	67	35.3	29	53.7		3	14.3	99	37.4
Digestive anastomosis	0–1	182	95.8	46	85.2	0.014	14	66.7	242	91.3
	2–5	8	4.2	8	14.8		7	33.3	23	8.7
Number of digestive anastomoses	Median	1	(0–1)	0	(0–1)	0.17	1	(1–2)	1	(0–1)
Omentoplasty	[Yes]	151	(79.5)	16	(29.6)	$< 10^{-11}$	13	(61.9)	180	(67.9)
Definitive digestive stoma	[Yes]	5	(2.6)	1	(1.9)	1	0	(0)	6	(2.3)
Definitive urinary stoma	[Yes]	2	(1.1)	2	(3.7)	0.21	0	(0)	4	(1.5)
Transfusion requirement, unit of packed red blood cells	[Yes]	76	(40)	12	(22.2)	0.02	4	19	92	35
	Median	2	(2–4)	3	(2–4)	0.51	3	(2–4.25)	2	(2–4)
Use of amines		72	(37.9)	17	(31.5)	0.49	12	(57.1)	101	(38.1)
Operative time, (min, median)		240	(196.25–300)	240	(150–330)	0.49	270	(240–360)	240	(195–300)
Margin										
	R0/R1	185	(97.4)	53	(98.1)		20	(95.2)	258	(97.4)
	R2	5	(2.6)	0	(0)	0.59	1	(4.8)	6	(2.3)

Table 2 (continued)

		Primary		Recurrence		*p*-value	persistence		Total	
		N	(%: *N* = 190)	N	(%: *N* = 54)			(%: *N* = 21)	N	(%: *N* = 265)
Morbidity										
Length of hospitalization (days)	Median	15	(12–22)	13	(9–16)	0.0015	14	(13–21)	14	(11–21.5)
Grade of complication (Clavien–Dindo)										
	3A	2	(1.1)	2	(3.7)	0.17	0	(0)	4	(1.5)
	3B	18	(9.5)	4	(7.4)	1	3	(14.3)	25	(9.43)
	4A	10	(5.3)	1	(1.9)	0.42	1	(4.8)	12	(4.5)
	4B	2	(1.1)	1	(1.9)	0.49	0	(0)	3	(1.1)
	5	5	(2.6)	1	(1.9)	1	0	(0)	6	(2.3)
	Total (3A–5)	37	(19.5)	9	(16.7)	0.64	4	(19)	50	(18.9)
Readmission	[Yes]	4	(2.1)	1	(1.9)	1	1	(4.8)	6	(2.3)

$p = 0.003$), number of digestive anastomoses (OR 3.15, $p = 0.013$), and pancreatic and/or major arterial resection (OR 2.25, $p = 0.032$). On multivariate logistic analysis (Table 5, right panel), only transfusion requirement (OR 2.16, $p = 0.026$) was significant.

The median follow-up was 27.1 months. The 3-year OS and 3-year LRFS of P were 84.9% (CI 0.79–0.91) and 70% (CI 0.63–0.78), with or without complications (HR 1.5, CI 0.65–3.49) and (HR 1.45, CI 0.76–2.77), respectively. The 3-year OS and 3-year LRFS of R were 83.9% (CI 0.72–0.98) and 61% (CI 0.47–0.81), with or without complications (HR 1.85, CI 0.21–16.25) and (HR 0.53, CI 0.07–4.13), respectively.

DISCUSSION

Despite different patient characteristics and surgical constraints, the rates of serious morbidity after surgery of primary RPS and relapses are similar, 18.5% overall, and are responsible for equivalent operative mortality. In the two multivariate analyses, the probability of suffering a severe postoperative adverse event increased with male sex, PS, DD LPS histology, low SAL, and transfusion requirement without impairing oncological outcomes. This outcome underscores that specific factors should be considered rather than the timing of surgery.

The optimization of the local treatment of RPS led to widening of the resection[8,9] to minimize the areas of positive margins and decrease the risk of tumor rupture by handling when necrotic since a large proportion of patients die from iterative local recurrences. Moreover, this process avoids considering multifocal tumors that encompass different organs. This "compartmental resection," pioneered by two centers[8,9] and recommended by TARPSWG guidelines,[2] is mostly adapted to LPS.[11,12,25] It is associated with up to threefold reductions in local recurrence rates of primaries and a gain in overall survival.[8,9] However, the subsequent morbidity with such multivisceral resection is a potential issue.[26] In the present study, the respective rate of serious morbidity after surgery for primary tumors and persistence after macroscopically incomplete surgery, 19.5 and 19%, respectively, and relapses, 16.7%, is comparable to that of previous series using this technique and gathering primaries, one bicentric, 18%,[14] and the series of TARPSWG, 16.4%,[15] and that of recurrent tumors of TARPSWG, 16%.[16] Small variations could be related to the exhaustive nature of the collection of complications; for example, drainage of superficial surgical site infections was considered in our series. This incompressible but < 20% rate of morbidity is related to the high constraints of multivisceral resection (MVR) but compares favorably with the older series in which surgery was mostly more limited. In Judge's series reporting data from the American College of Surgeons National Surgical

TABLE 3 Severe postoperative adverse events (Clavien–Dindo ≥ 3)

Type of complications and interventions	*N* patients (%, *N* = 265)
Patient re-operated	
Iterative laparotomy	15 (5.6)
Bowel anastomotic leak	7 (2.6)
Deep collections	3 (1.1)
Postoperative bleeding	3 (1.1)
Bowel obstruction	2 (0.8)
Superficial reintervention	5 (2)
Wound abscess	4 (1.6)
Postoperative superficial hematoma	1 (0.4)
Percutaneous treatment of vascular thrombosis	3 (1.1)
Transurethral prostate resection for urinary retention	1 (0.4)
Tracheotomy for respiratory failure	1 (0.4)
Total (re-operated patients)	25 (9.4)
Patient not re-operated	
ICU monitoring for pneumonia/respiratory failure	8 (3.4)
Temporary dialysis for renal failure	7 (2.6)
Percutaneous drainage for collection under local anesthesia	4 (1.5)
ICU monitoring for reversible cardiogenic shock	3 (1.1)
Venous thromboembolism	1 (0.4)
ICU monitoring for reversible cerebral vasoconstriction syndrome	1 (0.4)
Urinary retention	1 (0.4)
Total (non re-operated patients)	25 (9.4)
Total (re-operated and non re-operated patients)	50 (18.9)

ICU Intensive Care Unit

Quality Improvement Program (ACS-NSQIP) between 2012 and 2015, 41% of patients underwent MVR.[27] The results from the entire cohort showed 1.2% mortality and 19.1% morbidity with no difference between patients undergoing marginal excision and those undergoing MVR.

In the present series, there was no difference in severe morbidity or mortality rates among primary tumors (19.5%), persistence (19%), and relapses (16.7%), but the factor weighting might be different. Patients operated on from the primary tumor had larger tumors and required more frequent transfusion, whereas patients selected for surgery for recurrences were younger, had more WD LPS, but received more preoperative treatments, and more frequently had major arterial resections because the initial resection attempted to be conservative when the artery was not infiltrated, as recommended. Moreover, the normal anatomic planes were disrupted because of the initial surgery. The characteristics of patients with persistence of the tumor after incomplete surgery were similar to those of patients with primary tumors, but they were operated on when the tumor size was comparable to recurrence with the same rate of preoperative treatment. Therefore, some individual pre- and perioperative parameters should be considered, and are significant for morbidity, whereas the timing of operation is not globally considered.

Half of the serious complications were "medical," with respiratory and temporary renal failures being the most frequent, and two-thirds of the postoperative deaths were consecutive due to medical complications. The prevalence of these two medical complications was also detected in the Fiore study (6.9% respiratory complications and 3.5% renal failure).[28] This finding emphasizes the major role of postoperative nursing and physiotherapy in preventing at least respiratory and venous thromboembolism. Vascular filling is essential to prevent renal failure favored by nephrectomy, combined with possible bleeding and modifications of vessel pressure due to the "removal of the obstacle" consecutive to resection of the tumor.[2] Very few studies have explored the impact of these complications on long-term renal function. In Fiore's study, estimated glomerular filtration rate stage 3 (between 30 and 59 ml/mn) was observed in 37% of the patients at 12 months.[28] The other half of the serious complications were surgical, but only 5.6% of patients received an iterative laparotomy, with bowel anastomotic leakage being the most frequent reason, although patients with low SAL received significantly more temporary digestive derivation.

TABLE 4 Logistic analysis including all preoperative parameters

Preoperative prognostic factors	Severe morbidity		No severe morbidity		Univariate analysis		Multivariate analysis	
	N	%	*N*	%	OR	*p*-value	OR	*p*-value
Albumine								
< 3.5 g/dl	15	7	30	14	3.43 [1.58; 7.36]	0.002	2.86 [1.12; 7.14]	0.02
≥ 3.5 g/dl	22	10	151	69				
Unknown	13		34					
Histologic type								
DD LPS	35	13.2	107	40.4	2.36 [1.24; 4.68]	0.011	2.72 [1.11; 7.4]	0.03
Others	15	5.7	108	40.8				
Age								
< 72	34	13	180	68				
≥ 72	16	6	35	13	2.42 [1.19; 4.81]	0.013	1.4 [0.52; 3.54]	0.49
Sex								
Female	20	8	124	47				
Male	30	11	91	34	2.04 [1.09; 3.87]	0.026	2.46 [1.07; 5.96]	0.03
PS (ECOG)								
0	36	16	171	75				
1	8	4	13	6	2.92 [1.09; 7.47]	0.027	3.21 [0.95; 10.45]	0.05
Not significant								
Timing of surgery								
Primary+Persistance	41	15	170	64				
Recurrence	9	3	45	17	0.83 [0.36; 1.77]	0.64		
Primary	37	14	153	58				
Recurrence+Persistance	13	5	62	23	0.87 [0.42; 1.71]	0.69		
Cardiovascular disease								
No	31	12	156	59				
Yes	19	7	59	22	1.62 [0.84; 3.07]	0.14		
ASA								
1 to 2	37	14	177	67				
3	13	5	38	14	1.64 [0.77; 3.31]	0.18		
Other cancers								
No	45	17	177	67				
Yes	5	2	38	14	0.52 [0.17; 1.28]	0.19		
Obesity								
No	41	15	188	71				
Yes	9	3	27	10	1.53 [0.64; 3.39]	0.31		
Diabetes								
No	45	17	200	75				
Yes	5	2	15	6	1.48 [0.46; 4.05]	0.47		
Neoadjuvant CT								
No	46	17	191	72				
Yes	4	2	24	9	0.69 [0.20; 1.9]	0.51		
Neoadjuvant RT								
No	43	16	190	72				
Yes	7	3	25	9	1.24 [0.47; 2.91]	0.64		
Histologic size								
< 30 cm	34	13	152	58				
≥ 30 cm	16	6	62	23	1.15 [0.58; 2.21]	0.67		

Table 4 (continued)

Preoperative prognostic factors	Severe morbidity		No severe morbidity		Univariate analysis		Multivariate analysis	
	N	%	*N*	%	OR	*p*-value	OR	*p*-value
Side								
Left	24	9	109	41				
Right	26	10	106	40	1.11 [0.6; 2.07]	0.73		
Symptoms								
No	33	13	145	55				
Yes	17	6	67	26	1.14 [0.57; 2.12]	0.74		
Tobacco								
No	24	13	105	55				
Yes	11	6	51	27	0.94 [0.41; 2.037]	0.94		

Severe morbidity: postoperative adverse events (Clavien–Dindo ≥ 3), *DD LPS* de-differentiated liposarcoma, *ASA* American Society of Anesthesiologists score, *PS* (*ECOG*), performance status according to the Eastern Cooperative Oncology Group, *CT* chemotherapy, *RT* radiotherapy

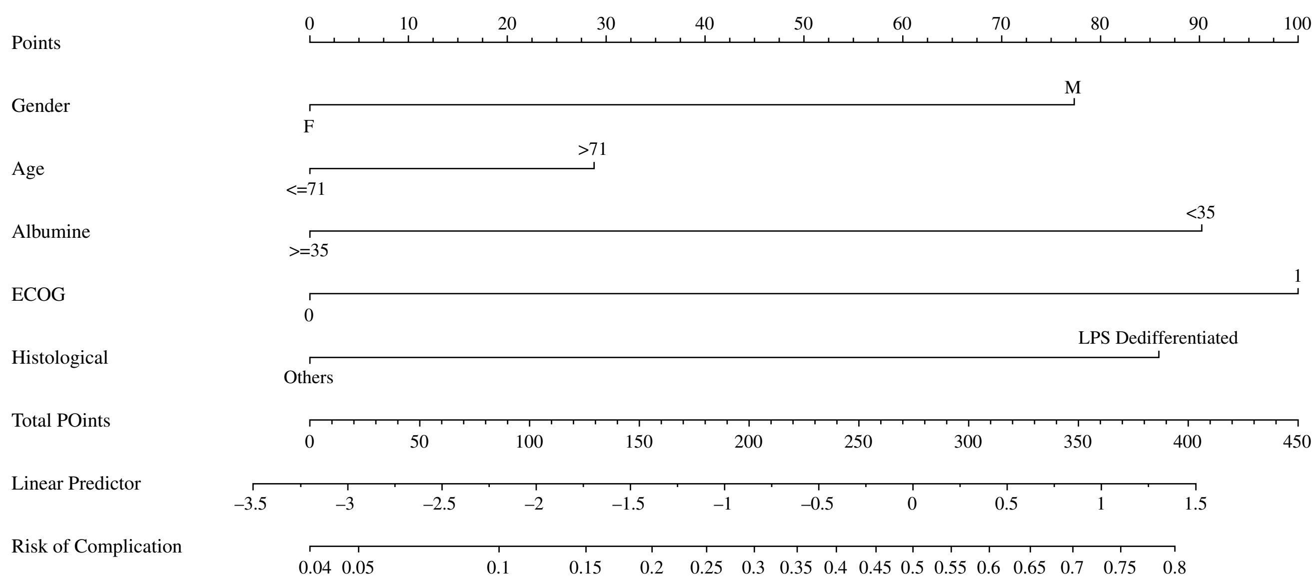

FIG. 1 Nomogram predicting morbidity risk according to preoperative parameters

To our knowledge, this study is the first to evaluate the impact of a large set of parameters that can be identified preoperatively. The intrinsic risks related to the patient and their tumor are essential for the patient's information and should be distinguished from those resulting from surgery. Their recognition could mitigate the extent of the surgery, specifically the resection of adherent organs not overtly invaded or the use of a temporary digestive derivation. In the multivariate analysis, a significant association was detected between severe adverse events and PS, male sex, DD LPS, and SAL < 3.5 g/dl. A nomogram was built to help preoperatively evaluate this risk, which included all of these parameters and age. Elderly patients had a higher risk of severe adverse events in the monovariate analysis, as reported in the TARP-SWG study and in the Royal Marsden Hospital series.[15,29] PS considers age and frailty, so this factor was an independent predictor of serious morbidity in the multivariate analysis. Male sex was another independent predictor, which could be related to higher visceral fat and a narrower pelvis, which can render abdominal surgery more difficult.[30] Moreover, the female immune system responds more efficiently to any pathogen.[31] Histology also significantly impacted serious morbidity: in contrast to well-differentiated LPS and LMS, de-differentiated parts of LPS are particularly adherent to the

TABLE 5 Severe morbidity: postoperative adverse events (Clavien–Dindo ≥ 3)

Per operative prognostic factor	Severe morbidity		No severe morbidity		Univariate analysis		Multivariate analysis	
	N	%	*N*	%	OR	*p*-value	OR	*p*-value
Transfusion								
No	23	9	149	56				
Yes	27	10	66	25	2.65 [1.42; 5]	0.0023	2.16 [0.044; 0.17]	0.026
Operative time								
< 240 mn	10	4	91	35				
≥ 240 mn	40	15	122	46	2.98 [1.47; 6]	0.003	1.9 [0.85; 4.5]	0.13
Digestive anastomoses								
0 to 1	41	15	201	76				
2 to 5	9	3	14	5	3.15 [1.24; 7.69]	0.013	2.45 [0.9; 6.49]	0.073
Resection pancreas or major artery								
No	37	14	186	70				
Yes	13	5	29	11	2.25 [1.05; 4.68]	0.032	1.38 [0.59; 3.11]	0.44
Not significant								
Vasoactive amines								
No	25	10	128	50				
Yes	23	9	78	31	1.51 [0.80; 2.85]	0.2		
Epiploplasty								
No	14	5	70	27				
Yes	35	13	145	55	1.21 [0.62; 2.45]	0.59		

adjacent organs without any plane of dissection,[28] which can increase operating time and bleeding, especially when the de-differentiated part is in the tumor periphery, in contact with the noble structures that one wishes to preserve (vessels). Although hypoalbuminemia can result from a variety of pathophysiologic processes, it is commonly associated with an increased risk of morbidity and mortality, as already shown in RPS surgery.[33,34] Albuminemia has the advantage of being a routine exam that is always available, in contrast to other more specific laboratory markers, such as the Prognostic Inflammatory and Nutritional Index (PINI), which is practically available in less than half of cases, including in expert centers.[34] Hypoalbuminemia identifies a high-risk group that might benefit from more intense nutritional support before surgery and a transitory digestive derivation. Body mass index (BMI) is not informative since significant tumor mass can change BMI.

Using a separate multivariable Cox model including per operative parameters, a significant association was detected between severe adverse events and operative time, ≥ 2 digestive anastomoses, resection of a major arteria and/or pancreas, and requirement for transfusion. Obviously, surgical complexity, which could be approached by these individual parameters or by a global resected organ score (ROS), as described in the TARPSWG series, increases the risk of complications.[15,16] In a bicentric study, a direct linear relationship was observed between a higher resected organ score and increasing units of red blood cell transfusion.[35] Similarly, pancreatic resection of soft pancreatic tissue exposes patients to pancreatitis and secondary bleeding, which was the only surgical cause of death in this series. In the TARPSWG series of patients with distal pancreatectomy for primary RPS, the 90-day severe complication rate was 40%, and the cumulative mortality rate was 6.9% at 90 days, emphasizing a higher risk compared with the general RPS population.[36] However, in the multivariate model, only transfusion requirement achieved statistical significance, as in the TARPSWG study on recurrent RPS.[16] Consequently, the surgical objective is not to multiply the parameters that will increase the risk of complications, but to consider these factors by adjusting the technique. For instance, major arterial grafts should prompt a discussion of cross-femoral bypass in cases of multiple digestive anastomoses, and the pancreas should be resected only if infiltrated. Tranexamic acid administration could decrease perioperative bleeding and was routinely used.[37]

Preoperative treatment with chemo- or radiotherapy did not increase operative risk, in line with previous data from TARPSWG.[15] In STRASS, the rates of postoperative death (approximately 2%) and reoperation (11%) were also similar with and without preoperative radiotherapy.[3] More insight will be provided by STRASS 2 on the impact of neoadjuvant chemotherapy on morbidity and mortality. Importantly, serious morbidity did not impact oncological outcomes when postoperative death was omitted, as found in previous studies.[15]

The main limitation of this study is that these results represent those of a high-volume center (HVC) trained in RPS surgery (38 RPS surgeries/year) with a dedicated team. They are not transferable to nonspecialized centers but are in line with those of TARPSWG, which reported collaborative data from HVCs, including our own experience. In addition, we previously showed that 3-year RPS overall survival was at least 20% better in HVCs.[6] All of these results call for the centralization of RPS surgeries in HVCs.

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