



Postoperative Morbidity After Radical Resection of Retroperitoneal Solitary Fibrous Tumor

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Background: This study aimed to investigate the clinicopathological characteristics of retroperitoneal solitary fibrous tumor (RSFT) and the safety of radical resection.

Methods: A retrospective analysis was conducted on the data of 32 RSFT patients who received surgery with curative intent from February 2011 and June 2021.

Results: This cohort included 16 (50%) male and 16 (50%) female patients, with the median age of 52 (29 to 72) years. Tumor burden ranged from 3 to 25 (median, 10) cm. Seven patients received arterial embolization before surgery. 15 (47%) patients received radiotherapy, nine (28%) of which received preoperative radiotherapy. Most of the patients (91%) achieved complete resection with median bleeding of 400 (20 to 5,000) ml. Nine (28%) patients received packed red blood cell (RBC) transfusion, with a median of 5 (2 to 10) U. All patients had the five-year progression-free survival rate and the overall survival rate of 75.8% and 80.0%, respectively. 11 (34%) patients were found with adverse events, and four (12%) patients were found with serious postoperative complications (Clavien-Dindo ≥ 3), of which one (3.1%) patient died after surgery. The univariate analysis found that tumor burden ($p = 0.022$), packed RBC transfusion ($p = 0.001$) and postoperative hospital stays (0.027) were correlated with overall morbidity. The multivariate analysis found packed RBC transfusion as an independent risk factor for postoperative morbidity (HR 381.652, 95% CI, 1.597–91213.029, $p = 0.033$).

Conclusion: RSFT was confirmed as an uncommon, slow-growing and recurring tumor, with acceptable postoperative morbidity and mortality after surgical resection.

Keywords: retroperitoneal, solitary fibrous tumor, neoadjuvant radiotherapy, preoperative embolization, morbidity, progression-free survival (PFS), overall survival (OS)

INTRODUCTION

Solitary fibrous tumor (SFT), previously named as hemangiopericytoma, has been found as a rare tumor derived from the mesenchyme. The incidence rate of SFT reaches nearly 0.2 per 100,000 population per year (1). Klemperer et al. first described SFT as a pleural tumor, and it was later found on the external thorax (e.g., adrenal glands, head and neck, retroperitoneum, kidney, liver and skeletal muscle) (2). Surgical resection is recognized as the cornerstone of treatment, which can make the optimal long-term prognosis of SFT. The recurrence-free survival rate of SFT is $>90\%$ with complete resection (3, 4), while large SFTs are often highly vascular (5). Besides, the

retroperitoneum is a huge anatomical space, which often has a greater tumor burden compared with other parts. Furthermore, the scope of resection is generally limited by the surrounding structures (6).

There have been rare studies on retroperitoneal SFT (RSFT), with only two literature reports previously. One literature report is conducted by Rahul Rajeev et al., which contained 18 RSFT patients (7), and the other is a report of 35 primary RSFT patients by Peng Luo et al. (8), whereas relevant postoperative complications data were not included.

This study aimed to investigate the clinicopathological features of RSFT and the safety of radical resection.

METHODS

This retrospective study was conducted at the South Hospital of Zhongshan Hospital/Shanghai Public Health Clinical Center. As approved by the ethics committee, this study retrospectively analyzed the clinicopathological data of patients pathologically diagnosed with SFT (or hemangiopericytoma) from February 2011 to June 2021. Further selection criteria included (1) the location at retroperitoneum, (2) for radical surgery, and (3) complete clinicopathological data and available follow-up information.

The data included gender, age, ASA score, symptoms, presentation status (primary or recurrence), tumor location (abdominal or pelvic), multifocality, tumor burden, malignancy, Ki-67, preoperative embolization, radiation, neoadjuvant radiotherapy, chemotherapy, complete resection, estimated blood loss, packed RBC transfusion, postoperative ICU stay, postoperative complications [Clavien-Dindo classification (9)], as well as postoperative hospital stays.

Tumor burden referred to the sum of the largest diameters of all tumors reported in the surgical record. Complete resection was defined as negative margins (R0) or positive micro margins (R1) without positive gross margin resection (R2). Malignant SFT was diagnosed for lesions with at least one of the characteristics below: hypercellularity, mitotic index > 4/10 at high power field, necrosis, margin of infiltration, as well as pleomorphism (10). Severe postoperative adverse events were classified as Clavien-Dindo 3 or higher.

For the postoperative follow-up, the respective follow-up required clinical and imaging examination (CT or MRI of the chest, abdomen and pelvis). Patients were followed up every 3–4 months for the first 2 years, every 6 months after 2 years, as well as every year after 5 years. Information acquired during follow-up involved disease progression and death. Imaging findings of new lesions or significant enlargement of the original lesions were defined as disease progression.

RESULTS

Baseline Characteristics

This study included 32 RSFT patients who received surgical resection with curative intent at South Hospital of Zhongshan Hospital/Shanghai Public Health Clinical Center, of which the details and the summary of clinicopathologic characteristics

are listed in **Table 1**. This cohort covered 16 (50%) male and 16 (50%) female patients, and the median age of all patients was 52 (29 to 72) years. There were eight (25%) patients with ASA classification over grade 1 and seven (22%) patients with recurrent disease. The tumors of most of the patients were located in the pelvic cavity (75%), and with monofocality disease (91%). Tumor burden ranged from 3 to 25 (median, 10) cm. Moreover, 12 (38%) patients were classified to be malignant, while 20 (62%) patients were classified to be benign. Seven patients had undergone arterial embolization before surgery with the median bleeding of 500 (range, 20–3,500) ml. A total of 15 (47%) patients received radiotherapy, nine (28%) patients of which received preoperative radiotherapy. Most patients achieved complete resection (91%), with median bleeding of 400 (range, 20–5,000) ml. Nine (28%) patients received packed RBC transfusion, with a median infusion of 5 (range, 2–10) U. At the median follow-up time of 58.2 (95%CI, 36.1–80.4) months, six (19%) patients had disease recurrence, and five (16%) patients died. The 5-year disease-free survival rate and the overall survival rate of all patients reached 75.8% and 80.0%, respectively (**Figure 1**).

11 (34%) patients were found with adverse events, and four (12%) were found with severe postoperative adverse events. The results showed that one (3.1%) patient died after surgery, one (3.1%) suffered bleeding, one (3.1%) had urinary tract infection, two (6.3%) had sepsis, two (6.3%) had wound infection, two (6.3%) had intraabdominal abscesses, and two (6.3%) had ascites.

Risk Factor Analysis

In the univariate analysis, the probability of patients with a postoperative adverse event increased significantly with tumor burden ($p = 0.022$), packed RBC transfusion ($p = 0.001$) and postoperative hospital stays (0.027). The variables with $p < 0.2$ (i.e., tumor burden, number of combined resections, estimated blood loss, packed RBC transfusion, as well as postoperative hospital stays) according to the univariate analysis were applied for the multivariate analysis. In the multivariate logistic analysis, only packed RBC transfusion was still statistically significant (HR 381.652, 95% CI, 1.597–91213.029, $p = 0.033$) (**Table 2**).

DISCUSSION

SFT has been found as a rare, slow-growing neoplasm of mesenchymal tissue origin, which largely occurs in middle-aged patients (3, 11). The incidence of ESFT is significantly higher than that of pleural counterpart, taking up nearly 70% of all SFTs (2), and retroperitoneum is one of the most common sites of ESFT (4, 12). Surgical resection remains the cornerstone of a radical cure (3). However, since SFT is a highly vascularized tumor, there has been no lack of case reports of intraoperative hemorrhage and even death from intraoperative hemorrhage (13–15). Moreover, since RPS often grows huge and requires multiple organ resections, the perioperative risk is elevated (16). Accordingly, the perioperative safety of RSFT should be verified urgently.

There have been only two cohort reports on RSFT in the past. Peng Luo et al. studied 35 patients with retroperitoneal SFT and reported that tumor size ≥ 10 cm was independently correlated

TABLE 1 | Patient and tumor characteristics in 32 patients with retroperitoneal solitary fibrous tumor.

Characteristics	N = 32	% of Total	Complication group	Non-complication group	P-value
Gender					0.458
Male	16	50	4	12	
Female	16	50	7	9	
Age, years median (range)	52 (29–72)		51 (30–70)	52 (29–72)	0.802
ASA score					0.397
1	24	75	7	17	
≥1	8	25	4	4	
Symptoms					0.703
Yes	8	25	2	6	
No	24	75	9	15	
Primary disease					1.000
Yes	25	78	9	16	
No	7	22	2	5	
Location					0.397
Abdominal cavity	8	25	4	4	
Pelvic cavity	24	75	7	17	
Multi-focal disease					1.000
Yes	3	9	1	2	
No	29	91	10	19	
Tumor burden, cm median (range)	10 (3–25)		15 (5–25)	7 (3–20)	0.012
Histologic subtypes					0.465
Benign	20	62	8	12	
Malignant	12	38	3	9	
Ki-67	5 (1–40)		5 (2–20)	5 (1–40)	0.346
Preoperative embolization					0.667
Yes	7	22	3	4	
No	25	78	8	17	
Radiation	15	47	5	10	0.907
Yes	15	47	5	10	
No	17	53	6	11	
Neoadjuvant radiotherapy					0.681
Yes	9	28	4	5	
No	23	72	7	16	
Chemotherapy					0.111
Yes	2	6	2	0	
No	30	94	9	21	
Complete resection					1.000
Yes	29	91	10	19	
No	3	9	1	2	
Number of combined resections					
0	16	50	5	11	
1	12	38	3	9	
2	2	6	1	1	
3	0	0	0	0	
4	2	6	2	0	
Estimated blood loss, ml median (range)	400 (20–5,000)		600 (50–5,000)	250 (20–2,200)	0.011

(Continued)

TABLE 1 | Continued

Characteristics	N = 32	% of Total	Complication group	Non-complication group	P-value
Packed RBC transfusion					<0.001
Yes	9	28	8	1	
No	23	72	3	20	
Packed RBC transfusion, unit median (range)	5 (2–10)		6 (6–6)		0.777
ICU Stay					0.730
Yes	10	31	4	6	
No	22	69	7	15	
Clavien–Dindo classification					0.206
NA	21	66	0	21	
1–2	7	22	7	0	
3–5	4	12	4	0	
Postoperative hospital stay, days median (range)	12 (4–55)		20 (8–55)	11 (4–30)	
Disease recurrence					0.637
Yes	6	19	1	5	
No	26	81	10	16	

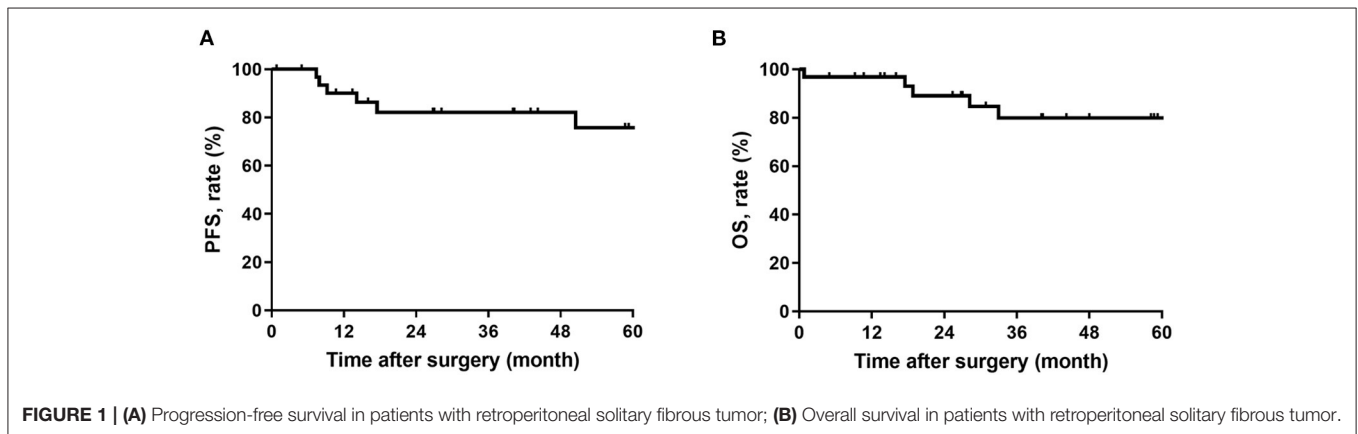


FIGURE 1 | (A) Progression-free survival in patients with retroperitoneal solitary fibrous tumor; (B) Overall survival in patients with retroperitoneal solitary fibrous tumor.

with short DFS. Compared with our cohort, the two groups had comparable malignant ratios (37 vs. 38%) and median tumor sizes (9 vs. 10 cm), but no one was treated with radiotherapy in Peng's cohort, and the postoperative morbidity and mortality of the patients were not reported (8). Another study was reported by Rahul Rajeev et al. (7) in 2015 by complying with The National Cancer Database data. Since the number of patients is limited (only 18 patients), postoperative complications were not systematically reported or analyzed. This is the first study to assess the postoperative morbidity and mortality of RSFT. In this study, adverse events were reported in 11 (34%) patients, four (12%) patients suffered from a serious complication after surgery, one (3.1%) patient died after surgery. The short-term prognosis of the patients in this study complied with the results reported in previous studies on RPS (17–19). For instance, Tseng et al. (17) used data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) to study the safety of radical RPS resection. In the ACS-NSQIP study, the

results of the entire cohort included a mortality rate of 1.3%, a morbidity rate of 26%, as well as a severe morbidity rate of 11.5%. Therefore, as indicated by the findings from our sarcoma center, RSFT radical resection is relatively safe.

In this study, transfusion requirements were the significant predictors of postoperative adverse events. In particular, nine (28%) patients received packed RBC transfusion in the perioperative period, and eight (89%) of them were found to develop postoperative complications. This proportion was only 13% who did not receive packed RBC transfusion, consistent with the results of two recent reports from the Transatlantic Australasian RPS Working Group (TARPSWG) on the perioperative safety of primary RPS and recurrent RPS (18, 19). For critically ill patients with massive blood loss or anemia, blood transfusion was found as a life-saving method. In patients who received major surgery, infusion of concentrated red blood cells, fresh frozen plasma, platelets or cryoprecipitate was found to be essential to maintain

TABLE 2 | Univariable and multivariable analyses to determine independent predictors of adverse events of retroperitoneal solitary fibrous tumor.

Variables	Univariate analysis		Multivariate analysis	
	Hazard ratio (95%CI)	P-value	Hazard ratio (95%CI)	P-value
Gender female vs. male	2.333 (0.520–10.478)	0.269		
Age (continuous)	1.008 (0.951–1.068)	0.794		
ASA score > 1 vs. 1	2.429 (0.470–12.542)	0.289		
Symptoms yes vs. no	1.429 (0.303–6.737)	0.652		
Primary disease yes vs. no	1.406 (0.225–8.783)	0.715		
Location Abdominal vs. Pelvic	2.429 (0.470–12.542)	0.289		
Multi-focal disease yes vs. no	0.950 (0.076–11.803)	0.968		
Tumor burden (continuous)	1.188 (1.025–1.377)	0.022	1.144 (0.897–1.459)	0.277
Histologic subtypes Malignant vs. Benign	0.500 (0.103–2.436)	0.391		
Ki-67 (continuous)	0.960 (0.883–1.044)	0.342		
Preoperative embolization yes vs. no	1.594 (0.286–8.871)	0.595		
Neoadjuvant radiotherapy yes vs. no	1.829 (0.374–8.937)	0.456		
Complete resection yes vs. no	0.975 (0.277–3.436)	0.968		
Number of combined resections (continuous)	1.882 (0.845–4.194)	0.122	1.504 (0.370–6.112)	0.569
Estimated blood loss (continuous)	1.001 (1.000–1.002)	0.073	0.999 (0.996–1.001)	0.316
Packed RBC transfusion yes vs. no	5.333 (4.804–592.100)	0.001	381.652 (1.597–91213.029)	0.033
ICU stay yes vs. no	1.429 (0.303–6.737)	0.652		

hemostasis, correct abnormal coagulation, and ensure adequate tissue perfusion and oxygenation (20). However, it has been extensively found that for patients who received surgery, whether to infuse RBC in the perioperative period is correlated with short-term and long-term prognoses (20–22). According to the relationship between perioperative blood transfusion and postoperative systemic inflammatory response, the interference of blood transfusion on postoperative immune disorders could be the mechanism leading to poor prognosis (23). Therefore, strict standards should be formulated based on the evaluation of the appropriateness of blood transfusion, and it is recommended to limit non-essential blood transfusion during the perioperative period.

Neoadjuvant radiotherapy can be used to shrink tumors, which has been found to improve local symptoms and facilitate surgical resection. Targeted radiotherapy of 50 to 60 Gy can decrease the tumor volume from pelvic or thoracic tumors by up to 60% (24–26). Radiation therapy has become one of the main treatments or adjuvant therapy for head, neck and chest SFT. (27, 28). The results of this study showed that there was no additional morbidity or mortality correlated with radiation therapy, consistent with the EORTC STRASS trial, in which the second mid-term safety analysis reported that adjuvant radiotherapy did not increase the risk of perioperative complications (29).

Arterial embolization blocks the terminal arterial supply of tumors, leading to hypoxia and ischemia. It has been employed to effectively treat blood-rich tumors. Since a huge SFT usually has a large blood supply vessel, it has been reported that the blood loss during surgery was large (13), so preoperative selective embolization of the supply vessel of SFTs could reduce

intraoperative blood loss without blood transfusion (30, 31). In this study, seven patients received preoperative arterial embolization, and preoperative embolization was not found as a risk factor for postoperative complications in the risk factor analysis. Due to the possibility of intestinal ischemia, especially for tumors with main blood supply as the inferior mesenteric artery, surgery should be performed in 1–2 days after embolization, and patients' abdominal signs should be carefully observed after embolization, so as not to ignore intestinal ischemia complication.

The univariate analysis found that the tumor size was correlated with postoperative complications, while there was no statistical difference in the multivariate analysis. Numerous researchers have reported that the tumor size is negatively correlated with the prognosis of ESFT. Demicco EG et al. and Smith SC et al. suggested that patients with large tumors had decreased DSS (32). Peng Luo et al. also highlighted that tumor size ≥ 10 cm could be conducive to the independent prognosis of shortened DFS (8). More advanced and larger tumors may lead to longer operation times, greater difficulty and greater inflammation and blood transfusion requirements, thus resulting in the increase in morbidity and mortality.

This study has certain limitations. First, it was a retrospective study, and there were still biases in statistical analysis. Furthermore, though the blood transfusion was found as a risk factor for postoperative disease, the 95% CI range was relatively large due to the limited sample size, so we should draw a careful conclusion. In addition, since only two patients in this study were treated with neoadjuvant chemotherapy and only nine patients received radiotherapy before surgery, it would be difficult to accurately evaluate the efficacy of adjuvant therapy strategies.

This was the first study that presented the clinicopathologic features and analyzed the postoperative morbidity factors for RSFT by using the data of 32 patients from a tertiary cancer center.

SFT refers to a blood-rich tumor, and retroperitoneal tumors are often huge, whereas the overall postoperative safety is controllable, and preoperative radiotherapy and interventional embolization are all possible methods to consider. Intraoperative packed RBC transfusion has been found as an independent risk factor for postoperative complications. We should fine-tune the operation to reduce intraoperative bleeding and reduce RBC transfusion.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Ethics Committee of South Hospital of Zhongshan Hospital/Shanghai Public Health Clinical Center. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

AZ, LM, and YF collected, analyzed, and interpreted the patient data. AZ was a major contributor in writing the manuscript. WL provided writing ideas, helped data analysis, and article proofreading. HT and YZ provided the research ideas and guidance and were responsible for the results of this study. All authors contributed to the article and approved the submitted version.

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