Surgical Approach and Oncologic Outcomes Following Multidisciplinary Management of Retrorectal Sarcomas

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ABSTRACT

Background. Retrorectal sarcomas are rare, and limited data are available on oncologic outcomes following surgery. Our aim was to evaluate outcomes in this patient population at our institution.

Materials and Methods. All patients who underwent surgical resection of a malignant retrorectal/presacral sarcoma between 1985 and 2005 were identified. Data analyzed included demographics, histopathologic diagnosis, surgical morbidity and mortality, use of adjuvant therapy, local and distant recurrence, and survival.

Results. A total of 37 patients were identified (20 males) with a median age of 49 years (range, 22–81 years). The most common histopathologic diagnosis was malignant peripheral nerve sheath tumor ($n = 8$). Also, 22 tumors were high grade and 15 were low grade. Surgical margin status was R0 in 31 patients and R1 in 6. Adjuvant therapy was given to 26 patients. Postoperative morbidity and mortality was 57% and 3%, respectively. Median length of follow-up in 16 patients alive at last contact was 4.7 years. The 5-year survival free of local (LDFS), distant (DDFS), and local or distant recurrence (DFS) was 51, 58, and 39%, respectively. Patient survival at 2, 5, and 10 years was 75, 55, and 47%, respectively. Disease-free survival was not significantly associated with gender ($P = .16$), primary vs

secondary ($P = .94$), R0 vs R1 resection ($P = .26$), low vs high tumor grade ($P = .17$), or the use of surgery with or without adjuvant therapy ($P = .33$).

Conclusions. Retrorectal sarcomas are often high grade and locally advanced. Most tumors are resectable with free margins, and long-term survival may be possible in up to one-half of patients following an aggressive surgical approach.

Patients with malignant tumors arising in the retrorectal or presacral space present a significant challenge to pelvic surgeons. Diverse pathology, delayed presentation, and locally advanced disease characterize these lesions. An aggressive surgical approach may not always be considered because of the lack of technical expertise, and the surgeon's concern that operative complications and post-operative disability will be too high.

Of the wide range of malignant tumors arising in the retrorectal space, sacrococcygeal chordomas are the most common.^{1–3} Surgical management and oncologic outcomes of these tumors have been well described with 5-year disease-free survival reported to be as high as 60%.⁴ On the contrary, surgical management of nonchordoma malignant retrorectal tumors has only been reported in small series or single-case reports, and therefore limited data exist on long-term oncologic outcomes.^{1,3} In a previous analysis of malignant retrorectal tumors by our institution, we found that the majority of nonchordoma retrorectal tumors were sarcomas.³ In that series, oncologic outcomes were poor, but this was early in our experience and prior to the routine use of a multidisciplinary approach.

Because of the location of some pelvic sarcomas in the retrorectal space, colorectal surgeons may be asked to

evaluate and make treatment recommendations for these patients. Given the advances in surgical technique and adjuvant therapy over the last 20 years, we aimed to evaluate our results in patients with retrorectal sarcomas in the modern era that included a multidisciplinary management approach.

METHODS

Following approval by the Institutional Review Board, the prospectively maintained Surgical Pathology and Tumor Registry databases at the Mayo Clinic Rochester (MCR) were examined to identify all patients who underwent surgery for a retrorectal tumor between 1985 and 2005. Operative notes and imaging studies were reviewed to confirm that all lesions extended into, or were primarily located in, the retrorectal or presacral space. Primary sacral-based tumors that extended into and occupied the retrorectal space were included. The anatomical definition of what constitutes this space has been published previously.⁵ Sarcomas confined to the sacrum, nonsarcoma retrorectal malignant lesions, and patients with distant metastatic disease at the time of initial evaluation were excluded from analysis.

Primary resections were defined as those patients who had an attempt at curative surgery at MCR for a newly discovered retrorectal sarcoma. Secondary resections were defined as those patients who had surgery at MCR for locally recurrent tumors and also those patients who had had breach of their tumor capsule by previous subtotal resection or by an open biopsy. Patients with locally recurrent disease, previous subtotal resection, and open biopsy were considered to be high risk for local recurrence, postoperative complications, and worse survival and so were combined into 1 group for analysis purposes to see how their outcomes compared with primary resection patients. A negative surgical margin is defined as an “R0 resection,” a microscopically positive surgical margins is defined as an “R1 resection.”

The type of hemipelvectomy performed depended on the extent of tumor. In patients in whom resection required loss of spinopelvic continuity, sacrifice of the lumbosacral trunk, and resection of the native hip joint, external hemipelvectomy (hindquarter amputation) was performed to obtain an R0 margin and provide viable tissue for flap closure. In patients with lesser extent of tumor, resection of a portion of the sacrum and hemipelvis (medial ilium) was possible with preservation of the limb.

Clinical records were reviewed, and data were extracted regarding demographics, clinicopathologic features, surgical technique, use of adjuvant therapy, including intraoperative radiation therapy (IORT), postoperative

morbidity, and mortality. Survival free of local recurrence (LDFS), survival free of distant recurrence (DDFS), and survival free of first recurrence, either local or distant (DFS), was calculated. The histopathology was reviewed and confirmed by a pathologist.

Statistical Analysis

Descriptive statistics are reported as a percentage of the group total and continuous variables as a median and range. The Kaplan-Meier method was used to estimate OS and DFS. Associations between variables and either OS or DFS were assessed using Cox proportional hazards regression, and results reported as hazard ratio (HR) and 95% confidence interval (95% CI). The alpha level was set at .05 for statistical significance.

RESULTS

A total of 37 patients (20 males) with a median age of 49 years (range, 22–81 years) were identified. Of these, 26 patients presented with primary tumors, 11 with secondary tumors (5 with locally recurrent lesions, 6 with incompletely excised lesions or open biopsies). Table 1 outlines the histopathological features of the tumors. The median tumor size was 10 cm (range, 4.5–27 cm), and most tumors were high grade. The stage distribution for our cohort is shown in Table 2. Stage III disease was the most common presentation, and no patients were node-positive.

TABLE 1 Histopathological features of cohort

Tumor type	No.	Tumor grade	
		High	Low
Malignant peripheral nerve sheath tumor	8	5	3
Pleomorphic undifferentiated sarcoma	6	6	0
Leiomyosarcoma	4	1	3
Chondrosarcoma			
Dedifferentiated	3	3	0
Conventional	3	0	3
Mesenchymal	1	1	–
Liposarcoma			
Well differentiated	3	0	3
Myxoid liposarcoma	2	0	2
Dedifferentiated	1	1	–
Osteosarcoma	3	3	0
Malignant solitary fibrous tumor	1	1	–
Fibromyxoid sarcoma	1	–	1
Gastrointestinal stromal tumor	1	1	–

TABLE 2 Stage distribution of cohort

Stage ^a	No. of patients ^b (%)
Stage IA	3 (9%)
Stage IB	5 (14%)
Stage IIA	4 (11%)
Stage IIB	6 (17%)
Stage III	17 (49%)
Stage IV	0

^a Based on AJCC Cancer Staging Manual²⁰

^b 2 of 37 patients could not be staged due to incomplete information

Presenting symptoms at the time of evaluation were pain (70%), constipation (5%), and no symptoms (24%).

Preoperatively, chemotherapy alone was given to 3 patients, radiotherapy alone to 8 patients, and combined chemoradiation to 9 patients. Also, 8 patients received IORT, 6 with R0 resections (less than 2-cm margins) and 2 with R1 resections. Postoperatively, chemotherapy alone was given to 2 patients, radiation alone to 7 patients, and combined chemoradiation to 4 patients.

A total of 28 patients underwent en-bloc resection of adjacent pelvic organs or bony structures because of local extension of their tumor. The most common pelvic organs removed were ureter and/or bladder ($n = 9$) and rectum ($n = 6$). The most common bony structures removed included sacrum ($n = 5$) and those associated with internal and external hemipelvectomy ($n = 11$). Resection margin status was R0 in 31 patients (84%) and R1 in 6 patients (16%). All patients with R1 resection had extensive pelvic sidewall disease, 4 of which with recurrent disease or previous subtotal resections.

Postoperative complications were recorded in 21 patients (58%), with bleeding in the postoperative period requiring transfusion ($n = 5$) and wound complications being the most common ($n = 4$). The majority of complications occurred in patients who had sacral resection and

hemipelvectomy (Table 3). The median intraoperative blood loss was 3000 mL (IQR, 1700–5375 mL). The median blood loss was greater in sacrectomy and hemipelvectomy patients compared with those without bony resection (5000 vs 2500 mL). A 30-day mortality occurred in 1 patient secondary to necrotizing fascitis of a soft-tissue flap. Two patients who had no nerve excision as part of their operation had postoperative lumbosacral plexopathy resulting in impaired lower extremity dorsiflexion (foot drop). The median length of stay in the 36 patients discharged from the hospital was 12.5 days (range, 4–150 days).

The median length of follow-up in the 16 patients alive at last contact was 4.7 years. Patient survival at 2, 5, and 10-years was 75% and 55% and 47%, respectively (Fig. 1). The 5-year LDFS, DDFS, and DFS were 51%, 58%, and 39%, respectively (Fig. 2). Disease-free survival was not significantly associated with female relative to male gender (HR = 1.8, $P = .16$), secondary relative to primary resection (HR = 1.0, $P = .94$), R0 relative to R1 resection (HR = 2.0, $P = .26$), high (III/IV) relative to low (I/II) tumor grade (HR = 1.8, $P = .17$), or the use of surgery with or without adjuvant therapy ($P = .33$) (Table 4). In the patients who have died, 16 of 21 (76%) was due to recurrent metastatic disease.

DISCUSSION

Review of the surgical outcomes in patients at our institution with retrorectal sarcomas revealed several significant findings: (1) most patients presented with large, locally advanced high-grade sarcoma variants, (2) up to 30% presented to our institution with either a locally recurrent or an incompletely excised tumor, (3) R0 resection could be achieved in almost all patients, but multiorgan and bony resection was often necessary, (4) operative mortality was low, but postoperative morbidity

TABLE 3 Postoperative complications in first 30 days

Postoperative complication	No. patients
Bleeding ^a	5
Flap dehiscence ^b	2
Intra-abdominal abscess ^c	2
Wound infection	2
Neurologic injury	2
Small bowel obstruction	1
Pulmonary embolus	1
Other	7

^a Requiring transfusion

^b Required reoperation

^c Required percutaneous drainage

FIG. 1 Overall survival

FIG. 2 Disease-free survival

was high, (5) local and distant recurrence was common, but 5-year survival was achieved in more than 50% of patients.

Retrorectal tumors are rare, and their true incidence is difficult to accurately assess.⁶ Tumors located in this anatomical space encompass a wide spectrum of pathology and typically fall under 1 of 4 categories; congenital, neurogenic, osseous, or miscellaneous. Malignant lesions have been described in each of these categories, and previous data published by our institution reported that 43% of all retrorectal lesions were malignant.³ Other published series report a 35%–67% rate of malignancy when all retrorectal lesions are pooled together.^{1,2,7}

Sarcomas located in the pelvis account for less than 5% of all sarcomas, with the majority limited to the genitourinary tract.^{8,9} Limited data exist on oncologic outcomes specifically for retrorectal sarcomas.^{1,3,7} In contrast,

patients with soft-tissue sarcomas of the retroperitoneum and pelvis have been reported, but oncologic outcomes vary. Mackenzie et al. reported a 5-year survival of 62% in a series of 61 patients when complete resection was achieved.¹⁰ Similar to our study, they found a high distant recurrence rate with long-term follow-up. Keyzer-Dekker et al. reported a series of 33 patients with pelvic sarcomas and found a high rate of local and distant recurrence and a 33% 5-year survival.¹¹ This lower survival may be explained by the fact that 61% of their patients had a marginal or intralesional resection.

Patients in our current study had an overall 5-year survival of 55%, which was much higher than 17% seen in the 21 patients in our previous series.³ Survival outcomes from the current series should be viewed in the context that no stage IV patients were included in the analysis and almost half of the patients had stage III disease. Small numbers in both our previous series, and this current one, make it difficult to determine statistical differences. However, we believe the improved survival in the current series is related to better surgical technique using a multidisciplinary team (higher number of R0 resections) and the more consistent use of adjuvant therapy. Patients in our past reported series were operated on without a pre-operative diagnosis in most cases and without the assistance of multiple specialists. Moreover, review of cases from that time period revealed that oncologic principles were not always followed and many patients underwent piecemeal, intralesional or marginal resections. In contrast, most patients in this series underwent wide, en-bloc resections with strict adherence to oncologic

TABLE 4 Univariate associations of factors with OS and DFS

Variable	OS		DFS	
	HR (95% CI)	P value	HR (95% CI)	P value
Gender				
Female	1.0 (0.4, 2.5)	.96	1.8 (0.8, 4.1)	.16
Male	1.0 (reference)		1.0 (reference)	
Margin status				
R0	1.0 (0.3, 3.2)	.94	2.0 (0.6, 6.8)	.26
R1	1.0 (reference)		1.0 (reference)	
Tumor grade				
High	2.4 (0.8, 6.7)	.10	1.8 (0.8, 4.2)	.17
Low	1.0 (reference)		1.0 (reference)	
Type of operation				
Secondary	0.7 (0.3, 2.0)	.55	1.0 (0.4, 2.4)	.94
Primary	1.0 (reference)		1.0 (reference)	
Adjuvant therapy ^a				
Surgery + chemo	5.8 (0.9, 35.2)	.06	1.9 (0.4, 9.6)	.43
Surgery + radiation	1.9 (0.5, 6.4)	.32	0.9 (0.3, 2.6)	.83
Surgery + chemoradiation	2.9 (0.8, 10.4)	.10	2.1 (0.8, 5.8)	.15
Surgery alone	1.0 (reference)		1.0 (reference)	

^a The overall association of Adjuvant Therapy with OS is $P = .21$; overall association of adjuvant therapy with DFS is $P = .33$

principles. Therefore, previous outcomes would not be expected to be similar to the more current approach.

There is general agreement that complete surgical resection, with negative margins, is the most important factor in improving survival when treating patients with soft tissue sarcomas.^{10,12,13} Several authors have stated that outcomes in pelvic sarcomas have been poor because the anatomical constraints of the pelvis and early involvement of adjacent structures limits the ability to perform a wide-margin resection.^{11,14} The high number of sacrectomies, hemipelvectomies, and proctectomies in our series attests to the need for radical resection to achieve clear margins in patients with deep pelvic sarcomas. Not all patients are willing to undergo extended resections that include hemipelvectomy or sacrectomy, especially if being operated for recurrent disease. In our study, 4 of the patients who had R1 resections had extensive pelvic sidewall disease that would have required hemipelvectomy for complete clearance, but amputation was not acceptable to these patients.

The use of adjuvant therapy for malignant retrorectal tumors in our series was tailored to tumor type, and the use of both chemotherapy and radiation was common. Adjuvant therapy used in our patients followed protocols typically for soft-tissue sarcomas.¹⁵ In our series, postoperative radiation was given to patients who did not receive it preoperatively and had less than 2-cm margins. Postoperative chemotherapy was given to patients with large (>5 cm) high-grade tumors. Use of adjuvant radiation and chemotherapy in patients with pelvic sarcomas remains controversial because of small sample sizes, mixed pathology, and lack of randomized data. Radiation therapy has been shown to significantly decrease local relapse following surgery for both extremity and retroperitoneal sarcomas, and by extrapolation, would be expected to decrease local relapse in patients with pelvic sarcomas if adequate dose can be safely delivered.^{16,17} Similar findings using chemotherapy alone, or in combination with radiation, have been seen for extremity and retroperitoneal soft tissue sarcomas, resulting in decreased local and distant relapse with trends toward improved survival.^{15,18,19} With the small numbers in our series, meaningful conclusions as to the utility of adjuvant therapy in this surgical setting cannot be drawn. However, given that improved survival in patients with soft-tissue sarcomas, especially those with high-grade lesions, has been limited by high rates of local and distant relapse, and aggressive multimodality approach seem warranted.¹⁵

Significant postoperative complications in our series were mainly related to infection (wound infection, intra-abdominal abscess) and wound healing. These occurred more commonly in patients undergoing major bony resection. Complications requiring surgical intervention in our cohort were secondary to dehiscence or infection of the

soft-tissue flaps (4 patients), all of which underwent extended bony resections. Our only postoperative mortality was related to necrotizing fascitis of a soft-tissue flap. Long operative times, radiated tissue, and periods of hypotension, which are common in these types of resections, are likely responsible for these complications. Two patients experienced postoperative foot drop following surgery not related to nerve resection. Both patients had extensive lumbosacral nerve mobilization to expose tumors, and these plexopathies were thought to be related to dissection and retraction. At last follow-up, these patients had improved with physical therapy.

Limitations of our study include: (1) retrospective analysis, (2) a long study period, (3) heterogeneity of tumors and, (4) a small cohort. The analysis of primary vs secondary resection, R0 vs R1, and the use of adjuvant therapy is constrained by the low numbers of patients in the comparison groups. However, given the limited data in the literature to guide treatment in these patients, and the fact that a prospective randomized trial is unlikely to be undertaken, our favorable results have reinforced the continued current approach to these patients.

Over the last 15 years, our practice has evolved in the approach to patients with retrorectal sarcomas. All tumors undergo a preoperative parasacral or transperineal computerized tomography (CT) guided biopsy to establish a definitive diagnoses. To determine the extent of local and distant disease, CT of the chest, abdomen, and pelvis is done. Pelvic MRI is performed to define the extent of local disease and plan the lines of resection. Flexible sigmoidoscopy is used to rule out transmural invasion of the rectum. A dedicated multidisciplinary pelvic tumor team consisting of a pelvic tumor radiologist, medical and radiation oncologists, and surgeons (colorectal, orthopedic spine, orthopedic oncology, urologic, vascular, neurologic, plastic) meet to review imaging, plan lines of resection, and sequence the steps of the surgical procedure for each specialty surgeon. If it is felt that the operation cannot technically achieve an R0 or R1 resection for the primary tumor, patients are not offered surgery unless palliation is required. Other contraindications for surgical resection include: (1) unresectable metastatic disease, (2) bilateral pelvic sidewall involvement, and (3) those with significant medical comorbidities. Patients with resectable metastatic disease are offered surgery. Wide en-bloc removal of adjacent organs and soft tissue and bone (if locally adherent) to achieve negative margins is the goal of resection. For bony lesions below the 3rd sacral body, and not invading local structures, we prefer a posterior-only approach. For lesions locally advanced, or those above the 3rd sacral body, a combined anterior-posterior approach is used. When extensive unilateral pelvic sidewall disease occurs in combination with sacral involvement,

concomitant hemipelvectomy is performed. All preoperative biopsy tracts are excised at the time of surgical resection.

Patients with large, locally advanced primary tumors, and those who have had their tumor capsule breached by open biopsy or incomplete resection, undergo chemotherapy and external beam radiation prior to definitive surgical resection, as margins in these patients are less well defined. If patients are not medically fit to undergo chemotherapy, then external beam radiation therapy and surgery are performed without chemotherapy. If patients have undergone previous chemotherapy or radiation, doses are adjusted to factor in overall risk of toxicity. Intraoperative radiotherapy is delivered when surgical margins are less than 2 cm, or if tumor spillage occurs during the operation. We considered postoperative chemotherapy for high-grade tumors greater than 5 cm in size. Postoperative radiation therapy is given to patients who did not receive preoperative therapy and who have less than 2-cm surgical margins. Patients are followed closely postoperatively with particular attention to local recurrence and pulmonary metastasis. Patients are offered repeat resection for local or distant recurrence if all disease can be removed by surgical resection. Adjuvant chemoradiation therapy is given depending on the extent of prior treatment.

In conclusion, retrorectal sarcomas may present as large, high-grade, locally advanced lesions. Most tumors are resectable, but the locally aggressive behavior of these tumors often requires extended resection. With an appropriate oncological surgical approach and adjuvant therapy, including IORT, it may be possible to achieve long-term survival in up to 50% of patients who do not have stage IV disease. Because of the rarity of these tumors, a multi-institutional review of management and outcomes is needed to draw definitive conclusions as to the best overall treatment approach. We believe that because of the inherent complexity in the management of these tumors, direct referral to experienced, specialized centers, before diagnostic and therapeutic interventions, is warranted to optimize patient outcomes. Greater awareness and appropriate management will lead to earlier diagnosis and improved survival in patients with retrorectal sarcomas.

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