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World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 27 September 26, 2022

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 27 September 26, 2022

Contents

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 27 September 26, 2022

Contents

LETTER TO THE EDITOR

World Journal of Clinical Cases

Thrice Monthly Volume 10 Number 27 September 26, 2022

Contents

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ORIGINAL ARTICLE

Observational Study

Intra and extra pelvic multidisciplinary surgical approach of retroperitoneal sarcoma: Case series report

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Abstract

BACKGROUND

Retroperitoneal sarcoma (RPS) is a rare malignancy arising from mesenchymal cells that most commonly presents as an abdominal mass and is associated with poor prognosis. Although several studies have assessed the survival benefits of wide excision, few have reported detailed methods for achieving wide excision in patients with RPS.

AIM

To describe our experience with multidisciplinary surgical resection of RPS using intra- and extra-pelvic approaches.

METHODS

Multidisciplinary surgery is an anatomical approach that combines intra- and extra-peritoneal access within the same surgery to achieve complete RPS removal. This retrospective review of the records of patients who underwent multidisciplinary surgery for RPS analyzed surgical and survival outcomes.

RESULTS

Eight patients underwent 10 intra- and extra-pelvic surgical resections, and their median mass size was 12.75 cm (range, 6-45.5 cm). Using an intrapelvic approach, laparoscopy-assisted surgery was performed in four cases and laparotomy surgery in six. Using an extrapelvic approach, ilioinguinal and posterior approaches were used in four cases each, and the prone position and midline skin

incision were shared in one. All patients' RPS masses were removed completely, and four achieved R0 resection through intra- and extra-pelvic surgery. The median estimated blood loss was 2000 mL (range, 300-20000 mL) and the median hospitalization was 12.6 d (range, 9-69 d). Reoperation was needed in two patients (one for wound necrosis and the other for bowel perforation and wound necrosis). The median overall survival rate and median progression-free survival were 64.6 and 13.7 mo, respectively.

CONCLUSION
RPS is therapeutically challenging because of its location and high risk of recurrence. Therefore, intra- and extra-pelvic surgical approaches can improve the macroscopic security of the surgical margin.

Key Words: Margins of excision; Retroperitoneal neoplasms; Sarcoma

Core Tip: Retroperitoneal sarcomas (RPS) are therapeutically challenging because of their location and high risk of recurrence. Multidisciplinary surgery is an anatomical approach that combines intra- and extra-peritoneal access within the same surgery to achieve complete RPS removal. This retrospective review of the records of eight patients who underwent multidisciplinary surgery for RPS analyzed surgical and survival outcomes. All patients' RPS masses were removed completely, and four achieved R0 resection through intra- and extra-pelvic surgery. Therefore, intra- and extra-pelvic surgical approaches can improve the macroscopic security of the surgical margin.

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INTRODUCTION

Retroperitoneal sarcoma (RPS) is a rare malignancy arising from mesenchymal cells that most commonly presents as an abdominal mass and is associated with poor prognosis[1]. Liposarcoma, either well-differentiated or dedifferentiated (WDLPS or DDLPS), is the most frequent histological subtype (50%-63%), followed by leiomyosarcoma (LMS) (19-23%)[2,3]. Other less frequent soft tissue sarcoma subtypes in the retroperitoneum include solitary fibrous tumor, malignant peripheral nerve sheath tumor (MPNST), synovial sarcoma, and undifferentiated pleomorphic sarcoma (UPS)[2,3]. The incidence is approximately 0.5-1 case per 100000, and these tumors are almost always sporadic[4]. Surgery is the mainstay of curative therapy, and local control is critical for an outcome[5]. In addition, the Korean obstetric gynecology group also noted that absent residual disease was an important prognostic factor in patients with leiomyosarcoma (hazard ratio 5.07, $P < 0.001$)[6]. Conversely, the role of chemotherapy in the management of localized RPS remains unclear; moreover, the potential benefit of radiotherapy (RT) remains controversial and is currently under evaluation[7]. Nevertheless, anatomical constraints in the retroperitoneum limit the ability to achieve a wide resection margin[1]. Considering this anatomical challenge, hospital volume may be a surrogate for the infrastructure and support necessary for the optimal management of these complex malignancies[8].

Although several studies have assessed the survival benefits of wide excision, few have reported detailed methods for achieving wide excision in patients with RPS. Therefore, the present study aimed to describe our experience with multidisciplinary surgical resection in patients with RPS, including intra- and extra-pelvic approaches. Our multidisciplinary surgical approach used an anatomical approach for tumor removal, combining intra- and extra-peritoneal RPS access (Figures 1 and 2). Although this two-step approach is more invasive than the conventional approach, it is a potential solution to overcome the surgical limitations of the anatomic location in the retroperitoneal space.

MATERIALS AND METHODS

Eligible patients seen at Seoul St. Mary's Hospital, College of Medicine at The Catholic University of Korea, were identified based on their surgical history of RPS. Only patients who underwent surgical

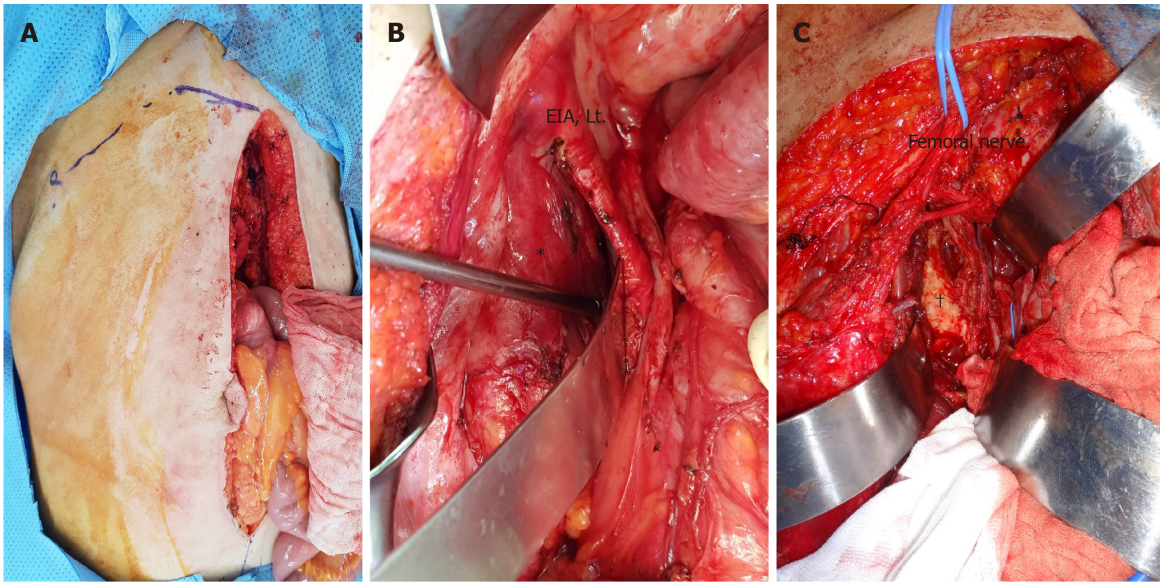

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Figure 1 Intra and extra pelvic multidisciplinary surgical approach. A: Incision of intra and extra pelvic approach (midline incision + ilioinguinal approach); B: Intra pelvic approach; C: Extrapelvic approach. ∗: Medial part of the sarcoma mass, soft tissue of the obturator internus; †: Lateral part of the sarcoma mass, from the ilium and ischium; EIA: External iliac artery.

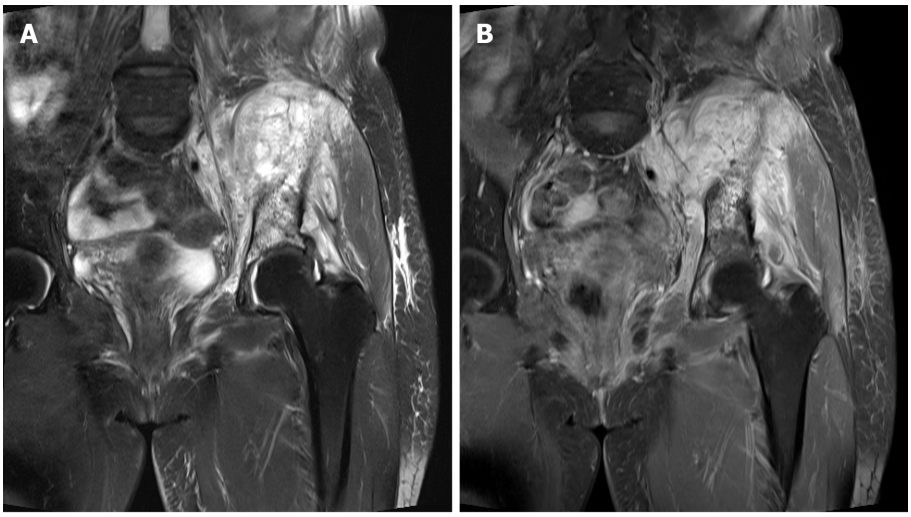

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Figure 2 Magnetic resonance image of retroperitoneal sarcoma involved Lt. pelvis (Lt. iliac bone, Lt. obturator internus muscles, Lt. common and internal iliac lymph node). A: Coronal T2 weighted image; B: Coronal T1 weighted fat suppression image.

treatment using intra- and extra-pelvic approaches were included in the current study, regardless of their disease state. We evaluated medical records between January 2001 and February 2020, including patient age, body mass index (BMI), mass size, use of neoadjuvant or adjuvant treatments, final histology following surgical resection and outcomes [*i.e.*, approach method, estimated blood loss, overall survival (OS), and progression-free survival (PFS) for each treatment]. The size of the retroperitoneal mass was reported based on its long axis. This study was approved by the institutional review board of Seoul St. Mary's Hospital (approval number: KC20RISI0350).

RESULTS

Ten intra- and extra-pelvic surgical treatments were administered to eight patients in September 2014. The patients' mean age and BMI were 42.75 years (range, 14-78 years) and 22.4 (range, 17.6-24), respectively. The median mass size was 12.75 cm (range: 6-45.5 cm). The masses extended from the

intra- to the retroperitoneal areas. Palpable mass or pain at specific sites was reported as the initial symptom in four patients. Three patients underwent multidisciplinary surgery as the primary surgical resection, whereas the others underwent a secondary or greater surgical resection (Table 1). Before surgery, all cases were discussed regarding resectability, necessary pre-operative procedures, and predicted complications in a multidisciplinary cooperative center at the Department of Oncology, Seoul St. Mary's Hospital. In routine systems, contact with specialized doctors is available at every surgical time, owing to hospital policy. Another surgical team could be requested to join our surgery at any time during the operation.

For the intrapelvic approach, laparoscopy-assisted surgery was performed on four patients, and laparotomy surgery with midline incision was performed on six. For the extrapelvic approach, ilioinguinal and posterior approaches were used in four patients, while the prone position and midline skin incision were shared in one. In all 10 procedures, wide or marginal mass excision was performed, with resection of suspicious tumor invasion structures. The pelvic organs (sigmoid colon and external or internal iliac vessels) were dissected and mobilized by several specialized doctors. Pelvic lymph node dissections, prophylactic fixation, or revision of the structures were performed. In all 10 cases, a median of three surgical teams (range, 2-5 teams) cooperated to remove the RPS. The colorectal or vascular team of general surgery, gynecologic oncology team, bone tumor or spine part of orthopedic surgery, and urology doctors participated in multidisciplinary surgery (Table 2).

Prior to surgery, six patients underwent arterial embolization to reduce blood loss; nevertheless, their estimated median blood loss was 2000 mL (range, 300-20000 mL). Furthermore, nine patients received transfused blood intraoperatively. Ligation of the internal iliac vessel in one patient and dissection with mobilization of the iliac vessel in three were performed by a vascular surgical team. In addition, the vascular surgical team performed an internal iliac artery-deep femoral artery allograft bypass on one patient. The gynecologic oncology team performed another dissection and primary closure of the iliac vessel. These procedures are necessary to achieve surgical margins and reduce blood loss.

The median hospitalization duration was 12.6 d (range: 9-69 d). Reoperation was needed in two patients, one for wound necrosis and the other for bowel perforation and wound necrosis. No postoperative deaths occurred.

All the patients had the total tumor mass removed macroscopically, and four (40%) achieved R0 resection through intra- and extra-pelvic surgical treatment. The most common histology of RPS (two patients) was the myxoid type of well-differentiated liposarcoma. LMS, MPNST, osteosarcoma, chondrosarcoma, low-grade fibromyxoid sarcoma (LGFMS), and malignant spindle cell tumor were also noted. Neoadjuvant chemotherapy was administered to two patients, and all patients received adjuvant treatment (RT and/or chemotherapy).

Five patients are currently alive. Two patients died due to RPS progression, and one was lost to follow-up. Among the five living patients, disease progression was reported in three, while two showed no progression. The median OS was 64.6 mo (range, 11.4-206.8 mo), and the median PFS following treatment was 13.7 mo (range, 4.3-50.6 mo).

DISCUSSION

RPS consists of a heterogeneous group of malignant tumors with very low incidence. Very little is known about their biological behavior, and no specific causative compounds have been identified[9]. Macroscopically clear margins are an important prognostic factor for patients[9]. However, securing a clear margin is challenging because of the tumor location. Malinka *et al*[10] reported a macroscopically clear margin in 84% (51, total 61). Hogg *et al*[11] in a separate study, reported it in 88.9% (80, total 90). Our finding that all patients had a macroscopically clear margin is superior to that of conventional studies.

Patients used all treatment methods currently available, including surgical approaches, chemotherapy or target therapy, and RT. RT was the treatment option used to treat these patients. RT is usually used to control local recurrence or improve surgical margins; however, it does not affect distant metastasis or OS[12]. Haas *et al*[12] reported that pre-operative RT was associated with better local control in an unadjusted univariate analysis among the three cohorts, but not after accounting for imbalances in prognostic variables. According to Turner *et al*[13] compared with resection alone, additional neoadjuvant RT was associated with multi-visceral resection (87.5% *vs* 66.1%, $P = 0.02$) and negative margins (72.5% *vs* 30.6%, $P < 0.001$). Roeder *et al*[14] also reported that the combination of neoadjuvant intensity-modulated RT, surgery, and intraoperative RT is feasible with acceptable toxicity and yields good results in terms of local control and OS in patients with high-risk retroperitoneal sarcomas (estimated 3- and 5-year local control rates of 72% and estimated 3- and 5-year OS rates of 74%). This method showed superior effectiveness in achieving a surgical margin compared with neoadjuvant RT alone [R0 in six patients (22%) and R1 in 22 (74%)]. The combination method showed a rate with a macroscopically clear margin similar to ours (100%) but included several side effects and limitations. First, the combination method has more reported postoperative side effects. Nine patients (30%) had more than grade 3 postoperative side effects, four (15%) needed reoperations, and two died

Table 1 Characteristics of patients with retroperitoneal sarcoma (*n* = 8)

Characteristics	Value
Mean age (yr)	42.75 ± 18.4
Mean BMI	22.4 ± 2.4
Initial symptoms, *n* (%)	
Palpable mass	4 (50)
Pain on the specific site	4 (50)
Median mass size (long axis, cm)	12.75 ± 11.7
Order of surgery, *n* (%)	
Primary	3 (30)
Secondary	2 (20)
Tertiary	2 (20)
More than tertiary	3 (30)
History of neoadjuvant or adjuvant treatment, *n* (%)	
Neoadjuvant treatment	2 (25)
Adjuvant treatment	8 (100)
Surgical outcome	
Median overall survival (mo, median)	64.6
Progression-free survival (mo, median)	13.7
Died patients due to disease, *n* (%)	2 (25)
Pathology, *n* (%)	
Liposarcoma	2 (25)
Leiomyosarcoma	1 (12.5)
Malignant peripheral nerve sheath tumor	1 (12.5)
Osteosarcoma	2 (25)
Chondrosarcoma	1 (12.5)
Low-grade fibromyxoid sarcoma	1 (12.5)

during the prolonged postoperative period. These rates are higher than ours: two patients (20%) underwent reoperation, and none died postoperatively. Another limitation of the combination method is that it should only be administered to inpatients in hospitals with appropriate facilities for intensity-modulated and intraoperative RT. Thus, a multidisciplinary surgical approach is a good option for treating patients with RPS to achieve a clear margin.

However, the efficacy of chemotherapy and immunotherapy for RPS is limited. The role of adjuvant/neo-adjuvant systemic therapy is not well-defined because of the rarity of the disease and the paucity of randomized controlled data. The role of palliative systemic therapy is better established, mostly through extrapolation of data from sarcomas at other locations[15]. Currently, anthracycline-based therapy is the standard first-line treatment[16]. However, it induces a response in only 15%-35% of patients, irrespective of the histological subtype[17]. Thus, complete surgical resection is considered a milestone in RPS treatment. Several agents have recently emerged as second-line treatment options, including gemcitabine/docetaxel, high-dose ifosfamide monotherapy, trabectedin, pazopanib, and eribulin. According to the PALETTE study, pazopanib significantly increased PFS compared with placebo in metastatic soft tissue sarcoma, progressing despite previous standard chemotherapy[18]. According to Dickson *et al*[19] the selective CDK4 and CDK6 inhibitor palbociclib inhibits growth and induces senescence in liposarcoma cell lines, favoring progression free; however, there was no significant difference in PFS between patients who had or had not received prior systemic therapy (P = 0.70). Depending on the histological type, there are several randomized controlled trials on neoadjuvant or systemic chemotherapy. The EORTC-1809-STBSG- STRASS 2 study was intended to be an international randomized multicenter, open-label phase 3 trial, with stratification by specific tumor histology, including only high-grade dedifferentiated liposarcoma and LMS[20]. This study aimed to evaluate whether neoadjuvant chemotherapy reduces the development of distant metastases in these well-

Table 2 Surgical approach and outcomes (total 10 cases)

PN	Number of surgery	Intra pelvic surgery	Extra pelvic surgery	Pathology	Resection margin		EBL (mL)	HD (d)	OS (mo)	PFS (mo)
		Approach method and operation title	Approach method and operation title		Intra pelvic surgery	Extra pelvic surgery				
1	Primary surgery	Laparoscopy Mass excision	Posterior approach of hip Wide excision	WDLPS	R0	R0	300	15	65.3	13.7
1	Secondary surgery	Laparotomy Mass excision Dissection and mobilization of Lt. internal iliac vessel Ligation of Lt. iliac vein	Laparotomy Marginal excision-neurolysis	WDLPS	R1	R1	2000	17	65.3	50
2	5th surgery	Laparotomy Mass excision	Ilioinguinal approach Wide excision	LMS	R1	R0	1250	19	97	9
3	Secondary surgery	Laparoscopy Rt. RSO and PLND Sigmoid colon mobilization Dissection of Rt. external and internal iliac vessel	Ilioinguinal approach Wide excision	MPNST	R0	R1	10000	42	63.9	4.3
4	Primary surgery	Laparotomy Mass excision Dissection of Lt. common and external iliac vessel Ligation of Lt. internal iliac artery	Posterior approach of hip Wide excision neurolysis	Myxoid liposarcoma	R0	R1	2000	16	55.7	49
5	Tertiary surgery	Laparotomy Mass excision Rectum mobilization	Posterior approach of hip Wide excision, neurotomy L5-S1	Osteosarcoma	R0	R0	20000	52	52	11.5
6	Tertiary surgery	Laparotomy Mass excision Int. iliac-deep femoral artery, allograft bypass Rt. D-J catheter insertion with primary bladder repair	Ilioinguinal approach Marginal excision skin flap and graft	LGFMS	R1	R0	12000	67	206.8	28.9
6	Quaternary surgery	Laparotomy Mass excision	Prone position Wide excision	Osteosarcoma	R1	R0	700	12	206.8	14.6
7	Primary surgery	Laparoscopy Mass excision Dissection and	Posterior approach of hip Wide excision neurolysis L5-S3, Lt.	Malignant spindle cell tumor	R0	R0	10000	69	11.4	7.5

		mobilization of Lt. external and internal iliac vessel								
8	5th surgery	Laparoscopy Mass excision, Rt. PLND Primary closure of Rt. external iliac vein	Ilioinguinal approach Marginal excision	Chondrosarcoma	R0	R0	300	9	115	13.7

EBL: Estimated blood loss; HD: Hospitalization days; LGFMS: Low-grade fibromyxoid sarcoma; LMS: Leiomyosarcoma; MPNST: Malignant peripheral nerve sheath tumor; OS: Overall survival; PFS: Progression-free survival; PN: Patient number; RSO: Right salpingo-oophorectomy; WDLPS: Well-differentiated liposarcoma; PLND: Pelvic lymph node dissection.

defined histologic entities[20]. Thus, we are awaiting this result to determine the efficacy of neoadjuvant chemotherapy.

Complete surgical resection and securing clear surgical margins are the most effective therapeutic methods. However, as described above, surgical treatment is challenging for most surgeons because of the RPS location. To overcome this obstacle, neoadjuvant and/or adjuvant therapy was developed, and the Trans-Atlantic RPS Working Group was established in 2013. This group insisted on the importance of presurgical imaging studies and multidisciplinary discussions for patients with RPS. They also noted that complete resection should be accomplished despite large resections of adjacent organs[1]. Thus, an interdisciplinary collaboration among teams of surgeons, anesthesiologists, and nurses is necessary to achieve a complete RPS resection.

Several side effects have been noted following a multidisciplinary approach for RPS resection. Although there were no deaths in our sample, reoperation was needed in two patients. One patient underwent wound revision and local flap coverage for wound necrosis 17 d after surgery. The other patient's complications were more severe (*i.e.*, bowel perforation and wound necrosis), requiring exploratory laparotomy with ileostomy and wound debridement with flap coverage almost one month postoperatively. Compared to pelvic exenteration for recurrent or advanced cervical cancer, which is one of the most challenging surgeries in gynecological cancer, our multidisciplinary two-step approach resulted in higher wound complications than pelvic exenteration (20% *vs* 4.3%)[21]. The Dana-Farber/Brigham and Women's Cancer Centre, which reviewed conventional surgical resection for RPS, reported a smaller median size of resected mass than this study [15.5cm (range, 1.8-60.0 cm) *vs* 12.75 cm (range, 6-45.5 cm)][22]. Long hospitalizations (range, 9-69 d) and large estimated blood loss volumes (range, 300-20000 mL) were also found, despite 60% of the patients receiving pre-operative arterial embolization. All 10 patients also required transfused packed red blood cells, fresh frozen plasma, and/or platelets. Moreover, almost 70% of all the patients had this surgery for recurrent diseases. Considering a few treatment options for recurrent RPS, a multidisciplinary approach is an essential option, though the surgical side effects are severe and the size that can be resected is rather small. This approach achieved a clear margin rate of 100%. Thus, it is a superior method to the conventional single-incision approach.

According to Bizzarri *et al*[23] minimal invasive surgery could be applied to challenging surgery, keeping the same survival outcomes compared to conventional surgery. This two-step approach can also be changed to minimally invasive surgery using a robotic system or other advanced surgical methods. This could decrease the complication rates in patients with RPS using a two-step approach. Furthermore, this complication rate was lower than that found in a combination of RT and surgery, which achieved a similar clear surgical margin rate. In addition, pre-operative vascular assessment (Tinelli's Score) could be a new option to achieve surgical margins and reduce blood loss[20,24]. We discussed several factors influencing the surgical status before surgery and performed arterial embolization if the cancerous mass was located or invaded the major vessel. However, we did not use this evaluation system pre-operatively. Therefore, we retrospectively analyzed our data using Tinelli's Score. Among the 10 cases, six (60%) were grade 1 or 2, and two were grade 3. One case each was grade 4 and 5, and a major vessel allograft was performed in the case of grade 5 vessel invasion. Among the four cases with upper grade 3, arterial embolization was performed in 3. However, for these cases that showed a large amount of bleeding even after embolization, if a large amount of bleeding during surgery is suspected, even with a low score, embolization should be considered before surgery. Therefore, checking the vessel invasion grade, performing arterial embolization before surgery, and co-operation with the vascular surgical team could achieve complete tumor resection and reduce blood loss and surgical complications in the next surgery. Finally, applying enhanced recovery after surgery (ERAS) or a modified ERAS method may reduce hospitalization and postoperative complications.

These findings support the need for a multicenter or randomized controlled study to test the effectiveness of the multidisciplinary approach, despite the Trans-Atlantic RPS Working Group's current guideline that the multidisciplinary approach is superior for complete tumor resection.

CONCLUSION

Therapeutic challenges associated with RPS are based on their location and high risk of recurrence. Therefore, a multidisciplinary approach is necessary to improve patient outcomes. The location of RPS and the benefits of using intra- and extra-pelvic treatments make this a good candidate for a multidisciplinary approach. This approach may improve the securing of the macroscopic surgical margins.

ARTICLE HIGHLIGHTS

Research background

Retroperitoneal sarcoma (RPS) is a rare malignancy and is associated with poor prognosis. Although several studies have assessed the survival benefits of wide excision, few have reported detailed methods for achieving wide excision in patients with RPS.

Research motivation

Considering poor prognosis of RPS, we'd like to find effective surgical approach to complete resection for RPS. This Multidisciplinary surgery is an anatomical approach that combines intra- and extraperitoneal access within the same surgery to achieve complete RPS removal.

Research objectives

We described our experience with multidisciplinary surgical resection of RPS using intra- and extrapelvic approaches.

Research methods

This study reviewed of the records of patients who underwent multidisciplinary surgery for RPS analyzed surgical and survival outcomes retrospectively.

Research results

All patients' RPS masses were removed completely, and four achieved R0 resection through intra- and extra-pelvic surgery.

Research conclusions

RPS is therapeutically challenging because of its location and high risk of recurrence. Therefore, intra- and extra-pelvic surgical approaches can improve the macroscopic security of the surgical margin.

Research perspectives

These findings support the need for a multicenter or randomized controlled study to test the effectiveness of the multidisciplinary approach, despite the Trans-Atlantic RPS Working Group's current guideline that the multidisciplinary approach is superior for complete tumor resection.

FOOTNOTES

Author contributions: Lee KH, Chung YG, and Song H designed this study; all other authors contributed to data collection; Song H, Ahn JH, Jung Y, Woo JY, and Cha J analyzed and interpreted the data, and Song H wrote the draft of the manuscript; Lee KH and Chung YG supervised and revised the manuscript for intellectual content.

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