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Analysis of the Onco-Vascular Approach in Retroperitoneal Sarcoma with Vascular Involvement

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Abstract

Background: Due to the limited number of clinical series and the lack of multi-institutional or national registries concerning retroperitoneal sarcoma (RPS) extending to major arterio-venous structures, the short and long-term benefits following concomitant resection of these major structures are still antagonistic. **Objective:** To present our institutional experience with RPS tumors, to assess their vascular involvement and to analyze the outcomes of onco-vascular approach. **Patients and methods:** A retrospective review of our institutional RPS patients' clinical charts was performed. All consecutive adult patients surgically treated for RPS were included. Resection of RPS tumors was followed by histopathological examination for grading. Types of vascular involvement were assessed preoperatively. RPS tumors were resected en bloc together with blood vessels according to the type of vascular involvement and the surgical standards. **Results:** This study included 14 patients; 8 males (57%) and 6 females (43%) with RPS. Vascular resection was performed in all patients. Adherent structures were resected in 43%. Resection was performed for 29% RPSs with arterial venous involvement, 14% with only arterial involvement, and 57% with only venous involvement. All RPSs were classified as high-grade lesions, and 64% showed secondarily major vessels involvement. 43% of patients were treated by arterial resection. 80% had venous involvement. Venous resections were followed by venous reconstruction in all patients with both arterial and venous involvement. The morbidity rate was 43% while the mortality rate was 7%. **Conclusion:** Complete resection with clear margins is important for long-term survival in patients with retroperitoneal soft tissue sarcomas.

Keywords

Outcomes, Retroperitoneal Sarcoma, Vascular Approach

1. Introduction

Retroperitoneal sarcomas (RPS) that arise from mesenchymal cells account for about 15% of soft tissue sarcomas [1]. Little is known about the biological behavior of the tumor, and no specific etiological associations have been identified [2]. Such tumors are usually large at initial presentation mounting no obvious clinical symptoms [3]. The management of the disease remains a challenge [4] and surgical resection of localized RPS aiming for gross or microscopically negative margins is still the best [5]. However, because of the high rate of local recurrence, the prognosis of the patients with RPS is generally poor [2]. Local recurrence accounts for 77% of RPS-related deaths without concomitant metastasis, it is, therefore, important to control the disease locally [6]. It is common for RPS to involve major arterio-venous structures [7]. Planned vascular resection is essential to achieve the oncologic standards of complete tumor resection with microscopically negative margins and the prevention of tumor spillage during surgery [8]. Still, limited knowledge is available on the extent of surgical resection and the best surgical approach [9]. Three major factors influence the need and the type of vascular replacement: the site of the lesion and especially the relation to renal veins; the extent of IVC involvement (partial or circumferential); and the presence of well-established collateral venous system [9]. RPS tumors extending to major arterio-venous structures might be rare. Due to the limited number of clinical series and the lack of multi-institutional or national registries, the short and long-term benefits following concomitant resection of major arterio-venous structures are still antagonistic [9].

Our aim in this work was to present our institutional experience with RPS tumors, assess their vascular involvement and to analyze the outcomes (Short and long-term) of onco-vascular approach.

2. Patients and Methods

2.1. Inclusion Criteria

All adult patients consecutively diagnosed with RPS and treated at the National Cancer Institute (NCI), Cairo University-Department of Surgical Oncology from 2004 to 2010 (n = 14). The primary disease involved major arterio-venous structures and hence an onco-vascular approach was followed. RPS tumors were imaged using ultrasonography (US), magnetic resonance imaging (MRI), computed tomography (CT), or a combination of the three with or without angiography. The indications for RPS resection en bloc together with major blood vessels were applied in patients with clear involvement of major blood vessels. Such an involvement was established when MRI or CT scans did not show a rim of normal tissue in-between the tumor and the vessel. Resection of RPS tumors was followed by histopathological examination. A dedicated pathologist assessed the resected specimens and finally commented on the grade guided by the degree of cellularity, differentiation, pleomorphism, necrosis and mitotic activity, and categorized them into low-grade, intermediate-grade, and high-grade RPS

[10]. Exclusion criteria: suprarenal vessels involvement by tumor.

2.2. Classification of Vascular Involvement

Types of vascular involvement were assessed preoperatively by high-resolution CT scans or MRI. Primary and secondary vessel involvements are indistinguishable by preoperative radiologic tomography or by clinical assessment. Therefore, both primary and secondary blood vessel involvement were classified as follows: type I, RPS involving major arteries and veins; type II, RPS affecting only arterial blood vessels; type III, RPS involving the veins without altering an artery; type IV, RPS without direct involvement of arterial or venous blood vessels [9].

2.3. Surgery, Radiation, and Vascular Replacement

RPS tumors were resected en bloc together with blood vessels according to the type of vascular involvement and the surgical standards [10] [11]. Radiotherapy was given in higher-grade and recurrent STSs with sparing of radiosensitive structures such as ureter or small bowel from intraoperative radiation by dissection, mobilization, and positioning [12].

Blood flow was restored with respect to the resection site and the extent of the vascular defect and collateral blood flow (e.g., venous drainage). Arterial reconstructions were usually performed by the appropriate method, such as primary anastomosis, reinsertion, or synthetic prostheses (expanded polytetrafluoroethylene [ePTFE] or Dacron), preferably in an anatomic position. Autologous vein (reversed great saphenous vein) was considered in selective cases (visceral or iliac arteries). Circular venous defects of the IVC were reconstructed by ePTFE prostheses when a primary anastomosis was impossible. For localized defects of the IVC, either a synthetic or a venous patch was used or venoplasty (longitudinal suture) was performed. Veins occluded by thrombosis were not reconstructed (ligation of the proximal and distal venous stump).

Patients routinely received prophylactic antibiotic treatment (cephalosporin) both preoperatively and postoperatively. Bowel preparations were not routinely administered. Perioperatively, a low-dose regimen of heparin was administered (unfractionated heparin intraoperatively and low-molecular-weight heparin in the postoperative phase). After discharge, oral anticoagulants were not routinely administered.

2.4. Follow-Up

Patients were seen regularly during the observation period at our outpatient clinic. The standard follow-up was weekly for one month, then monthly for the first 3 months, then every 3 months for a year, followed by a visit every 6 months for 2 years. Patients were assessed clinically following a CT imaging organized beforehand to evaluate the patency of arterial and venous reconstructions.

3. Results

A retrospective review of our institutional retroperitoneal sarcoma database and

patients' clinical charts was performed. All consecutive adult patients surgically treated at our NCI from 2004 to 2010 for primary RPS directly arising from or secondarily involved blood vessels were included. This study included 14 patients; 8 males (57%) and 6 females (43%), their age ranged from 29 - 68 years with median age 51 years. The size of the tumor ranged from 5 - 15 cm with median size of 5 cm in diameter.

3.1. Respectability and Vascular Infiltration

Vascular resection was performed in all 14 patients. Adherent organs or structures were resected in 43% of patients (n = 6); kidney (n = 4), large bowel (n = 1), and small bowel (n = 1) were the resected organs.

Resection was performed for four (29%) RPSs with arterial venous involvement (type I), 2 (14%) with only arterial involvement (type II), and eight (57%) with only venous involvement (type III). Histopathologic examination of the specimens showed that five (36%) RPSs originated in the blood vessel wall, including four leiomyosarcomas of the inferior vena cava and one angiosarcoma of the aortic wall (infrarenal segment) (Table 1). All these RPSs were classified as high-grade lesions, and nine (64%) secondarily involved major vessels. Of these nine RPSs infiltrating the vessel wall (44.4%, n = 4/9 showed both arterial and venous infiltration, 44.4%, n = 4/9 with venous infiltration only, and 11.2%, n = 1/9 with arterial infiltration only).

Diverse histologic subtypes (e.g., liposarcoma, malignant fibrous histiocytoma, and clear cell sarcoma) and either primary disease (66.7% n = 6/9) or locally recurring tumors (33.3%, n = 3) were diagnosed for secondary vascular involvement. Tumor growth also affected adjacent retroperitoneal or visceral organs. Of six patients in whom organs were resected, 66.7% (n = 4/6) presented with organ infiltration on histopathologic examination: kidney (75%, n = 3/4); and small bowel (25%, n = 1).

3.2. Morbidity and Mortality

Morbidity was observed in 43% (n = 6) of patients. Infection of the graft (14%, n = 2)

Table 1. Results of histopathologic evaluation of the surgical specimen concerning vascular and organ involvement in 14 patients with retroperitoneal soft tissue sarcomas.

Characteristics	Number (14)	Rate (%)
Primary involvement	5	36
Inferior vena cava	4	29
Aorta (infrarenal segment)	1	7
Secondary involvement (vascular infiltration)	9	64
Inferior vena cava and aorta (type I)	4	29
Right common iliac artery (type II)	1	7
Inferior vena cava (type III)	1	7
Superior mesenteric vein (type III)	1	7
Right and left common iliac bifurcation vein (type III)	2	14

was the most common complication. Patients with wound infections were successfully treated conservatively by IV antibiotics. One patient had intraoperative bleeding that had been controlled by blood transfusion. Pulmonary embolism was observed in one patient and had been properly managed. A thromboembolic complication treated by blood vessel reconstruction was observed in one patient. Abdominal wall dehiscence was observed in one patient.

The mortality rate was 7% owing to the death of one patient on the first postoperative day from massive intraoperative blood loss with subsequent multiorgan failure.

3.3. Arterial Resection and Graft Function

43% of the 14 patients (n = 6) were treated by arterial resection. Four arterial resections (29%) were performed for RPSs that involved both arteries and veins (type I), and two arterial resections (14%) were for tumors that only involved arteries (type II). All arterial resections were followed by vessel reconstruction. In 83% of the six reconstructions (n = 5), synthetic grafts were used, and one reimplantation of the celiac trunk was done.

No patient was lost to follow-up. Median follow-up was 19 months for surviving patients. The overall patency rate of arterial reconstructions was 83% (5 of 6 reconstructions).

3.4. Venous Resection and Graft Function

80% of patients (n = 12) had venous involvement: four with arterial involvement also (type I RPS) and eight with only venous involvement (type III). Venous resections were followed by venous reconstruction in all patients with both arterial and venous involvement. Resections were reconstructed in 88% of the patients (n = 7) with venous involvement alone. In one patient, the vessels could not be reconstructed because of scarring in the operation field.

3.5. Tumor Control and Survival

After complete tumor resection, 21% of patients (n = 3) presented with local recurrences. One patient was from the type II group (Aorta involvement) and had the recurrence within 1 year; the other two patients were from the type I (both arterial & venous involvement) and had the recurrence within 2 years. At the last follow-up (2 years), 7 patients (50%) were alive.

4. Discussion

Surgical risks were high, and the long-term prognosis is usually poor when there is involvement of major blood vessels in tumor making a limiting factor for curative surgery [13]. Advances in surgical techniques have allowed extending the limits of surgery beyond major vascular resection, with a relatively low rate of postoperative complications [14].

The number of patients with retroperitoneal STSs requiring major vascular

resections is unknown [9]. Leiomyosarcomas, liposarcomas, and other types of sarcomas were associated with vascular involvement [15]. Most studies focus selectively on the very rare entity of primary leiomyosarcoma of the vena cava, neglecting all other sarcomas that involve blood vessels in the retroperitoneum [16] [17] [18] [19] [20]. Most of the STSs secondarily involved vascular structures either by histologically proven vascular infiltration or by vascular encasement [9].

Retroperitoneal sarcomas are usually large at diagnosis, and the differentiation between primary or secondary blood vessel involvements is not made before the pathologist examines the specimen [10]. This implicates that both have to be treated by a common procedural algorithm and resection strategy [20]. Schwarzbach suggested a four-stage classification that describes the pattern of vascular involvement by retroperitoneal STSs [9]. In the current study, the most common type of vascular involvement was type III, venous involvement (57%). This was in agreement by a large number of reports about leiomyosarcomas of the inferior vena cava [16] [17] [18] [19] [20]. In type III tumors, surgery is performed on the vena cava or iliac veins [16] [17] [18] [19] [20].

The present study also shows that the simultaneous involvement of retroperitoneal arteries and veins by type I sarcomas occurred with a lower frequency (29%). Dzsinich *et al.*, [16] reported 7.7% prevalence of both arterial and venous involvement in 13 cases with leiomyosarcomas. Less common, in this study, is isolated arterial involvement by retroperitoneal sarcomas (type II) (14%). Chiche *et al.*, [21] reported five patients with sole arterial growth pattern. Type II sarcomas usually require vascular reconstruction [18] [21].

The decision of whether to resect blood vessels depends especially on preoperative radiologic imaging results [10] [11]. angiography or contrast-enhanced MRI can be used as diagnostic procedure [10] [22]. In patients with palpable pulses, routine angiography or MR angiography is not necessary, and venography is usually not required [22]. Intravascular ultrasound scans can be used as a complementary diagnostic tool. The value of positron emission tomography is still unclear [23].

Arterial replacement was usually accomplished by implanting a synthetic vascular prosthesis in anatomic position. Visceral arteries must be resected for tumors extending into the mesenteric root. In such cases, reconstruction can necessitate primary anastomosis, reinsertion, or bridging by small-diameter grafts (e.g., great saphenous vein, synthetic 6-mm ePTFE, or Dacron prostheses). Good long-term patency rates (83%) were observed in this study when preferably synthetic grafts were used for arterial reconstructions. Arterial bypass grafting after sarcoma surgery has been recognized in the literature in few series [21] [24].

Central venous repair after resection prevents lower limb edema and the clinical sequelae such as pain, swelling, tension, and skin alterations [25]. Expanded PTFE tube prostheses or ePTFE patches are preferred for reconstruction of the inferior and middle portion of the vena cava. Only in case of pre-existing venous

thrombosis should caval ligation be done below the renal veins or in the iliac veins. Retroperitoneal venous reconstructions after STS resection have been previously reported [16]-[21].

The morbidity and reoperation rates in our study were acceptable and thus favor the concept of vascular resection with consecutive repair. As bleeding was the most common complication in some series [9]; careful hemostasis and cautious intraoperative administration of heparin have been suggested [9].

According to our institutional surgical policy, 43% of patients received multi-visceral resection to improve quality of margins and subsequently local control [26] [27].

One of the most common complications in venous reconstruction is graft occlusion, ranging between 7% and 28% [9] [16] [20] [28]. The most used reported graft is PTFE: it is claimed to be more resistant to abdominal viscera compression and consequently less prone to thrombosis [9] [13] [20] [28]. The venous graft is preferable for its theoretical superiority against infection. Whenever a banked homograft of adequate size is available, anatomic restoration of IVC integrity and size matching are more easily achievable than with autologous venous graft (surgical technique).

Bood vessel resection should be considered feasible whenever necessary in RSTS. This is of high importance; especially that completeness of surgical resection is the predominant prognosticator in RSTS [29].

Some authors reported the prognosis of patients who undergo complete resection of retroperitoneal sarcoma with major vascular resection to be very poor, with no long-term survivors [26] [30] [31]. Indeed this bad outcome may be possibly related to disease extent of the patients reported in those series, as indirectly reflected by the need to perform vascular resection, rather than to the procedure itself [32].

5. Conclusion

This study shows that complete resection with clear margins is important for long-term survival in patients with retroperitoneal soft tissue sarcomas. Primary sarcomas or local recurrences, as well as tumors with primary vascular involvement or secondary vascular involvement, require resection of diseased blood vessels necessary to improve the completeness of tumor clearance. The extent of vascular resection and the appropriate vascular repair has to be assessed in the individual patient according to the preoperative imaging, intraoperative findings, and extent of resection, and it should be carefully planned on the basis of the stage of the disease. The proposed classification and treatment algorithm can be used to plan resection and vascular replacement.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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