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Assessment of Surgical Management Modalities and Their Postoperative Outcome of Retroperitoneal Sarcomas: A Study in a Tertiary Care Hospital, Dhaka, Bangladesh

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Abstract **Original Research Article**

Background: Retroperitoneal sarcomas(RPS) are rare tumors with an expected incidence of 5-1 new cases/100,000 inhabitants per year.1 Despite the advent of modern imaging, the associated increase incidental diagnoses, retroperitoneal soft tissue sarcoma (RPS) remains sararemalignancy occurring 0.5 to 1.0 per 100,000 populations.1 The rarity of these tumors and the complexity of their treatment require multi-disciplinary management in specialized centers to improve oncologic and clinical outcomes.2 Moreover, sarcomas in the retroperitoneum have a worse prognosis than sarcomas in the extremities.3 Surgery remains the curative treatment for RPS. Unlike extremity sarcomas, however, RPS can expand massively in the confines of the retroperitoneum prior to detection and diagnosis, making these resections challenges. ***Objective:*** The main objective of this study was to assess the surgical management modalities and their post-operative outcomes of retroperitoneal sarcomas. ***Methods and Materials:*** This was a cross-sectional study from initially all the patients were enrolled by purposive sampling. Thereafter, they were scrutinized by eligibility criteria. All the patients underwent definitive surgery. A preformed structured peer-reviewed data collection sheet was prepared which was used to collect data. Data were compiled, edited, and analyzed by SPSS version 24.0. The result was tabulated in table and figure form. Data analysis was done by Pearson's chi-square test and student's t-test. P-value was significant at <0.05. ***Results:*** Out of 30 patient's maximum of 13(43.33%) patients belonged to the 50-59 years ' age group which was subsequently followed by 6(20%) in the>60 years' age group. Rest 5(16.67%), 4(13.33%) and 2(6.66%) patients belonged to 40-49 years, 30-39 years, and ≤ 29 year's age group respectively. Out of 30 patients, 25(83.33%) were male and 5(16.67%) were female. The male-female ratio was 5:1. Among the total 30 patients, 22(73.33) and 8(26.67%) were primary and recurrent retroperitoneal sarcomas respectively. Out of 30 patients 22(100%) patients in recurrent retroperitoneal sarcoma presented with an abdominal mass. But only 11(50%) in primary cases had pain or discomfort in comparison to 3(37.5%) out of 8 in recurrent cases (p=0.4). The median radiological tumor size in primary and recurrent cases was 15 cm and 12 cm respectively (p=0.003). Out of 22 patients and 8 patients in primary and recurrent retroperitoneal sarcoma respectively; focality and invasiveness showed statistically significant differences as well as a number of resected organs/structured (p-0.006, 0.001, and 0.09 respectively). On the contrary tumor resection margins, grade, histology, and resection of adjacent visceral structures showed no statistically significant differences between the groups (p=>0.05). ***Conclusion:*** In this study, retroperitoneal sarcoma, tumor size, histologic grade, incomplete resection, increasing age, and male sex are strongly associated with recurrence. Complete (R0) resection appeared most significant. Retroperitoneal sarcoma is a giant abdominal tumor that takes it huge size silently. The surgical outcome of primary retroperitoneal sarcoma is relatively better than recurrent retroperitoneal sarcoma.

Keywords: Retroperitoneal sarcomas, post-operative outcome, radiotherapy, chemotherapy, surgery.

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I. INTRODUCTION

Retroperitoneal sarcoma (RPS) is a rare tumor whose diagnosis and management can be challenging and for which management requires a multidisciplinary team in a specialized center. An important part of the diagnosis-identification of the histologic subtype-depends on pathology; identifying the histologic subtype is important because this can affect prognosis

and treatment options. Complete surgical resection with negative margins remains the cornerstone of treatment of no metastatic RPS and is the only chance for cure. In order to achieve negative margins, multivisceralen block resection is often necessary. Neoadjuvant therapies (chemotherapy, external beam radiation, or combination radiation and chemotherapy) are safe in well-selected patients and maybe considered after careful review by a multidisciplinary sarcoma tumor board when the recurrence risk is high. The retro peritoneum is the portion of the lumboiliacregi on limited anteriorly by the peritoneal covering, posteriorly by the posterior abdominal wall, superiorly by the twelfth rib and vertebra, inferiorly by the base of the sacrum and iliac rest, and laterally by the side borders of the quadrates lumborum muscles. The management remains a challenge and surgical resection of localized RPS with microscopically negative margins, as the standard of care is usually used. Complete resection is, however, often difficult to carry out because of the frequently large size of the tumor at the time of diagnosis, the deep-seated location and common infiltration of adjacent vital organs [1]. A thorough excision of retroperitoneal sarcoma is feasibleinupto70% of patients, leading to a five-year local recurrence-free survival and overall survival of 55-80% and 39-90%, respectively [2,3]. Considering the relatively high incidence of local relapse and the infiltrative pattern of growth of RS, some author shave advocated wider resection to improve the thoroughness of surgery [4]. This approach has been called aggressive surgery and consists of their section of the tumor mass with wide excisional margins, which includes adjacent organs located around the tumor although not clinically (i.e. macroscopically) involved. Aggressive surgery for RS has led to promising outcomes as local recurrence were observed in 21-22% of patients and 5-year overall survival was 65-68% [5]. The short term outcomes are common to any abdominal surgery e.g. anastomotic failure, wound infection, embolism, DVT etc. And long term outcome is considered depending on their recurrence. There has been a paucity of well documented study on retroperitoneal sarcomas and its surgical aspects in Bangladesh. In this context, the objective of this study is to evaluate the surgical management modalities of retroperitoneal sarcomas and their outcome in a tertiary care hospital in Bangladesh.

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II. OBJECTIVES

General Objectives

To determine the surgical modalities of treatment and their early outcome of retroperitoneal sarcoma

Specific Objectives

- To discuss the demographic findings of the patients suffering from retroperitoneal sarcoma.
- To analysis the post-surgery outcomes of the selected patients.

III. MATERIALS AND METHODS

This was an across sectional study. Took place in a Tertiary Care Hospital, Dhaka, Bangladesh, from July 2017 to June 2018. All patients admitted in Department of Surgical Oncology, in the tertiary care hospital. Purposive sampling was followed according to the availability of the patients. Total 30 patients were recruited as study population. The study was undertaken on the patients diagnosed with retroperitoneal sarcoma. The diagnosis was done after proper history taking, imaging and FNAC investigations. The purpose and procedure of the study was discussed with the patient. Written consent was taken from those who agreed to participate in the study. On receipt of the informed written consent, data was collected from the patients on variables of interest using the structured design by interview, observation, clinical examination, and diagnostic imaging and biochemical investigations. The analyzed variables were preoperative data (gender, age, tumor location, size, symptoms), preoperative data (date of surgery, resection performed, mortality and postoperative morbidity, histology, microscopic margins, perioperative radiotherapy and/or chemotherapy) but due to time constraint, long term data was possible to be analyzed. Histological Grade 1 & 2 was grouped a slow and grade 3 & 4 high. The primary RPS was defined as a tumor which was untreated before definitive surgical intervention. Local vs. distant recurrence was separated as the sample size was small. Surgical resection was classified into completed (R_0) or incomplete (R_1 & R_2). The patients were followed up 1 and 3 months. Collected data was checked and edited first. They were then processed with the help of software SPSS version 23.0. Data was complied, edited and plotted in tabular and figure form. Descriptive statistics was performed and all data was expressed as mean ± SD and percentage ratio. Ethical clearance for the study was taken from the department of Surgical Oncology and concerned authority in a tertiary care hospital, Dhaka, Bangladesh. The study population was thoroughly appraised about the nature, purpose and implications of the study, as well entire spectrum of benefits and risks of the study. There was physical, psychological, social and legal risk during collection of blood and physical examinations and surgery; proper consent was taken. Interest of the study population was being compromised to safeguard their rights and health. Operative and post-operative complications were explained to the patients. For safeguarding confidentiality and protecting anonymity each of the patients was given a special ID no. which was followed in sample collection, transport to lab and reporting in each and every step of the procedure. All study population was assured of adequate treatment of any complications developed in relation to the study purpose and freedom to withdraw them from the study anytime.

IV. RESULTS

Table-1: Distribution of patients according to age (N=30)

1.	Age group	2.	Frequency (%)
3.	≤29	4.	2(6.67)
5.	30–39	6.	4(13.33)
7.	40–49	8.	5(16.67)
9.	50–59	10.	13(43.33)
11.	>60	12.	6(20.0)
13.	Median (in years)	14.	5
15.	Age range (in years)	16.	29–67

Table-1 shows that out of 30 patient's maximum 13 (43.33%) patients belonged to 50-59 years' age group which was subsequently followed by 6 (20%) in >60 year's age group. 5(16.67%), 4 (13.33%) and 2 (6.66%) patients belonged to 40-49 years,30-39 years and≤29 year's age group respectively.

Table-2: Patient, disease, and treatment characteristics (N=30)

Characteristics	No. of patients	Percentage (%)
Age (yrs), median (range)	55 (29-67)	
Sex		
Male	25	83.33
Female	5	16.67
Tumor site		
Retroperitoneum	22	73.33
Abdomen+pelvis	8	26.67
Tumor size (cm), median (range)	12.0(4.0-37.0)	
≤5	3	10.0
5.1-10	7	23.33
>10	19	63.33
Unknown	1	3.34
Grade		
Low	14	46.67
High	13	43.33
Unknown	3	10.0
Histologic sub type Liposarcoma		
Leiomyo sarcoma	13	43.33
Malignant fibrous histiocytoma	8	26.67
Rhabdomyo sarcoma	5	16.67
Spindle cell sarcoma	2	6.67
Synovial sarcoma	1	3.33
Others	1	3.33
Margin status		
Negative	10	33.33
Microscopic positive	14	46.67
Macroscopic positive	4	13.33
Unknown	2	6.67
Tumor presentation		
Primary	22	83.33
Recurrence	8	16.67
Adjuvant chemotherapy		
No	21	70.0
Yes	9	30.0

Table 2 showed, out of 30 patients, male was 25(83.33%) and female 5(16.67%). The ratio of Male: Female was 5:1, that's mane was dominating absolutely. Largest tumor size (>10cm) was highest 19, followed by (5.1-10 cm) was 7. Tumor size (cm), median (range) was 12.0(4.0-37.0). Tumor presentation primary was 22(83.33) and recurrence 8(16.67). Adjuvant chemotherapy needed Yes 9(30%) and No 21(70%).

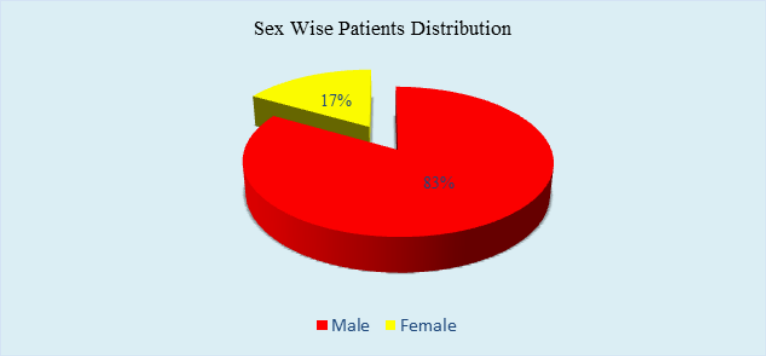

Fig-I: Distribution of patients according to sex (N=30)

Figure-I showed that, out of 30 patients 25(83.33%) and 5(16.67%) were male and female respectively. The male to female ratio was 5:1.

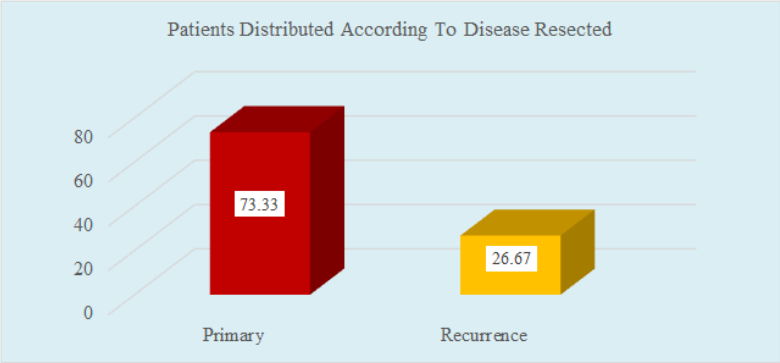

Fig-II: Distribution of patients according to Disease resected (N=30)

Figure II showed that, out of 30 patients 22(73.33%) and 8(26.67%) were primary and recurrent retroperitoneal sarcoma respectively.

Table-3: Distribution of patients according to post-operative outcome (N=30)

Post-operative outcome	Primary (n=22)		Recurrent (n=8)		P value
	n	%	n	%	
Uneventful outcome					
Yes	13	59.09	3	37.50	0.29^{ns}
No	9	40.91	5	62.50	
Emergency					
Reoperation Required	2	9.09	1	12.50	0.78^{ns}
Not required	20	90.91	7	87.50	
Percutaneous					
Drainage Required	22	100.0	8	100.0	-
Not required	0	0.00	0	0.0	
Peritoneal					
Hemorrhage Happened	4	18.18	2	25.00	0.67^{ns}
Not happened	18	81.82	6	75.00	
Septic complications					
Yes	1	4.55	1	12.50	0.40^{ns}
No	21	95.45	7	87.50	
Wound infection					
Present	7	31.82	3	37.50	0.77^{ns}
Absent	15	68.18	5	62.50	
Mean hospital stay (days)	15.39±2.31		18.73±4.33		0.39^{ns}
p-Value was calculated by chi square test ns: not significant p-Value was significant at <0.05.					

Table 4 showed that, out of 22 patients in primary retroperitoneal sarcoma, wound infection was the highest complication 31.82%) whereas the in recurrent sarcoma it was (37.5%). Subsequently, peritoneal hemorrhage was observed as 15.39±2.31and 18.73±4.33 days respectively. No postoperative outcome was observed as statistically differences.

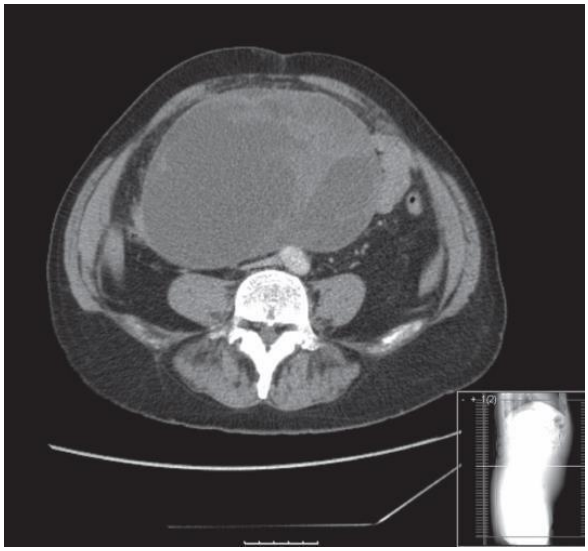

Fig-III: CT scanned Image of an 80 years old Male Patients

Figure-III: showed a CT scanned image of an 80-year-old male showing a central abdominal mass probably arising from within the mesentery or a small bowel loop. A core needle biopsy confirmed a gastrointestinal stromal tumor with amutation found inexon11oftheKITgene. The patient was commenced on imatinib.

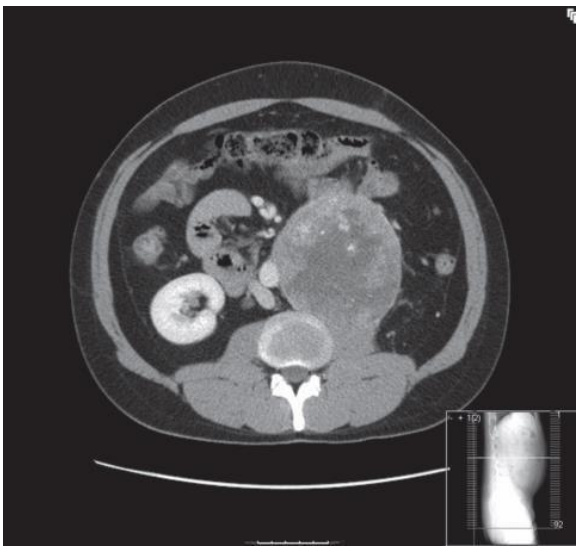

Fig-IV: CT scanned image of a 27 years old Male Patient

Figure IV showed that, a CT scanned image of a 27 years old male patient showing left retroperitoneal mass closely applied to the aorta. Acoreneedle biopsy was consistent with a diagnosis of Ewing's sarcoma and genetic analysis demonstrated a Trans location involving the EWSR 1 gene. The patient received neo adjuvantchemo therapy and <10% viable tumor was found on post resection histology. Intra-abdominal lymphoma is not uncommon and may present as a midline mass, which can displace or encase the aorta, cava or iliac vessels. Management options for retroperitoneal sahwan no mas include radiological surveillance in asymptomatic patients or surgical resection in symptomatic patients [6]. Once a retroperitoneal tumor has been identified, a number of clinical entities must be considered, including and nonfunctioning adrenal tumors, renal tumors, pancreatic tumors, advanced gastrointestinal carcinomas, germ cell tumors. And soft tissue sarcomas. A detail history and physical examination can help to distinguish many of these entities and direct further studies. Testicular examination, ultrasonography and measurements of serum βhuman chorionic gonadotropin (β-hCG) are indicated in case of suspected testicular cancer with retroperitoneal metastasis. In patients with lymphadenopathy, either core needle or excisional biopsy of enlarged lymph nodes may be diagnostic for lymphoma. Some recommend surgical exploration as the most appropriate next step for a retroperitoneal mass suspected of being a sarcoma [7]. When the diagnosis may change the preoperative therapy, we perform a percutaneous biopsy. A negative biopsy does not justify a period of observation, and we proceed to surgery. Examples include the use of imatinib mesylate (Gleevec) for gastrointestinal stromal tumors or primary chemotherapy for germ cell tumors or lymphomas. Distinguishing between these diagnoses can be difficult, with nonspecific physical findings and imaging studies.

V. DISCUSSION

The guideline for the treatment of RS recommended complete surgery of the resection of the localized tumor mass with clinically-negative excision margins. As histopathological margin is recognized as being the most important prognostic factor contributing to long term local disease free survival [8], aggressive surgery consisting of the excision of organs and viscera adjacent to the tumor mass although clinically uninvolved, has been proposed to improve local tumor control in patients with primary RS [5]. Complete and aggressive have been directly compared in retrospective series [5], suggesting a possible improvement in tumor control after aggressive specially in patients with low-grade tumors [9]. Several concerns exist regarding the retrospective sign of such studies (including a limited length of follow-up), as well as a lack of standardization of the aggressive surgical technique, and the absence of prospective studies designed to complete and aggressive surgery [10]. We have evaluated 30 patients in department of Surgical Oncology where it was evident that 22(73.33%) cases were primary RPS and rest 8(26.67%) were secondary RPS. The overall median age of the respondents was 55 years. Age range was 29-

67 years. Approximately 6.67% patientsbelongedto50-59 year's age group which was subsequently followed by 23.33% patients in >60 year's age group. Sex distribution revealed that among 30 patients, 25(83.33%) was male and 5(16.67%) was female. The male female ratio was 5:1. Both the variables findings were in accordance with the findings of N.V. Vanitha's study. Stoeckle et al. [11] showed in their study the male and female ratio was 1:1.2 and 1:1.22 respectively. But Lewis et al. [8] showed male patients was higher than female patients like 1.34:1, 1.2:1 and 2:1 respectively. Interestingly, we have found male patients were 5 times higher which was for higher in comparison to other above mentioned studies. It might be due to smaller sample size and influenced of patriarchy socio-economic profile of Bangladesh society where most of the poverty-stricken women get less importance to seek medical attention for complicated disease that deserved costly and long term treatment. All most all the patients in primary (n=22) and recurrent (n=8) cases presented with abdominal mass. But 50% and 37.5% patients respectively presented with pain or discomfort for the median radiological size of primary tumor was 15 cm but the same parameter in recurrent tumor was 8 cm. This is the only variable that showed statistically significant difference in clinical presentation (p=0.003). The similar result was observed in the study by Carlo Ricardo Rossietal [12] where they showed the median tumor size were 15 cm and 12 cm respectively. The highest resection margin category in primary RPS was R_1 (59.09%) and same (62.5%) in recurrent category (p=0.98). Combinedly in our study it was a little lower (86.67%) than their study. For the point of view of NCLCC: tumor grade 12(54.54%) and 6(75%) were the highest the primary and recurrent RPS respectively. Carlo Ricordo Rossi's results agreed with our findings were differentiated limosarcoma was the highest histological category (50% each) in both the groups. This was also similar like previous study [13]. Focality, invasiveness and number of rejected organs revealed statistically significant differences between primary and recurrent RPS groups (p=<0.05) that was also agreed by previous study [13]. Recent publications have described the invasive behavior of RPS, helping to explain the propensity to local recurrence. Previously, only high grade RPS was thought to be invasive but Mussietal found invasive behavior in 25% and 33% respectively of the well differentiated liposarcoma (WDLS) cases they reported [14]. Half (50%) of the tumors resected in our series demonstrated invasive behavior on histopathological examination but the proportion was reduced (35%) when considering WDLS patients only. The difficulty of microscopically examining the surface of a 20 cm tumor completely is noted. In their extensively histologically sampled prospective series, Mussi et al. describe infiltration of at least one organ in 80% of their patients [14]. Wound infection (p=0.77) peritoneal hemorrhage (p=0.67) and septic complications (p=0.43) were the frequent complications though none of them showed statistically significant difference between primary and recurrent RPS category. According to postoperative outcome, out of 22 patients 13(59.09%) in primary RPS showed uneventful outcome. On the contrary 3(37.5%) out of 8 patients in recurrent RPS revealed uneventful outcome.

VI. CONCLUSION

Retroperitoneal Sarcomas are relatively uncommon tumors with varied manifestations, ill-defined prognostic factors and uncertain management modalities. We undertook this study to review patients who presented with primary or recurrent RPS during the study period. Retroperitoneal sarcoma is a giant abdominal tumor that takes it huge size silently. The surgical outcome of primary retroperitoneal sarcoma is relatively better than recurrent retroperitoneal sarcoma.

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