ISSN 2689-8268 | Volume 8

American Journal of Surgery and Clinical Case Reports

Case Report Open Access

Giant Retroperitoneal Liposarcoma, Does Size Matter?

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Received: 20 May 2025
Accepted: 26 May 2025
Published: 01 Jun 2025
J Short Name: AJSCCR

Keywords: Liposarcoma; Giant Retroperitoneal Liposarcoma; Compartmental Surgery

Citation: AJG Moriana.Giant Retroperitoneal Liposarcoma, Does Size Matter?. Ame J Surg Clin Case Rep. 2025; 8(16): 1-5

1. Abstract

1.1. Introduction

Liposarcomas are rare tumors, with their most common location being the retroperitoneum. The retroperitoneal cavity provides large space for the growth of retroperitoneal liposarcomas (RPL), often leading to a late diagnosis when they reach significant size and generate symptoms due to compression. Very few cases of giant RPL are described in the literature, mostly as case reports, or case series. The aim of our study is to analyze the largest case series of RPL described in the literature to date.

1.2. Materials and Methods

Ambispective observational study including a cohort of patients with giant retroperitoneal liposarcoma (GRPL) operated on at our center from January 2016 to February 2024.

1.3. Results

During the study period, a total of 12 patients were diagnosed with a GRPL and operated on. The mean age of the patients was 57 years old, and 66.7% of them were female. The most common ASA score was II (58.3%), followed by ASA score III (41.7%). The most frequent symptom was due compression of the tumoral mass to nearby organs, present in 41.7% of patients. All cases were diagnosed with a CT and a biopsy, with an average size of 33.79 cm in height, 26.09 cm in width, and 18.32 cm in depth, and a mean weight of 7.73 kg. The GRPL was left-sided in the 58.3% of patients and crossed the midline in 75% of cases.

1.4. Conclusions

The treatment of GRPL is associated with significant morbidity and mortality, due to the need for extensive compartmental surgeries. Therefore, this type of pathology should be treated at high-volume referral centers by a multidisciplinary team of experts.

2. Introduction

Soft tissue tumors (STTs) represent approximately 1% of neoplasms in adults [1]. According to the World Health Organization (WHO), they have an incidence of 2-5 cases per 100,000 people, with over 100 subtypes, each with different clinical presentations, treatments, and prognoses [2]. The most common locations are the extremities (41%), trunk (13%), and retroperitoneum (7%) [3].Liposarcomas are the most common STTSs that develop in the retroperitoneum. They have a mesodermal origin, derived from adipose tissue. The WHO has classified liposarcomas into four subtypes: well-differentiated, dedifferentiated, pleomorphic, and myxoid. Well-differentiated and dedifferentiated subtypes are most frequently found in the retroperitoneum, while pleomorphic and myxoid subtypes more commonly originate in the extremities [4-5].The retroperitoneal cavity provides ample space for the growth of retroperitoneal liposarcomas (RPLs). This allows RPLs in their early stages to be asymptomatic and not produce symptoms until they reach a large size due to compression of neighboring structures. As a result, the average size at diagnosis is typically around 20-25 cm and weighs approximately 15-20 kg [4,6]. This aligns with a T4 category in the AJCC Cancer Staging Manual [7]. A giant retroperitoneal tumor is defined as one with a diameter equal to or greater than 30 centimeters or a weight exceeding 20 kilograms [8].

There are very few cases described in the literature of giant retroperitoneal liposarcoma (GRPLs), most of which are presented as clinical cases or case series. The aim of this study is to analyze the largest case series of GRPLs described in the literature to date.

3. Materials and Methods

This is an observational ambispective study comprising a cohort of patients with giant retroperitoneal sarcoma who underwent surgery at our center from January 2016 to February 2024. The study was conducted at the Department of Peritoneal and Retroperitoneal Oncologic Surgery of the Virgen del Rocío University Hospital (Seville, Spain) (Level 1). Informed consent was obtained from all patients prior to their inclusion in the study.

3.1. Sample

A total of 12 patients diagnosed with GRPL were treated between January 2016 and February 2024.Inclusion criteria were: age over 18 years old, confirmed diagnosis of retroperitoneal liposarcoma by pathological anatomy, patients operated on for primary retroperitoneal liposarcoma with a size exceeding 30 cm or weight exceeding 20 kg at our center, and acceptance and signing of the informed consent.Exclusion criteria were: age under 18 years old, patients operated on for recurrences of retroperitoneal liposarcoma, and refusal by patients to participate in the study.

3.2. Study Design

3.2.1. Diagnosis: The Diagnosis was Made Using CT or MRI Plus Biopsy

3.2.1.1. Procedure: all patients were presented to a multidisciplinary committee prior to surgery, where the intervention was individualized according to the patients' characteristics. Patients were admitted one day before the surgical intervention, and mechanical bowel preparation with sodium phosphate was performed in those anticipated to undergo colonic resection.The surgical technique was individualized for each patient following the principles of compartmental surgery and the decision of the multidisciplinary committee. All patients received general anesthesia and antibiotic prophylaxis.

3.3. Postoperative Follow-Up

Patients were evaluated in consultation at one month, six months, and subsequently annually until reaching five years of follow-up.

3.4. Variables

The variables studied are presented in Table 1.

3.5. Characteristics of The Sample

During the period from January 2016 to February 2024, 45 retroperitoneal liposarcomas were operated on, 12 of which were giant. Demographic characteristics are shown in Table 2.Twelve giant retroperitoneal liposarcomas were operated on, with an average size of 33.79 +/- 4.31 cm in height, 26.09 +/- 5.64 cm in width, and 18.32 +/- 5.78 cm in depth. The mean weight was 7.73 +/- 2.29 kg, as recorded in the pathology laboratory. The remaining characteristics are presented in Table 3.

4. Statistical Analysis

A descriptive study of the variables was conducted. Patient characteristics were summarized using continuous and categorical variables. Continuous variables were presented as mean ± standard deviation (SD) or median. Categorical variables were presented with frequencies and percentages (%). Kaplan-Meier curves with 95% confidence intervals were used to study disease-free interval and overall survival. Data analysis was performed using IBM® SPSS® Statistics 21 software.

Table 1: Variables studied.

Qualitative variables	Sex (man (M)/ female (F)
	ASA (American Society of Anesthesiologists Classification) (I, II, III, IV, V, VI
	Admission to ICU (yes/no)
	Readmission to ICU (yes/no)
	Compartmental Surgery (R0, R1, R2)
	Clinical presentation at diagnosis (compressive symptoms, mass, pain, weight loss)
	Diagnosis method (CT scan, Biopsy, MRI)
	Laterality (Right, Left)
	Midline crossing (yes/no)
	Subtype (well-differentiated, poorly-differentiated, myxoid, pleomorphic)
	Surgical procedure (nephrectomy, adrenalectomy, pancreatectomy, splenectomy, small bowel resection, right hemicolectomy, left hemicolectomy, segmental transverse resection, recto-sigmoidectomy, oophorectomy, hysterectomy)
	Intestinal anastomosis (yes/no)
	Vascular resection (arterial, venous)
	Reintervention (yes/no)
	Clavien-Dindo classification (I, II, III, IV, V)
	Complications (anastomotic leak, pancreatic fistula, superficial surgical site infection (SSI), deep surgical site infection, evisceration, hemoperitoneum)
	Readmission (yes/no)
	Outcome (recurrence, persistence, cure)
	Survival (yes/no)
	Median: 12 (7-39) months
Quantitative variables	Age (years)
	Disease duration (months)
	Length of stay (days)
	Size (centimeters (cm)
	Weight (kilograms (Kg))
	Organs resected (number)
	Disease-free interval (DFI) (months)
	Overall survival time (months)

5. Results

5.1. Surgery Characteristics

In 11 cases, compartmental R0 surgery was performed with an open approach followed by ICU stay, while the remaining case was not completely resectable due to involved structures, resulting in R1 surgery. The total postoperative stay was 30.33 +/- 19.79 days, and the most frequently resected organ was the kidney. The most common complication was deep SSI. The characteristics of the intervention are presented in Table 4.

5.2. Prognosis

The overall cure rate in our series is 75%. The disease-free interval was 27.45 +/- 6.25 months (95% CI = 15.21-39.69) (Figure 1). Overall survival was 83.3% with a total survival time of 65.25 +/- 9.49 months (95% CI = 46.64-83.85) (Figure 2). Prognosis and survival are shown in Table 5.

Table 2: Demographic characteristics.

Sex	M = 4 (33.3%) F = 8 (66.7%)
Age	57.08 +/- 14.18 years
ASA	I = 0 II = 7 (58.3%) III = 5 (41.7%) IV = 0

Table 3: Characteristics of GLPS.

Clinical Presentation at Diagnosis	Compressive symptoms = 5 (41.7%) Mass = 4 (33.3%) Pain = 2 (16.7%) Weight loss = 1 (8.3%)
Disease duration	Median: 12 (7-39) months
Size	Height = 33.79 +/- 4.31 cm Width = 26.09 +/- 5.64 cm Depth = 18.32 +/- 5.78 cm
Weight	7.73 +/- 2.29 Kg
Laterality	Right = 5 (41.7%) Left = 7 (58.3%)
Subtype	Well-differentiated = 6 (50%) Poorly-differentiated = 6 (50%) Myxoid, = 0 Pleomorphic = 0
Midline crossing	Yes = 9 (75%) No = 3 (25%)

6. Discussion

Currently, there is limited research on giant retroperitoneal liposarcomas (GLPS) due to their low incidence, which hinders the conduct of prospective studies and the development of specific treatments [2-3]. Consequently, the treatment of GLPS follows the same surgical principles as normal-sized liposarcomas (NLS). We acknowledge the primary limitation of our study as the sample size, which may overestimate or underestimate some of the presented results.The demographic characteristics of the study population show a peak incidence of GLPS between 43-71 years, predominantly among females (66.7%), consistent with findings by Hassan et al. and Zeng et al. [9-10], who reported a peak incidence between 40-60 years and a slight female predisposition. Symptoms in scientific literature are nonspecific, with a prolonged time to diagnosis, similar to our case series where nonspecific symptoms of neighboring structure compression predominate (41.7%), with a median duration of symptoms until diagnosis of 12 months (7-39).Another feature worth noting in our study is the weight of the tumor. In our case, the weight of the GLPS is on average 7.73 +/- 2.29 Kg, much lower than that described in the literature, for example, Zeng et al. [10] in their review obtained an average weight of 40kg. This is because we used the weight recorded after the pathological anatomy process instead of the weight at extraction, as we did not have the latter in the older cases.Compartmental surgery is the cornerstone of non-metastatic GLPS treatment, involving en-bloc resection of all organs and structures in contact with the neoplasm regardless of infiltration. This results in multivisceral resections aimed at achieving R0 resection [11-12]. In our study, we observed high rates of organ resection with a mean of 4.25 +/- 1.28, major morbidity (Clavien-Dindo ≥3) of 50%, and mortality of 16.7%. These data significantly differ from those described in the literature; for example, MacNeill et al. found only 16.7% of their 1007 patients experiencing major postoperative morbidity (Clavien-Dindo ≥3), with a mortality of 1.8%. The number of resected organs was also significantly lower, with a mean of 2 (1-4) [12]. This disparity suggests that compartmental surgery in GLPS is more aggressive, with greater organ resection and higher postoperative morbidity.Given the significance of R0 compartmental surgery as a prognostic factor, strategies are

Table 4: Surgical characteristics.

Compartmental Surgery	R0 = 11 (91.7%) R1 = 1 (8.3%)
Length of Stay	30.33 +/-19.79 days
Number of Organs Resected	4.25 +/- 1.28
Surgical Procedure	Nephrectomy = 12 (100%) Adrenalectomy = 9 (75%) Pancreatectomy = 5 (41.7%) Splenectomy = 4 (33.3%) Small bowel resection = 0 Right Hemicolectomy = 4 (33.3%) Left Hemicolectomy = 7 (58.3%) Segmental transverse resection = 0 Recto-sigmoidectomy = 5 (41.7%) Oophorectomy = 9 (75%) Hysterectomy = 9 (75%)
Intestinal anastomosis	Yes = 10 (83.3%) No = 2 (16.7%)
Vascular resection	Arterial = 0 Venous = 1 (8.3%)
Clavien-Dindo classification	0 = 2 (16.7%) I = 1 (8.3%) II = 3 (25%) III = 3 (25%) IV = 2 (16.7%) V = 1 (8.3%)
Reintervention	Yes = 3 (25%) No = 9 (75%)
Complications	Anastomotic leak (n=10) = 1 (10%) Pancreatic fistula (n=5) = 3 (60%) Superficial SSI (n=12) = 2 (16.7%) Deep SSI (n=12) = 7 (58.3%) Evisceration (n=12) = 0 Hemoperitoneum (n=12) = 2 (16.7%)
Readmission	Yes = 1 (8.3%%) No = 11 (91.7%)

Table 5: Prognosis and overall survival of GLPS.

Cure	Recurrence= 2 (16.7%) Persistence = 1 (8.3%) Cure = 9 (75%)	
Disease-free Interval	27.45 +/- 6.25 months	IC 95% (15.21-39.69)
Survival	Yes = 10 (83.3%) No = 2 ((16.7%)	
Overall Survival Time	65.25 +/- 9.49 months	IC 95% (46.64-83.85)

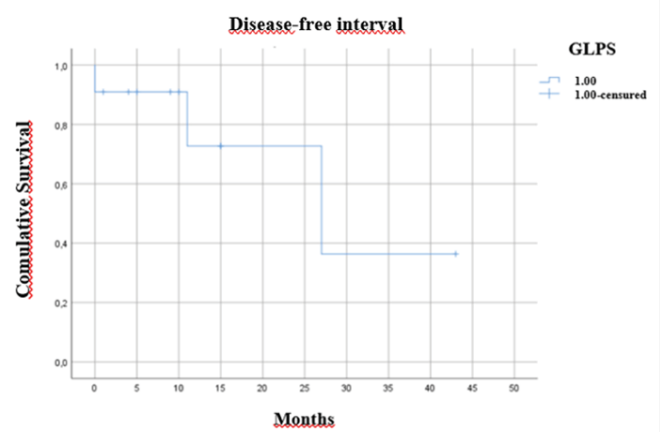

Figure 1: Disease-free-interval of GLPS.

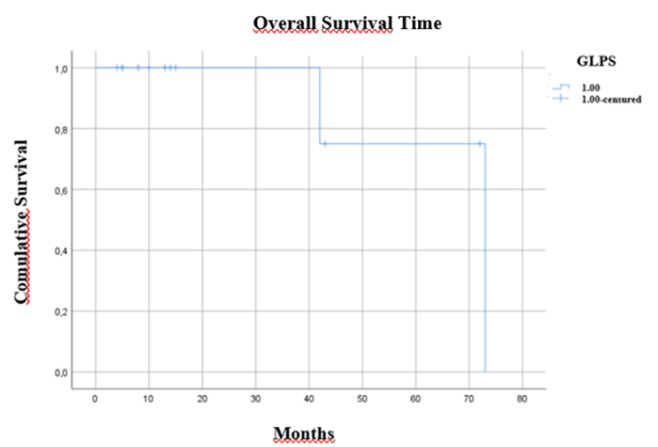

Figure 2: Overall Survival Time of GLPS.

being sought to reduce its morbidity. For example, Gronchi et al. have begun to propose personalized surgeries for each patient based on their GLPS characteristics [13]. The Trans-Atlantic RPS Working Group recommends managing these patients in specialized multidisciplinary teams and high-volume compartmental surgery centers [14]. We believe that for the proper treatment of GLPS, personalized surgery and concentration of cases in referral centers with multidisciplinary committees are essential.The impact of R0 surgery on Overall Survival (OS) and Disease-Free Survival (DFS) in these tumors has been demonstrated. Lewis et al. in 1988 observed in their cohort of 500 patients that the median survival in R0 cases was 103 months compared to 18 months in R1-R2 cases [15]. Similarly, Gronchi et al. in their retrospective study of 288 patients comparing compartmental surgery versus standard surgery observed a decrease in local recurrence (28% CS vs 48% Non-CS) and metastasis (13% CS vs 22% Non-CS) with compartmental surgery [16].When comparing our global survival results with those obtained by Lewis et al. [15], we observe that our GS is somewhat lower than theirs (mean 65.25 months vs 103 months). This discrepancy may be primarily influenced by the follow-up time, which was 12 years in their case and 6 years in ours. On the other hand, our DFS was 75%, higher than the 53% reported by Gronchi et al. [16] in the compartmental surgery group. Therefore, although the data must be interpreted cautiously, in GLPS, lower OS is observed despite higher DFS, which may be related to the increased morbidity and mortality associated with extensive compartmental surgery these patients require.Efforts to improve DFS and OS have relied on complementary treatments such as chemotherapy and radiotherapy. However, few clinical trials have been conducted to date to evaluate the role of radiotherapy in LPS treatment. The ACOSOG trial ended prematurely due to low patient recruitment. The EORTC randomized clinical trial STRASS found improvement in DFS in patients treated with radiotherapy and compartmental surgery, although no significant differences were found in the rate of local recurrence in patients who underwent R0 surgery, regardless of whether they received radiotherapy or not [17]. Regarding chemotherapy, given the hematogenous metastatic spread of sarcomas, perioperative chemotherapy has been proposed as a therapeutic tool for controlling microscopic disease or achieving tumor size reduction to achieve a higher rate of R0 surgeries [18]. However, studies such as those by Bremjit et al. or Miura et al. found no benefit in chemotherapy in terms of global survival [19,20]. Therefore, the roleof chemotherapy or radiotherapy should be assessed and individualized in each case within a Multidisciplinary Expert Committee.

In conclusion, the size of GLPS matters, as it increases morbidity and decreases OS, probably due to the need for extensive compartmental surgery, despite DFS increasing in our series compared to those published in the literature. Based on these results, we consider that the best option for the surgical treatment of these patients is to manage them in centers with high expertise and multidisciplinary team presence.

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