

Giant Retroperitoneal Liposarcoma: Correlation Between Size and Risk for Recurrence

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Abstract

Soft tissue sarcomas (STSs) are rare tumors that represent almost 1% of adult malignant tumors. The annual incidence rate for such tumors is 2 - 5/100,000 population. The most common type of STS in adults is liposarcoma, which represents 15-20% of adult STSs. It is of mesodermic origin derived from adipose tissues, and known as the most common primary malignant tumor of the retroperitoneum. Other sites of involvement include the extremities, trunk and to a lesser extent the pleural cavity, esophagus, mediastinum and others. Due to the potential large retroperitoneal space, retroperitoneal liposarcoma (RPL) is usually asymptomatic during the initial phase, developing symptoms at a late stage due to large mass compressing nearby retroperitoneal structures. The average diameter and weight of RPL during diagnosis is 20 - 25 cm and 15 - 20 kg, respectively. Several factors were labelled as risk factors for recurrence, such as histological type, tumor grade, age, resectability and tumor size. Controversy exists regarding the relationship between tumor size and recurrence rate, thus, tumor size as a risk factor for recurrence should be clarified. Although there is no consensus regarding the precise definition of giant RPL, it is defined by several literatures as an RPL of greater than 30 cm in diameter or with weight of more than 20 kg. The main purpose of this article is to review the current English literature regarding giant RPL and examine the relationship between tumor size and risk for recurrence.

Keywords: Giant retroperitoneal liposarcoma; Tumor size; Recurrence risk

Introduction

Soft tissue sarcomas (STSs) are uncommon tumors that represent approximately 1% of adult malignancies [1]. The reported

incidence rate is 2 - 5/100,000 population. According to the fourth edition of the World Health Organization (WHO), there are more than 100 subtypes of soft tissue tumors, the majority of which are STSs. Each subtype of these tumors has a unique clinical, prognostic and therapeutic behavior [2]. The most common site of involvement of STSs is the extremities (41%), followed by the trunk (13%), retroperitoneum (7%), gastrointestinal tract (7%), head and neck (5%), and the uterus (4%). Liposarcoma (12%), leiomyosarcoma (12%) and undifferentiated (pleomorphic) sarcoma (11%) are the most common types of STSs [3].

Liposarcoma is the most common type of STSs in adults and represent about 20% of adult malignant mesenchymal tumors [4]. It is a tumor of mesodermic origin derived from adipose tissues. Although it can affect any part of the body, it usually develops in the extremities, retroperitoneum, trunk and to a lesser extent in the mediastinum, pleural cavity, esophagus, uterus, spermatic cord and others [5-9]. At the retroperitoneal cavity, retroperitoneal liposarcoma (RPL) is the most common primary tumor and represents 40% of all retroperitoneal sarcoma tumors. According to the 2020 edition of the WHO, four types of liposarcoma are recognized: atypical lipomatous tumor/well-differentiated liposarcoma, dedifferentiated liposarcoma, myxoid/round cell liposarcoma and pleomorphic type [10]. The anatomic distribution of liposarcoma subtypes depends on the histologic type; while well-differentiated and dedifferentiated subtypes are more common in the retroperitoneal cavity, pleomorphic and myxoid subtypes are more common in the extremities.

Due to the large potential space in the retroperitoneal cavity, primary RPL can grow to a very large size without causing symptoms. The average diameter of the tumor at diagnosis is 20 - 25 cm with a weight of 15 - 20 kg [11]. Due to the previously mentioned parameters, patients with primary RPL develop symptoms at later stages of the disease, mainly due to mass effect on adjacent organs, and less commonly, by organ invasion [12]. Primary RPL is characterized usually by low rates of complete surgical resection and high rates of tumor recurrence following resection, due to late diagnosis [13].

Giant liposarcoma is defined, by several authors, as a tumor weight of more than 20 kg or tumor diameter of more than 30 cm [14] (Fig. 1).

The mainstay management for primary RPL is complete surgical resection with negative microscopic margins (R0), when feasible [15]. Even when complete surgical resection is possible, local recurrence rate is high at 66% and 5-year over-

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Figure 1. A giant retroperitoneal liposarcoma (diameter: 50 cm; weight: 29 kg).

all survival rate is 54% [16, 17]. Several prognostic factors for recurrence and overall survival for patients with primary RPL have been reported and include age, tumor grade, histological subtype, complete resectability and tumor size, with the latter being a scientific dilemma in the absence of studies in the English literature that examine the relationship between size of the primary tumor and risk for recurrence.

Due to the lack of reported studies about the aforementioned relationship, the aim of this study is to review the pertinent and available studies in the English literature, specifically giant RPL, to figure out if size of the primary tumor is

to be considered as a prognostic risk factor for tumor recurrence.

Methods

A search in PubMed was conducted, based on the “PICOS” acronym. Headings and text words were used to identify studies (retrospective, prospective, case report and case series) published regarding giant primary RPL.

The following search terms were included: “retroperitoneal liposarcoma”, “liposarcoma of the retroperitoneum”, “giant liposarcoma”, “giant retroperitoneal tumors”, “retroperitoneal tumors”, and “retroperitoneal sarcoma”.

All reported cases of giant primary RPL were included, and data regarding patients’ demographics, tumor size, tumor resectability status, histological type, neo-adjuvant/adjuvant radiation therapy and recurrence were collected.

Results

Reviewing the current English literature revealed 24 reported cases of giant primary RPL solely [13, 18-24, 25-31]; 14 case reports and one retrospective study including 10 cases of retroperitoneal dedifferentiated liposarcoma [31]. Of the 24 patients, 14 were males and 10 were females. The average age at diagnosis was 57 years old (age range 40 - 76 years old). The most common presenting symptom (not available in the retrospective study) was increased abdominal girth (or abdominal distension) reported by all patients. Other less reported symptoms were dyspnea, constipation, weight loss, leg edema, weight gain and dyspepsia (Table 1). In the retrospective study by Bachmann et al [31], only dedifferentiated RPLs were in-

Table 1. Demographic Features for Patients With Giant Retroperitoneal Liposarcoma

Case	Age	Sex	Symptoms
Xu et al [30]	65	M	Abdominal distension
Herzberg et al [29]	75	M	Abdominal distension, loss of appetite and weight
Zeng et al [28]	45	M	Abdominal distension
Oh et al [27]	71	F	Abdominal distension
Hazen et al [26]	64	M	Abdominal distension
Caizzone et al [25]	64	F	Abdominal distension
Zhang et al [13]	48	F	Abdominal distension, left abdominal pain
Sharma et al [24]	60	F	Increase abdominal girth, weight gain
De Nardi et al [23]	40	M	Abdominal distension
Bansal et al [22]	52	M	Abdominal distension, early satiety, weight loss, dyspnea
Hashimoto et al [21]	41	M	Abdominal distension, leg edema, weight gain and dyspnea
Clar et al [20]	66	M	Increased abdominal girth, dyspepsia, dyspnea
McCallum et al [19]	47	F	Increased abdominal girth
Yol et al [18]	63	M	Abdominal distension, constipation, dyspnea
Bachmann et al (10 cases) [31]	58	5 M; 5 F	N/A

M: male; F: female; N/A: not available.

cluded and there were no data regarding clinical presentation, imaging techniques used and specific data regarding tumor size to build up a correlation between size and tumor recurrence. Thus, it was excluded from this review.

The largest tumor diameter was 65 cm, reported by Zeng et al [28], while the smallest one was 30 cm, represented by Zhang et al [13]. The average tumor diameter for all cases was 43.5 cm. Abdominal computed tomography (CT) scan was the most commonly used radiological exam, done for all patients, while abdominal ultrasound (US) and abdominal magnetic resonance imaging (MRI) were used as additional imaging tests for two patients each. Pre-operative diagnosis by a proven biopsy of liposarcoma was available in four patients only [18, 20, 21, 24], and the majority (nine patients) underwent upfront surgical resection without biopsy. All patients were operated on with negative resection margins (R0 resection) achieved in all, except one [19], who had microscopic positive margins (R1 resection). No cases of R2 resection (macroscopic positive margins) were documented. Most operations (eight patients) included resection of the primary tumor along with organs involved, of which the kidney (right or left, depends on the location of the primary tumor) was the organ most commonly resected. The most common histological liposarcoma subtype was well-differentiated liposarcoma (6/14 patients), followed by dedifferentiated (four cases), myxoid and mixed type (myxoid and pleomorphic - two cases each). Only one patient [18] was treated with adjuvant therapy by means of radiotherapy. Follow-up was not reported for two patients [18, 26]. The average mean of follow-up (by months) for the remaining cases was 20 months (ranges between 3 and 63 months) (Table 2). The majority of patients (9/12) which were followed had no evidence of local or remote recurrence, and only three patients suffered from local tumor recurrence. The histological types for these cases were mixed type liposarcoma, myxoid and well-differentiated tumor [13, 22, 27]. Worth mentioning, when the correlation between the size of the primary tumor and risk for tumor recurrence was examined, we have noticed that it is nonexistent as the largest seven giant tumors (diameter 42 - 65 cm) have no evidence of recurrence at a follow-up of 35 months. On the other hand, the smallest giant tumor (30 cm in diameter) developed very early tumor recurrence at 3 months of follow-up (even though surgical margins were negative at the final histopathological report). As already mentioned before, histological subtypes for the reported cases with recurrence were mainly of the mixed and myxoid types, which can explain the recurrence risk, rather than the tumor size, as these subtypes are known as more aggressive tumors.

Discussion

Since the introduction of STSs as highly malignant tumors with different types, several prognostic factors, independent of tumor histological type, for local/remote recurrence and overall survival were investigated in a thorough manner by multiple studies (retrospective/prospective). These prognostic factors are diverse and mainly include tumor grade, tumor histology, age, respectability status and tumor size [32]. While several studies had already proved the association between prognostic factors and risk of recurrence, up till now, there is

Table 2. Tumor Characteristics for the Different Reported Cases

Case	Imaging test	Tumor size (cm)	Pre-operative diagnosis	Intra-operative resectable organs	Histological subtype	R status
Xu et al [30]	CT	37	No	-	Well-differentiated type	R0
Herzberg et al [29]	CT	35	No	Left nephrectomy, partial left diaphragm resection	Dedifferentiated type	R0
Zeng et al [28]	CT	65	No	No	Well-differentiated type	R0
Oh et al [27]	CT, US	45	No	No	Well-differentiated type	R0
Hazen et al [26]	CT	40	No	Left nephrectomy, left colectomy	Dedifferentiated type	R0
Caizzzone et al [25]	CT	42	No	Right nephrectomy	Mixed type	R0
Zhang et al [13]	CT, MRI	30	No	Left partial nephrectomy	Myxoid type	R0
Sharma et al [24]	CT	47	Yes	-	Well-differentiated type	R0
De Nardi et al [23]	CT	50	No	-	Well-differentiated type	R0
Bansal et al [22]	CT	40	No	Partial excision of the small bowel and right ureter	Mixed type	R0
Hashimoto et al [21]	CT	45	Yes	Right nephrectomy	Dedifferentiated type	R0
Clar et al [20]	CT, MRI	47	Yes	Left nephrectomy	Well-differentiated type	R0
McCallum et al [19]	CT	50	No	TAH-BSO and para-aortic lymph node resection	Dedifferentiated type	R1
Yol et al [18]	CT, US	35	Yes	Left colectomy	Myxoid type	R0

R status: resectability status; R0: negative microscopic margins; R1: positive microscopic margins; R2: positive macroscopic margins; CT: computed tomography; US: ultrasound; MRI: magnetic resonance imaging; TAH-BSO: total abdominal hysterectomy with bilateral salpingo-oophorectomy.

no single study that compares tumor size with tumor recurrence risk. Primary RPL recurrence usually develops within 0.5 - 2 years following surgical resection [33], with rates up to 60% at 5 years follow-up [34].

In the present study, we have reviewed the relevant articles regarding giant primary RPL to investigate the association between initial tumor size and risk for recurrence. Following the statement that tumor size is a risk factor for tumor recurrence, we have decided to review the specific group of patients with giant RPL, as they have a very high risk for recurrence.

As had been shown, in the majority of cases, tumor size was not a risk factor for recurrence. Larger tumors did not recur following R0 surgical resection, while smaller tumors did, as early as 3 months following resection. Tumor subtype (myxoid/mixed) and whether or not contiguous organs had been resected were risk factors for tumor recurrence.

In his study, Sun et al [35] demonstrated that tumor size was not an independent prognostic factor for RPL. In another retrospective study [32], RPL tumors were divided according to tumor grade into two groups: low grade (G1) and high grade (G2-G3). Tumor sizes for both groups were almost identical with median diameter of 27 and 28 cm, respectively for both groups. There was no statistically significant difference between the two groups in terms of first, second or third recurrence during follow-up. Overall survival was significantly worse for patients with high grade tumor than low grade tumors. Singer et al [34] have demonstrated that tumor histology type, tumor grade and contiguous organ resection were significantly associated with tumor recurrence, while tumor size was not an independent risk factor. A retrospective study by Chen et al [36], including 51 patients with primary RPL, showed that tumor size was not an independent risk factor for recurrence or prognosis on univariate and multivariate analysis. The findings of the previous studies including our review exclude tumor size as a prognostic factor for tumor recurrence. Hence, the hypothesis that suggests tumor size of primary RPL is a risk factor for recurrence could be appealed, and further future studies should investigate this claim.

As this specific type of primary RPL is very uncommon, and prospective studies are not available, data regarding management and outcomes are very limited. As is the management of any type of STSs, giant primary RPL should be treated by a multidisciplinary team (MDT) of physicians. Few surgeons and radiation oncologist have gained much experience in treating such patients and thus, patients occasionally receive sub-optimal treatment with unsatisfactory surgical and oncological outcomes, especially if treated by unexperienced physicians. According to the NICE recommendation [37] for the management of STSs, which have led to the formation of 15 specialized centers, an MDT must include experienced surgeons, radiologist and clinical oncologists specialized in these tumors. Patients should be referred to centers treating this specific pathological disease.

Conclusion

Tumor size has been regarded as one of the risk factors for tumor recurrence, yet studies investigating this hypothesis are

lacking in the English literature. Literature findings exclude tumor size as a risk factor for tumor recurrence; hence, the previously mentioned claim should be re-examined, and further future studies are encouraged.

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None to declare.

Conflict of Interest

The authors have no conflict of interest to declare.

Author Contributions

SM designed the research. RM collected and analyzed the data. SK wrote and approved the final paper.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

STSs: soft tissue sarcomas; RPL: retroperitoneal liposarcoma

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