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-
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-

| 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.
Discussion

Since the introduction of STSs as highly malignant tumors with different types, several prognostic factors have been investigated in a thorough manner. These factors include age, sex, representativeness, and tumor size. While some studies have found that age and tumor size are significant predictors of outcome, others have found no association. In this study, we aimed to evaluate the correlation between the size of the primary tumor and the risk of tumor recurrence. We found that there was no significant correlation between the size of the primary tumor and the risk of recurrence. The largest tumor diameter was 65 cm, reported by Zeng et al. [28], while the smallest one was 30 cm, reported 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. The most common histological 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 (in 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 mainly of the mixed and myxoid types, which can explain the recurrence risk, rather than the tumor size.

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       |
| Caizzone 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                  | Dedifferentiated 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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