Diagnosis and Prognosis of Retroperitoneum Liposarcoma: a single Asian center cohort of 57 cases

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Abstract

Background

Liposarcoma is a form of malignancy found in soft tissues, mostly observed in the extremities. However, retroperitoneum liposarcoma has been seldom reported, and such diagnosis is also neglected. This study aims to present the clinical characteristics, diagnosis and prognosis of 5 different subtypes of liposarcoma and report our experience of treatment of the patients.

Methods

We conducted a single-center non-intervention retrospective study of 57 retroperitoneal liposarcoma patients who were admitted to Peking Union Medical College Hospital (PUMCH, Beijing, China) from December 2007 to May 2018. We collected and analyzed the demographic, clinical, imaging, histologic, therapeutic and prognostic data for these patients over a mean 4.5-year follow up period.

Results

Twenty-five (44%) patients were asymptomatic prior to diagnosis, with abdominal distension as the chief complaint for 18 (32%) patients and abdominal pain observed in 16 (28%) patients. Masses were evaluated by CT (n=48, 84%) or ultrasound (n=25, 44%). Laparotomy (n=52, 91%) was the preferred dominant therapeutic modality rather than laparoscopy (n=5, 9%). All patients were treated with R0 resection except 2 patients who underwent R2 resection. We conducted regular follow-up every 6 months after surgery for a mean duration of 4.5 years. Recurrence was experienced by 15 (26%) patients and a further 11 (19%) died during follow up.

Conclusions

Abdominal distension and pain are main chief complaints of liposarcoma. As extremity is the main location for liposarcoma occurrence, diagnosis of retroperitoneum liposarcoma is usually neglected. Since half of the patients are asymptomatic, timely diagnosis and treatment are highly dependent on regular ultrasound and CT imaging. R0 resection is the key to retroperitoneal liposarcoma treatment. Comparingly, patients underwent R2 resection, which is considered as a palliative treatment, have bad prognosis. Dedifferentiated liposarcoma, especially those with organ invasion, tend to have bad prognosis, and prognosis for well-differentiated or myxoid liposarcoma is relatively good.
Background

Accounting for only approximately 10% of all soft tissue sarcomas or 15% of all sarcomas, liposarcoma (LPS) is a frequently observed tumor generated from adipocytic differentiated primitive mesenchymal cells. Its incidence peaks in the age range 50–60 years.[1, 2] Although occurring predominantly in the deep soft tissues of the extremities, LPS is also reported in the abdomen, such as the esophagus, stomach and descending mesocolon.[3, 4] In general, the retroperitoneum is a rare location for LPS to occur, with only a few publications discussing its diagnosis, clinical characteristics and prognosis.[2, 5, 6] LPS is generally classified into 5 subtypes: well-differentiated LPS (WDLPS), dedifferentiated LPS (DLPS), myxoid LPS (MLPS), pleomorphic LPS (PLPS) and mixed LPS. WDLPS is the most common retroperitoneal LPS, accounting for 40–45% of all LPS.[2, 7–9] Gene amplification in 12q12-21 and 10p11-14 is often spotted in WDLPS and DLPS, and DLPS has an additional gene amplification in 6q23 and 1p32.[8, 10] Also, WDLPS has about 10% probability to convert into DLPS, a more invasive subtype of LPS.[8] Approximately 95% of MLPS patients have a t(12;16)(q13;p11) reciprocal chromosomal translocation resulting in an in-frame fusion of fused in sarcoma (FUS) to DNA damage inducible transcript 3 (DDIT3), and the remaining 5% patients exhibit a t(12;22)(q13;q12) translocation.[8, 11] For PLPS, the rarest case among all subtypes, there is so far no constant chromosomal aberration or molecular alternation reported.[8] Diagnosis of LPS is currently highly dependent on pathological findings, with CT or magnetic resonance imaging (MRI) responsible for the majority of pre-surgical diagnoses.[11, 12] Since many liposarcomas can be asymptotic before diagnosis, and symptoms, if there are any, are mainly nonspecific such as abdominal pain or distention, pre-operative diagnosis for LPS is difficult.[2, 13] Although golden standard for diagnosis remains to be biopsy, imaging is currently widely accepted means for diagnosis.[2, 14] Via imaging, presence of macroscopic fat arouses alert for LPS.

Upon diagnosis, surgery was first treatment of retroperitoneal LPS, but extent of resection remain controversial.[15] Although it is a convention to only resect those directly involved adjacent organ, more aggressive approach, which proposes to resect uninvolved adjacent organ partially, has also been suggested.[15, 16] Besides, some phase II or III clinical trials have proven that chemotherapy,
such as trabectedin and eribulin, may improve prognosis of LPS.\cite{17, 18} Also, immunotherapy for LPS is now under development.

Prognosis of LPS is highly dependent on surgical approach and histological subtype. WDLPS, together with low-grade MLPS, has a 5-year survival rate above 90%. Contrastingly, 5-year survival rate of PLPS, DLPS and high-grade MLPS is all below 75%, among which PLPS has the lowest one of only 50%.\cite{2, 19}

Methods

The medical records of all retroperitoneal LPS patients presenting at Peking Union Medical College Hospital (PUMCH), Beijing, China between July 2011 and December 2019 were retrospectively reviewed. Informed consent was obtained from each patient. The study was approved by the Institutional Review Board of PUMCH.

Detailed demographic and clinical data, such as histological subtype of tumor, symptoms and physical signs from all 57 patients were reviewed. All available imaging examinations, including those of ultrasound, computed tomography (CT) and MRI, were also collected. Also, surgery approach, together with surgical details such as surgery duration and pathological findings, was recorded. To assess prognosis, the patients were questioned regularly to obtain details of any relapse, post-surgical chemotherapy or other adjuvant therapies. Regular follow-up every 3–9 months after surgery, including CT imaging or ultrasound, together with tumor markers, were conducted for all patients, and the most recent follow-up was in February 2020.

All data were recorded and analyzed using Python 3.7. Descriptive data were expressed in numbers (%) for categorical variables and means (SD) for continuous variables, as appropriate. A t-test was used to analyze continuous variables. All tests were two-sided with $P < 0.05$ considered statistically significant.

Results

A total of 57 patients suffering from retroperitoneal LPS were recruited from PUMCH, of which 26 were males and 31 were females. Mean age at treatment was 57.0 (12.2) years. These patients were followed-up regularly, the mean duration of follow-up being 4.5 (2.6) years.
Collation of the history of the current illness demonstrated that 25 (44%) patients had been completely asymptomatic, LPS having been detected during routine medical examination. Abdominal discomfort was the most common symptom, with 18 (32%) patients complaining abdominal distention and 16 (28%) patients complaining abdominal pain, including 2 (4%) who had complained of both. Besides abdominal discomfort, lower extremity symptom, including swelling and pain, was also reported in 6 (11%) patients. Different subtypes of LPS had different chief complain. Half of the WDLPS patients and 75% PLPS patients were asymptotic before diagnosis, but 57% MLPS patients had abdominal distention as their chief compliant, and 48% DLPS patients complained abdominal pain (Table 1).

Table 1  
Demographic and clinical characteristics of retroperitoneal LPS patients

| Demographic characteristics n = 57 |
|----------------------------------|
| Sex male/female                  | 26/31 |
| Age at diagnosis, mean (S.D.), years | 57.0 (12.2) |
| Duration of follow-up, mean (S.D.), years | 5.3 (2.6) |

| Clinical characteristics n = 57 |
|--------------------------------|
| Location                      |
| Retroperitoneum               | 57 (100%) |
| Pelvis invasion               | 7 (12%) |
| Left retroperitoneum          | 29 (51%) |
| Right retroperitoneum         | 24 (42%) |
| Both retroperitoneum          | 4 (7%) |
| Symptoms                      |
| WDLPS                          | 18 |
| Asymptotic                    | 10 (56%) |
| Abdominal pain                | 6 (33%) |
| Abdominal Pain                | 2 (11%) |
| DLPS                           | 23 |
| Abdominal pain                | 11 (48%) |
| Asymptotic                    | 9 (39%) |
| Abdominal distention          | 5 (21%) |
| Lower extremity discomfort    | 5 (21%) |
| Fever                         | 2 (9%) |
| Vomiting                      | 1 (4%) |
| Frequent micturition          | 1 (4%) |
| PLPS                           | 4 |
| Asymptotic                    | 3 (75%) |
| Abdominal pain                | 1 (25%) |
| MLPS                           | 7 |
| Abdominal distention          | 4 (57%) |
| Asymptotic                    | 3 (43%) |
| Abdominal pain                | 2 (29%) |
| Mixed LPS                     | 6 |
| Abdominal distention          | 3 (50%) |
| Asymptotic                    | 1 (17%) |
| Lower extremity discomfort    | 1 (17%) |
| Dysuria                       | 1 (17%) |
| Overall                       | 57 |
| Asymptotic                    | 25 (44%) |
| Abdominal distention          | 18 (32%) |

| Overall                        |
|--------------------------------|
| Abdominal pain                | 16 (28%) |
| Lower extremity discomfort    | 6 (11%) |
| Urinary system symptom        | 2 (4%) |
Detailed physical examination (PE) was conducted on each patient. Only 18 (32%) among the total of 57 had no apparent positive signs of the disease, the retroperitoneal mass tangible in all the other 39 (68%) patients. Among the 39 patients with tangible mass, 29 (74%) had little mobility, and 29 (74%) had a clear margin. Tenderness pain was reported by only 14 (36%) patients. As for subtypes, half of WDLPS patients had tangible retroperitoneal mass while the other half did not. Among 23 DLPS patients, retroperitoneal mass of 16 (70%) patients were tangible, and 7 (30%) were not tangible. All PLPS and mixed LPS patients had tangible retroperitoneal mass. (Table 1).

For all 57 patients, retroperitoneal LPS was diagnosed via pre-surgical imaging and post- surgical pathological analysis. The form of pre-surgical imaging used for diagnosis included ultrasound, CT and MRI. All cases of LPS were located within the retroperitoneum, and the tumor mass of 7 (12%)
patients also invaded pelvis. The liposarcoma of 53 (93%) patients were anchored in only half of the retroperitoneum, with 29 of on the left side and 24 right-sided LPS reported. No family history of LPS was reported in any of the 57 patients (Table 1). Patients were divided into 3 subgroups according to longest tumor diameter indicated by imaging examination (larger than 25 cm, medium or smaller than 15 cm) (Table 2). Characters demonstrated by ultrasound or CT, such as echoic and density, fail to be pre-surgical factors to predict pathological subtypes: both mixed and low CT density were reported in each subtype, and the ratio had no significant difference. (Table 3, Fig. 1, 2).
Table 2
Size of tumor decided by different methods

| No.* | PE  | CT  | Ultrasound | Resection | Subgroup |
|------|-----|-----|------------|-----------|----------|
| 1    | 7*4 | 12*11 | NA**       | 18.5*17*10.3 | Small    |
| 2    | 10  | NA   | 11.6*9.6*10.4 | 15*8*6 | Small    |
| 3    | 10*5 | 10.8*5.4 | 7.8*5.9 | 11*7.5*6 | Small    |
| 4    | 20*9 | 17.9*17.7*12.1 | 15.8*11.7 | 22.8*19.5*10 | Middle |
| 5    | Intangible | NA | 10*8       | 20*20*5.5 | Small    |
| 6    | Intangible | 9.6*7.6 | NA         | 12.5*8.5*6 | Small    |
| 7    | 10*10 | 17.2*13 | No data*** | 18*15*9 | Middle |
| 8    | Intangible | 7.4*6 | NA         | 11.4*9*5.8 | Small    |
| 9    | 10  | 25.2*13.7*10 | NA       | 30*28*17 | Large    |
| 10   | 10*10 | 12.5 | 14.9*12.9*10.7 | 9*9*4.8 | Small    |
| 11   | 10  | 12.3*11.0*8.9 | NA     | 16*12*6 | Small    |
| 12   | Intangible | 5.7*4.9*3.8 | NA      | 7.5*5*4.2 | Small    |
| 13   | 15*15 | 20.6*16.1*9.7 | NA | 19*16*6.5 | Middle |
| 14   | 25*20 | 20*14*25 | NA         | 30*25*10 | Middle |
| 15   | Intangible | 12.9*12.3*17.2 | NA | 19*15*8 | Middle |
| 16   | 20*15 | 24.4*17.5*21.4 | NA       | 22*20*4.5 | Middle |
| 17   | 10  | 21.2*12.9 | NA     | 25*22*9.5 | Middle |
| 18    | Intangible | 34.3*31.7*23.8 | NA | 37*30*16.5 | Large |
| 19    | 10  | 30*30*20 | NA     | 21*18*3.5 | Large |
| 20    | 10  | 4.2*3 | NA       | 5.5*3*1.5 | Small |
| 21    | Intangible | 4.5*4.5*2.7 | 4.5*3.2 | 4*3.5*3 | Small |
| 22    | Intangible | NA | NA         | 4.5*2*2 | Small |
| 23    | 15*15 | 15.8*15.3 | No data | 20*17*12 | Middle |
| 24    | 10  | 10*9.7*9.6 | NA | 11*9*8 | Small |
| 25    | No data | 26.5*13.1*36.6 | No data | 32*40*20 | Large |
| 26    | 25  | 24.9*23.9*28.2 | NA | 48*36*12 | Middle |
| 27    | No data | 23*20 | 25*17 | 33*21*12 | Middle |
| 28    | 20  | NA   | 25.3*18.8*14.2 | 15*13*3 | Large |
| 29    | 25*15 | 16*9.5 | NA     | 25*17*9 | Middle |
| 30    | 18*10 | 18.0*12.5*11.4 | 18.6*11.6 | 18*12*9 | Middle |
| 31    | No data | 30.5*20.9 | NA | 40*35*20 | Large |
| 32    | 20  | NA   | 17.5*12.2*13.6 | 30*25*6 | Middle |
| 33    | 30  | No data | NA     | 38*30*8.5 | Large |
| 34    | Intangible | NA | 10.3*5.9 | 13.5*11.5*8.5 | Small |
| 35    | 12*12 | 12*12 | NA | 18*13*7 | Small |
| 36    | Intangible | 8.6*5.5 | NA | 15*11*5 | Small |
| 37    | Intangible | 8.9*7.3*9.7 | NA | 11.7*9*9 | Small |
| 38    | 10  | 14*14*16.5 | NA | 20*20*12 | Middle |
| 39    | 10*10 | 14.3*9.7 | NA | 19.5*15.8*9.5 | Middle |
| 40    | Intangible | NA | 10*7.2 | 20*16*5 | Small |
| 41    | 25*15 | 17.6*8.9 | NA | 15.5*8 | Middle |
| 42    | 12*12 | 12*8 | 11.8*9.5*9.2 | 15*14*14 | Small |
| 43    | Intangible | 12.2*9.9*8.5 | NA | 15*12*7 | Small |
| 44    | 25  | 26.4*25.4*16.5 | NA | 36*32*8 | Large |
| 45    | Intangible | 16*13 | 20.2*16.1*15.5 | 23*15.5*14.5 | Middle |
| 46    | No data | 7.5*5.4*6.6 | NA | 9*8.5*1.5 | Small |
| 47    | 15  | 19.2*9.3 | NA | 17*14*8 | Middle |
| 48    | 25*20 | NA | NA | 15*15*10 | Middle |
| 49    | Intangible | 5.1*4.1 | 5.6*4.7 | 13*11*5 | Small |
| 50    | 15*5 | 6.9*2.5*4.5 | 13.7*18*6.2 | 22.5*15*7 | Middle |
| 51    | Intangible | NA | 11.2*5.3 | 15*13*4 | Small |
| 52    | 15*10 | No data | NA | 17*14*12 | Small |
| 53    | 8    | 13.3*12.0*27.8 | 15.3*13.2*11.2 | 25*14*13 | Large |
| 54    | 20*15 | 24.5*12.7*23.3 | 14.7*8.48 | 29*16*11 | Middle |
| 55    | Intangible | NA | 9.3*5.4 | 15*11*3 | Small |
| 56    | 10*10 | 9.21*9.95*9.26 | NA | 16*12*7 | Small |
| 57    | 7*8 | 16.5*16.2*13.7 | 11.4*7.4*6.6 | 16.8*9*6.5 | Middle |

*All data is in centimeters.

**NA:** corresponding examination was not performed.

***No data:** corresponding examination was performed, but no specific number was recorded.

****No. 18: Though large, the tumor mass was intangible, maybe because of hernia.
Table 3
Characteristics of tumor decided by different methods

| Patient No. | PE     | Ultrasound-Echoic | CT-Density | Pathology |
|-------------|--------|-------------------|------------|-----------|
| 1           | Tangible | NA*               | Low        | PLPS      |
| 2           | Tangible | Mixed-Echoic      | NA         | PLPS      |
| 3           | Tangible | Hypo-Echoic       | Low        | PLPS      |
| 4           | Tangible | Mixed-Echoic      | Mixed      | PLPS      |
| 5           | Intangible | Mixed-Echoic     | NA         | WDLPS     |
| 6           | Intangible | NA               | Mixed      | WDLPS     |
| 7           | Tangible | Hyper-Echoic      | Low        | WDLPS     |
| 8           | Intangible | NA               | Low        | WDLPS     |
| 9           | Tangible | NA                | Mixed      | WDLPS     |
| 10          | Tangible | Hyper-Echoic      | Low        | WDLPS     |
| 11          | Tangible | NA                | Low        | WDLPS     |
| 12          | Intangible | NA              | Mixed      | WDLPS     |
| 13          | Tangible | NA                | Mixed      | WDLPS     |
| 14          | Tangible | NA                | Low        | WDLPS     |
| 15          | Intangible | NA              | Low        | WDLPS     |
| 16          | Tangible | NA                | Low        | WDLPS     |
| 17          | Tangible | NA                | Low        | WDLPS     |
| 18          | Intangible | NA             | Mixed      | WDLPS     |
| 19          | Tangible | NA                | Mixed      | WDLPS     |
| 20          | Intangible | NA              | Low        | WDLPS     |
| 21          | Intangible | Hypo-Echoic    | Low        | WDLPS     |
| 22          | Intangible | NA              | NA         | WDLPS     |
| 23          | Tangible | Mixed-Echoic      | Low        | Mixed LPS |
| 24          | Tangible | NA                | Mixed      | Mixed LPS |
| 25          | Tangible | Hypo-Echoic       | Mixed      | Mixed LPS |
| 26          | Tangible | NA                | Mixed      | Mixed LPS |
| 27          | Tangible | Hyper-Echoic      | Low        | Mixed LPS |
| 28          | Tangible | Hyper-Echoic      | NA         | DLPS      |
| 29          | Tangible | NA                | Low        | DLPS      |
| 30          | Tangible | Hypo-Echoic       | Low        | DLPS      |
| 31          | Tangible | NA                | Mixed      | DLPS      |
| 32          | Tangible | Hyper-Echoic      | NA         | DLPS      |
| 33          | Tangible | NA                | Mixed      | DLPS      |
| 34          | Intangible | Hypo-Echoic    | Mixed      | DLPS      |
| 35          | Tangible | NA                | Mixed      | DLPS      |
| 36          | Intangible | NA              | Mixed      | DLPS      |
| 37          | Intangible | NA              | Mixed      | DLPS      |
| 38          | Tangible | NA                | Low        | DLPS      |
| 39          | Tangible | NA                | Low        | DLPS      |
| 40          | Intangible | Hyper-Echoic    | NA         | DLPS      |
| 41          | Tangible | NA                | Mixed      | DLPS      |
| 42          | Tangible | Hypo-Echoic       | Low        | DLPS      |
| 43          | Intangible | NA              | Low        | DLPS      |
| 44          | Tangible | NA                | High       | DLPS      |
| 45          | Intangible | Hypo-Echoic    | Mixed      | DLPS      |
| 46          | Tangible | NA                | Mixed      | DLPS      |
| 47          | Tangible | NA                | Low        | DLPS      |
| 48          | Tangible | NA                | NA         | DLPS      |
| 49          | Intangible | Hypo-Echoic    | Mixed      | DLPS      |
| 50          | Tangible | NA                | Low        | MMLPS     |
| 51          | Intangible | Hypo-Echoic    | High       | MMLPS     |
| 52          | Tangible | Hyper-Echoic      | Low        | MMLPS     |
| 53          | Tangible | Hypo-Echoic       | Mixed      | MMLPS     |
| 54          | Tangible | Mixed-Echoic      | Mixed      | MMLPS     |
| 55          | Intangible | Hypo-Echoic    | NA         | MMLPS     |
| 56          | Tangible | NA                | Mixed      | MMLPS     |
| 57          | Tangible | Hyper-Echoic      | Mixed      | MMLPS     |

*NA: corresponding examination was not performed. LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma; All 57 patients received surgery, of which 52 (91%) were open surgery and 5 (9%) were laparoscopic, and all laparoscopic surgery were given because of a tumor size less than 10 cm. Besides tumor
tissue resection, the invaded organs were also removed during surgery, but all uninvolved nearby organs were kept. The most commonly involved organ was pancreas and kidney, with 5 (9%) patients had their pancreas resected, and 2 (4%) patients had one-side kidney removed. Though not directly involved, LPS of 10 patients grew surrounding kidney, and such tumor were completely resected since a macroscopic fissure between kidney existed. All post-surgical histopathological reports were obtained for analysis, the diagnosis of LPS having been confirmed in every patient. Bleeding during surgery ranged from 30 to 8400 mL, with a mean of 910 mL. Bleeding of 8400 mL was because of separation of tumor mass from psoas major, and pitifully we lost connection with this patient 2 years after surgery. Duration of surgery ranged from 2 to 8 hours, the mean of which was 4.18 hours.

Neither surgical bleeding nor duration was related to the size of LPS mass ($R^2$ for bleeding and size: 0.02, $R^2$ for duration and size: 0.03). Fourteen (25%) patients were admitted to the intensive care unit (ICU) in PUMCH for better post-surgical care.

Mean duration of hospital stay was 18.6 (8.9) days (7.6 days prior to surgery and 11.0 days after surgery). There was no significant association observed between length of hospital stay and size of LPS (greatest diameter greater than 15 cm by ultrasound or CT) (large vs small: 17.97 vs 19.61, $p = 0.492$). Post-surgical pathological results confirmed that all patients had LPS, including 5 subtypes.

During the average 4.5-year follow-up, 15 (26%) recurrences and 11 (19%) deaths were reported among the 57 patients. Two (4%) patients received radiotherapy, and 2 (4%) received chemotherapy following surgery. A complaint of hypoleukemia, lymphopenia and herpes zoster was received from an 81-year-old female who underwent radiotherapy following surgery. No severe post-surgical complications were reported from other patients.

Four patients received post-surgical radiotherapy or chemotherapy, the latter being standard MAID therapy comprising Mesna, adriamyein, ifosfamide and dacarbazine. Recurrence was not observed in any of the 4 patients during follow-up.

Follow-up every 3–9 month, including CT imaging or ultrasound, and tumor marker, was conducted regularly. Until the latest follow-up in February 2020, there are 11 (19%) deaths and 15 (26%)
recurrence, and we lost connection with 9 (16%) patients. Among all subtypes, DLPS had the highest recurrence rate of 42% and the highest death rate of 26%. (Table 4) Defining death or recurrence as bad prognosis, no recurrence as good prognosis, using Fisher’s exact probability, there is no statistically significant difference among prognosis of 5 subtypes (p = 0.247, Table 5).
Table 4
Prognosis of retroperitoneal LPS patients

| Patient No. | Pathology  | Subgroup | Adjuvant       | Prognosis   |
|-------------|------------|----------|----------------|-------------|
| 1           | PLPS       | Small    | None           | Death       |
| 2           | PLPS       | Small    | None           | Loss        |
| 3           | PLPS       | Small    | Chemotherapy   | Recurrence  |
| 4           | PLPS       | Middle   | None           | No recurrence |
| 5           | WDLPS      | Small    | None           | No recurrence |
| 6           | WDLPS      | Small    | None           | Loss        |
| 7           | WDLPS      | Middle   | None           | Recurrence  |
| 8           | WDLPS      | Small    | None           | No recurrence |
| 9           | WDLPS      | Large    | None           | No recurrence |
| 10          | WDLPS      | Small    | None           | No recurrence |
| 11          | WDLPS      | Small    | None           | No recurrence |
| 12          | WDLPS      | Small    | None           | Death       |
| 13          | WDLPS      | Middle   | None           | Death       |
| 14          | WDLPS      | Middle   | None           | No recurrence |
| 15          | WDLPS      | Middle   | None           | No recurrence |
| 16          | WDLPS      | Middle   | None           | Loss        |
| 17          | WDLPS      | Middle   | None           | No recurrence |
| 18          | WDLPS      | Large    | None           | No recurrence |
| 19          | WDLPS      | Large    | None           | Recurrence  |
| 20          | WDLPS      | Small    | None           | No recurrence |
| 21          | WDLPS      | Small    | None           | Loss        |
| 22          | WDLPS      | Small    | None           | Recurrence  |
| 23          | Mixed LPS  | Middle   | None           | Death       |
| 24          | Mixed LPS  | Small    | None           | Recurrence  |
| 25          | Mixed LPS  | Large    | None           | Death       |
| 26          | Mixed LPS  | Middle   | None           | No recurrence |
| 27          | Mixed LPS  | Middle   | None           | Loss        |
| 28          | DLPS       | Large    | None           | No recurrence |
| 29          | DLPS       | Middle   | None           | Recurrence  |
| 30          | DLPS       | Middle   | None           | Loss        |
| 31          | DLPS       | Large    | None           | No recurrence |
| 32          | DLPS       | Middle   | None           | Death       |
| 33          | DLPS       | Large    | None           | Recurrence  |
| 34          | DLPS       | Small    | None           | Recurrence  |
| 35          | DLPS       | Small    | None           | Death       |
| 36          | DLPS       | Small    | None           | Loss        |
| 37          | DLPS       | Small    | None           | Recurrence  |
| 38          | DLPS       | Middle   | None           | No recurrence |
| 39          | DLPS       | Middle   | None           | Recurrence  |
| 40          | DLPS       | Small    | None           | Death       |
| 41          | DLPS       | Middle   | None           | Death       |
| 42          | DLPS       | Small    | None           | No recurrence |
| 43          | DLPS       | Small    | None           | No recurrence |
| 44          | DLPS       | Large    | None           | Loss        |
| 45          | DLPS       | Middle   | None           | No recurrence |
| 46          | DLPS       | Small    | None           | Recurrence  |
| 47          | DLPS       | Middle   | None           | Recurrence  |
| 48          | DLPS       | Middle   | None           | Recurrence  |
| 49          | DLPS       | Small    | None           | Death       |
| 50          | MLPS       | Middle   | None           | Recurrence  |
| 51          | MLPS       | Small    | Radiotherapy   | No recurrence |
| 52          | MLPS       | Small    | Chemotherapy   | No recurrence |
| 53          | MLPS       | Large    | None           | Death       |
| 54          | MLPS       | Middle   | None           | Loss        |
| 55          | MLPS       | Small    | None           | No recurrence |
| 56          | MLPS       | Small    | Radiotherapy   | No recurrence |
| 57          | MLPS       | Middle   | None           | Recurrence  |

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma;
### Table 5
Fisher`s Exact Probability for Prognosis among 5 Subtypes

| Subtype     | Good prognosis | Bad prognosis |
|-------------|----------------|---------------|
| WDLPS       | 10             | 5             |
| DLPS        | 6              | 13            |
| PLPS        | 1              | 2             |
| MLPS        | 4              | 3             |
| Mixed LPS   | 1              | 3             |
| Fisher`s Exact Probability | 0.247          |               |

**Discussion**

As a subtype of sarcoma, liposarcoma accounts for approximately 15% of all sarcomas, making it the most common soft tissue sarcoma.[5] LPS mostly occurs in extremities, followed by retroperitoneum, and there are also literatures reporting LPS founded in rare locations, such as mediastinum, larynx or paratesticular.[20-22] High occurrence of retroperitoneum may be attributed to metastasis of LPS from other parts of body, especially where fat is abundant.[1, 2, 23] Primary retroperitoneal LPS usually originates in the perirenal fat, and there were 19 (33%) perirenal LPS or LPS directly invading kidney in our cohort. LPS peaks in the range of 50-60 years, and in our 57-person cohort, mean average when diagnosed is 57.0 years old, and 20 (35%) patients were in the range between 50 and 60. We consider this phenomenon as a result of high tolerance of older patients and severity of younger patients, since PUMCH gathers severe cases of kinds of diseases in China. LPS were founded no significant gender difference, and the ratio of our cohort was 26 (46%) male to 31 (54%) female. Different subtypes of LPS have their own driven genetic mutation. For example, the t(12;16)(q13;p11) reciprocal translocation results in MLPS,[8, 11] gene amplification in 12q12-21 and 10p11-14 explains for WDLPS and DLPS, and an additional amplification in 6q23 and 1p32 is also necessary in DLPS.[8, 10] Additionally, no former researches disclosed relationship between occurrence of LPS and exterior factors such as trauma or usage of drugs.

Usually, LPS was found accidentally or regular physical check-ups. The clinical symptoms reported were principally abdominal pain and distention, both in the present cohort and in that previously
published ones.[9, 24-26] Since abdominal pain and distention were nonspecific and tolerable to patients, it was difficult to diagnose retroperitoneal LPS or differentiate subtypes of LPS via clinical symptoms.

As for pre-surgical imaging diagnosis, CT and MRI are regarded the most appropriate modality. Different subtypes can be distinguished using CT and MRI. WDLPS typically has above 75% adipose tissue with septations thicker than 2 mm and small internal nodular areas. Using CT, such nodular can be found with soft-tissue attenuation. Septations and nodular areas of WDLPS show hyperintense character on T2-W1 MRI, distinguishing it from other types of LPS[14]. Though similar with WDLPS, DLPS can still be identified by larger non-lipomatous components can nodular areas.[27] MLPS often shows multilobulated, hypoechoic structure on ultrasound.[28] Moreover, MLS usually exhibits low signal intensity in T1W and intermediate signal intensity in T2W, making it recognizable with other types of tumors.[12, 25] PLPS, due to its special component, shows little fat attenuation on CT.[14] However, hemorrhage and necrosis occur frequently in PLPS, causing heterogeneity on imaging, making diagnosis difficult.[29] Though theoretically distinguishable, no specific subtype was diagnosed before surgery in this cohort. Because surgery modality was the same among all subtypes, the pre-surgical diagnosis of ‘huge retroperitoneal mass’ was enough for surgery. So far, post-surgery pathological results remain to be golden standard for differentiating subtypes,[14] based on which we make prediction on prognosis and choose chemotherapy or radiotherapy.

The size of LPS ranged from 1.2 × 1.2 cm to 36.6 × 26.5 cm in the present cohort, with a median diameter of 14.6 cm. Using the longest diameter of 15 cm and 25 cm as thresholds, the patients were categorized into 3 subgroups, denoted as large, medium and small (Table 2). Using chi-square test, defining death or recurrence as bad prognosis, no recurrence as good prognosis, pre-surgical size had no statistically significant influence on prognosis (p = 0.750) (Table 4,6).
Table 6
Chi-square Test for Prognosis among 3 Subgroups

|     | Good prognosis | Bad prognosis |
|-----|---------------|--------------|
| Small | 11            | 11           |
| Middle | 7              | 11           |
| Large  | 4              | 4            |

Chi-square 0.559
P value 0.750

Though extent of resection remains under debate, surgery is still the key of treatment for LPS.[30]

Traditionally, a macroscopically negative margin is sufficient for treatment, regardless of histological subtypes. In our 57-patient cohort, all patients received R0 resection with a macroscopically negative resection margin except 2 R2 resections, which were both because of high age and bad body condition. Two patients who received R2 resections died within 1 year after surgery.

Histological subtype is an important factor to predict prognosis, including local recurrence, distant recurrence and death. Previous cohort studies have demonstrated that DLPS has the highest risk for both local and distant recurrence, while WDLPS has the lowest risk.[19, 31] In this cohort, however, no statistically significant difference exists in different subtypes (Table 4, 5). Nonetheless, recurrence and death rate was lowest in WDLPS subtype, and highest in DLPS subtype, which was in accordance with previous researches. All recurrences reported in our cohort were local recurrence.

Bad prognosis for DLPS drove surgeons to find extended surgery modality, which includes en bloc resection of adjacent organs, even though uninvolved.[15, 30] Extended resection, proven by other series, lowers risk for local recurrence, but its effect on overall survival stays unclear.[16, 32] No extended resection was operated in our cohort, due to worries about low life quality after adjacent uninvolved organ resection.

There are other approaches to improve prognosis for LPS besides extended surgery modality, such as radiotherapy and chemotherapy. Although retroperitoneal LPS is relatively radiosensitive, so is its nearby organs. Overdose of radiotherapy deals damage to surrounding radiosensitive organs, such as liver and kidney, so the timing and technique of delivery of radiotherapy for retroperitoneal LPS matter.[2] Among all subtypes, MLPS is the most chemo sensitive one, making chemotherapy
possible.\[12, 17, 18\] In our cohort, 4 patients received post-surgery adjuvant therapy, among which 3 were diagnosed MLPS by post-surgery pathological result. None of the 4 patients had recurrence or death, showing efficiency of radiotherapy and chemotherapy, but no conclusion could be drawn due to small sample size.

There are several limitations to this study. Firstly, as a retrospective study, missing data, recall bias and errors in the initial medical records may exist. Secondly, the sample size of 57 is relatively small, and number for each subtype is sometimes less than 10. Thirdly, PUMCH is among the most comprehensive third-grade class-A hospitals in China, the high number of severe cases and difficult surgical cases of which may give rise to bias.

We collected and analyzed detailed demographic and clinical data of all 57 patients. Pre-surgery imaging helps to diagnose LPS, and specific subtypes can also be distinguished via CT or MRI.

Prognosis for different subtypes was different. Recurrence and death were easy to occur for DLPS patients, contrastingly, WDLPS had a relatively low recurrence rate and death rate. A macroscopically negative margin was surgery goal for most of the patients in this cohort, and an aggressive surgery modality to resect adjacent uninvolved organ was also proposed by other researchers. Radiotherapy and chemotherapy may further improve prognosis. Generally, this cohort has helped deepen our understanding of LPS, and provides characteristics of a Chinese retroperitoneal LPS cohort.

**Summary**

We collected and analyzed available data of 57 retroperitoneum myxoid liposarcoma patients during an average follow-up time of 4.5 years. Via analysis of current data and comparison with previous researches, we made conclusions mainly on pre-surgery diagnosis, factors influencing prognosis and treatment. Comparing with clinical symptoms, imaging, including CT, ultrasound and MRI provides more evidence when diagnosing LPS and its subtypes. The most important factor deciding prognosis is subtype. Among all subtypes, WDLPS has the best prognosis while DLPS has the worst. R0 resection is key of treatment for all subtypes, and an aggressive surgery modality to resect uninvolved adjacent organ for DLPS, chemotherapy and radiotherapy for MLPS, are also alternative choices.

**Abbreviations**
PUMCH: Peking Union Medical College Hospital; CT: computed tomography; MRI: magnetic resonance imaging; LPS: liposarcoma; WDLPS: well-differentiated liposarcoma; DLPS: dedifferentiated liposarcoma; MLPS: myxoid liposarcoma; PLPS: pleomorphic liposarcoma; DNA: deoxyribonucleic acid; DDIT3: DNA damage inducible transcript3; SD: standard deviation; PE: physical examination; ICU: intensive care unit.

Declarations
Ethics approval and consent to participate: This manuscript was established according to the guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of PUMCH. Written informed consent was obtained from individual.
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References
1. Huh WW, Yuen C, Munsell M, Hayes-Jordan A, Lazar AJ, Patel S, Wang WL, Barahmani N, Okcu MF, Hicks J et al: Liposarcoma in children and young adults: a multi-institutional experience. Pediatr Blood Cancer 2011, 57(7):1142-1146.
2. Vijay A, Ram L: Retroperitoneal liposarcoma: a comprehensive review. Am J Clin Oncol 2015, 38(2):213-219.
3. Sonoda A, Sawayama H, Miyanari N, Mizumoto T, Kubota T, Baba H: Giant myxoid liposarcoma of the stomach: Report of a case. Int J Surg Case Rep 2019, 60:234-238.
4. Uslukaya O, Taskesen F, Aliosmanoglu I, Arikanoglu Z, Gul M, Dusak A: Giant myxoid liposarcoma of descending mesocolon origin. *Prz Gastroenterol* 2014, **9**(6):361-364.

5. Grasso E, Marino F, Bottalico M, Simone M: A case of myxoid liposarcoma of the retroperitoneum: a challenging tumour for diagnosis and treatment. *Case Rep Surg* 2014, **2014**:572805.

6. Setsu N, Miyake M, Wakai S, Nakatani F, Kobayashi E, Chuman H, Hiraoka N, Kawai A, Yoshida A: Primary Retroperitoneal Myxoid Liposarcomas. *Am J Surg Pathol* 2016, 40(9):1286-1290.

7. Lee A, Thway K, Huang P, Jones R: Clinical and Molecular Spectrum of Liposarcoma. *Journal of Clinical Oncology* 2018, **36**(2):151-159.

8. Yang L, Chen S, Luo P, Yan W, Wang C: Liposarcoma: Advances in Cellular and Molecular Genetics Alterations and Corresponding Clinical Treatment. *J Cancer* 2020, **11**(1):100-107.

9. Thway K: Well-differentiated liposarcoma and dedifferentiated liposarcoma: An updated review. *Semin Diagn Pathol* 2019, **36**(2):112-121.

10. Pedeutour F, Maire G, Pierron A, Thomas DM, Garsed DW, Bianchini L, Duranton-Tanneur V, Cortes-Maurel A, Italiano A, Squire JA et al: A newly characterized human well-differentiated liposarcoma cell line contains amplifications of the 12q12-21 and 10p11-14 regions. *Virchows Arch* 2012, **461**(1):67-78.

11. Yu JSE, Colborne S, Hughes CS, Morin GB, Nielsen TO: The FUS-DDIT3 Interactome in Myxoid Liposarcoma. *Neoplasia* 2019, **21**(8):740-751.

12. Abaricia S, Hirbe AC: Diagnosis and Treatment of Myxoid Liposarcomas: Histology Matters. *Curr Treat Options Oncol* 2018, **19**(12):64.

13. Chouairy CJ, Abdul-Karim FW, MacLennan GT: Retroperitoneal liposarcoma. *J Urol*
14. Teniola O, Wang KY, Wang WL, Tseng WW, Amini B: Imaging of liposarcomas for clinicians: Characteristic features and differential considerations. *J Surg Oncol* 2018, **117**(6):1195-1203.

15. Fairweather M, Gonzalez RJ, Strauss D, Raut CP: Current principles of surgery for retroperitoneal sarcomas. *J Surg Oncol* 2018, **117**(1):33-41.

16. Gronchi A, Lo Vullo S, Fiore M, Mussi C, Stacchiotti S, Collini P, Lozza L, Pennacchioli E, Mariani L, Casali PG: Aggressive surgical policies in a retrospectively reviewed single-institution case series of retroperitoneal soft tissue sarcoma patients. *J Clin Oncol* 2009, **27**(1):24-30.

17. Saponara M, Stacchiotti S, Gronchi A: Pharmacological therapies for Liposarcoma. *Expert Rev Clin Pharmacol* 2017, **10**(4):361-377.

18. Suarez-Kelly LP, Baldi GG, Gronchi A: Pharmacotherapy for liposarcoma: current state of the art and emerging systemic treatments. *Expert Opin Pharmacother* 2019, **20**(12):1503-1515.

19. Singer S, Antonescu CR, Riedel E, Brennan MF: Histologic subtype and margin of resection predict pattern of recurrence and survival for retroperitoneal liposarcoma. *Ann Surg* 2003, **238**(3):358-370; discussion 370-351.

20. Yang YS, Bai CY, Li ZC, Li WJ, Li Y: Giant primary liposarcoma of the anterior mediastinum: A case report. *Medicine (Baltimore)* 2018, **97**(42):e12873.

21. Han Y, Yang L, Liu T, Wang J, Li H, Yu G, Wang Z, Lv J, Zhao H, Wang E: Liposarcoma of the Larynx Report of a Case and Review of Literature. *Int J Clin Exp Pathol* 2014, **8**(1):1068-1072.

22. Mouden K, Wakrim S, Semmar A: Paratesticular liposarcoma: a case report. *Pan Afr Med J* 2019, **33**:282.
23. Sheah K, Ouellette HA, Torriani M, Nielsen GP, Kattapuram S, Bredella MA: 
   Metastatic myxoid liposarcomas: imaging and histopathologic findings. 
   Skeletal Radiol 2008, 37(3):251-258.

24. Thway K, Jones R, Noujaim J, Zaidi S, Mian A, Fisher C: Dedifferentiated 
   Liposarcoma Updates on Morphology, Genetics, and Therapeutic Strategies. 
   Adv Anat Pathol 2016, 23(1):30-40.

25. Durr HR, Rauh J, Baur-Melnyk A, Knosel T, Lindner L, Roeder F, Jansson V, Klein A: 
   Myxoid liposarcoma: local relapse and metastatic pattern in 43 patients. BMC 
   Cancer 2018, 18(1):304.

26. Wang L, Luo R, Xiong Z, Xu J, Fang D: Pleomorphic liposarcoma: An analysis of 6 
   case reports and literature review. Medicine (Baltimore) 2018, 97(8):e9986.

27. Murphey M, Arcara L, Smith F: From the archives of the AFIP imaging of 
   musculoskeletal liposarcoma with radiologic-pathologic correlation. 
   RadioGraphiccs 2005, 25:1371-1395.

28. Jagannathan JP, Tirumani SH, Ramaiya NH: Imaging in Soft Tissue Sarcomas: 
   Current Updates. Surg Oncol Clin N Am 2016, 25(4):645-675.

29. Craig W, Smith F, Henry L, Guerrero R, Barton F: Fat-containing lesions of the 
   retroperitoneum radiologic-pathologic correlation. RadioGraphics 2009, 29:261- 
   290.

30. Mansfield SA, Pollock RE, Grignol VP: Surgery for Abdominal Well-Differentiated 
   Liposarcoma. Curr Treat Options Oncol 2018, 19(1):1.

31. Bartlett EK, Curtin CE, Seier K, Qin LX, Hameed M, Yoon SS, Crago AM, Brennan MF, 
   Singer S: Histologic Subtype Defines the Risk and Kinetics of Recurrence and 
   Death for Primary Extremity/Truncal Liposarcoma. Ann Surg 2019.

32. Bonvalot S, Rivoire M, Castaing M, Stoeckle E, Le Cesne A, Blay JY, Laplanche A:
Primary retroperitoneal sarcomas: a multivariate analysis of surgical factors associated with local control. *J Clin Oncol* 2009, **27**(1):31-37.

Figures

Figure 1

CT scan of retroperitoneal MLPS patients. A. Huge retroperitoneal MLPS at kidney level. B. Huge retroperitoneal MLPS at colon level. C. Huge retroperitoneal MLPS, coronary view.
Figure 2

Ultrasound of retroperitoneal MLPS patient. Retroperitoneal MLPS, indicated by while ‘+’ symbols.