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 asymptomatic 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.[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%.[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 asymptomatic before diagnosis, but 57% MLPS patients had abdominal distention as their chief complaint, 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%)

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma; S.D.: Standard Deviation.

Demographic characteristics n = 57	
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%)
Abdominal pain	16 (28%)
Lower extremity discomfort	6 (11%)
Urinary system symptom	2 (4%)
Physical signs	
WDLPS	18
Absent	9 (50%)
Tangible mass	9 (50%)
DLPS	23
Absent	7 (30%)
Tangible mass	16 (70%)
PLPS	4
Tangible mass	4 (100%)
MLPS	7

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma; S.D.: Standard Deviation.

Demographic characteristics n = 57	
Absent	2 (29%)
Tangible mass	5 (71%)
Mixed LPS	5
Tangible mass	5 (100%)
Overall	57
Absent	18 (32%)
Tangible mass	39 (68%)
Characteristics of retroperitoneal mass	
WDLPS	9
Clear border	8 (89%)
Good mobility	3 (33%)
Tenderness pain	2 (22%)
DLPS	16
Clear border	9 (56%)
Good mobility	3 (19%)
Tenderness pain	8 (50%)
PLPS	4
Clear border	4 (100%)
Good mobility	1 (25%)
Tenderness pain	1 (25%)
MLPS	5
Clear border	5 (100%)
Good mobility	2 (40%)
Tenderness pain	2 (40%)
Mixed LPS	5
Clear border	3 (60%)

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma; S.D.: Standard Deviation.

Demographic characteristics n = 57	
Good mobility	1 (20%)
Tenderness pain	1 (20%)
Overall	39
Clear border	29 (74%)
Good mobility	10 (26%)
Tenderness pain	14 (36%)
LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma; S.D.: Standard Deviation.	

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*18.5*3.5	Large
20	Intangible	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
*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.					

No.*	PE	CT	Ultrasound	Resection	Subgroup
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

*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.

No.*	PE	CT	Ultrasound	Resection	Subgroup
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

*NA: corresponding examination was not performed.

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma;

Patient No.	PE	Ultrasound-Echoic	CT-Density	Pathology
24	Tangible	NA	Mixed	Mixed LPS
25	Tangible	Hypo-Echoic	Mixed	Mixed LPS
26	Tangible	NA	Mixed	Mixed LPS
27	Tangible	Hypo-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

*NA: corresponding examination was not performed.

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma;

Patient No.	PE	Ultrasound-Echoic	CT-Density	Pathology
49	Intangible	Hypo-Echoic	Mixed	DLPS
50	Tangible	NA	Low	MLPS
51	Intangible	Hypo-Echoic	High	MLPS
52	Tangible	Hyper-Echoic	Low	MLPS
53	Tangible	Hypo-Echoic	Mixed	MLPS
54	Tangible	Mixed-Echoic	Mixed	MLPS
55	Intangible	Hypo-Echoic	NA	MLPS
56	Tangible	NA	Mixed	MLPS
57	Tangible	Hyper-Echoic	Mixed	MLPS
*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, adriamycin, 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

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma;

Patient No.	Pathology	Subgroup	Adjuvant	Prognosis
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

LPS: Liposarcoma; WDLPS: Well-differentiated liposarcoma; DLPS: Dedifferentiated liposarcoma; PLPS: Pleomorphic liposarcoma; MLPS: myxoid liposarcoma;

Patient No.	Pathology	Subgroup	Adjuvant	Prognosis
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

WDLPS	
Good prognosis	10
Bad prognosis	5
DLPS	
Good prognosis	6
Bad prognosis	13
PLPS	
Good prognosis	1
Bad prognosis	2
MLPS	
Good prognosis	4
Bad prognosis	3
Mixed LPS	
Good prognosis	1
Bad prognosis	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

Small	
Good prognosis	11
Bad prognosis	11
Middle	
Good prognosis	7
Bad prognosis	11
Large	
Good prognosis	4
Bad prognosis	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. Pervious 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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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 white '+' symbols.