Original Article

Undifferentiated pleomorphic sarcoma of the extremity and trunk: a retrospective cohort study of 166 cases in a large institution

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Background: An imperative need for better management strategies to improve the survival in patients with undifferentiated pleomorphic sarcoma (UPS).

Methods: The retrospective analysis of clinicopathological data of 166 UPS patients, who have undergone surgical treatment in our hospital, was carried out from January 2005 to January 2018. Cox regression model and Kaplan-Meier method were employed to identify the relevant factors affecting the rate of local recurrence (LR), distant metastasis (DM), and overall survival (OS) via univariate and multivariate analysis. The $P<0.05$ were found to be statistically considerable.

Results: At the end of follow-up, the rate of LR, DM and OS in 166 UPS patients was 22.9% (38/166), 32.5% (54/166) and 75.3% (125/166) with a median follow-up time of 55 months. The existing study reveals that the UPS in trunk, tumor size ≥5 cm and R1/R2 resection margin are the prognostic markers of poor survival rate. Women are more susceptible to LR, and R1/R2 resection margin is significantly correlated with a high rate of LR. Old Patients (>60 years), the UPS in trunk and R1/R2 resection margin are susceptible to DM.

Conclusions: R0 resection margin was an only independent favorable prognostic factor, which was correlated with LRFS, DMFS, and OS.

Keywords: Undifferentiated pleomorphic sarcoma (UPS); R0 resection margin; prognosis

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Introduction

Soft tissue sarcoma (STS) is a type of malignant tumor that develops from mesenchymal tissue, which is estimated to be 1–2% of all malignant tumors, and contains more than 50 histological subtypes (1,2). Undifferentiated pleomorphic sarcoma (UPS) is one of the most common subtypes of STS, previously known as malignant fibrous histiocytoma (MFH) (1,3,4). In 1964 and 1978, O'Brien & Stout and Weiss *et al.* (5,6) studied the features of MFH and for the first time and then revealed transitions from an area of extremely arranged storiform pattern to a less differentiated area with a pleomorphic appearance. In 2002, the World Health Organization (WHO) reconsidered the definition of MFH, and pointed out that it should be a diagnosis of exclusion. In this view, the term 'malignant fibrous histiocytoma' was exchanged by the UPS (7). UPS should be labeled as the exclusion of particular directions of differentiation (8-10), along with the key element which is composed of several types of pleomorphic sarcoma cells with heterogeneity (7). As the most common histological subtype in STS (11), once a clear direction of differentiation can be ruled out, the diagnosis must be considered first in the STSs.

The deep-seated, aggressive and enlarged progressively without pain, always represents the clinical manifestations of

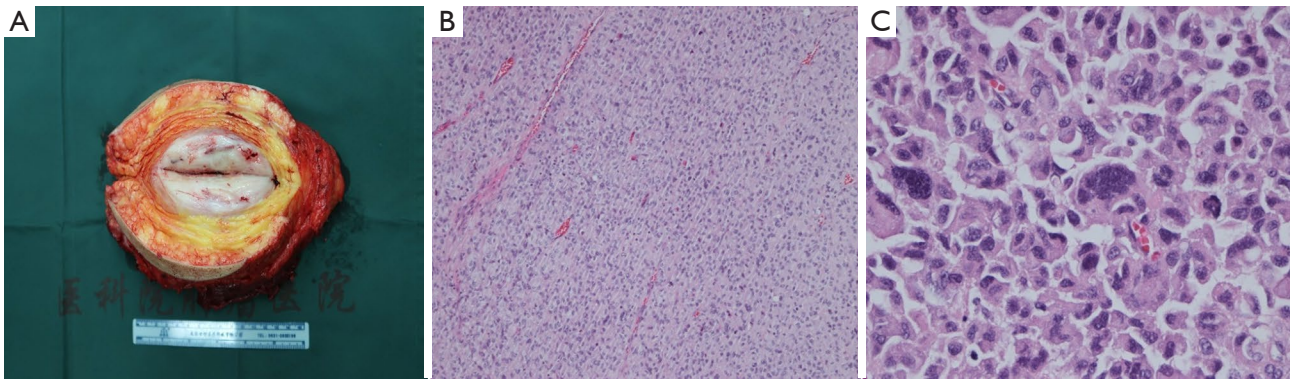

Figure 1 Macroscopic and HE staining pictures of tumor samples from UPS patients. (A) Isolated, leaf-like or fish-like masses, and the cut surface is mostly gray or white; (B,C) HE staining (10× and 40×), it appears as a mixed growth pattern of matted areas and polymorphic areas with a large number of polymorphic areas appearance. Multinucleated giant cells with chromatin and irregular nucle. HE, hematoxylin-eosin; UPS, undifferentiated pleomorphic sarcoma.

STS, and 60–70% occurs in the extremity (3). In addition, approximately 19% of STS originate in the trunk wall (12).

Related reports suggest that the recurrence rate of UPS is greater than 31% (13). Compared with other STSs, the 5-year overall survival (OS) rate is lower in UPS, around 50–70% (9,14-16), and some studies revealed that the 5-year OS rate could be 72% (17). Surgical treatment is largely followed in the UPS (16,18), which can achieve significantly local control for primary UPS. Forty percent of patients with these tumors develop pulmonary metastases (15), which was with 8–12 months of median survival (19).

The current mainstay of treatment for STS is wide resection. And radiotherapy and chemotherapy are effective and recommended adjuvant therapy, its curative effect is not very satisfactory (18,20-22). This research work mainly focuses on the analysis of clinical and pathological features of UPS to confirm the prognostic factors correlated with the OS, metastatic survival and local survival. We aimed to provide the risk factors regarding the survivals in patients with UPS at trunk and extremity. We present the following article in accordance with the STROBE reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1795/rc).

Methods

Basic information

One hundred and sixty-six UPS patients (AJCC II and III in trunk and extremity) were included in the existing study, who underwent surgical treatment at the Cancer Hospital of the Chinese Academy of Medical Sciences and Peking Union Medical College from January 2005 to January 2018. Detailed clinical features were carefully collected and classified, and the main clinical features include epidemiological statistics of UPS (gender and age of onset), tumor-associated data [site of the tumor, local recurrence (LR) at diagnosis, tumor size, AJCC stage, and resection quality, etc.] and treatment methods (surgery, adjuvant chemotherapy, and adjuvant radiotherapy). The 8th edition AJCC staging for STS of the trunk/extremities divides T-stage into 4 categories and upstages nodal disease to stage IV (23).

The patient's age was recorded at the moment when the initial diagnosis was carried out in our hospital. The tumor size was the largest diameter of the tumor, and the data comes from pathological results or imaging data. Resection quality were classified into R0 and R1/R2. R0, referred to microscopic tumor-negative surgical margins; R1, referred to microscopic tumor-positive surgical margins; and R2, referred to macroscopic tumor-positive surgical margins.

All histopathological specimens of 166 patients were confirmed by two pathologists. UPS usually appears as isolated, leaf-like, or fish-like masses, and the cut surface is commonly white or gray. Under hematoxylin-eosin (HE) staining, it mostly appears as a mixed growth pattern of matted areas and polymorphic areas with a large number of polymorphic areas. The chromatin and irregular nuclei were present in multinucleated giant cells, as depicted in *Figure 1*.

The inclusion/exclusion criteria for patients enrolled

in this study were: (I) surgery, must be performed at our hospital; (II) patients who only received radiotherapy and/or chemotherapy were excluded; (III) the pathological diagnosis, as well as the surgical margins, must be determined by our pathology department; and (IV) long-term follow-up data must be detailed and reliable completely.

The study was established, according to the ethical guidelines of the Helsinki Declaration (as revised in 2013) and was approved by the Human Ethics Committee of National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital (No. NCC2020C-341). Written informed consent was obtained from individual or guardian participants.

Treatment and follow-up data

The resection quality of all patients was evaluated at our hospital, and those cases who just received chemotherapy and/or radiotherapy were excluded. Postoperative pathological indications were as follows; 90.4% (150/166) and 9.6% (16/166) patients were R0 and R1/R2 resection, respectively. For patients with high recurrence rate and/or high metastasis rate, we generally recommend radiotherapy and/or chemotherapy. Fifty point six percent (84/166) patients underwent adjuvant radiation therapy in the period of the disease, with an average radiotherapy dose of 50 Gy (15–76 Gy) and a median radiation dose of 60 Gy. Thirty-three point seven percent (56/166) patients received adjuvant chemotherapy. Ifosfamide and doxorubicin were mainly used as chemotherapeutic drugs. The regular checkups including regular chest CT and local MRI scans were carried out post operation in our hospital. Follow-up data were collected by phone calls and medical records. The follow-up time of 166 patients was 6–168 months, with a mean follow-up time of 62 months and a median follow-up of 55 months.

Statistical analysis

The statistical analysis was carried out by SPSS 22.0 and GraphPad Prism 6. While the Kaplan-Meier method and Cox regression model were employed for univariate and multivariate analysis. P value less than 0.05 was regarded as statistically considerable.

Results

Among them, male patients and female patients were 54.2% (90/166) and 45.8% (76/166), respectively and their ages were 24 to 83 years with median and the average age of 57 and 55.5 years, respectively. The UPS in the trunk, upper extremity and lower extremity accounted for 30.1% (50/166), 15.7% (26/166), and 54.2% (90/166), respectively. Patients with no recurrence tumors and recurrent tumors accounted for 62.7% (104/166) and 37.3% (62/166), respectively. The tumor size ranged from 1 to 22 cm, with an average size of 5.52 cm. The diameter of tumors was 5 cm or less in 57.8% (96/166), while in 42.2% (70/166) the diameter of the tumor was more than 5 cm. According to the American Joint Committee on Cancer (AJCC) staging criteria, stage II and stage III accounted for 57.8% (96/166) and 42.2% (70/166), accordingly, as presented in *Table 1*.

LR

At the end of follow-up, 22.9% (38/166) was the LR rate of 166 UPS patients with a median follow-up of 55 months. The 3- and 5-year LR-free survival (LRFS) rate were 79.2% and 74.4%, respectively (*Figure 2A*). Factors influencing LRFS in univariate analyses and multivariate analysis were listed in *Table 2*. Univariate analysis revealed that the significant factors correlated with higher LR rate were female, recurrence patients and R1/R2 (*Table 2*, *Figure 2B-2D*). The multivariate analysis revealed that gender (P=0.008, HR =0.410, 95% CI: 0.212–0.796) and resection quality (P=0.001, HR =3.626, 95% CI: 1.675–7.846) were two independent risk factors for LR in patients with UPS post operation (P<0.05), which was presented in *Table 2*. The female patients had a 1.92-fold increased risk of developing LR than male patients (HR =2.285, 95% CI: 1.213–4.383, P=0.0111), as depicted in *Figure 2B*. With respect to the resection quality, a considerable variation was found between the two groups for LRFS (HR =3.758, 95% CI: 3.064–33.63, P=0.0002), as given in *Figure 2D*. R1/R2 resection margins had a high LR rate in UPS (24), which was confirmed again by us. Radiotherapy is an important means to control tumor recurrence after surgery. In this article, it is not found that radiotherapy is meaningful for the control of postoperative recurrence of UPS.

Distant metastasis (DM)

In 166 UPS patients, the rate of DM was 32.5% (54/166). The 3- and 5-year distant metastasis-free survival (DMFS) rates were 74.5% and 67.6%, respectively (*Figure 2A*). In the existing study, univariate analysis revealed that prognostic

Table 1 Tumor status and prognosis of 166 UPS patients

Variables	Quantity	Percentage (%)
Demographic characteristics		
Age (years)		
≤60	101	60.8
>60	65	39.2
Gender		
Male	90	54.2
Female	76	45.8
Tumor features		
Tumor site		
Trunk	50	30.1
Upper extremity	26	15.7
Lower extremity	90	54.2
Local recurrence at diagnosis		
No recurrence	104	62.7
Recurrence	62	37.3
Tumor size (cm)		
≤5	96	57.8
>5	70	42.2
Tumor grades		
AJCC grades		
II	96	57.8
III	70	42.2
Pathological features		
Resection quality		
R0	150	90.4
R1/R2	16	9.6
Adjuvant treatment		
Radiotherapy	84	50.6
Chemotherapy	56	33.7
Combined	42	25.3
Nil	62	37.3
Prognosis		
Post-treatment local recurrence	38	22.9
Post-treatment metastases	54	32.5
Death	41	24.7

UPS, undifferentiated pleomorphic sarcoma.AJCC, American Joint Committee on Cancer.

factors i.e., older (>60 years), LR at diagnosis, trunk and R1/R2 had considerable variations in DMFS (*Table 3*, *Figure 2E-2H*). The significant results of the univariate analysis were incorporated into the cox multivariate analysis, and then we revealed the independent factors i.e., older (>60 years) (P=0.044, HR =1.780, 95% CI: 1.016–3.116), trunk (P=0.002, HR =0.396, 95% CI: 0.219–0.718), R1/R2 (P=0.006, HR =2.566, 95% CI: 1.315–5.005), and adjuvant chemotherapy (P<0.001, HR =2.992, 95% CI: 1.666–5.371) had a more possibility of DM (all P<0.05), as presented in *Table 3*.

OS

The OS rate of 166 UPS patients was 75.3% (125/166) until the end of follow-up, while the 3- and 5-year OS rates were 81.7% and 76.4%, respectively. In our study, univariate analysis reveals that prognostic factors i.e., older (>60 years), LR at diagnosis, tumor size (>5 cm), AJCC stage (III) and R1/R2 were considerably associated with the poor OS rate (P<0.05) (*Table 4*, *Figure 2I-2L*). The effective results of the univariate analysis were incorporated into the cox multivariate analysis which confirms the three independent factors i.e., trunk (P=0.047, HR =0.526, 95% CI: 0.279–0.992), R1/R2 (P<0.001, HR =3.742, 95% CI: 1.853–7.554) and tumor size (>5 cm) (P=0.022, HR =2.093, 95% CI: 1.110–3.944) which correlated with a poorer OS, as presented in *Table 4*. In this study, in 54 patients with metastases, whether chemotherapy or not was significantly related to overall prognosis.

Discussion

UPS, called MFH previously, which was recognized as the most common STS in adults, accounting for 50% of diagnoses. However, the pathological diagnosis of UPS shown no evidence of true histiocytic differentiation, meaning it encompasses the morphologic manifestations of a variety of poorly differentiated tumors rather than being a single entity (15). So the diagnosis and treatment of UPS are still highly challenging because of the confused pathological classification. MRI is commonly used as a non-invasive effective diagnostic tool for STS.

R1/R2 resection margins identified as predictors of poor outcomes. Herein, the R0 resection margin was an only independent favorable prognostic factor that was correlated with LRFS, DMFS, and OS. The resection margin was found to be the prognostic factor that was effectively

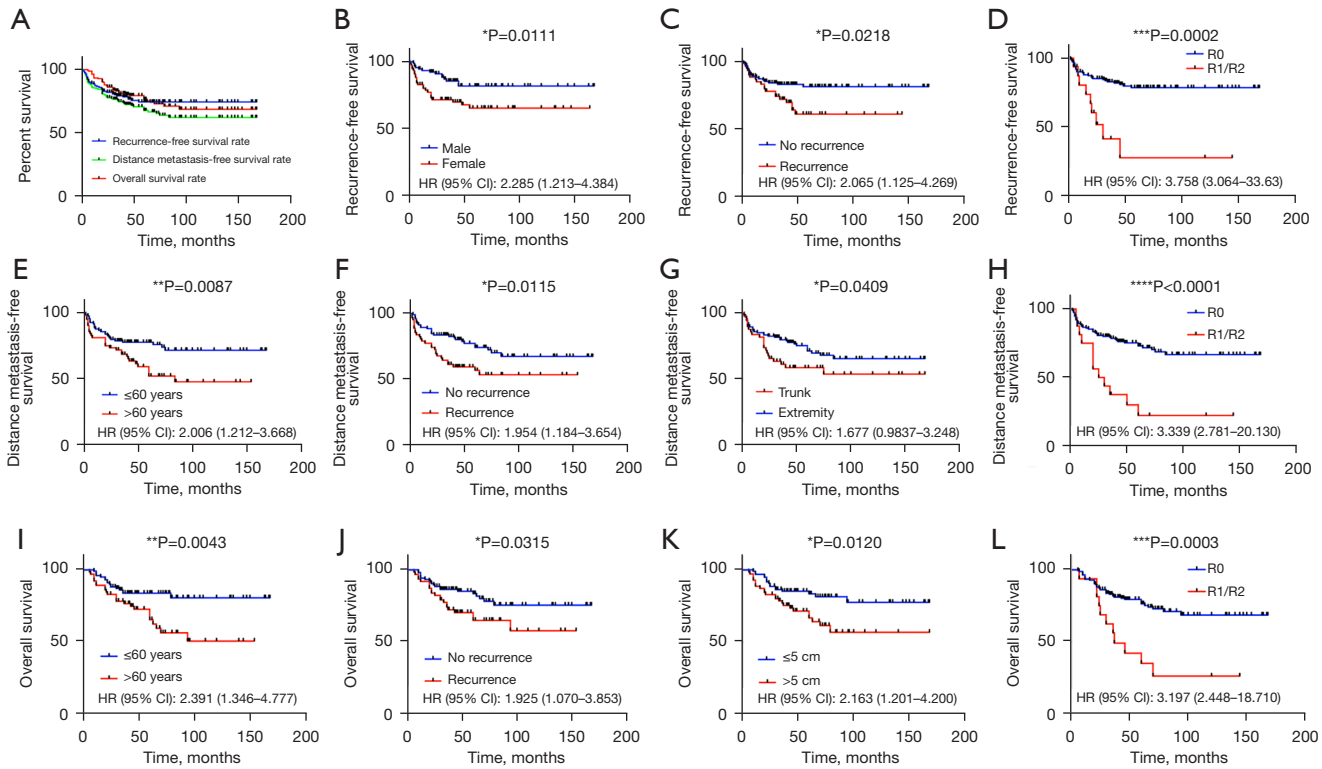

Figure 2 Kaplan-Meier curve for LRFS, DMFS and OS based on different prognostic variables. (A) Local recurrence-free survival rates, distant metastasis-free survival rates and overall survival rates at 3 and 5 years for 166 patients were 79.2% and 74.4%, 74.5% and 67.6% and 81.7% and 76.4%, respectively; (B-D) Kaplan-Meier curve for LRFS based on the gender, local recurrence at diagnosis and surgical margin. Patients with female, recurrence patients and R1/R2 have a worse LRFS than patients with male, no recurrence patience and R0 in all tumor groups; (E-H) Kaplan-Meier curve for DMFS based on the age, local recurrence at diagnosis, tumor location and surgical margin. Patients with age (>60 years), recurrence patients, trunk and R1/R2 have a worse DMFS than patients with age (≤60 years), no recurrence patients, extremity and R0 in all tumor groups; (I-L) Kaplan-Meier curve for OS based on the age, local recurrence at diagnosis, tumor size and surgical. Patients with age (>60 years), recurrence patients, tumor size (>5 cm) and R1/R2 after metastasis have a worse OS than patients with age (≤60 years), no recurrence patience, tumor size (≤5 cm) and R0 in all tumor groups. HR, hazard ratio; LRFS, local recurrence-free survival; DMFS, distant metastasis-free survival; OS, overall survival.

correlated with the duration of survival. Peiper *et al.* (13) proposed that positive microscopic margins were correlated with an elevated LR rate (RR =4.8, P<0.01). Özkurt *et al.* (25) studied 14 cases of confirmed bone UPS and it was found that the 5-year survival rate of patients with wide resection and border resection were 81.9% and 33.3% (P<0.05), which reveals that surgical excision with wide margins and adjuvant chemotherapy provided adequate control of the disease and longer survival. Just like some article says that surgery striving for negative margins, with radiotherapy, is the treatment of choice (10,15,24).

With respect to tumor size, Winchester *et al.* (26) evaluated the prognostic factors of 319 UPS patients and revealed that tumor size (greater than 5 cm) and deep subcutaneous fat infiltration were significant factors that affect the LR rate. In the existing study, compared with those with tumor sizes ≤5 and >5 cm, the 5-year LR, DM and OS rates decreased by 11.3%, 18.4% and 16.7%, respectively (*Table 2*). The extensive analysis of the data of more cases may contribute to better resolve the underlined problem.

The metastasis predominantly occurs in the lungs (10,27) relative to regional lymph nodes (28). Winchester *et al.* (26) suggested that the main factors that affect the DM of UPS were the tumor site, tumor size larger than 2 cm, invasion beyond subcutaneous fat, and lymphovascular invasion. In

Table 2 Univariate and multivariate analysis of factors influencing post-treatment local recurrence-free survival in 166 patients

Variables	Univariate analysis			Multivariate analysis		
	3-year LRFS rate	5-year LRFS rate	P value	HR	95% CI	P value
Gender			0.011			0.008
Male	85.5	81.9		0.410	0.212–0.796	
Female	71.5	65.3				
Age (years)			0.113			–
≤60	82.8	79.5		–	–	
>60	73.6	66.3		–	–	
Local recurrence at diagnosis			0.022			0.076
No recurrence	83.3	81.6		1.800	0.939–3.450	
Recurrence	72.2	61.2				
Tumor sites			0.696			–
Trunk	83.7	76.7		–	–	
Extremity	77.5	73.4		–	–	
Tumor size (cm)			0.183			–
≤5	81.7	78.8		–	–	
>5	75.7	67.5		–	–	
AJCC grade			0.183			–
II	81.7	78.8		–	–	
III	75.7	67.5		–	–	
Resection quality			0.000			0.001
R0	82.7	78.5		3.626	1.675–7.846	
R1/R2	41.3	27.6				
Adjuvant radiotherapy			0.329			–
Yes	81.1	78.9		–	–	
No	77.3	70.1		–	–	
Adjuvant chemotherapy			0.221			–
Yes	74.4	68.3		–	–	
No	81.8	77.5		–	–	

LRFS, local recurrence-free survival; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer.

the existing study, cox multivariate survival analysis found that >60 years were at a higher risk of metastasis than the younger patients, and the chances of metastasis were lower in the R0 resection margin, as presented in *Table 3*. Furthermore, in multivariate analysis, the tumor site was an independent predictor correlated with DMFS, as depicted in *Figure 2F*. Our findings of increased metastatic disease for the UPS in trunk is likely due to trunk tumors being more possibility and visible to hematogenous metastasis in the early stages of disease.

In the analysis of OS, the Cox multivariate survival analysis revealed that tumor site (P=0.026), tumor size (P=0.048), AJCC stage (P=0.048), and resection quality (P=0.001) were independent factors that affect postsurgical

Table 3 Univariate and multivariate analysis of factors influencing post-treatment distant metastasis-free survival in 166 patients

Variables	Univariate analysis			Multivariate analysis		
	3-year DMFS rate	5-year DMFS rate	P value	HR	95% CI	P value
Gender			0.695			–
Male	70.6	65.9		–	–	
Female	78.5	69.6		–	–	
Age (years)			0.009			0.044
≤60	78.1	76.3		1.780	1.016–3.116	
>60	68.9	52.4				
Local recurrence at diagnosis			0.012			0.091
No recurrence	82.5	77.3		1.603	0.928–2.769	
Recurrence	61.3	56.8				
Tumor site			0.041			0.002
Trunk	61.4	58.8		0.396	0.219–0.718	
Extremity	80.0	71.5				
Tumor size (cm)			0.070			0.386
≤5	80.1	75.4		1.276	0.736–2.213	
>5	66.7	57.0				
AJCC grade			0.070			–
II	80.1	75.4		–	–	
III	66.7	57.0		–	–	
Resection quality			0.001			0.006
R0	78.5	73.0		2.566	1.315–5.005	
R1/R2	37.5	22.5				
Adjuvant radiotherapy			0.863			–
Yes	74.7	68.0		–	–	
No	74.2	67.4		–	–	
Adjuvant chemotherapy			0.001			<0.001
Yes	79.8	75.8		2.992	1.666–5.371	
No	64.2	52.5				

DMFS, distant metastasis-free survival; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer.

survival in UPS patients (all P<0.05), as represented in *Table 4*. According to our cohort, for the patients having tumors of the trunk, the tumor size ≥5 cm and R1/R2, a more significant and effective approach should be adopted. Winchester *et al.* (26) found that age, immunosuppression, tumor size larger than 2 cm, and lymphovascular invasion were independent risk factors affecting overall prognosis. Simultaneously, the existing study revealed that patients with severe subcutaneous fatty infiltration of tumors had a bad prognosis rate. In the AJCC staging system, tumor size and tumor depth were significantly associated with the prognosis.

In the AJCC staging guidelines, tumor size is an important criteria for the judgment of soft tissue staging.

Table 4 Univariate and multivariate analysis of factors influencing overall survival in 166 patients

Variables	Univariate analysis			Multivariate analysis		
	3-year OS rate	5-year OS rate	P value	HR	95% CI	P value
Gender			0.758			–
Male	84.2	77.3		–	–	
Female	81.5	75.0		–	–	
Age (years)			0.004			–
≤60	86.1	83.8		–	–	
>60	78.2	65.5		–	–	
Local recurrence at diagnosis			0.031			–
No recurrence	86.4	83.5		–	–	
Recurrence	74.1	65.0		–	–	
Tumor site			0.128			0.047
Trunk	75.3	72.4		0.526	0.279–0.992	
Extremity	84.3	80.9				
Tumor size (cm)			0.012			0.022
≤5	85.2	83.4		2.093	1.110–3.944	
>5	76.9	66.7				
AJCC grade			0.012			–
II	85.2	83.4		–	–	
III	76.9	66.7		–	–	
Resection quality			<0.001			<0.001
R0	84.5	81.3		3.742	1.853–7.554	
R1/R2	56.3	35.2				
Adjuvant radiotherapy			0.843			–
Yes	82.1	77.0		–	–	
No	81.2	75.9		–	–	
Adjuvant chemotherapy			0.226			–
Yes	84.4	79.0		–	–	
No	76.6	71.5		–	–	

OS, overall survival; HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer.

Univariate analysis revealed that the size of the tumor was not considerably associated with LRFS and DMFS, but was closely associated with OS (P=0.012), as shown in *Figure 2K*. In multivariate analysis, tumor size (≥5 cm) was not an independent prognostic factor affecting LRFS and DMFS (all P>0.05). Furthermore, in 2009, Lehnhardt *et al.* (17) also shown that tumor size ≥5 cm was considerably associated with the OS, which was in line with Chen and Al-Agha (27,29). Our study also confirmed that tumor size ≥5 cm was also one of the most important factors affecting OS. Peiper *et al.* (13) found that tumor size (RR =6.0, P<0.01) was a significant factor that affects the DFS of UPS patients. Larger tumors suggest a higher ability to divide and proliferate, a wider range of invasion, a higher degree

of malignancy, and more complicated surgical methods, so the first visit to the professional sarcoma center is critical.

In the existing study, Univariate K-M analysis revealed that the LR at diagnosis was a significant factor that affects the LR rate, DM rate, and OS rate (P<0.05). But in multivariate analysis, the presentation of tumor was not an independent prognostic factor affecting LR rate, DM rate, and OS rate, with P values of 0.076, 0.091, and 0.162, respectively. Lehnhardt *et al.* (17) shown that a considerable variation was found between the group presenting with primary tumors (5-year survival: 84%, P<0.05) and recurrent tumors (5-year survival: 62%, P<0.05), which is correlated with our existing research work. The prognosis for patients with UPS of the extremities depends predominantly on adequate wide resection of the primary tumor, which is same to the idea that complete surgical resection was the most important UPS treatment strategy for UPS (18). In short, the LR at diagnosis and then R0 resection in the first therapy may play a crucial role in patient prognosis.

The value of adjuvant radiotherapy and chemotherapy in the diagnosis and treatment of STS has been mixed. Radiotherapy is mostly considered to be an effective mean to control local tumor recurrence, but in this study, it was not found that radiotherapy has any significance in the control of UPS. Trials from Gronchi suggested an OS benefit with five cycles of adjuvant full-dose epirubicin plus ifosfamide in localised high-risk soft-tissue sarcoma of the extremities or trunk wall (30,31). Adjuvant chemotherapy was associated with improved LRFS only in patients ≥30 years (32). Pazopanib and immune checkpoint inhibitors are a new attempt in UPS treatment (33-35). UPS is an immunologically active subtype of STS, which is particularly amenable to immune checkpoint inhibitors (35). Immunohistochemical biomarkers significantly contribute to predicting the rate of recurrence, metastasis, and OS rate. A significant predictive index for evaluating the effect of VEGFR receptor inhibitors in the treatment of advanced STS, TP53 plays a significant role in the diagnosis and treatment of UPS (36). Therefore, an extensive study on the molecular mechanism is needed to explore the targeted therapy and feasibility of immune checkpoint inhibitors(18,37-39).

As a retrospective study, although this study has given us a crucial hint, there are some shortcomings in the existing study. Firstly, the statistics on chemotherapy and radiotherapy are not sufficient due to the low incidence rate of the underlined disease, limited samples, and a large time span and the significant evaluation of the adjuvant therapy is also very difficult. Nevertheless, the accumulation and analysis of more comprehensive medical data for UPS can objectively reflect the characteristics and outcome of the disease that needs to be improved.

Conclusions

The existing study determines that the UPS in trunk, tumor size ≥5 cm and R1/R2 resection margin are prognostic markers of poor over survival. R1/R2 resection margin significantly correlated with high LR rate and women are more susceptible to LR. The UPS in trunk and R1/R2 resection margin are significantly correlated with DM and old patients (>60 years) are more susceptible to DM.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1795/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1795/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1795/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was established, according to the ethical guidelines of the Helsinki Declaration (as revised in 2013) and was approved by the Human Ethics Committee of National

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