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Original Article

Clinical outcomes of undifferentiated sarcomas are similar with that of other spindle cell sarcomas of specific histologic types: an institutional experience

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Abstract: Background: Clinical, epidemiological and pathologic data about undifferentiated sarcoma (US) is not sufficient. This study aimed to provide the basic data including clinical outcomes about US. Materials and methods: For this study, we selected 135 cases of sarcomas including 49 cases of US and 86 cases of specific sarcomas diagnosed from 2000 to 2012 at St. Vincent Hospital, The Catholic University of Korea. Among the specific sarcomas, we selected some high grade spindle cell sarcomas which grouped as non-US and used for comparison and analysis. We compared clinical and histological characteristics and overall survival between these two groups. Results: US occupied 36.3% of sarcomas and occurred mainly in older ages more than 41 years (82%), and lower extremities were prevalent sites. 6 cases were accompanied by metastasis (12.2%), and lung and bone were major target organs. 22 cases (44.9%) were grade 2 by FNCLCC and 27 (55.1%) were grade 3. When compared with non-US, there were no significant differences. Clinically, presence of metastasis alone affected their overall survival not only in US but also in non-US. Conclusions: Because US and other spindle cell sarcoma showed similar clinical outcomes according to this study, clinical approaches for US could be followed safely that of other high grade sarcomas.

Keywords: Undifferentiated sarcoma, epidemiology, immunohistochemistry, molecular pathology, overall survival

Introduction

Undifferentiated sarcoma (US) refers a soft tissue sarcoma showing no identifiable line of differentiation even though present available diagnostic tools such as immunohistochemistry and tumor genetic assays are applied [1]. US includes several kinds of tumors, and US is diagnostic term used only after possible specific entities are excluded as described in the definition of US. Therefore, this entity can be reckoned as a kind of wastebasket. In the category of US, dedifferentiated sarcomas of other specific soft tissue tumors are not included [1, 2].

The clinical, epidemiological and pathologic data about US is not sufficient. This study aimed to provide the basic data about US such as clinical and histological characteristics, and its overall survival. Especially, because several sarcomas of specific types such as leiomyosarcoma, synovial sarcoma or fibrosarcoma are reckoned as principal entities for differential diagnosis with US, we aimed to know whether there were significant differences in their clinical courses between US and above mentioned sarcomas.

Materials and methods

For this study, we selected 135 cases of sarcomas including 49 cases of US and, for comparison, 86 cases of specific sarcomas diagnosed from 2000 to 2012 at St. Vincent Hospital, The Catholic University of Korea. Because the diagnostic term of US was changed several times, diagnostic term of these cases were variable. Therefore, 49 US cases included 38 malignant fibrous histiocytomas, 2 undifferentiated pleomorphic sarcomas, 2 high grade sarcomas, and 7 poorly differentiated sarcomas. Although some cases showed ambiguous diagnostic term, we grouped these cases as US according

Table 1. Clinical characteristics of sarcomas

Diagnosis	No. (%)	Sex		Ages (years)			
		M	F	0-20	21-40	41-60	61-80
Dedifferentiated liposarcoma	6 (4.4)	4	2	0	0	4	2
Myxoid liposarcoma	16 (11.9)	4	12	0	5	9	2
Pleomorphic liposarcoma	1 (0.7)	1	0	0	0	0	1
Fibrosarcoma	3 (2.2)	3	0	0	2	1	0
Myxofibrosarcoma	4 (3.0)	3	1	0	1	2	1
Leiomyosarcoma	5 (3.7)	3	2	0	1	2	2
Rhabdomyosarcoma	8 (5.9)	3	5	3	3	1	1
Kaposi sarcoma	6 (4.4)	3	3	0	0	1	5
Angiosarcoma	4 (3.0)	4	0	1	0	2	1
MPNST	5 (3.7)	4	1	0	5	0	0
Synovial sarcoma	11 (8.1)	6	5	0	2	9	0
Epithelioid sarcoma	5 (3.7)	4	1	1	3	1	0
Alveolar soft part sarcoma	5 (3.7)	2	3	0	3	1	1
Clear cell sarcoma	4 (3.0)	3	1	1	1	1	1
Extraskeletal Ewing sarcoma	3 (2.2)	3	0	2	0	0	1
Undifferentiated sarcoma	49 (36.3)	29	20	0	9	21	19
Tatal	135 (100.0)	79 (58.5)	56 (41.5)	8 (5.9)	35 (25.9)	55 (40.7)	37 (27.5)

to the 2013 WHO classification [1], because these cases showed no definite line of differentiation histologically and immonohistochemically in common. Among the specific sarcomas, we excluded well differentiated liposarcoma and dermatofibrosarcoma protuberans.

We considered following conditions before selection of US, the methods provided by Goldblum [3]: any kind of specific line of differentiation was not identified immunohistologically, any possibility of dedifferentiated sarcoma should be excluded, and the possibility of sarcomatous carcinoma from other body sites was not present. We selected the cases of US only after above mentioned criteria is fulfilled. For other specific sarcomas, we selected them according to the classification of 2013 WHO classification.

We examined clinical characteristics such as age, sex, site, and metastatic rate of these sarcomas. We reviewed HE slides and immunohistochemical results of US and other sarcomas. Tumor grade were applied according to Federation Nationale des Centres de Lutte Contre le Cancer (FNCLCC). This system consists with scoring system including tumor differentiation (score 1 to 3), mitotic count (score 1 to 3), and tumor necrosis (score 0 to 2). Histologic grade is 1 if total score is 2 or 3, grade 2 if total score is 4 or 5, and grade 3 if total score is 6, 7, or 8 [1]. For the comparison of histologic grades and overall survival, we selected fibrosarcoma, myxofibrosarcoma, dedifferentiated liposarcoma, leiomyosarcoma, MPNST and synovial sarcoma as a group of non-US because these tumors are most frequently referred diagnostic entities for the differential diagnosis of US. We compared overall survival between US and selected specific sarcomas above mentioned (non-US below). We used the chi-square test and Kaplan-Meier survival analysis to examine the statiatical significance of the results, using SAS software (version8; SAS Inc., Cary, NC, USA). A p-value of <0.05 was considered significant. This study was approved by the Clinical Study Medical Ethics Committee (VC15RISI-0002).

Results

Among sarcomas diagnosed in this institute, US occupied 36.3%. Male to female ratio was about 1.5:1.0. US occurred mainly in older ages more than 41 years (82%). Other specific sarcomas composed of various diagnoses. Their sex ratio was variable. As US, these sarcomas were also more frequent in older ages more than 41 years (61%) (**Table 1**).

Table 2. Metastatic rates of soft tissue sarcomas

Diagnosis[a]	No. (%)	Rate of metastasis No (%)	Sites of metastasis
DLS	6 (4.4)	0 (0.0)[b]	-
MLS	16 (11.9)	2 (12.5)	Liver, bone
PLS	1 (0.7)	0 (0.0)	-
FS	3 (2.2)	1 (33.3)	Lung
MFS	4 (3.0)	1 (25.0)	Lung
LMS	5 (3.7)	0 (0.0)	-
RMS	8 (5.9)	3 (37.5)	Lung, bone
KS	6 (4.4)	0 (0.0)	-
AS	4 (3.0)	2 (50.0)	Lung, brain
MPNST	5 (3.7)	2 (40.0)	Lung, bone
SS	11 (8.1)	4 (36.4)	Lung
ES	5 (3.7)	1 (20.0)	Lung
ASPS	5 (3.7)	5 (100.0)	Lung, bone
CCS	4 (3.0)	4 (100.0)	Lung, bone, brain, regional lymph node
EES	3 (2.2)	1 (33.3)	Brain
US	49 (36.3)	8 (16.3)	Lung, bone
Tatal	135 (100.0)		

[a]DLS, dedifferentiated liposarcoma; MLS, myxoid liposarcoma; PLS, pleomorphic liposarcoma; FS, fibrosarcoma; MFS, myxofibrosarcoma; LMS, leiomyosarcoma; RMS, rhabdomyosarcoma; KS, kaposi sarcoma; AS, angiosarcoma; MPNST, malignant peripheral nerve sheath tumor; SS, synovial sarcoma; ES, epithelioid sarcoma; ASPS, alveolar soft part sarcoma; CCS, clear cell sarcoma; EES, extraskeletal Ewing sarcoma; US, undifferentiated sarcoma; [b]Percentage within individual sarcoma.

These sarcomas showed various rates of metastasis from 0 to 100%. Angiosarcoma, alveolar soft part sarcoma and clear cell sarcoma showed high rate (more than 50%) of metastasis. Most frequent metastatic sites were lung and bone. Other sites included liver, brain and regional lymph node. Among 49 US, 6 cases were accompanied by metastasis (12.2%), and lung and bone were major target organs (**Table 2**).

Immunohistochemistry was done in 49 cases of US. Generally performed items were cytokeratin, vimentin, alpha 1-antitrypsin, desmin, actin, lysozyme, myoglobin, S-100 protein, CD68 and CD34. Our cases showed nonspecific or occasional positive reactions to vimentin, alpha 1-antitrypsin, CD68 and lysozyme, but negative reactions to other items except 3 cases which showed weal or focal positive reaction to actin, and a case with faint reaction to S-100protein. Other antibodies such as HMB-45, c-kit, EMA, CD99, CD56 and beta-catenin were applied in certain cases, but showed negative reactions in majority cases (**Table 3**).

Following results are comparisons between US and non-US as these were major concern of this study. For this comparison, we selected 34 sarcomas of specific histologic types including 3 fibrosarcomas, 4 myxofibrosarcomas, 6 dedifferentiated liposarcomas, 5 leiomyosarcomas, 5 malignant peripheral nerve sheath tumors, and 11 synovial sarcomas. Histologically, US could be divided into 24 pleomorphic type (49.0%), 19 spindle cell type (38.8%), 5 epithelioid type (10.2%), and 1 round cell type (2.0%) (**Table 4**; **Figure 1**). In US, 22 cases (44.9%) were grade 2 and 27 (55.1%) were grade 3. Grade 1 tumor was not found. Among the 34 cases of non-US, 15 cases (41.7%) were grade 2 and 21 (58.3%) were grade 3. Grade 1 tumor was not found either. Statistical difference of histologic grade between US and non-US group was insignificant (*P=0.827*) (**Table 4**).

We compared the sites of occurrence between US and non-US. More than 60.0% of US, fibrosarcomas, myxofibrosarcomas, Leiomyosarcomas, MPNST and synovial sarcomas occurred in the extremities. Dedifferentiated liposarcomas occurred in intraabdominal area more frequently (66.7%). In US, 34 cases (69.4%) occurred in extremities, especially in lower extremities - 5 (10.2%) in upper and 29 (59.2%) in lower extremities. 9 cases (18.4%) were found in the trunk, and 6 cases (12.2%) were found as intraabdominal tumor (**Table 5**).

In the aspects of overall survival, there was no difference between US and non-US (P= 0.362) (**Figure 2A**). Among the grade 2 tumors, there was no difference between them (P= 0.562) (**Figure 2B**) and showed same results among the grade 3 (P=0.552) (**Figure 2C**). Among non-US, there was no difference between grade 2 and 3 (p=0.378) (**Figure 2D**) and showed same result with US (P=0.392)

Table 3. Immunohistochemical results of US

Cases	CK	vim	AT	DM	S-100	MG	LZ	A1A	c-kit	CD34	CD68	HMB45	CD56	CD99	BC
1	-[a]	P	-	N	-	-	N	-	-	-	-	-	-	-	-
2	-	P	-	N	-	N	P	P	-	-	-	-	-	-	-
3	-	P	-	-	-	-	WP	P	-	-	-	-	-	-	-
5	-	P	-	N	N	-	-	P	-	-	-	-	-	-	-
6	N	P	-	-	-	-	P	P	-	-	-	-	-	-	-
7	-	P	N	N	N	-	-	P	-	-	-	-	-	-	-
8	N	P	N	-	N	-	-	-	-	N	-	-	-	-	-
9	-	P	N	-	N	-	-	P	-	-	-	-	-	-	-
10	-	-	N	-	N	-	-	-	-	N	-	-	-	-	-
11	-	-	-	-	-	-	P	P	-	-	-	-	-	-	-
12	-	-	N	-	N	-	P	P	-	-	-	-	-	-	-
13	N	P	N	N	N	N	N	P	P	-	-	-	-	-	-
14	-	-	N	-	N	-	-	-	-	N	-	-	-	-	-
15	-	P	N	N	N	-	-	P	-	-	-	-	-	-	-
16	-	P	-	-	N	-	P	P	-	-	-	-	-	-	-
17	-	P	-	-	N	-	P	P	-	-	-	-	-	-	-
18	N	P	-	N	N	-	-	-	-	-	-	-	-	-	-
19	-	-	N	N	-	-	N	P	N	N	-	-	-	-	-
20	-	P	N	N	N	N	N	-	-	-	-	-	-	-	-
21	-	-	N	-	N	-	-	P	-	N	-	-	-	-	-
22	-	P	P	N	N	-	P	-	-	-	-	-	-	-	-
23	-	P	N	N	-	N	N	P	-	-	-	-	-	-	-
24	-	P	N	-	N	-	N	P	-	-	-	-	-	-	-
25	-	P	WP	N	N	N	P	-	-	-	-	-	-	-	-
27	-	-	N	N	N	N	-	-	N	-	N	-	-	-	-
28	-	P	N	N	N	-	-	-	-	N	P	-	-	-	-
29	-	P	N	N	N	-	-	N	-	N	P	-	-	-	-
30	-	P	N	-	N	-	-	-	-	-	-	-	-	-	-
31	-	P	N	N	N	-	N	-	-	-	-	-	-	-	-
32	N	P	-	-	P	-	-	-	-	-	-	N	N	-	-
33	N	-	-	-	N	-	-	-	-	-	-	-	-	N	-
34	N	P	-	N	N	N	-	-	-	N	N	N	-	-	-
35	N	P	-	-	-	-	-	-	-	-	-	-	-	-	-
36	N	-	WP	N	N	-	-	-	-	N	-	-	-	-	-
37	N	P	N	N	N	-	-	-	N	N	-	-	-	-	-
38	-	P	N	N	N	-	-	-	-	-	-	-	-	-	-
40	N	-	N	N	N	-	N	-	-	-	P	-	-	N	-
41	-	-	N	N	N	-	-	-	N	N	P	-	-	-	N
42	-	P	N	N	N	-	P	-	-	-	P	-	-	-	-
43	-	-	N	N	N	-	-	-	-	-	-	-	-	-	-
44	N	-	N	-	N	N	N	-	-	-	-	-	-	-	-
45	-	P	N	-	N	-	P	-	-	-	-	-	-	-	-
46	-	P	N	N	N	N	P	P	-	-	-	-	-	-	-
48	-	P	N	N	N	-	-	N	-	N	-	-	-	-	-
49	-	-	N	N	N	N	-	P	-	N	-	-	-	-	-

CK, cytokeratin; vim, vimentin; AT, actin; DM, desmin, S-100, S-100protein; MG, myoglobin; LZ, lysozyme; A1A, alpha-1 antitrypsin; BC, beta-catenin. a. N, negative; P, positive, WP, weak positive; FP, focal positive; -, not done.

Table 4. Histologic grades of US and sarcomas of control

Histologic types		No. (%)				
		Tumor grade[a]			Total	*p-value*[d]
		1	2	3		
US	Pleomorphic	0	9	15	24 (49.0)[b]	
	Spindle	0	12	7	19 (38.8)	
	Epithelioid	0	0	5	5 (10.2)	
	Round	0	1	0	1 (2.0)	
	Total	0 (0.0)	15 (30.6)	34 (69.4)	49 (100.0)	
Fibrosarcoma		0	3	0	3 (8.8)[c]	
Myxofibrosarcoma		0	4	0	4 (11.8)	
Dedifferentiated liposarcoma		0	0	6	6 (17.6)	
Leiomyosarcoma		0	3	2	5 (14.7)	
MPNST		0	0	5	5 (14.7)	
Synovial sarcoma		0	5	6	11 (32.4)	
Total		0 (0.0)	15 (44.1)	19 (55.9)	34 (100.0)	*0.827*

a. Tumor grades were based on FNCLCC system; b. Percentage within US; c. Percentage within non-US including fibrosarcoma, myxofibrosarcoma, Leiomyosarcoma, MPNST and synovial sarcoma; d. Chi-square test.

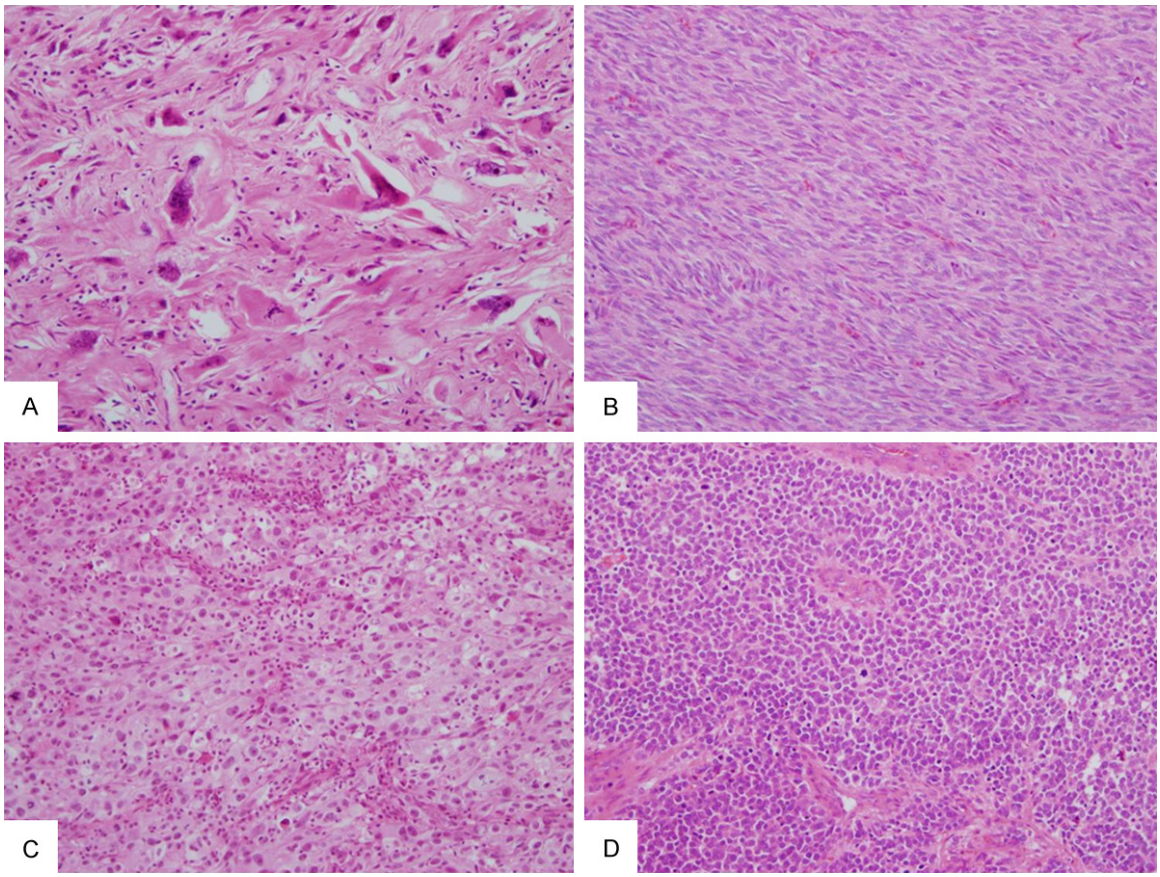

Figure 1. Histologic types of undifferentiated sarcoma. Pleomorphic type shows bizarre cytology and multinucleated giant cells as dominant morphology (A). Spindle cell type is characterized by fascicular pattern of spindle cells (B). Epithelioid type is composed of tumor cells which are similar to metastatic carcinoma or mesothelioma (C). Round cell type is consisted with homogenous small round cell pattern (D).

Table 5. Sites of US and sarcomas of control

Sites	No. (%)						
	US	FS	MFS	DLS	LMS	MPNST	SS
Extremities	34 (69.4)[a]	2 (66.7)	4 (100.0)	2 (33.3)	3 (60.0)	3 (60.0)	11 (100.0)
Upper	5 (10.2)	2 (66.7)	1 (25.0)	0 (0.0)	1 (20.0)	1 (20.0)	3 (27.3)
Lower	29 (59.2)	0 (0.0)	3 (75.0)	2 (33.3)	2 (40.0)	2 (40.0)	8 (72.7)
Trunk	9 (18.4)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)
Neck	2 (4.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CW	4 (8.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)
Back	2 (4.1)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Abd	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
IA	6 (12.2)	0 (0.0)	0 (0.0)	4 (66.7)	2 (40.0)	1 (20.0)	0 (0.0)
O/M	2 (4.1)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
RP	4 (8.2)	0 (0.0)	0 (0.0)	3 (50.0)	2 (40.0)	1 (20.0)	0 (0.0)
Total	49 (100.0)	3 (100.0)	4 (100.0)	6 (100.0)	5 (100.0)	5 (100.0)	11 (100.0)

a. Percentage within individual sarcoma US, undifferentiated sarcoma; FS, fibrosarcoma; MFS, myxofibrosarcoma; DLS, dedifferentiated liposarcoma; LMS, leiomyosarcoma; MPNST, malignant peripheral nerve sheath tumor; SS, synovial sarcoma; CW, chest wall; Abd, abdominal wall; IA, intraabdominal; O/M, omentum/mesentery; RP, retroperitoneum.

(**Figure 2E**). Survival difference between grade 2 and 3 among total sarcomas which included US and non-US was also insignificant (P=0.146) (**Figure 2F**; **Table 6**).

As the overall survivals were examined in the aspect of metastasis, cases with metastasis showed worse prognosis than cases without metastasis among total sarcomas which included US and non-US (P=0.001) (**Figure 3A**). Among the cases without metastasis, there was no survival difference between US and non-US (P=0.305) (**Figure 3B**). Among the cases with metastasis, there was no survival difference between US and non-US too (P=0.218) (**Figure 3C**). Among non-US, cases with metastasis showed worse prognosis than cases without metastasis (P=0.036) (**Figure 3D**) and same result was found among US (P=0.009) (**Figure 3E**; **Table 6**).

Discussion

Diagnostic term of US changed several times. In the previous editions of WHO classification, malignant fibrous histiocytoma (MFH) and high grade undifferentiated pleomorphic sarcoma were used as diagnostic terms [4]. At 2013 edition of WHO classification, these tumors are grouped under the term of undifferentiated sarcoma (US). Under the name of US, WHO classification includes undifferentiated round cell sarcoma, undifferentiated spindle cell sarcoma, undifferentiated pleomorphic sarcoma, undifferentiated epithelioid sarcoma, and undifferentiated sarcoma, NOS [1, 5].

US is known as aggressive sarcoma, and occupy 20% of sarcomas, and most frequently arised in extremities [1, 5]. Also, US is known as most common soft tissue sarcoma which occurs in older adult [6]. But, precise percentage of this tumor is still in controversy [7]. Recent report from Syria listed the percentages of sarcomas as malignant fibrous histiocytoma (23%), liposarcoma (22%), rhabdomyosarcoma (9%), leiomyosarcoma (8%), malignant schwannoma (5%), dermatofibrosarcoma protuberans (5%), synovial sarcoma (10%), fibrosarcoma (13%), extraskeletal chondrosarcoma (1%), and extraskeletal Ewing sarcoma (4%) [3]. When compared with this data, we could notice that diagnostic rate of US was somewhat higher in this institute. According to the statistical data from Jamaica, sarcoma, not otherwise specified (NOS) occupied 20.1% and MFH was 17.9% [8]. If these cases were gathered in one category, it became similar diagnostic rate with that of our study. According to a report, pediatric US is characterized by predominant round cell type, but comparison with our case is not feasible because of small number of round cell type in our study [9]. Altogether, the epidemiologic reports about US are not sufficient. Comprehensive statistical study in USA showed similar incidences of various sarcomas with our results [10]. Report in Nigeria showed that incidence of sarcomas was 11.3% of all sarcomas,

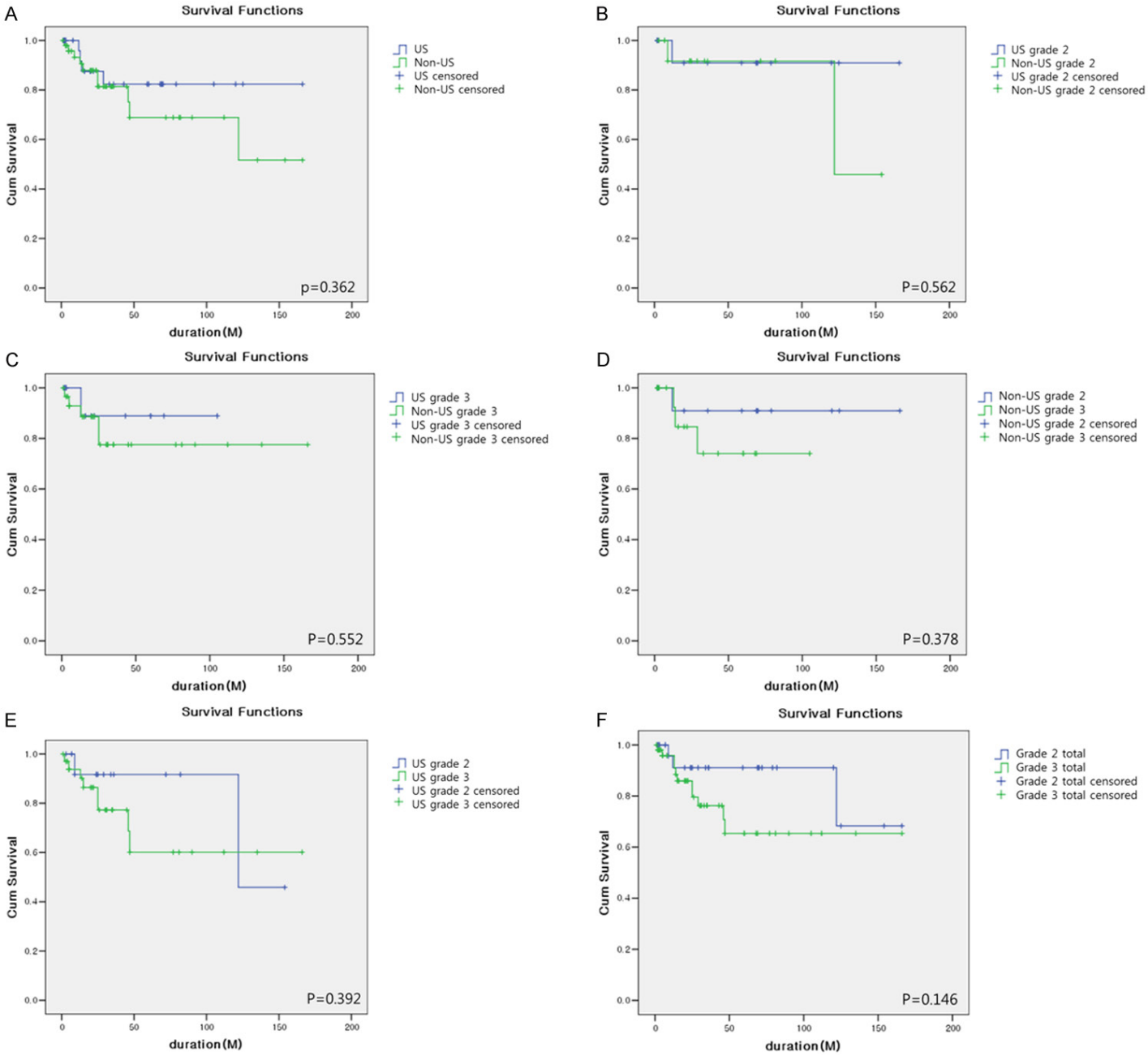
A
Survival Functions
US
Non-US
US censored
Non-US censored
Cum Survival
duration(M)
p=0.362
B
Survival Functions
US grade 2
Non-US grade 2
US grade 2 censored
Non-US grade 2 censored
Cum Survival
duration(M)
P=0.562
C
Survival Functions
US grade 3
Non-US grade 3
US grade 3 censored
Non-US grade 3 censored
Cum Survival
duration(M)
P=0.552
D
Survival Functions
Non-US grade 2
Non-US grade 3
Non-US grade 2 censored
Non-US grade 3 censored
Cum Survival
duration(M)
P=0.378
E
Survival Functions
US grade 2
US grade 3
US grade 2 censored
US grade 3 censored
Cum Survival
duration(M)
P=0.392
F
Survival Functions
Grade 2 total
Grade 3 total
Grade 2 total censored
Grade 3 total censored
Cum Survival
duration(M)
P=0.146

Figure 2. In the aspects of overall survival, there was no difference between US and non-US (P=0.362) (A). Among the grade 2 tumors, there was no difference between them (P=0.562) (B) and showed same result among the grade 3 (P=0.552) (C). Among non-US, there was no difference between grade 2 and 3 (P=0.378) (D) and showed same result with US (P=0.392) (E). Survival difference between grade 2 and 3 among total sarcomas which included US and non-US was also insignificant (P=0.146) (F).

Table 6. Comparisons of overall survival between US and non-US

Histologic types	No. (%)	Mean survival (M) ± SD	*p-value*
Non-US	34	141.968 ± 11.045	
US	49	117.505 ± 13.496	*0.362*
Non-US, grade 2	15	152.000 ± 13.348	
US, grade 2	15	127.250 ± 14.611	*0.562*
Non-US, grade 3	19	82.885 ± 11.130	
US, grade 3	34	111.296 ± 16.392	*0.552*
Non-US, grade 2	15	152.000 ± 13.348	
Non-US, grade 3	19	82.885 ± 11.130	*0.378*
US, grade 2	15	127.250 ± 14.611	
US, grade 3	34	111.296 ± 16.392	*0.392*
Non-US and US, grade 2	30	142.139 ± 12.278	
Non-US and US, grade 3	53	117.645 ± 12.589	*0.146*
Non-US and US, without meta	66	142.391 ± 9.151	
Non-US and US, with meta	17	45.094 ± 6.797	*0.001*
Non-US, without meta	25	157.000 ± 8.731	
US, without meta	41	134.658 ± 12.542	*0.305*
Non-US, with meta	9	51.875 ± 9.331	
US, with meta	8	32.688 ± 7.123	*0.218*
Non-US, without meta	25	157.000 ± 8.731	
Non-US, with meta	9	51.875 ± 9.331	*0.036*
US, without meta	41	134.658 ± 12.542	
US, with meta	8	32.688 ± 7.123	*0.009*

US, undifferentiated sarcoma; non-US, spindle cell sarcomas other than US.

and among them US occupied 21.1% of all sarcomas. Their prevalent sites were lower extremities [11].

Clinically, age and sex distributions of US in this study were similar with other specific high grade sarcomas. This study showed 12.2% of metastatic ratio with lung and bone as dominant target organs. Comparisons of metastatic ratios with other sarcomas were not feasible because there were so many kinds of specific sarcomas and their numbers of cases were not sufficient. Other report insisted that more than 30% of metastatic rate could be estimated [12]. Overall survival of US was not significantly different with other high grade sarcomas in this study. At present, prognosis of these tumors may be more dependent on adequate surgical treatment [13].

There are some controversies about the diagnosis of US. For example, if Murine double-minute 2 (MDM2) amplification was identified by immunohistochemistry or by molecular method, this tumor should be considered as dedifferentiated sarcoma [14]. Even though US was finally diagnosed, there still remain the possibility of other disease entity. As said before, presence of other specific line of differentiation, possibility of dedifferentiated sarcoma, and possibility of non-mesenchymal neoplasm, especially sarcomatoid carcinoma should be considered before diagnosis of US is made. In this study, although histological findings were matched with US, studies about the specific line of differentiation were not sufficiently done in some cases as seen in the immunohistochemical results. We think that the supplimentation of this point should be made.

For the strict limitation of the ranges of US, we should provide some strategies. At first, clinical and pathological informations should be meticulously examined. For example, in the case of high grade sarcoma found in intraabdominal site without evidence of definite line of differentiation, the possibility of dedifferentiated sarcoma should be considered as a differential diagnosis. In this study, considerable portion of intraabdominal sarcomas were dedifferentiated sarcoma. If there was history of carcinoma in certain case, the possibility of metastatic

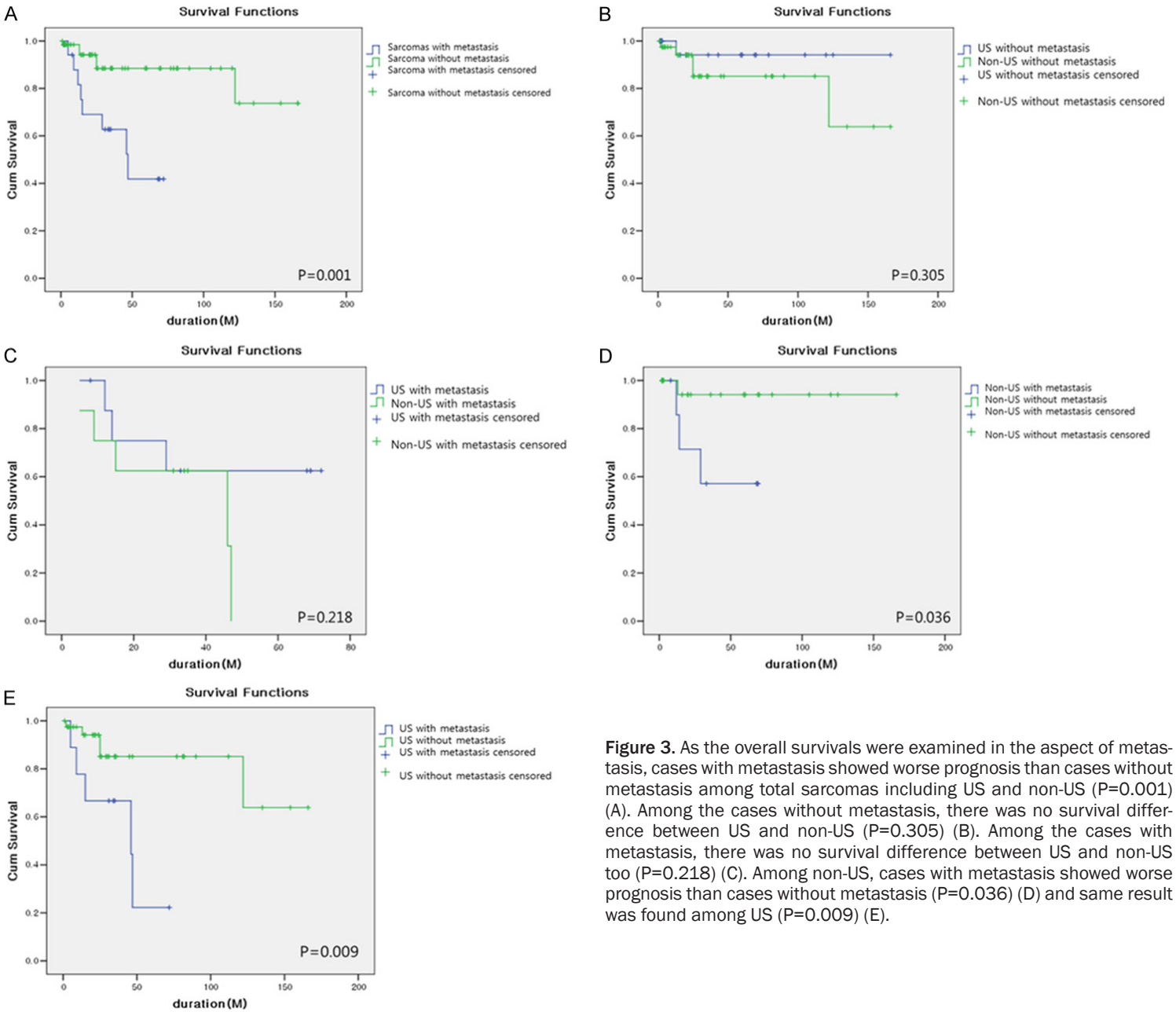

Figure 3. As the overall survivals were examined in the aspect of metastasis, cases with metastasis showed worse prognosis than cases without metastasis among total sarcomas including US and non-US (P=0.001) (A). Among the cases without metastasis, there was no survival difference between US and non-US (P=0.305) (B). Among the cases with metastasis, there was no survival difference between US and non-US too (P=0.218) (C). Among non-US, cases with metastasis showed worse prognosis than cases without metastasis (P=0.036) (D) and same result was found among US (P=0.009) (E).

carcinoma in the form of high sarcomatoid carcinoma should be considered. In this case, use of wide range immunohistochemical panel containing several antibodies for the detection of epithelial differentiation may be great help for the differential diagnosis. As shown in immunohistochemical results, in many cases of this study, immunohistochemical studies for the epithelial differentiation were not done. We think some kind of cytokeratin should be included in the immunohistochemical panel to diagnose US. If histologic findings such as myxoid change and complex capillary pattern were found, myxofibrosarcoma can be a possible diagnosis. Immunohistochemically, brand-new antibodies can be useful in the differential diagnosis. As mentioned above, MDM2 is known as associated with atypical lipomatous tumor and dedifferentiated liposarcoma which is closely related with atypical lipomatous tumor [14, 15]. In certain cases of myxofibrosarcoma, AMACR amplification was identified [16]. Other report showed that LMP2/beta-1i and cyclin B1 can be useful for the diagnosis of uterine leiomyosarcoma [17], but the application for the cases of soft tissue leiomyosarcoma is not known.

Recently, molecular pathology has appeared as important diagnostic method. Already, many important genetic translocations were identified and used as diagnostic markers using fluorescent in situ hybridization (FISH). Not only the translocations, but also complex genetic abnormalities were found [18, 19]. Some kind of genetic abnormalities were reported for US [20-22], but their diagnostic values are investigational. Collectively, US in this institute showed higher diagnostic rate than preexisting but limited reports. To establish accurate epidemiology of US in stricter range, not only clinical and pathological examination, but also reinforcement and supplementation in the field of immunohistolochemistry and especially molecular pathology is mandatory. It may be certain that there will be no great changes in classification and differential diagnosis of US even though discrimination of specific sarcomas from US is important task of pathologists. Because US and other spindle cell sarcoma showed similar clinical outcomes according to this study, clinical approaches for US could be safely followed that of other high grade sarcomas. We hope this study could contribute to be a data base about US and useful data for further research.

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Disclosure of conflict of interest

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