Soft tissue sarcoma in adolescent and young adult patients: A retrospective study using a nationwide bone and soft tissue tumor registry in Japan.

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Research article

Keywords: Soft tissue sarcoma, Adolescents and young adults, Cancer survival, Japan, Database, MPNST

DOI: https://doi.org/10.21203/rs.2.20871/v2

Abstract

Background

Compared to young children or older adults, the prognoses of adolescent and young adult (AYA) patients with cancer, i.e., those aged from 15 to 39 years, have not improved. In this study, we focused on soft tissue sarcoma (STS) in AYA patients and aimed to determine whether there is a correlation between the AYA age group and overall poor cancer survival in STS. We further aimed to determine which histologic subtypes are more common in AYA patients and investigate the cause of poor outcomes in this group.

Methods

The medical records of 5853 Japanese patients diagnosed with STS between 2006 and 2013 were accessed from the Bone and Soft Tissue Tumor registry (BSTT). We analyzed and compared the epidemiological features of AYA patients with those of other age groups. The cancer survival rates were calculated using the Kaplan-Meier method. Cox proportional hazards models were used to analyze the prognostic factors for cancer survival. The primary endpoint for prognosis was the occurrence of tumor-related death.

Results

On multivariate analysis, age was not a prognostic factor for poor cancer survival among these patients. Compared to the same categories in other age groups, the proportions of myxoid/round cell liposarcomas, synovial sarcomas, malignant peripheral nerve sheath tumors (MPNST), primitive neuroectodermal tumor, and rhabdomyosarcoma in AYA patients were the highest, but none of the categories were significantly more prevalent in AYA patients. The cancer survival rates of AYA patients with MPNST were poorer than those of the other age groups; however, AYA age was not a prognostic factor on multivariate analysis in MPNST patients.

Conclusions

Our study is the first to investigate STS in AYA patients using the nationwide BSTT registry. Our findings demonstrate that AYA age is not a prognostic factor for poor cancer survival among those with STS in Japan.

Background

Cancer survival rates have significantly improved over time, except among adolescent and young adult (AYA) patients with cancer, i.e., those aged from 15 to 39 years [1]. This has been partly related to the difference in biological behavior, a lower enrollment in clinical trials, and the variability of treatment across settings [2]. AYAs with cancer comprise a unique population and have gained research and media attention in recent years. In 2005, the Joint Progress Review Group of the National Cancer Institute and

the LiveStrong Foundation in Adolescent and Young Adult Oncology convened to examine the state of science associated with cancer among AYAs [3].

Lymphoma, melanoma, testicular cancer, sarcoma, thyroid cancer, leukemia, and breast cancer are the most common cancers in AYA patients [4]. Of these, sarcomas are the most frequent, accounting for up to 9% of total malignancies in this population [5]. However, sarcoma is a rare disease with an annual incidence rate of 5.6 per 100,000 individuals in Europe [6]. Furthermore, they have widely diverse pathologies with more than 70 histological subtypes [7], and may develop at any age including childhood, occurring anywhere from the head to the feett, with varying aggressiveness, even within the same histological subtype [8]. It is therefore difficult to obtain the data of sarcoma in AYAs. Moreover, studies focusing on the clinical outcomes of AYAs with sarcoma are scarce.

In 2014, the Bone and Soft Tissue Tumor (BSTT) registry in Japan became available for clinical research. The BSTT is a nationwide organ-specific cancer registry for bone and soft tissue tumors and allows large-scale nationwide epidemiological investigations in AYA patients with sarcoma in Japan. We have previously used this database for a retrospective study of bone sarcoma in AYA patients in Japan [9]. In this study, we performed a large-scale nationwide epidemiological investigation of AYA patients with soft tissue sarcoma (STS) in Japan with the aim to determine whether there is a correlation between the AYA age group and overall poor cancer survival for STS and to identify the more common histologic subtypes in this age group. We also investigated the risk factors of the poor outcomes in AYA patients with STS.

Methods

Data source

The Japanese Orthopaedic Association (JOA) launched the BSTT registry in the 1950s. It is a nationwide patient data collection system for organ-specific bone and soft tissue tumors. This system includes almost all musculoskeletal malignant tumors in Japan. [8] Detailed data on patients with primary bone and soft tissue tumors (both benign and malignant) and metastatic bone tumors treated at the participating hospitals were collected annually. The survey included basic demographic data of the patient as well as information on the tumor, surgery, and any non-surgical treatment. The follow-up survey was conducted 2, 5, and 10 years after the initial registration. It included information on several outcomes at the time of the latest follow-up.

Although it is similar to the National Cancer Institute's Surveillance, Epidemiology, and End Results Program database, our registry has several advantages. One of these is that treating physicians registered several disease-specific detailed data including histologic findings, treatment modalities, and surgical, functional, and oncologic outcomes. These advantages improved the precision of our registry for detailed epidemiological studies. Use of the data from the BSTT registry for clinical research was approved by the Musculoskeletal Tumor Committee of the JOA in 2014 [9] [10]. This study was approved by the Institutional Review Board of the JOA.

Data extraction

A total of 7759 patients with STS listed in the BSTT registry between 2006 and 2013 were identified. Data including the year of registration, demographic characteristics, tumor size, location, grade, histological characteristics, Tumor-Node-Metastasis and Enneking stages, treatment details (surgical vs. non-surgical), and prognosis at the last follow-up visit (no evidence of disease, alive with disease, death from disease, or death from other causes) were obtained from the database. Liposarcomas were subdivided owing to the variable behavior of the different subtypes. Well-differentiated liposarcomas were excluded because they were considered borderline malignant. Histologic subtypes with larger absolute numbers or a higher ratio in AYA patients were analyzed as an independent histological subtype. The other subtypes were assigned to the high-grade or low-grade sarcoma groups. Patients who were registered less than 1 year from the study enrollment date and those with missing data were excluded. Therefore, the data of 5853 patients with primary STS and a prognosis of over one year were extracted from the database.

Statistical analyses

The primary endpoint for prognosis was tumor-related death. Cancer survival was defined as the period from the date of diagnosis until tumor-related death and was estimated using the Kaplan-Meier method. Patients without tumor-related deaths or those who died from other causes were censored at their last follow-up visit. The factors associated with survival were analyzed using Cox proportional hazards models. Control variables for multivariate analysis were indicated as “references.” These included AYA, female sex, low-grade tumor, tumor size ≤5 cm, location of the tumor in the upper extremity, non-surgical treatment, limb salvage after surgical removal of tumor, non-chemotherapy regimen, non-radiation therapy, non-metastatic, and superficial. The alpha level for significance was set at a p value of 0.05. All statistical analyses were conducted using IBM SPSS version 19.0 (IBM SPSS, Armonk, NY, USA).

Results

Of the 7759 patients with STS (4309 male and 3450 women) identified, 210 (2.7%) were aged ≤14 years (children), 1467 (18.9%) were aged 15–39 years (AYAs), 2771 (35.7%) were aged 40–64 years (adults), and 3311 (42.7%) were aged ≥65 years (elderly). The common histologic subtypes were undifferentiated pleomorphic sarcomas, 2030 (26.2%); myxoid/round cell liposarcomas (MRLS), 956 (12.3%); synovial sarcomas (SySa), 555 (7.2%); and malignant peripheral nerve sheath tumors (MPNST), 478 (6.2%). Meanwhile, the histologic subtypes with a higher ratio in AYA patients were MRLS, 286 (19.5%); SySa, 259 (17.7%); MPNST, 130 (8.9%); primitive neuroectodermal tumor (PNET), 111 (7.6%); and rhabdomyosarcoma (RMS), 94 (6.4%).

Table 1 shows the patient characteristics and treatments according to the age groups. The most predominant subtype among the AYA patients was MRLS, 286(19.5%), followed by SySa, 259 (17.7%). No other categories demonstrated differences in prevalence in the AYA patient groups when compared to the same categories in other age groups.

Table 2 shows the overall 5-year cancer survival rates among patients with STS with unadjusted and adjusted hazard ratios (HRs) derived from Cox proportional hazard models. The cancer survival rates of AYA patients with STS were poorer than those of adult age groups. However, they were not poorer than that of the child and the elderly age groups. On multivariate analysis, age was not a prognostic factor for poor cancer survival among AYA patients with STS.

Overall, the prognostic factors for poor cancer survival in patients with STS were age 40-64 years (HR: 1.35, 95% confidence interval [CI]: 1.11–1.65, *P*=0.003), age ≥65 years (HR: 2.28, 95% CI: 1.47–2.34, *P*<0.001), high tumor grade (HR: 3.41, 95% CI: 2.37-4.91, *P*<0.001), tumor size >5 cm and ≤10 cm and >10 cm (HR: 1.71 and 2.57, 95% CI: 1.38-2.12 and 2.06-3.19, *P*<0.001, respectively), multiple tumor location (HR: 2.32, 95% CI: 1.59-3.39, *P*=0.014), non-surgical treatment compared with surgery (HR: 0.58, 95% CI: 0.49-0.69, *P*<0.001), amputation (HR: 1.69, 95% CI: 1.35-2.11, *P*<0.001), positive surgical margins (HR: 1.65, 95% CI: 1.27-2.14, *P*<0.001), chemotherapy (HR: 1.59, 95% CI: 1.35-1.87, *P*<0.001), radiation (HR: 1.38, 95% CI: 1.20-1.59, *P*<0.001), the presence of metastases (HR: 4.68, 95% CI: 3.97-5.51, *P*<0.001), and deep tumor location (HR: 1.34, 95% CI: 1.07-1.67, *P*=0.041). The prevalence of these poor prognostic factors excluding age was not higher among the AYA patients compared with other age groups.

Figure 1 shows the Kaplan-Meier plots for cancer survival rates in patients with STS in general and its subtypes. The cancer survival rates of AYA patients with MPNST were poorer than those of other age groups, whereas those for AYA patients with other histologic subtypes were not significantly different from those of other age groups. Therefore, data from AYA patients with MPNST were analyzed to better understand the factors that caused these poor outcomes.

Table 3 shows the characteristics of MPNST based on age groups. MPNST was more prevalent in male AYA patients, had a larger tumor size, appeared predominantly on the head and neck and in deeper layers, had a higher rate of positive surgical margins, and presented with more metastatic lesions at the first visit in AYA patients than in other age groups.

Table 4 shows the results of univariate and multivariate analyses of the prognostic factors for cancer survival in patients with MPNST. The cancer survival rates of AYA patients with MPNST were poorer than those of other age groups on univariate analyses. Tumor size >5 cm and ≤10 cm (HR: 2.20, 95% CI: 1.01–4.77, *P*=0.046), tumor size >10 cm (HR: 2.54, 95% CI: 1.17–5.50, *P*=0.018), non-surgical treatment compared with surgery (HR: 0.51, 95% CI: 0.29-0.92, *P*=0.024), radiation (HR: 1.70, 95% CI: 0.67-2.06, *P*=0.035), the presence of metastases (HR: 3.11, 95% CI: 1.76-5.51, *P*<0.001), and deep tumor location (HR: 2.71, 95% CI: 1.23–5.98, *P*=0.014) were prognostic factors for poor cancer survival in patients with MPNST, but who were not AYA.

Discussion

In this study, we presented the nationwide statistics and outcomes in AYA patients with STS. The cancer survival rates of AYA patients with STS were poorer than those of adult age groups; however, they were not poorer than those of the child and the elderly age groups. Among those with STS, the AYA age range

was not a prognostic factor for poor cancer survival on multivariate analysis. Although few reports have compared cancer survival in AYA patients and other age groups, it has been suggested that AYA patients with STS have poorer outcomes than those of the child and adult age groups [5]; this differed from our findings. This difference may be related to the functioning of the Japanese health insurance system, in which public medical insurance covers 70–90% of the treatment costs. This increases to 100% for people in need. This ensures universal and equal access to medical treatment. Insurance coverage rates are significantly lower in AYA patients in the United States [11], and cancer survivors in this group with no health insurance may not receive cancer-related medical care, as opposed to those with insurance [12].

In this cohort, MRLS was the predominant subtype of STS among AYA followed by SySa, consistent with previous reports [5,8,13–15]. We could not compare our results with those of previous reports owing to the differences in age ranges. In addition, those studies also included patients with gastrointestinal stromal tumors and/or Kaposi's sarcomas.

Despite the small number of children included in this study, the survival rates of AYA patients with MPNST were poorer than those of the other age groups. However, multivariate analysis demonstrated that being an AYA was not an independent poor prognostic factor for cancer survival in patients with MPNST. Tumor size >10 cm, deep tumor location, non-surgical treatment, the presence of metastases, and deep tumor location were poor prognostic factors for cancer survival in patients with MPNST. Compared to other age groups, the characteristics that were more prevalent in AYA patients with MPNST were tumor size >10 cm, non-surgical treatment, radiation, metastatic lesion(s) at presentation, and deep tumor location. Therefore, certain prognostic factors for MPNST were found particularly more frequently in AYA patients with this tumor. This concordance may be attributed to the poorer survival rates in AYA patients with MPNST than in the other age groups.

One possible reason why the survival rates of AYA patients with MPNST were poorer than those of the other age groups is that a larger part of AYA patients with MPNST may have neurofibromatosis type 1 (NF1). MPNST patients with NF1 have been reported to be significantly younger at the time of MPNST diagnosis than those with sporadic tumors (median age, 26 years vs. 53 years) and have poor outcomes [16,17]. Thus, the mean age of MPNST patients with NF1 is within the AYA age group. The 5-year survival rate of MPNST patients with NF1 ranges from 21% to 49.7%. Meanwhile, the 5-year survival rate of MPNST patients with non-NF1 ranges from 42% to 64.9% [17–20]. However, our study did not distinguish NF1 patients. Thus, future analysis is required to validate this finding.

Our study has several limitations. First, findings from long-term observation of patients in the past 10 years were not available. Second, although the JOA-certified hospitals treat almost all patients with STS in Japan and the participation of all 89 JOA-certified hospitals in this nationwide registry is compulsory, the participation of other hospitals is voluntary. Therefore, only data from the participating hospitals were analyzed. Third, data on structures (pediatric department, adult department, mixed structures) in which these patients were treated were not included in the database. Fourth, the quality of life (QOL) including social functioning and employment in AYA cancer survivors has become an important health issue in

recent years; however, the factors related to the QOL were not registered in BSTT [21]. Thus, the QOL of AYA cancer survivors was not analyzed. Fifth, our database does not contain chronological information about chemotherapy and radiotherapy, just contain adjuvant or palliative. Thus, the chemotherapy and/or radiotherapy administered pre- or postoperatively or both were analyzed as merged data.

Conclusion

In this study, we evaluated the descriptive epidemiology and clinical outcomes of AYA patients with STS using a nationwide and large-scale database. We found that AYA age is not a prognostic factor for poor cancer survival among those with STS in Japan. However, AYA patients with MPNST had a poorer survival compared to other age groups. Our findings will provide useful information for the clinical management of AYA patients with STS. Further studies including larger cohorts with more diverse characteristics are warranted to validate our findings.

Abbreviations

ASPS, alveolar soft part sarcoma

AYA, adolescent and young adult

BSTT, Bone and Soft Tissue Tumor

CCS, clear cell sarcoma

CI, confidence interval

HR, hazard ratios

JOA, Japanese Orthopaedic Association

MPNST, malignant peripheral nerve sheath tumors

MRLS, myxoid/round cell liposarcoma

NF1, neurofibromatosis 1

PNET, primitive neuroectodermal tumor

QOL, quality of life

RMS, rhabdomyosarcoma

SySa, synovial sarcoma

Declarations

Ethics approval and consent to participate

The research was approved by the Ethics Committee of the Japanese Orthopaedic Association on March 17, 2016. This was a retrospective study performed using data from the Bone and Soft Tissue Tumor registry; the authors were not involved in the collection of this data. Patients were informed that their data would be used for research, and the data were de-identified before addition to the database. Retrieval of the data from this database occurred in an unlinked manner. As the data had been anonymized, the Ethical Guidelines for Epidemiological Research (Ministry of Education, Culture, Sports, Science and Technology, and Ministry of Health, Labour and Welfare of Japan) were not applicable to this study. Based on the Ethical Guidelines on Biomedical Research Involving Human Subjects (Ministry of Education, Culture, Sports, Science and Technology, and Ministry of Health, Labour and Welfare of Japan), clinicoepidemiological studies conducted on medical databases constitute research carried out on pre-existing material and data and do not require any interventions or interactions with patients. For these studies, including this one, written informed consent was not compulsory.

Consent for publication

Not Applicable.

Availability of data and materials

The datasets generated or analyzed during the current study are not publicly available as they are anonymized patient data from the Japanese Orthopaedic Association. However, the data are available from the authors upon reasonable request and with permission of the Japanese Orthopaedic Association.

Competing interests

The authors declare that they have no competing interests.

Funding

None.

Authors' contributions

TF, KO, TA, and AK contributed to the conception and design of the study. TF, KO, TA, and KT contributed to the analysis of data. All authors contributed to the interpretation of results. TF drafted the article; all authors revised it critically and approved the final version submitted for publication. All authors have read and approved the final manuscript.

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Acknowledgments

We would like to thank all the patients who volunteered for this study.

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Tables

Table 1. Patient characteristics by age group

	AYA (15-39years)		Overall		Child (≤14years)		Adult (40-64years)		Elderly (65- years)		P value
	N	%	N	%	N	%	N	%	N	%	
Total	1467		7759		210		2771		3311		
Sex											<0.001
Male	778	53.0%	4309	55.5%	91	43.3%	1571	56.7%	1869	56.4%	
Female	689	47.0%	3450	44.5%	119	56.7%	1200	43.3%	1442	43.6%	
Histologic grade											<0.001
Low	301	20.5%	1454	18.7%	16	7.6%	616	22.2%	521	15.7%	
High	1166	79.5%	6305	81.3%	194	92.4%	2155	77.8%	2790	84.3%	
Histologic subtype											<0.001
MRLS	286	19.5%	956	12.3%	3	1.4%	449	16.2%	218	6.6%	
SySa	259	17.7%	555	7.2%	36	17.1%	188	6.8%	72	2.2%	
MPNST	130	8.9%	478	6.2%	14	6.7%	173	6.2%	161	4.9%	
PNET	111	7.6%	210	2.7%	29	13.8%	54	1.9%	16	0.5%	
RMS	94	6.4%	271	3.5%	79	37.6%	51	1.8%	47	1.4%	
UPS	90	6.1%	2030	26.2%	3	1.4%	629	22.7%	1308	39.5%	
ASPS	77	5.2%	110	1.4%	13	6.2%	17	0.6%	3	0.1%	
EpiSa	73	5.0%	146	1.9%	4	1.9%	51	1.8%	19	0.5%	
CCS	51	3.5%	107	1.4%	2	1.0%	37	1.3%	17	0.5%	
High grade others	182	12.4%	2109	27.2%	16	7.6%	790	28.5%	1121	33.9%	
Low grade others	114	7.8%	787	10.1%	11	5.2%	332	12.0%	330	10.0%	
Tumor size (cm)											<0.001
≤5 cm	484	33.0%	2142	27.6%	97	46.2%	716	25.8%	845	25.5%	
>5 cm and ≤10 cm	530	36.1%	2916	37.6%	78	37.1%	989	35.7%	1319	39.8%	
>10 cm	333	22.7%	2138	27.6%	21	10.0%	839	30.3%	945	28.5%	
Unknown	120	8.2%	563	7.3%	14	6.7%	167	6.0%	202	6.1%	
Tumor location											<0.001

Upper extremity	182	12.4%	963	12.4%	48	22.9%	289	10.4%	444	13.4%	
Lower extremity	671	45.7%	3904	50.3%	88	41.9%	1412	51.0%	1733	52.3%	
Trunk	486	33.1%	2493	32.1%	45	21.4%	950	34.3%	1012	30.6%	
Head and neck	80	5.5%	216	2.8%	17	8.1%	56	2.0%	63	1.9%	
Multiple disease	48	3.3%	183	2.4%	12	5.7%	64	2.3%	59	1.8%	
Surgery	1120	76.3%	6200	79.9%	150	71.4%	2227	80.4%	2703	81.6%	<0.001
Chemotherapy	795	54.6%	2567	33.2%	148	72.2%	1159	41.9%	465	14.1%	<0.001
Adjuvant	536	67.4%	1653	64.4%	112	75.5%	760	65.6%	245	52.7%	
Palliative	246	30.9%	858	33.4%	29	19.6%	371	32.0%	212	45.6%	
Unknown	13	1.6%	56	2.2%	7	4.7%	28	2.4%	8	1.7%	
Radiotherapy	370	25.5%	1925	25.0%	80	39.6%	645	23.4%	830	25.2%	<0.001
Adjuvant	196	53.0%	1156	60.1%	46	57.5%	398	61.7%	516	62.2%	
Palliative	70	18.9%	322	16.7%	4	5.0%	114	17.7%	134	16.1%	
Radical	94	25.4%	393	20.4%	30	37.5%	108	16.7%	161	19.4%	
Unknown	10	2.7%	54	2.8%	0	0%	25	3.9%	19	2.3%	

SD: standard deviation, AYA: adolescent and young adult, MRLS: myxoid/round cell liposarcoma, SySa: synovial sarcoma, MPNST: malignant peripheral nerve sheath tumors, PNET: primitive neuroectodermal tumor, RMS: rhabdomyosarcoma, UPS: undifferentiated pleomorphic sarcoma, ASPS: alveolar soft part sarcoma, EpiSa: epithelioid sarcoma, CCS: clear-cell sarcoma

Table 2. Univariate and multivariate analyses of prognostic factors for overall cancer survival in soft tissue sarcoma

	No. of patients (%)	5-year survival (%)	Univariate analysis		Multivariate analysis	
			Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Total	5853	72.9%				
Age						
AYA (15-39 years)	1149	69.9%	Reference		Reference	
Child (≤14 years)	165	71.8%	0.80 (0.55-1.17)	0.25	0.94 (0.59-1.49)	0.800
Adult (40-64 years)	2127	75.2%	0.84 (0.71-0.99)	0.033	1.35 (1.11-1.65)	0.003
Elderly (≥65 years)	2412	72.5%	0.98 (0.84-1.15)	0.812	2.28 (1.85-2.79)	<0.001
Sex						
Female	2638	75.5%	Reference		Reference	
Male	3215	70.7%	1.33(1.18-1.50)	<0.001	1.14(0.99-1.31)	0.061
Histologic grade						
Low	1065	93.2%	Reference		Reference	
High	4788	68.2%	6.96 (5.05-9.58)	<0.001	3.41(2.37-4.91)	<0.001
Tumor size(cm)						
≤5 cm	1635	85.8%	Reference		Reference	
>5 cm and ≤10 cm	2216	74.3%	2.23 (1.84-2.70)	<0.001	1.71 (1.38-2.12)	<0.001
>10 cm	1587	57.2%	4.07 (3.38-4.90)	<0.001	2.57 (2.06-3.19)	<0.001
Tumor location						
Upper extremity	728	83.8%	Reference		Reference	
Lower extremity	2955	76.8%	1.38 (1.09-1.75)	0.007	1.14 (0.88-1.49)	0.331
Trunk	1870	65.7%	2.51 (1.98-3.17)	<0.001	1.77 (1.34-2.32)	<0.001
Head and neck	173	66.2%	2.62 (1.83-3.75)	<0.001	1.73 (1.07-2.78)	0.025
Multiple	127	35.2%	6.69 (4.87-9.20)	<0.001	2.32 (1.59-3.39)	<0.001
Surgery						
−	692	51.7%	Reference		Reference	
+	4272	77.3%	0.315 (0.278-0.357)	<0.001	0.58 (0.49-0.69)	<0.001
Limb salvage status						
Limb salvage	5072	76.4%	Reference		Reference	

Amputation	322	53.0%	1.98 (1.62-2.43)	<0.001	1.69 (1.35-2.11)	<0.001
Chemotherapy						
–	3737	83.1%	Reference		Reference	
+	2106	56.4%	2.69 (2.39-3.03)	<0.001	1.59 (1.35-1.87)	<0.001
Radiation						
–	4231	79.6%	Reference			
+	1604	56.7%	2.42 (2.15-2.72)	<0.001	1.38 (1.20-1.59)	<0.001
Metastasis						
–	5030	80.5%	Reference		Reference	
	771	22.9%	7.95 (7.04-8.98)	<0.001	4.68 (3.97-5.51)	<0.001
Tumor Depth						
Superficial	1453	87.3%	Reference		Reference	
Deep to fascia	4280	78.3%	2.83 (2.35-3.42)	<0.001	1.34 (1.07-1.67)	0.010

AYA: Adolescent and Young Adult, CI: confidence interval

Table 3. Characteristics of MPNST patients according to age group

	AYA (15-39 years)		Overall		Child (≤14 years)		Adult (40-64 years)		Elderly (≥65 years)		P value
	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%	No. of patients	%	
Sex											
Male	61	58.7%	185	52.6%	2	33.3%	72	54.5%	50	45.5%	0.181
Female	43	41.3%	167	47.4%	4	66.7%	60	45.5%	60	54.5%	
Histologic grade											
Low	17	16.3%	56	15.9%	2	33.3%	21	15.9%	16	14.5%	0.676
High	87	83.7%	296	84.1%	4	66.7%	111	84.1%	94	85.5%	
Tumor size (cm)											
Total											
≤5 cm	22	22.4%	83	25.4%	3	50.0%	31	25.2%	27	27.0%	0.204
>5 cm and ≤10 cm	38	38.8%	147	45.0%	1	16.7%	61	49.6%	47	47.0%	
>10 cm	38	38.8%	97	29.7%	2	33.3%	31	25.2%	26	26.0%	
Tumor location											
Upper extremity	12	11.5%	46	13.1%	1	16.7%	14	10.6%	19	17.3%	0.706
Lower extremity	26	25.0%	119	31.3%	2	33.3%	47	35.6%	35	31.8%	
Trunk	48	46.2%	153	43.5%	3	50.0%	57	43.2%	45	40.9%	
Head and neck	12	11.5%	27	7.7%	0	0.0%	9	6.8%	6	5.5%	
Multiple disease	6	5.8%	16	4.5%	0	0.0%	9	3.8%	6	4.5%	
Surgery	76	73.1%	285	81.0%	4	66.7%	111	84.1%	94	85.5%	0.064

Chemotherapy	57	55.3%	134	38.2%	2	33.3%	63	47.7%	12	10.9%	
Adjuvant	28	49.1%	64	47.8%	2	100%	30	47.6%	4	33.3%	<0.001
Palliative	29	50.9%	67	50.0%	0	0%	30	47.6%	8	66.7%	
Unknown	0	0%	3	2.2%	0	0%	3	4.8%	0	0%	
Radiotherapy	34	33.0%	106	30.2%	1	16.7%	42	31.8%	29	26.4%	
Adjuvant	14	41.2%	56	52.8%	1	100%	23	54.8%	18	62.1%	0.619
Palliative	13	38.2%	28	26.4%	0	0%	11	26.2%	4	13.8%	
Radical	6	17.6%	20	18.9%	0	0%	7	16.7%	7	24.1%	
Unknown	1	2.9%	2	1.9%	0	0%	0	0%	0	0%	
Metastasis	21	20.2%	51	14.7%	0	0.0%	18	13.7%	12	11.2%	
											0.197
Depth											
superficial	16	16.0%	87	25.7%	0	0.0%	32	25.0%	39	37.1%	0.003
deep	84	84.0%	252	74.3%	6	100.0%	96	75.0%	66	62.9%	

MPNST: malignant peripheral nerve sheath tumors, CI: confidence interval

Table 4. Univariate and multivariate analyses of prognostic factors for cancer survival in MPNST patients

		Univariate analysis		Multivariate analysis	
	No. of patients (%)	Hazard ratio (95% CI)	P value	Hazard ratio (95% CI)	P value
Total	256				
Age					
AYA (15-39 years)	68	Reference		Reference	
Child (≤14 years)	4	0.000 (0.000-2.69E+□□□)	0.95	0.000 (0.000-)	0.971
Adult (40-59 years)	101	0.62 (0.39-0.97)	0.036	0.73 (0.43-1.25)	0.250
Elderly (≥65 years)	83	0.45 (0.26-0.77)	0.004	0.71 (0.36-1.40)	0.318
Sex					
Female	122	Reference		Reference	
Male	134	1.63 (1.07-2.46)	0.022	1.17 (0.73-1.89)	0.510
Histologic grade					
Low		Reference		Reference	
High		4.09 (1.66-10.06)	0.002	2.71 (0.94-7.84)	0.065
Tumor size					
≤5 cm	66	Reference		Reference	
>5 cm and ≤10 cm	125	2.65 (1.28-5.46)	0.009	2.20 (1.01-4.77)	0.046
>10 cm	65	3.71 (1.78-7.72)	<0.001	2.54 (1.17-5.50)	0.018
Tumor location					
Upper extremity	34	Reference		Reference	
Lower extremity	89	1.00 (0.49-2.01)	0.99	0.74 (0.34-1.58)	0.430
Trunk	110	1.10 (0.57-2.14)	0.775	0.78 (0.38-1.61)	0.504
Head and neck	16	1.53 (0.64-3.70)	0.342	1.14 (0.41-3.20)	0.801
Multiple	7	2.59 (1.00-6.70)	0.049	1.48 (0.51-4.31)	0.474
Surgery					
−	67	Reference		Reference	
+	285	0.28 (0.18-0.42)	<0.001	0.51 (0.29-0.92)	0.024
Chemotherapy					

–	217	Reference		Reference	
+	134	2.44 (1.62-3.67)	<0.001	1.17 (0.67-2.06)	0.579
Radiation					
–	245	Reference		Reference	
+	106	2.44 (1.63-3.65)	<0.001	1.70 (0.67-2.06)	0.035
Metastasis					
–	235	Reference		Reference	
	21	5.47 (3.57-8.37)	<0.001	3.11 (1.76-5.51)	<0.001
Tumor Depth					
Superficial	68	Reference		Reference	
Deep to fascia	125	3.92 (1.89-8.10)	<0.001	2.71 (1.23-5.98)	0.014

AYA: Adolescent and Young Adult, CI: confidence interval

Figures

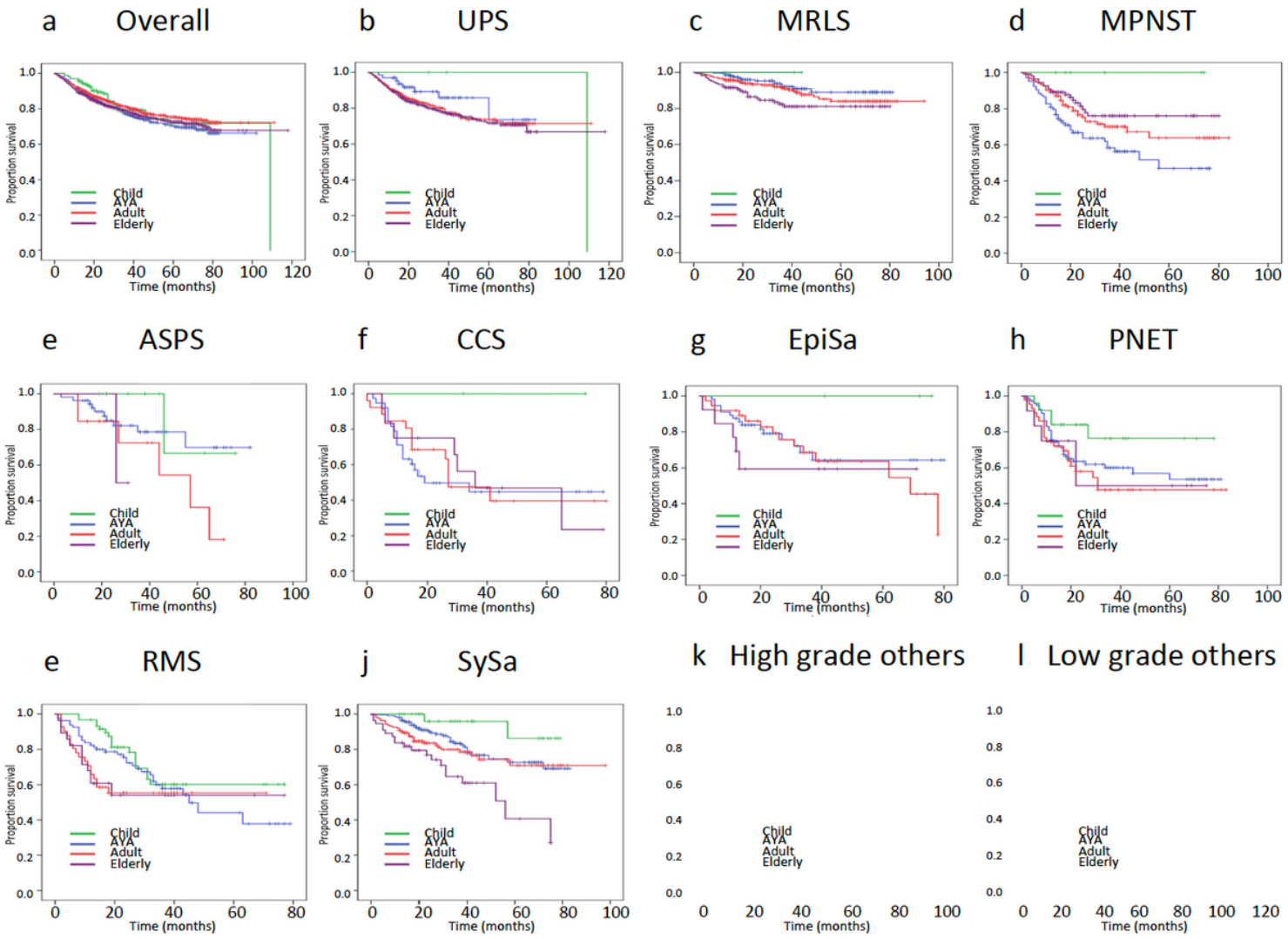

Figure 1

Kaplan-Meier survival curves showing survival rates for all tumors. The results show survival for overall sarcomas (a), UPS (b), MRLS (c), MPNST (d), ASPS (e), CCS (f), EpiSa (g), PNET (h), RMS (i), SySa (j), other high-grade tumors (k), and other low-grade tumors (l) stratified by age. Child: ≤14 years, adolescent and young adult (AYA): 15–39 years, adult: 40–64 years, and elderly: ≥65 years.