# Descriptive Epidemiology and Outcomes of Soft Tissue Sarcomas in Adolescent and Young Adult Patients in Japan

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**Research article**

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

**Posted Date:** January 15th, 2020

**DOI:** https://doi.org/10.21203/rs.2.20871/v1



**Version of Record:** A version of this preprint was published at Japanese Journal of Clinical Oncology on April 1st, 2021. See the published version at https://doi.org/10.1093/jjco/hyab044.

## 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

The survival rates for cancer 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]. Further, they have widely diverse pathologies, with more than 70 histological subtypes [7], and may develop at any age including childhood, occurring anywhere from head to foot, with varying aggressiveness, even within the same histological subtype [8]. It is therefore difficult to obtain 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 the present 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 aimed to investigate 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 are collected annually. The survey includes basic demographic data of the patient as well as information on the tumor, surgery, and any treatment other than surgery. The follow-up survey is conducted 2, 5, and 10 years after the initial registration. It includes 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 register several disease-specific detailed data including histologic findings, treatment modalities, and surgical, functional, and oncologic outcomes. These advantages improve the precision of our registry for detailed epidemiological studies. Use of the data from the BSTT registry for purposes of 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, TNM 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 different subtypes of liposarcoma. Well-differentiated liposarcomas were excluded because they were considered borderline malignant. Histologic subtypes that had 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. Date on 5853 patients with primary soft tissue sarcoma 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 hazard models. Control variables for multivariate analysis were indicated as "references"; these included AYA, female sex, low-grade tumor, tumor size $\leq$5 cm, location of the tumor in the upper extremity, limb salvage after surgical removal of tumor, surgical margin negative, non-metastatic, and superficial. The alpha level for statistical 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 $\leq$ 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 $\geq$ 65 years (elderly). The common histologic subtypes were undifferentiated pleomorphic sarcomas (UPS), myxoid/round cell liposarcomas (MRLS), synovial sarcomas (SySa), and malignant peripheral nerve sheath tumors (MPNST). Meanwhile, the histologic subtypes with a higher ratio in AYA patients were MRLS, SySa, MPNST, primitive neuroectodermal tumor (PNET), and rhabdomyosarcoma (RMS).

Table 1 shows the patient characteristics and treatments according to the age groups. The most predominant subtype among AYA was MRLS (19.5%), followed by SySa (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, it was 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 > 65 years (HR: 1.86; 95% confidence interval [CI]: 1.47–2.34; P < 0.001), male sex (HR: 1.20; 95% CI: 1.02–1.42; P = 0.028), high tumor grade (HR: 4.08; 95% CI: 2.72–6.12; P <

0.001), tumor size > 5 cm and ≤ 10 cm and > 10 cm (HR: 1.73 and 2.61; 95% CI: 1.35–2.22 and 2.02–3.37; P < 0.001, respectively), multiple tumor location (HR: 1.92; 95% CI: 1.14–3.21; P = 0.014), amputation (HR: 1.77; 95% CI: 1.39–2.25; P < 0.001), positive surgical margins (HR: 1.85; 95% CI: 1.43–2.38; P < 0.001), metastasis (HR: 5.54; 95% CI: 4.57–6.72; P < 0.001), and deep tumor location (HR: 1.29; 95% CI: 1.01–1.65; 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. Male sex (HR: 1.88; 95% CI: 1.05–3.35; P = 0.033), tumor size > 10 cm (HR: 3.43; 95% CI: 1.26–9.35; P = 0.0016), positive surgical margins (HR: 2.77; 95% CI: 1.31–5.83; P = 0.007), and the presence of metastasis (HR: 4.97; 95% CI: 2.49–9.92; P < 0.001) were prognostic factors for poor cancer survival in patients with MPNST, but not being an 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 were not able to compare our results with that of previous reports owing to 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 the current 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, positive surgical margins, and the presence of metastasis 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 male sex, tumor size > 10 cm, positive surgical margins, and metastatic lesion(s) at presentation. 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 21–49.7%. Meanwhile, the 5-year survival rate of MPNST patients with non-NF1 ranges from 42–64.9% [17–20]. However, our cohort does not distinguish NF1 patient. 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. 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.

# 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 patients with STS did not have poorer survival compared to other age groups. However, AYA patients with MPNST had 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.

# Declarations

### Ethics approval and consent to participate

The research has been 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 the present one, written informed consent is 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.

## 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

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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 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 |
| **Radiotherapy** | 370 | 25.5% | 1925 | 25.0% | 80 | 39.6% | 645 | 23.4% | 830 | 25.2% | <0.001 |

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 | 0.95 (0.54-1.68) | 0.872 |
| Adult (40-59 years) | 2127 | 75.2% | 0.84 (0.71-0.99) | 0.033 | 1.17 (0.92-1.49) | 0.201 |
| Elderly (≥65 years) | 2412 | 72.5% | 0.98 (0.84-1.15) | 0.812 | 1.86 (1.47-2.34) | <0.001 |
| **Sex** | | | | | | |
| Female | 2638 | 75.5% | Reference | | Reference | |
| Male | 3215 | 70.7% | 1.33(1.18-1.50) | <0.001 | 1.20(1.02-1.42) | 0.028 |
| **Histologic grade** | | | | | | |
| Low | 1065 | 93.2% | Reference | | Reference | |
| High | 4788 | 68.2% | 6.96 (5.05-9.58) | <0.001 | 4.08(2.72-6.12) | <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 | 1.73 (1.35-2.22) | <0.001 |
| >10 cm | 1587 | 57.2% | 4.07 (3.38-4.90) | <0.001 | 2.61 (2.02-3.37) | <0.001 |
| **Tumor location** | | | | | | |
| Upper extremity | 728 | 83.8% | Reference | | Reference | |
| Lower extremity | 2955 | 76.8% | 1.38 (1.09-1.75) | 0.007 | 1.22 (0.91-1.65) | 0.181 |
| Trunk | 1870 | 65.7% | 2.51 (1.98-3.17) | <0.001 | 1.97 (1.45-2.69) | <0.001 |
| Head and neck | 173 | 66.2% | 2.62 (1.83-3.75) | <0.001 | 2.49 (1.29-4.79) | 0.006 |
| Multiple | 127 | 35.2% | 6.69 (4.87-9.20) | <0.001 | 1.92 (1.14-3.21) | 0.014 |
| **Limb salvage status** | | | | | | |
| Limb salvage | 5072 | 76.4% | Reference | | Reference | |
| Amputation | 322 | 53.0% | 1.98 (1.62-2.43) | <0.001 | 1.77 (1.39-2.25) | <0.001 |
| **Surgical margin** | | | | | | |
| Negative (wide or marginal) | 4491 | 79.1% | Reference | | Reference | |
| Positive (intralesional) | 290 | 56.6% | 2.82 (2.26-3.51) | <0.001 | 1.85 (1.43-2.38) | <0.001 |
| **Metastasis** | | | | | | |
| – | 5030 | 80.5% | Reference | | Reference | |
| □ | 771 | 22.9% | 7.95 (7.04-8.98) | <0.001 | 5.54 (4.57-6.72) | <0.001 |
| **Tumor Depth** | | | | | | |
| Superficial | 1453 | 87.3% | Reference | | Reference | |
| Deep to fascia | 4280 | 78.3% | 2.83 (2.35-3.42) | <0.001 | 1.29 (1.01-1.65) | 0.041 |

CI: confidence interval

**Table 3.** Characteristics of MPNST patients according to age group

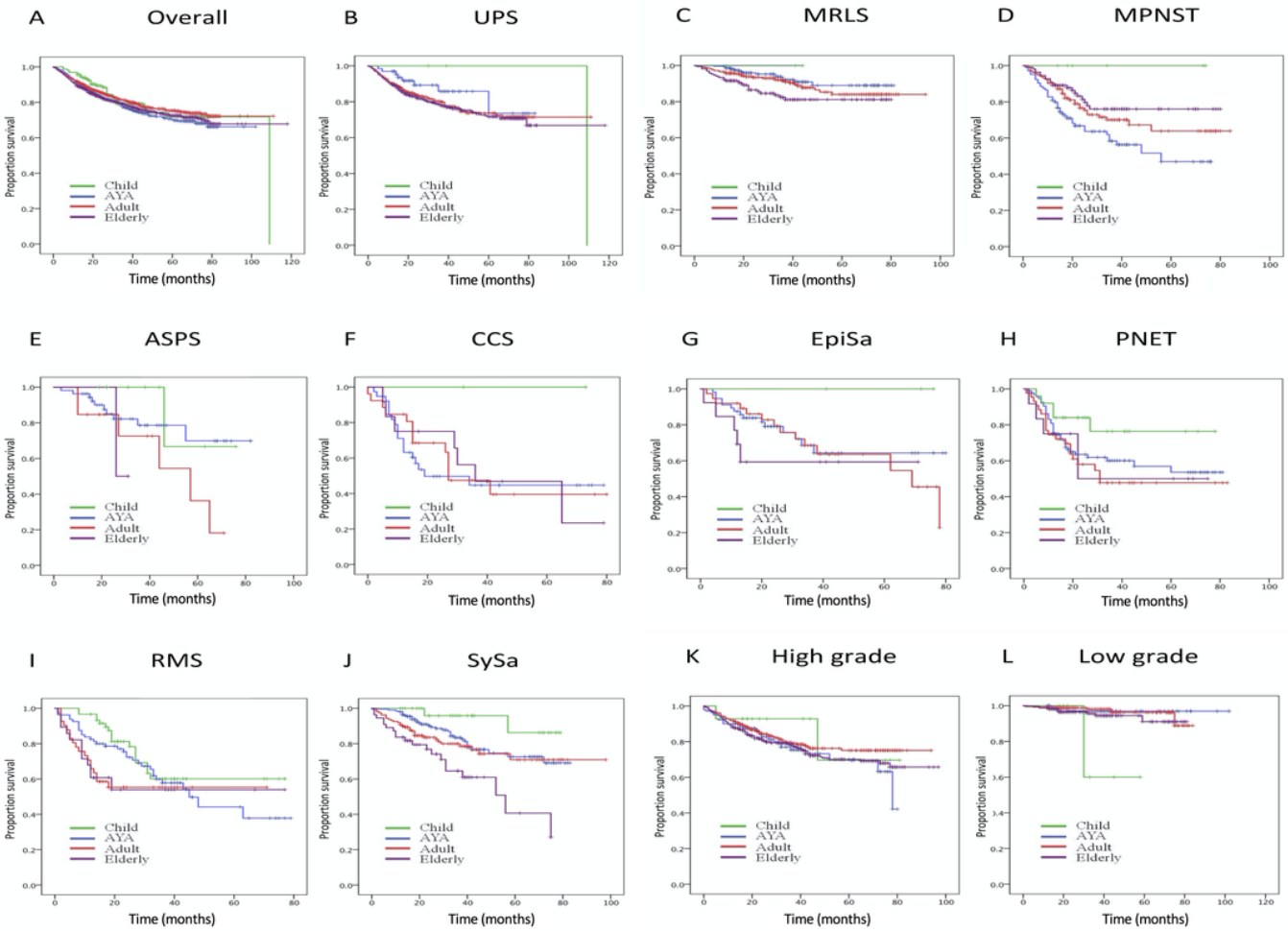
| | AYA (15-39 years) | | Overall | | Child (≤14 years) | | Adult (40-64 years) | | Elderly (≥65 years) | | P value |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. of patients | % | No. of patients | % | No. of patients | % | No. of patients | % | No. of patients | % | |
| **Sex** | | | | | | | | | | | |
| 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% | |
| **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% | |
| **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% | |
| **Surgical margin** | | | | | | | | | | | |
| Negative (wide or marginal) | 63 | 84.0% | 252 | 89.7% | 4 | 100.0% | 97 | 89.8% | 88 | 93.6% | 0.199 |
| Positive (intralesional) | 12 | 16.0% | 29 | 10.3% | 0 | 0.0% | 11 | 10.2% | 6 | 6.4% | |
| **Metastasis** | | | | | | | | | | | |
| - | 83 | 79.8% | 297 | 85.3% | 6 | 100.0% | 113 | 86.3% | 95 | 88.8% | 0.197 |
| + | 21 | 20.2% | 51 | 14.7% | 0 | 0.0% | 18 | 13.7% | 12 | 11.2% | |

**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-) | 0.977 |
| Adult (40-59 years) | 101 | 0.62 (0.39-0.97) | 0.036 | 0.83 (0.44-1.57) | 0.563 |
| Elderly (≥65 years) | 83 | 0.45 (0.26-0.77) | 0.004 | 0.79 (0.38-1.65) | 0.527 |
| **Sex** | | | | | |
| Female | 122 | Reference | | Reference | |
| Male | 134 | 1.63 (1.07-2.46) | 0.022 | 1.88 (1.05-3.35) | 0.033 |
| **Tumor size** | | | | | |
| ≤5 cm | 66 | Reference | | Reference | |
| >5 cm and ≤10 cm | 125 | 2.65 (1.28-5.46) | 0.009 | 2.08 (0.79-5.52) | 0.14 |
| >10 cm | 65 | 3.71 (1.78-7.72) | <0.001 | 3.43 (1.26-9.35) | 0.016 |
| **Tumor location** | | | | | |
| Upper extremity | 34 | Reference | | Reference | |
| Lower extremity | 89 | 1.00 (0.49-2.01) | 0.99 | 0.80 (0.34-1.89) | 0.607 |
| Trunk | 110 | 1.10 (0.57-2.14) | 0.775 | 0.84 (0.37-1.92) | 0.678 |
| Head and neck | 16 | 1.53 (0.64-3.70) | 0.342 | 0.36 (0.07-1.92) | 0.229 |
| Multiple | 7 | 2.59 (1.00-6.70) | 0.049 | 0.79 (0.10-6.64) | 0.831 |
| **Surgical margin** | | | | | |
| Negative (wide or marginal) | 227 | Reference | | Reference | |
| Positive (intralesional) | 29 | 2.46 (1.28-4.74) | 0.007 | 2.77 (1.31-5.83) | 0.007 |
| **Metastasis** | | | | | |
| – | 235 | Reference | | Reference | |
| □ | 21 | 5.47 (3.57-8.37) | <0.001 | 4.97 (2.49-9.92) | <0.001 |
| **Tumor Depth** | | | | | |
| Superficial | 68 | Reference | | Reference | |
| Deep to fascia | 125 | 3.92 (1.89-8.10) | <0.001 | 2.87 (0.99-8.25) | 0.051 |

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.