

# Sarcoma Patients Admitted to the Intensive Care Unit (ICU): Predictive Relevance of Common Sepsis and Performance Parameters

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**Purpose:** Prognosis of sarcoma patients is improving, with a better understanding of sarcomagenesis revealing novel therapeutic targets. However, aggressive chemotherapy remains an essential part of treatment, bearing the risk of severe side effects that require intensive medical treatment. Available data on the characteristics and clinical outcome of sarcoma patients admitted to intensive care units (ICU) are sparse.

**Patients and Methods:** We performed a retrospective analysis of sarcoma patients admitted to the ICU from 2005 to 2022. Patients  $\geq 18$  years with histologically proven sarcoma were included in our study.

**Results:** Sixty-six patients were eligible for analysis. The following characteristics had significant impact on overall survival: sex ( $p=0.046$ ), tumour localization ( $p=0.02$ ), therapeutic intention ( $p=0.02$ ), line of chemotherapy ( $p<0.001$ ), SAPS II score ( $p=0.03$ ) and SOFA score ( $p=0.02$ ).

**Conclusion:** Our study confirms the predictive relevance of established sepsis and performance scores in sarcoma patients. For overall survival, common clinical characteristics are also of significant value. Further investigation is needed to optimize ICU treatment of sarcoma patients.

**Keywords:** soft tissue sarcoma, intensive care unit, sepsis and performance scores, SOFA, SAPS II, ICU-specific survival

## Introduction

With an incidence rate of about 1.8–5.0 per 100,000 per year worldwide, soft-tissue sarcomas (STS) represent about 1% of the malignancies in adults.<sup>1,2</sup> The 5-year survival rate of these rare mesenchymal neoplasms is about 60% across all disease stages in Europe.<sup>2,3</sup> With over 70 different histopathologically defined subtypes, it remains difficult to establish a common therapeutic standard.<sup>4</sup> Diagnosed at an early stage, many STS can be cured by surgery alone. Local recurrence and metastatic disease, however, continue to be a therapeutic challenge especially

in high-grade STS, often requiring multimodal approaches. To date, the standard of care for the majority of advanced STS remains doxorubicin, either as single-agent therapy or in combination with other substances.<sup>5</sup> Whenever possible, therapy should include multiple modalities, eg, local irradiation and/or chemotherapy combined with surgery.<sup>5</sup>

The therapeutic regimen utilized in the LMS 04 trial illustrates a trend towards intensified perioperative therapy in STS: combination treatment with doxorubicin and trabectedin enhances therapeutic efficacy but is accompanied by relevant toxicity, such as significantly more febrile neutropenia (24% vs 11%), thrombocytopenia (20% vs 0%) and gastrointestinal toxicity (12% vs 1%).<sup>6</sup> Thus, intensive treatment strategies may lead to a rising demand for intensive care, especially in older patients.

Until recently, there were no established guidelines regarding the selection of oncologic patients for intensive care unit admission.<sup>7</sup> In 2018, a consensus statement was published concluding the necessity to assess tumour patients like other severely ill non-oncologic patients.<sup>8</sup>

In a work by Biskup et al, the authors showed that the main reasons for admission of cancer patients to the ICU are hypotension, acute respiratory failure, sepsis, acute kidney injury, and bleeding. The indications for ICU admission are rarely related to the underlying malignancy.<sup>7</sup>

Analyses on the outcome of oncologic patients after intensive care treatment are sparse. A critical illness requiring ICU admission occurs in about 5% during the course of malignant disease. Overall, cancer patients account for about 15% of all intensive care treatments.<sup>8–10</sup>

A French single-centre analysis comparing ICU admission data from the years 2007–2008 and 2017–2018 showed an increase in patients with metastatic disease and of patients admitted for drug- or procedure-related adverse events. Interestingly, the overall ICU survival rate of about 77% and the 1-year survival rate of 33% did not change significantly during the specified periods.<sup>11</sup>

For critically ill oncologic patients, no sarcoma specific scoring system predicting clinical outcome is available.<sup>7</sup> It has been shown, however, that mortality rates and clinical prognosis depend on the number of organ failures, the need of mechanical ventilation, vasopressors, and preceding therapies.<sup>7</sup>

The Acute Physiology and Chronic Health Evaluation (APACHE) score and the Sequential Organ Failure Assessment (SOFA) score are most commonly used to estimate ICU mortality.<sup>7</sup>

To date, APACHE exists in four versions (I–IV). To derive a severity score able to predict hospital mortality and sometimes even the length of stay, the input of several clinical variables is required.<sup>12,13</sup> APACHE II consists of three different parts: an acute physiological score, age, and chronic health points. The parameters are evaluated within the first 24 hours after admission to intensive care, the maximum score is 71 points.<sup>14</sup> Mortality increases in parallel with the respective score level.<sup>15</sup>

The Simplified Acute Physiologic Score (SAPS), on the other hand, is based on dichotomous and continuous variables. Severity is calculated based on the worst values measured within the first 24 hours after admission to the intensive care unit. The number of variables is 14 and thus smaller than those included in the APACHE score.<sup>16–18</sup> The maximum score is 163 points. Patients with the highest score have the worst prognosis.<sup>19</sup>

In cancer patients, older age, number of organ system failures, respiratory failure, and requirement of vasopressors as well as isolated lung injury influence mortality. Notably, the type of tumour has not been shown to be prognostic for ICU survival.<sup>7</sup> No such surrogate parameters indicating prognosis have been defined for sarcoma patients as of yet.

Our analysis aims to optimize the selection of sarcoma patients for ICU admission and to improve intensive care algorithms for this group of patients.

## Materials and Methods

This retrospective analysis comprises patients  $\geq 18$  years treated at Charité-Universitätsmedizin Berlin from 2005 to 2022. We included all patients with histologically proven sarcoma who had been admitted to the ICU during this period. We excluded patients with oncological neoplasms other than STS. In addition, patients who were only

monitored perioperatively in the ICU were also excluded. In total, 66 of 834 screened patients were eligible for analysis.

Informed consent following institutional guidelines was obtained from all patients. Data was retrospectively extracted from archived patient records with approval of the local ethical review committee of Charité-Universitätsmedizin Berlin (EA2/240/20) and in accordance with the Declaration of Helsinki.

This study aimed to characterize sarcoma patients admitted to the ICU by means of explorative, descriptive statistics. Factors influencing the survival of these patients were analysed. Laboratory analysis was performed within the first 24 hours after admission to the ICU. Primary endpoint was the ICU mortality, and secondary endpoints were the in-hospital survival and the overall survival. The in-hospital survival comprised the percentage of patients who survived the ICU treatment, but died during the same hospital stay. The overall survival was defined as the time from ICU admission to death or if survival status was unknown, to last contact. The Kaplan–Meier method with Log rank tests was used for univariable survival analyses.

To evaluate and examine the ICU scores, we calculated the median scores of all patients admitted, of the ICU-survivors and of ICU non-survivors. The interquartile range (IQR) containing the second and third quartile of the ICU scores was used to show the range of our data.

In general, p-values <0.05 (calculated 2-sided) were considered significant.

Data analysis was performed using SPSS (IBM Corp. Released 2021. IBM SPSS Statistics for Windows, Version 28.0. Armonk, NY: IBM Corp).

## Results

### Patient and Treatment Characteristics

#### Overall Study Population

The characteristics of 66 included patients are shown in [Table 1](#). The vast majority of patients (71.2%) had distant metastases at the time of ICU admission. The lung was the main location of these metastases.

More than half of the patients (62%) had progressive disease during the course of a mainly palliative treatment concept (83%). They were often (56%) multimodally pre-treated. Most commonly, the current therapy was a systemic treatment (58%) with an anthracycline-based combination chemotherapy (27%). In the majority of cases, it was the first-line treatment (56%). For details, please refer to [Table 1](#).

#### ICU Survivors/Surv versus ICU Non-Survivors/Non-Surv

Altogether, 17 patients died during ICU treatment. The median age was 59 years, and 53% of those patients were female. Undifferentiated, high-grade sarcoma and “other” sarcoma was the most common histologic subtype (each 24%). In the majority of cases, the primary location of the sarcoma was the abdomen/pelvis (ICU non-survivors 47% vs ICU survivors 35%). Most of the patients had multiple distant metastases (82%). Almost all non-survivors (94%) were treated in palliative intention. The current chemotherapy was primarily an anthracycline-based combination chemotherapy or trabectedin (31%). Infection was the most common reason for ICU admission (77%). ICU non-survivors were also more likely to receive vasopressor therapy (71% vs 35%), invasive ventilation (53% vs 18%) and renal replacement therapy (35% vs 6%). For details, please refer to [Table 2](#) as well as [Table 3](#).

Both groups also showed major differences in the common sepsis and performance scores: The group of ICU non-survivors showed higher median scores in all reviewed ICU-scoring systems. For details, please refer to [Table 4](#).

### Survival Analysis

#### Overall Survival

Survival data was available in n=66 patients (100%). In the overall study population, median OS was 7 months 95% CI, 0 to 30.6 months ([Figure 1A](#)). Median OS in the ICU surv population was not reached ([Figure 1B](#)). The median survival in the ICU non-surv study population was 6 days ([Figure 1C](#)).

**Table 1** General Patient Characteristics

	All Patients (n=66)	ICU Surv (n=49)	ICU Non-Surv (n=17)
Age			
Years (median (IQR))	57 (40–69)	57 (40–69)	59 (45–69)
Sex			
Female	34 (53%)	25 (51%)	9 (53%)
Male	32 (49%)	24 (49%)	8 (47%)
Histology			
Bone sarcoma (incl. osteo, chondro, and EFT)	15 (23%)	12 (24%)	3 (18%)
GIST	2 (3%)	2 (4%)	-
Leiomyosarcoma	8 (12%)	6 (12%)	2 (12%)
Liposarcoma	11 (17%)	9 (18%)	2 (12%)
Myxofibrosarcoma	5 (8%)	3 (6%)	2 (12%)
Solitary fibrous tumor	2 (3%)	1 (2%)	1 (6%)
Synovial sarcoma	3 (8%)	3 (6%)	-
Undifferentiated pleomorphic sarcoma (UPS)	5 (7%)	4 (8%)	1 (6%)
Undifferentiated, high-grade	4 (6%)	2 (4%)	2 (12%)
Vascular	3 (5%)	2 (4%)	1 (6%)
Other	8 (12%)	5 (10%)	3 (18%)
Grading			
None	24 (36%)	18 (37%)	6 (35%)
Low grade	6 (9%)	5 (10%)	1 (6%)
High grade	36 (54%)	26 (53%)	10 (59%)
Primary tumor location			
Extremity	27 (41%)	22 (45%)	5 (29%)
Abdomen/pelvis	25 (38%)	17 (35%)	8 (47%)
Thorax	10 (15%)	7 (14%)	3 (18%)
Head/neck	4 (6%)	3 (6%)	1 (6%)
Pulmonary metastases			
Not present	33 (50%)	27 (55%)	6 (35%)
Present	33 (50%)	22 (45%)	11 (65%)
Metastatic status			
None	10 (15%)	8 (16%)	2 (12%)
Localized	8 (12%)	7 (14%)	1 (6%)
Multiple	47 (71%)	32 (67%)	14 (82%)
Unknown	1 (2%)	1 (2%)	-

**Abbreviations:** Chondro, chondrosarcoma; EFT, Ewing family of tumors; GIST, gastrointestinal stromal tumor; ICU, intensive care unit; IQR, interquartile range; surv, survival; non-surv, non-survival; osteo, osteosarcoma.

## Role of Therapy

For ICU-survival, Kaplan–Meier analysis showed significant differences regarding the current chemotherapy ( $p=0.02$ ) and the chemotherapy line ( $p<0.01$ ). Univariate analysis showed a better clinical outcome for patients receiving a first-line chemotherapy than for those who received a chemotherapy regimen for relapse or progression. The median ICU-survival for a first-line chemotherapy was 19 days compared to 2 days for a fourth line chemotherapy. Median time from last chemotherapy to admission to the ICU was 11 days (range 1–27 days).

For the overall survival, univariate analysis showed significant differences regarding the intention of therapy ( $p=0.05$ ) (Figure 2). Line of therapy also had a significant impact on OS of the overall patient population ( $p<0.001$ ) and on OS of the non-surv population ( $p<0.001$ ). There was a trend towards improved overall survival depending of disease status: first diagnosis/progressive disease vs stable disease/partial/complete remission ( $p=0.039$ ) and towards the current chemotherapeutic regimen: anthracycline-based vs gemcitabine-based regimen vs trabectedin vs taxan vs Ewing sarcoma regimen vs other ( $p=0.034$ ). Neither previous nor current therapy (chemotherapy vs resection vs multimodal vs none) significantly influenced prognosis.

**Table 2** ICU-Related Characteristics

	All Patients (n=66)	ICU Surv (n=49)	ICU Non-Surv (n=17)
Clinical symptom at ICU admission			
Infection	32 (49%)	19 (39%)	13 (77%)
Cardiac	4 (6%)	3 (6%)	1 (6%)
Respiratory	9 (14%)	7 (14%)	2 (12%)
Neurological	5 (8%)	5 (10%)	-
Other	16 (24%)	15 (31%)	1 (6%)
Reason for ICU admission			
Therapy-related	33 (50%)	21 (43%)	12 (71%)
Tumor-related	23 (35%)	19 (39%)	4 (24%)
Therapy- and tumor-related	10 (15%)	9 (18%)	1 (6%)
Leucopenia prior to ICU admission			
Present	18 (27%)	13 (27%)	5 (29%)
Not present	40 (61%)	29 (59%)	11 (65%)
Vasopressor therapy			
Present	29 (44%)	17 (35%)	12 (71%)
Not present	37 (56%)	32 (65%)	5 (29%)
Ventilation			
Oxygen/non-invasive	41 (62%)	33 (67%)	8 (47%)
Invasive	18 (27%)	9 (18%)	9 (53%)
None	7 (11%)	7 (14%)	-
Renal replacement therapy			
Present	9 (14%)	3 (6%)	6 (35%)
Not present	57 (86%)	46 (94%)	11 (65%)
Blood transfusions			
Present	34 (52%)	23 (47%)	11 (65%)
Not present	32 (49%)	26 (53%)	6 (35%)
Location of infection			
Abdominal	3 (5%)	3 (6%)	-
Catheter-associated	3 (5%)	4 (8%)	-
Fever of unknown origin	4 (6%)	4 (8%)	-
Lung	16 (24%)	8 (16%)	8 (47%)
Urogenital	3 (5%)	3 (6%)	-
Other	2 (3%)	1 (4%)	1 (6%)
None	35 (52%)	27 (55%)	8 (47%)

**Abbreviations:** ICU, intensive care unit; surv, survival; non-surv, non-survival.

## Laboratory results

As stated before, systemically pre-treated patients had a shorter ICU-survival, as did those with an elevated potassium  $>5$  mmol/l ( $p=0.001$ ) and a decreased haemoglobin  $<9$  mg/dl ( $p=0.04$ ). Median ICU-survival for patients with normokalaemia was 19 days vs 4 days for patients with hyperkalaemia. Patients with a haemoglobin  $<9$  mg/dl had a mean ICU-survival of 19 days vs 25 days with a haemoglobin  $>9$  mg/dl.

Elevated potassium levels  $>5$  mmol/l ( $p=0.011$ ) as well as hyperuricemia  $>50$  mg/dl ( $p<0.001$ ) significantly influenced overall survival. Furthermore, liver parameters such as an elevated alkaline phosphatase  $>90$  U/l ( $p=0.02$ ) and an elevated bilirubin  $>1,2$  mg/dl ( $p=0.01$ ) were significantly associated with a reduced OS.

Haematological parameters such as anaemia, thrombopenia and leukopenia had no relevant impact on overall survival, whereas a pronounced anaemia adversely influenced ICU-surv.

**Table 3** Treatment Characteristics

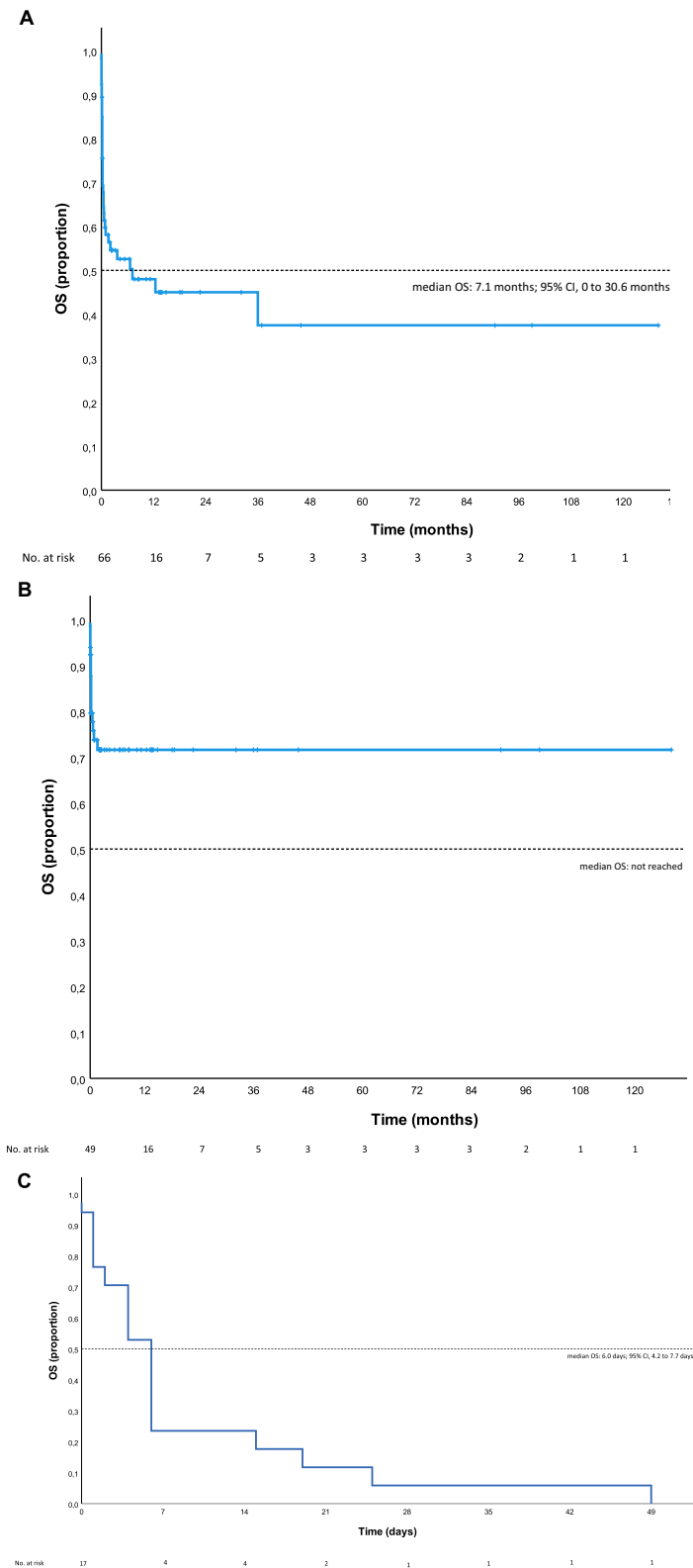
	All Patients (n=66)	ICU Surv (n=49)	ICU Non-Surv (n=17)
<b>Disease status</b>			
Treatment-naïve/first cycles	11 (17%)	8 (17%)	3 (18%)
Progressive disease	41 (62%)	31 (65%)	10 (59%)
Stable disease	8 (12%)	5 (10%)	3 (18%)
Partial remission	5 (8%)	4 (8%)	1 (6%)
<b>Treatment concept</b>			
Curative	11 (17%)	10 (21%)	1 (6%)
Palliative	54 (82%)	38 (79%)	16 (94%)
<b>Previous treatment modality</b>			
Chemotherapy	9 (14%)	7 (14%)	2 (12%)
Resection	8 (12%)	6 (12%)	2 (12%)
Multimodal	37 (56%)	27 (55%)	10 (59%)
None	12 (18%)	9 (18%)	3 (18%)
<b>Current treatment modality</b>			
Chemotherapy	38 (58%)	26 (53%)	12 (71%)
Resection	3 (5%)	3 (6%)	-
Radiation	4 (6%)	2 (4%)	2 (12%)
Multimodal	7 (11%)	6 (12%)	1 (6%)
None	14 (21%)	12 (25%)	2 (12%)
<b>Current chemotherapy</b>			
Anthracycline ± olaratumab	5 (8%)	5 (10%)	-
Anthracycline-based combination	11 (17%)	7 (14%)	4 (24%)
Trabectedin	8 (12%)	4 (8%)	4 (24%)
Ewing sarcoma regimen	5 (8%)	5 (10%)	-
Taxan	1 (2%)	-	1 (14%)
Gemcitabine-based regimen	3 (5%)	2 (4%)	1 (14%)
Other	5 (8%)	6 (12%)	3 (18%)
<b>Chemotherapy line</b>			
First-line	32 (49%)	26 (53%)	6 (35%)
Second-line	17 (26%)	11 (22%)	6 (35%)
Third-line	6 (9%)	5 (10%)	1 (6%)
Fourth-line	2 (3%)	-	2 (12%)
<b>Duration of ICU treatment</b>			
Median days (IQR)	3 (1–7)	3 (1–7)	6 (1.5–10.5)
<b>Duration of hospitalization</b>			
Median days (IQR)	17 (11–29.5)	17.5 (13.3–30)	12 (6–39)

**Abbreviations:** ICU, intensive care unit; IQR, interquartile range; surv, survival; non-surv, non-survival.

**Table 4** ICU-Scores

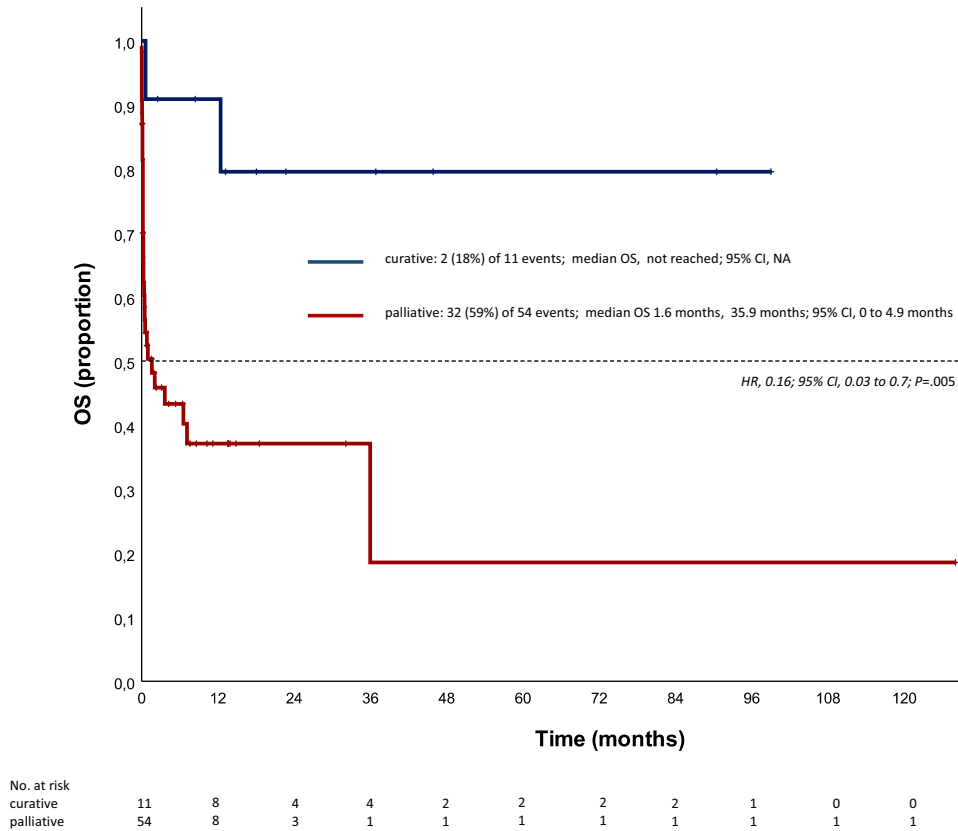
	All Patients (n=66)	ICU Surv (n=49)	ICU Non-Surv (n=17)
<b>APACHE II</b>			
Median (IQR)	15.5 (10–26.3)	15 (10–22)	26 (11.5–36.5)
<b>SAPS II</b>			
Median (IQR)	43 (30.8–64.3)	36 (30–48.5)	65 (47–78)
<b>SOFA</b>			
Median (IQR)	3 (0–8)	2 (0–4)	9 (6.3–14.3)

**Abbreviations:** APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; IQR, interquartile range; SAPS, Simplified Acute Physiologic Score; SOFA: Sequential Organ Failure Assessment; surv, survival; non-surv, non-survival.



**Figure 1** (A) Survival estimates of the overall patient population. (B) Survival estimates of the ICU surv patient population. (C) Survival estimates of the ICU non-surv patient population.

**Abbreviations:** CI, confidence interval; no., number; OS, overall survival; ICU, intensive care unit; surv, survival; non-surv, non-survival.



**Figure 2** Kaplan–Meier estimates for OS with respect to the therapeutic intention (curative vs palliative).

**Abbreviations:** CI, confidence interval; HR, hazard ratio; NA, not applicable; no., number; OS, overall survival.

### Patient and Tumour Characteristics

Female patients showed better overall survival than male patients, see [Figure 3A](#). Primary tumours located at the extremity were associated with an improved prognosis compared to tumours of other locations, see [Figure 3B](#). Comorbidities such as cardiovascular, renal or metabolic disorders did not relevantly influence survival.

### ICU Scores and Treatment

Regarding the ICU-scoring systems, we identified a SOFA score >5 (p=0.004) and a SAPS II score >50 (p=0.007) as predictive for ICU survival and for OS. For the latter, refer to [Figure 4A](#) and to [Figure 4B](#). By contrast, APACHE II did not predict survival. Patients of the non-surv population who needed vasopressors or renal replacement therapy showed worse survival (p=0.016 and p=0.006, respectively). The use of non-/invasive ventilation had no relevant impact on prognosis.

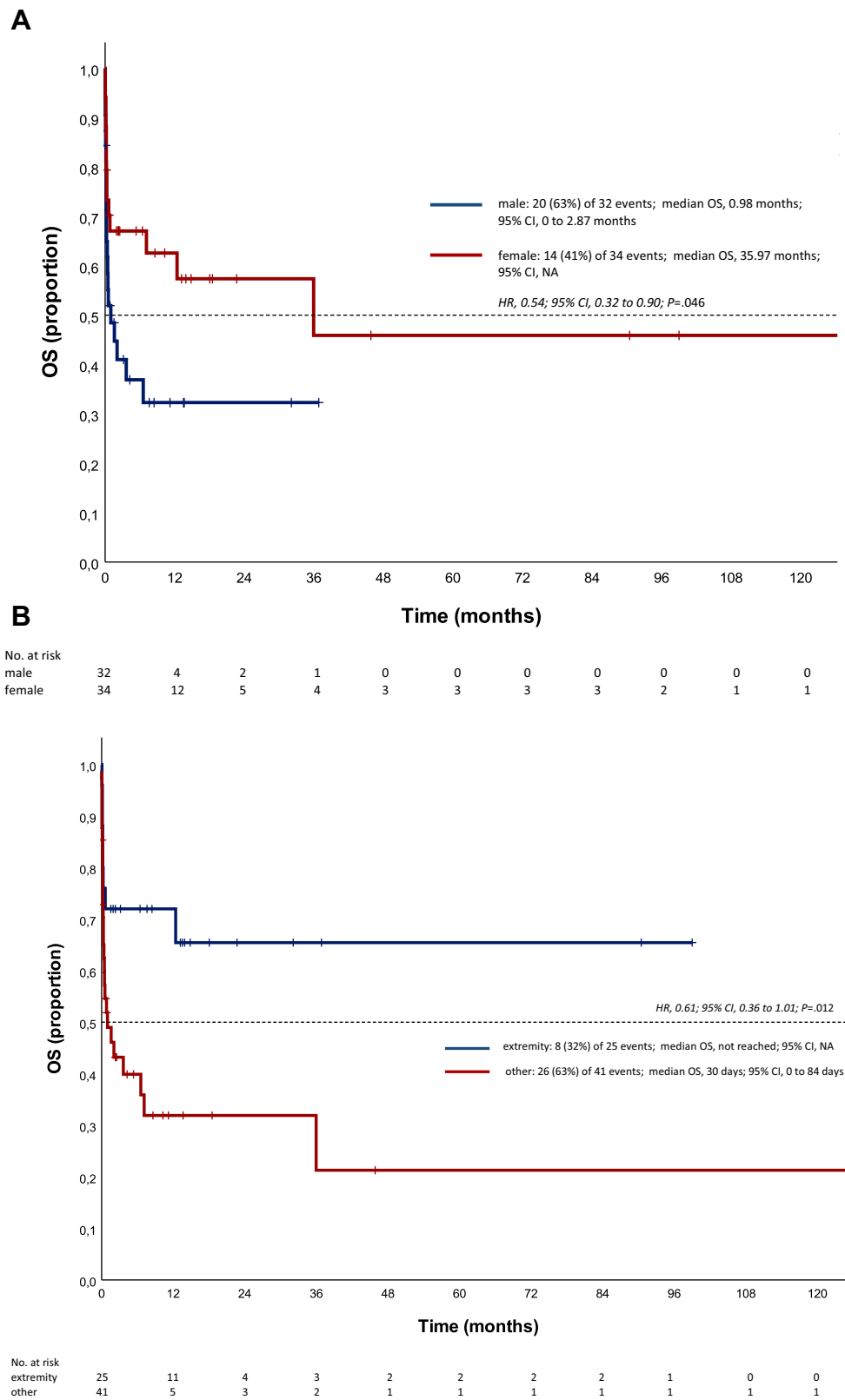
## Discussion

Sarcomas are rare neoplasms, and data regarding intensive care mortality, survival, and prognostic factors in this specific patient population are sparse, with only one other published analysis regarding sarcoma patients treated in the ICU.<sup>20</sup> Therefore, our data contribute to further improve intensive care treatment of this specific population.

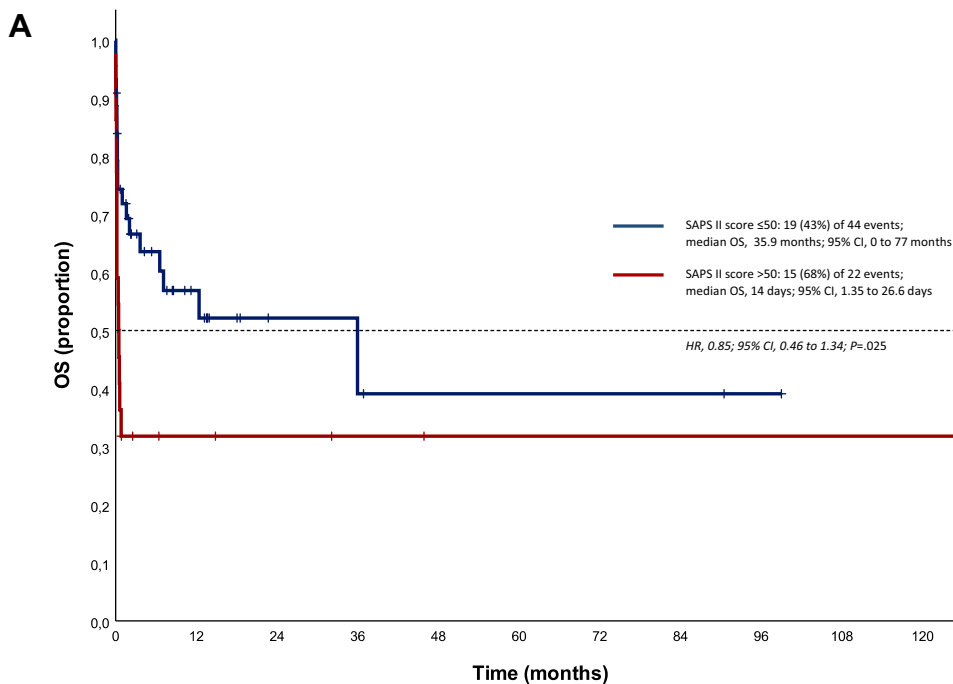
Overall, ICU-survival of sarcoma patients appears to be comparable to those of patients with other solid cancer types.<sup>21–24</sup> By contrast, ICU mortality in case of haematological disease is relevantly higher.<sup>23,25,26</sup>

We were able to confirm the value of common sepsis and performance scores (SOFA and SAPS II) to grade disease severity and to estimate ICU-related survival through the objective classification of organ dysfunction in sarcoma patients. Patients with a relevant organ dysfunction and a higher risk score showed a relevant increase in ICU-related

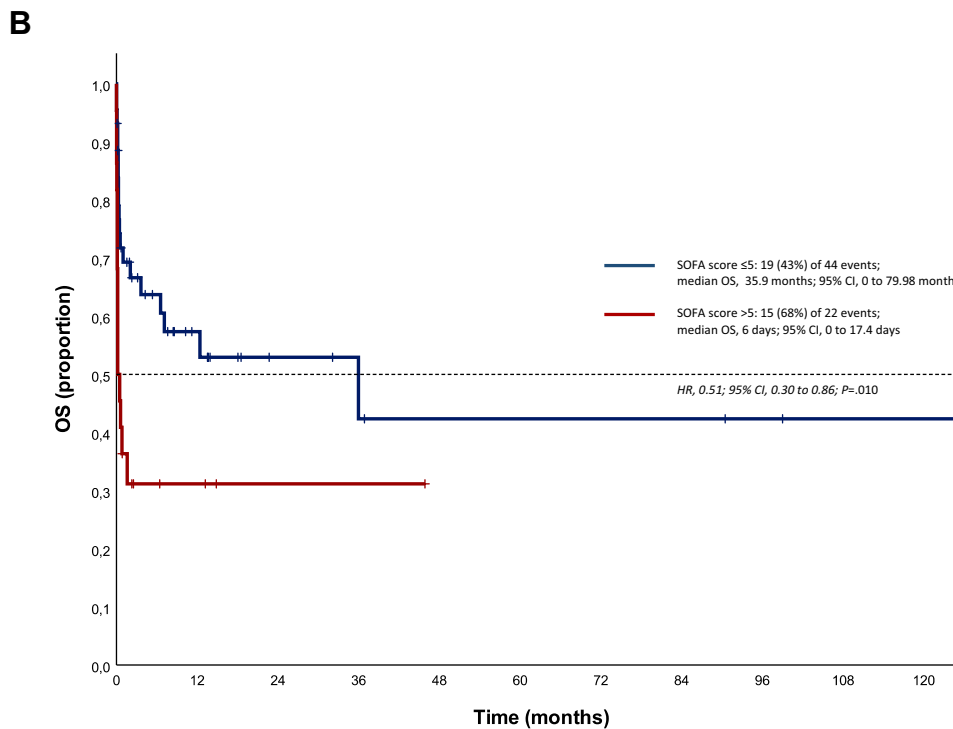




**Figure 3 (A)** Kaplan–Meier estimates for OS with respect to sex (male vs female). **(B)** Kaplan–Meier estimates for OS with respect to primary tumor location (extremity vs other). **Abbreviations:** CI, confidence interval; HR, hazard ratio; NA, not applicable; no., number; vs, versus.



No. at risk	0	12	24	36	48	60	72	84	96	108	120
SAPS II ≤50	44	12	4	3	2	2	2	2	1	0	0
SAPS II >50	22	4	3	3	1	1	1	1	1	1	1



No. at risk	0	12	24	36	48	60	72	84	96	108	120
SOFA ≤5	44	13	6	4	3	3	3	3	3	3	3
SOFA >5	22	3	1	1	0	0	0	0	0	0	0

**Figure 4 (A)** Kaplan–Meier estimates for OS with respect to the SAPS II score. **(B)** Kaplan–Meier estimates for OS with respect to the SOFA score. **Abbreviations:** CI, confidence interval; HR, hazard ratio; no., number; OS, overall survival; SAPS, Simplified Acute Physiologic Score; SOFA, Sequential Organ Failure Assessment.

mortality. The same applies to heavily chemotherapy pre-treated patients. As previously stated, ICU-related survival in the course of first-line tumour therapy was slightly better than in subsequent lines.

In addition, there was a significant impact of individual clinical characteristics such as sex and primary tumour location on OS.

In general, the investigated cohort is comparable to other sarcoma patient populations.<sup>1</sup> The sex ratio is well balanced, the majority of primary tumours was located at the extremity, and pulmonary metastases were the most common. Regarding STS, leiomyosarcoma as well as liposarcoma were the predominant histologic sub entities.

In accordance with prior publications, the most common indication for admittance to intensive care in our cohort were infectious complications (49%), followed by neurologic disturbances (14%). In total, 50% of the admissions were therapy-related, 35% tumour-associated, and 15% both therapy- and tumour-related. This is in line with previous analyses of oncologic patients requiring intensive care, with sepsis or septic shock being the most common reason for ICU treatment.<sup>27</sup> In contrast to Torres et al, we did not observe a negative impact of tumour-related critical illness compared to therapy-associated or other reasons on overall prognosis.<sup>28</sup>

As shown before in patients with lung cancer, those patients who died in the ICU received significantly vasopressors, invasive ventilation, and haemodialysis significantly more often, reflecting the respective severity of sepsis.<sup>27,29,30</sup>

In the ICU, prognostic scores are usually used to assess survival probability and severity of illness. Thus, we included APACHE II, SAPS II as well as SOFA score into our analysis. We did not find any significant impact of APACHE II. However, there was a significant association between a high SAPS II and SOFA score at admission and both ICU mortality and median ICU survival. Our results are thus in accordance with Gupta et al.<sup>20</sup>

In general, a higher grade of organ dysfunction might represent an important risk factor for ICU mortality.<sup>31</sup> Consistent with this observation, results of laboratory chemistry indicating organ failure are different in the cohort of patients who died in the ICU. To some extent, the relevant parameters are already part of the respective scoring systems, which might explain the applicability of these scores. Accordingly, in univariate analysis, we observed a worse ICU-survival in patients with a high SOFA score.

Patients receiving first-line chemotherapy at admission to intensive care showed a slightly better ICU survival than those receiving a later line of therapy. As anthracycline-based combination therapy still represents the first-line therapeutic standard in soft tissue sarcoma, patients receiving trabectedin or any other second- or further line treatment had worse outcomes than those receiving the former.<sup>32,33</sup> Hypothetically, accumulated therapy-associated toxicity in pre-treated patients might also contribute to the poor prognosis of this specific population. Additionally, in the situation of progressive disease, tumour-associated complications are more common.<sup>33</sup> In univariate analysis, female sex had a positive impact on overall survival. This survival advantage in malignant disease was shown before in diverse entities.<sup>34–37</sup> To date, a multifactorial cause such as gender-specific, biological and socio-cultural features is assumed.<sup>34</sup>

In addition, location of the primary tumour might have an influence on prognosis. In our cohort, patients with extremity tumour had a better OS than those with tumours of other locations. Tumours of the extremity are likely to be diagnosed at an early stage of disease due to a more rapid onset of symptoms. In addition, they are more accessible to surgery and/or radiation therapy.

In our study, disease stage as well as the respective therapeutic concept had an impact on OS. Thus, we were able to confirm previous analyses showing a negative prognostic role of progressive disease and of a palliative situation.<sup>20</sup>

In the analysed cohort, ICU mortality was 25.8%, whereas overall in-hospital mortality was 43.4%. ICU survival of sarcoma patients was therefore comparable to previously published results.<sup>20</sup> In contrast, in-hospital mortality was higher than observed before (42 vs 30%). This might be explained by a relevantly higher proportion of patients with progressive disease (63 vs 34%) and thus a lower percentage of stable disease as well as partial remission (20 vs 38%) in our cohort. However, the ICU-mortality rate found in this analysis was lower than the one observed for oncologic patients admitted to intensive care at tertiary institutions in previous publications by other authors.<sup>27,30</sup>

Median OS in our cohort was 7 months, which is relatively short compared to oncologic patients with other carcinomas treated at the ICU.<sup>38</sup> A potential reason is the heterogeneity as well as the limited efficacy of chemotherapeutic substances in soft tissue and bone sarcomas.

There are some limitations regarding our trial. First of all, it is a monocentric retrospective study with only a limited number of patients included. Multicentric, prospective analyses are desirable to minimize selection bias. Our analysis was realised in a high-volume university hospital setting; thus, data can only partially be compared to smaller non-academic institutions.

Additionally, sarcomas are a very heterogeneous tumour entity and conclusions are not easily generalisable. Therefore, subsequent studies might further distinguish between histologic sub entities and collect additional data regarding quality of life or other long-term information. We did not analyse a control group, eg, sarcoma patients with critical illness who were managed outside of the ICU or even patients with other cancer types needing intensive care treatment. Moreover, due to the limited number of patients, we were not able to perform multivariate statistics to eliminate confounding factors.

However, despite the rarity of sarcomas, we were able to analyse a relevant number of cases reflecting the real-life care of patients treated at a high-volume university hospital.

## Conclusion

So far, there is only one other published monocentric analysis evaluating intensive care outcomes in sarcoma patients. To the best of our knowledge, this trial represents the first retrospective analysis of this specific patient population in Europe. Given the diverse scoring systems utilized in the intensive care setting, we analysed not only the SOFA score but also SAPS II and APACHE II. These scoring systems are well established in intensive care medicine. Patients with a relevant organ dysfunction and a higher risk score showed a relevant increase in ICU-related mortality.

Our analysis can contribute to optimising clinical decision-making based on objective data as well as individual patient characteristics. To date, there are no defined criteria for triaging in this distinct patient population. Of significant importance might be the definition of clear goals for each individual patient.

In a palliative setting, ICU admittance of patients for tumour-related reasons and with progressive disease should be reconsidered carefully as the clinical benefit in this constellation might be limited. Further investigation is necessary to enable an optimisation of the ICU treatment of sarcoma patients.

## Abbreviations

APACHE, Acute Physiology and Chronic Health Evaluation; chondro, chondrosarcoma; CI, confidence interval; dl, decilitre; eg, *exempli gratia*; EFT, Ewing family of tumours; GIST, gastrointestinal stromal tumour; HR, hazard ratio; ICU, intensive care unit; incl, inclusive; IQR, interquartile range; l, litre; mg, milligram; NA, not applicable; no., number; non-surv, non-survival; NR, not reached; OS, overall survival; osteo, osteosarcoma; SAPS, Simplified Acute Physiologic Score; SOFA, Sequential Organ Failure Assessment; STS, soft tissue sarcoma; surv, survival; U, unit; vs, versus.

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## Disclosure

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