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# Prognostic Significance of the Systemic Immune-Inflammation Index and Pan-Immune-Inflammation Value in Metastatic Soft Tissue Sarcoma

## Metastatik Yumuşak Doku Sarkomunda Sistemik İmmün-İnflamasyon İndeksi ve Pan-İmmün-İnflamasyon Değerinin Prognostik Önemi

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## Prognostic Significance of the Systemic Immune-Inflammation Index and Pan-Immune-Inflammation Value in Metastatic Soft Tissue Sarcoma


### ABSTRACT

**Objective:** Soft tissue sarcomas (STS) are rare types of cancer that have many different histological subtypes. New prognostic markers are needed to predict the prognosis of patients with metastatic disease. We aimed to investigate the prognostic importance of the systemic immune-inflammation index (SII) and pan-immune-inflammation value (PIV) in patients diagnosed with metastatic STS.

**Material and Method:** A total of eighty-eight patients were evaluated retrospectively. The SII and PIV were calculated with the blood parameters that were checked before treatment. The Kaplan-Meier method was used for survival analysis. Factors impacting survival times were investigated via Cox regression analysis.

**Results:** The median value was calculated as 1019.6 for the SII and 586.0 for the PIV. The median progression-free survival (mPFS) was 7.1 months (95% CI 5.0–9.1) for PIV<586 patients and 4.1 months (95% CI 3.0–5.15) for PIV≥586 patients (*p=0.007*). The median overall survival (mOS) was 20.7 months (95% CI 12.9–28.4) for PIV<586 patients and 10.7 months (95% CI 8.6–12.7) for PIV≥586 patients (*p=0.001*). The mPFS was 6.3 months (95% CI 3.3–9.2) for those with an SII<1019.6 and 4.3 months (95% CI 3.1–5.4) for those with an SII≥1019.6 (*p=0.086*). The mOS was 17.6 months (95% CI 11.1–24.2) for patients with an SII<1019.6 and 11.0 months (95% CI 10.1–11.9) for those with an SII≥1019.6 (*p=0.005*). In multivariate Cox regression analysis, elevated PIV was found to be an independent prognostic factor for decreased OS (*p=0.009*).

**Conclusion:** The SII and PIV indices can guide the determination of high-risk cases and poor prognostic groups in patients diagnosed with metastatic STS in clinical practice.



**Keywords:** Pan-Immune-Inflammation Value, Sarcoma, Systemic Immune-Inflammation Index.


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## Metastatik Yumuşak Doku Sarkomunda Sistemik İmmün-İnflamasyon İndeksi ve Pan-İmmün-İnflamasyon Değerinin Prognostik Önemi


### ÖZ

**Amaç:** Yumuşak doku sarkomları (YDS), çok sayıda histolojik alt grup içeren nadir bir kanser türüdür. Metastatik hastalıkta prognozu öngörebilmek için yeni belirteçlere ihtiyaç vardır. Çalışmamızda metastatik YDS tanılı hastalarda sistemik immün-inflamasyon indeksi (SII) ve pan-immün-inflamasyon değerinin (PIV) prognostik önemini araştırmayı amaçladık.

**Gereç ve Yöntem:** Toplamda seksen sekiz hasta retrospektif olarak değerlendirildi. Hastaların tedavi öncesi kan parametreleri ile SII ve PIV hesaplandı. Sağkalım analizleri için Kaplan-Meier yöntemi kullanıldı. Sağkalım süreleri üzerinde etkisi olan faktörler Cox regresyon analizi ile araştırıldı.

**Bulgular:** Medyan değer SII için 1019,6, PIV için 586,0 olarak bulundu. Medyan progresyonsuz sağkalım (mPFS), PIV<586 için 7,1 ay (%95 CI 5,4-9,8) ve PIV≥586 için 4,1 ay (%95 CI 3,2-5,5) olarak hesaplandı (*p=0.007*). Medyan genel sağkalım (mOS) PIV<586 için 20,7 ay (%95 CI 13,9-30,5) ve PIV≥586 için 10,7 ay (%95 CI 9,2-13,7) olarak bulundu (*p=0.001*). Medyan PFS, SII<1019.6 için 6,3 ay (%95 CI 3,5-9,9) ve SII≥1019.6 için 4,3 ay (%95 CI 3,4-5,8) olarak hesaplandı (p=0.086). Medyan OS, SII<1019.6 için 17,6 ay (%95 CI 11.9-25.9) ve SII≥1019,6 için 11,0 ay (%95 CI 10,9-12,8) olarak bulundu (*p=0.005*). Çok değişkenli Cox regresyon analizinde artmış PIV değeri düşük OS için bağımsız bir prognostik faktör olarak saptandı (*p=0.009*).

**Sonuç:** SII ve PIV indekslerinin metastatik YDS tanılı hastalarda yüksek riskli olguların ve kötü prognostik grupların belirlenmesinde, klinik pratikte yol gösterici olabileceği düşünüldü.



**Anahtar Sözcükler:** Pan-İmmün-İnflamasyon Değeri, Sarkom, Sistemik İmmün-İnflamasyon İndeksi.

## Introduction

Soft tissue sarcomas (STS) are cancers that originate from mesenchymal cells and encompass a variety of histological subtypes. It is a fairly heterogeneous type of disease and includes many different histological subtypes (1). Anthracycline containing chemotherapy regimens are the primary choice of treatment, and the use of targeted therapies and immunotherapy is limited (2). The grade, tumor diameter, and stage are the most important prognostic factors (3). Since the incidence of STS is low and contains many different histological subtypes, individualized treatment decisions are needed. Therefore, new prognostic markers are needed to predict patient prognosis.

Inflammation, which involves the release of cytokines from cancer cells and the tumor microenvironment, is important for tumor proliferation and metastasis. Additionally, inflammation is associated with low response rates to systemic treatment (4,5). Many inflammatory scoring systems have been developed on the basis of laboratory parameters measured in blood. The systemic immune-inflammation index (SII) and pan-immune-inflammation value (PIV) are immune scoring systems developed using blood neutrophil, lymphocyte, platelet, and monocyte values and can be easily applied in clinical practice (6,7).

The prognosis in metastatic soft tissue sarcoma is poor, and there is a need for practical tools that can predict high-risk individuals. The use of SII and PIV indices, which have been shown to be associated with prognosis in various cancer types, raises curiosity about their applicability in metastatic soft tissue sarcomas. In our study, we aimed to investigate the prognostic significance of the SII and PIV indices in patients with metastatic STS.

## Material and Method

Patients with a diagnosis of metastatic STS in our center between May 2010 and June 2023 were retrospectively evaluated. Data were accessed through patient files and the hospital electronic system. The following criteria were used for inclusion: 1) Being eighteen years of age or older, 2) Being diagnosed with metastatic STS, and 3) Being able to access clinical and laboratory data. The following criteria were used for exclusion: 1) Diagnosis of bone sarcoma, gastrointestinal stromal tumor or another type of cancer other than STS; 2) Diagnosis of chronic hematological disease; and 3) Inability to access clinical and laboratory data.

The hemogram test parameters at the time of diagnosis of metastatic disease were evaluated. For SII neutrophil ($10^3$/μL) × platelet ($10^3$/μL) /lymphocyte ($10^3$/μL) and for PIV neutrophil ($10^3$/μL) × monocyte ($10^3$/μL) × platelet ($10^3$/μL) /lymphocyte ($10^3$/μL) were calculated. Since no significant cutoff value for survival could be obtained with receiver operating characteristic (ROC) analysis for the SII and PIV, the median values for both indices were determined as the cutoff point.

Categorical variables are expressed as numbers and percentages, and the relationships between categorical variables were analyzed with the chi-square test. Numerical variables conforming to a normal distribution were analyzed with means (± standard deviations), and variables not conforming to a normal distribution were analyzed with median (minimum–maximum) values. Overall survival (OS) and progression-free survival (PFS) were calculated via the Kaplan–Meier method. PFS is defined as the time from the diagnosis of metastatic disease to progression or death, whereas OS is defined as the time from the diagnosis of metastatic disease to death or the time of the most recent follow-up. Univariate and multivariate Cox regression tests were used to analyze the factors affecting OS and PFS. Parameters with a $p\text{-value}<0.05$ identified in the univariate Cox regression analysis were further tested using multivariate Cox regression analysis. The data were analyzed with the IBM SPSS 23 statistical program, and a value of $p<0.05$ was considered significant.

Approval from the Karadeniz Technical University Faculty of Medicine Ethics Committee, dated 19.10.2023 and protocol number 2023/195, was obtained before the study. The study protocol was carried out in accordance with the Helsinki Declaration.

## Results

The data of 88 patients were evaluated. The mean age was 55.2 ± 15.4 years. Thirty-seven (42.0%) of the patients were male, and 51 (58.0%) were female. The primary tumor was located in the extremity in 58 (65.9%) cases and was located in the non-extremity in 30 (34.1%) cases. Leiomyosarcoma (26.1%), malignant mesenchymal tumor (13.6%), liposarcoma (11.4%), and undifferentiated pleomorphic sarcoma (11.4%) were the most common histological subtypes. Fifty (56.8%) of the cases were de novo metastatic disease, and 38 (43.2%) were recurrent disease. Anthracycline-based chemotherapy was preferred in the first-line treatment in 60 (68.2%) patients. Among the patients who received anthracycline as first-line treatment, 31 (51.6%) were treated with a combination of anthracycline and ifosfamide. Clinical and demographic data of the patients are shown in Table I.

**Table I.** Relationship between Inflammatory Indices and Clinical and Demographic Variables

| Variable | | Total | SII <1019.6 | SII ≥1019.6 | *p* | PIV<586 | PIV≥586 | *p* |
|---|---|---|---|---|---|---|---|---|
| | | n (%) | n (%) | n (%) | | n (%) | n (%) | |
| **Age (years)** | mean±SD | 55.2±15.4 | | | | | | |
| | <65 | 24 (27.3) | 13 (29.5) | 11 (25.0) | *0.632* | 12 (27.3) | 12 (27.3) | *1.000** |
| | ≥65 | 64 (72.7) | 31 (70.5) | 33 (75.0) | | 32 (72.7) | 32 (72.7) | |
| **Gender** | Male | 37 (42.0) | 16 (36.4) | 21 (47.7) | *0.280* | 14 (31.8) | 23 (52.3) | *0.052** |
| | Female | 51 (58.0) | 28 (63.6) | 23 (52.3) | | 30 (68.2) | 21 (42.7) | |
| **ECOG** | 0-1 | 73 (83.0) | 38 (86.4) | 35 (79.5) | *0.395* | 39 (88.6) | 34 (77.3) | *0.156** |
| | 2-4 | 15 (17.0) | 6 (13.6) | 9 (20.5) | | 5 (11.4) | 10 (22.7) | |
| **Tumor location** | Extremity | 58 (65.9) | 27 (61.4) | 31 (70.5) | *0.368* | 24 (54.5) | 34 (77.3) | ***0.025**** |
| | Non-Extremity | 30 (34.1) | 17 (38.6) | 13 (29.5) | | 20 (45.5) | 10 (22.7) | |
| **Histological subtype** | Leiomyosarcoma | 23 (26.1) | 9 (20.5) | 14 (31.8) | *0.099* | 13 (29.5) | 10 (22.7) | ***0.021**** |
| | Malignant mesenchymal tumor | 12 (13.6) | 5 (11.4) | 7 (15.9) | | 3 (6.8) | 9 (20.5) | |
| | Liposarcoma | 10 (11.4) | 6 (13.6) | 4 (9.1) | | 6 (13.6) | 4 (9.1) | |
| | Undifferentiated pleomorphic sarcoma | 10 (11.4) | 5 (11.4) | 5 (11.4) | | 4 (9.1) | 6 (13.6) | |
| | Endometrial stromal sarcoma | 7 (8.0) | 7 (15.9) | 0 (0.0) | | 7 (15.9) | 0 (0.0) | |
| | Synovial sarcoma | 8 (9.1) | 5 (11.4) | 3 (6.8) | | 5 (11.4) | 3 (6.8) | |
| | Rhabdomyosarcoma | 5 (5.7) | 3 (6.8) | 2 (4.5) | | 3 (6.8) | 2 (4.5) | |
| | Other subtypes* | 13 (14.8) | 4 (9.1) | 9 (20.5) | | 3 (6.8) | 10 (22.7) | |
| **Tumor grade** | 1 | 5 (5.7) | 3 (6.8) | 2 (4.5) | *0.948* | 4 (9.1) | 1 (2.3) | *0.434** |
| | 2 | 15 (17.0) | 8 (18.2) | 7 (15.9) | | 9 (20.5) | 6 (13.6) | |
| | 3 | 36 (40.9) | 18 (40.9) | 18 (40.9) | | 16 (36.4) | 20 (45.5) | |
| | Not evaluated | 32 (36.4) | 15 (34.1) | 17 (38.6) | | 15 (34.1) | 17 (38.6) | |
| **Metastasis status** | De novo disease | 50 (56.8) | 24 (54.5) | 26 (59.1) | *0.667* | 22 (50.0) | 28 (63.6) | *0.197** |
| | Recurrent disease | 38 (43.2) | 20 (4.5) | 18 (40.9) | | 22 (50.0) | 16 (36.4) | |
| **Brain metastasis** | Present | 6 (6.8) | 4 (9.1) | 2 (4.5) | *0.676* | 5 (11.4) | 1 (2.3) | *0.202** |
| | Absent | 82 (93.2) | 40 (90.9) | 42 (95.5) | | 39 (88.6) | 43 (97.7) | |
| **Liver metastasis** | Present | 8 (9.1) | 7 (15.9) | 1 (2.3) | *0.058* | 7 (15.9) | 1 (2.3) | *0.058** |
| | Absent | 80 (90.9) | 37 (84.1) | 43 (97.7) | | 37 (84.1) | 43 (97.7) | |
| **Lung metastasis** | Present | 68 (77.3) | 34 (77.3) | 34 (77.3) | *1.000* | 33 (75.0) | 35 (79.5) | *0.611** |
| | Absent | 20 (22.7) | 10 (22.7) | 10 (22.7) | | 11 (25.0) | 9 (20.5) | |
| **Bone metastasis** | Present | 29 (33.0) | 14 (31.8) | 15 (34.1) | *0.821* | 13 (29.5) | 16 (36.4) | *0.496** |
| | Absent | 59 (67.0) | 30 (68.2) | 29 (65.9) | | 31 (70.5) | 28 (63.6) | |
| **Palliative radiotherapy** | Present | 40 (45.5) | 18 (40.9) | 22 (50) | *0.392* | 20 (45.4) | 20 (45.4) | *0.640** |
| | Absent | 48 (54.5) | 26 (59.1) | 22 (50) | | 24 (54.6) | 24 (54.6) | |
| **First-line treatment** | Anthracycline-based chemotherapy | 60 (68.2) | 26 (59.1) | 34 (77.3) | *0.067* | 31 (70.5) | 29 (65.9) | *0.647** |
| | Other treatments (anthracycline-free chemotherapy, pazopanib) | 28 (31.8) | 18 (40.9) | 10 (22.7) | | 13 (29.5) | 15 (34.1) | |

*Chi-Square Test; **ECOG:** Eastern Cooperative Oncology Group Scale; ***Other subtypes:** Fibrosarcoma (n=4), alveolar sarcoma (n=2), angiosarcoma (n=2), solitary fibrous tumor (n=1), Kaposi sarcoma (n=1), hemangioendothelioma (n=1), malignant peripheral nerve sheath tumor (n=1), poorly differentiated sarcoma (n=1); **PIV:** Pan-immune-inflammation value; **SII**: Systemic immune-inflammation index

The median value was calculated as 1019.6 for SII and as 586.0 for PIV. Median PFS was calculated as 7.1 months (95% CI 5.0–9.1) for PIV<586 and 4.1 months (95% CI 3.0–5.15) for PIV≥586 (*p=0.007*). Median OS was found to be 20.7 months (95% CI 12.9-28.4) for PIV<586 and 10.7 months (95% CI 8.6-12.7) for PIV≥586 (*p=0.001*).

Median PFS was calculated as 6.3 months (95% CI 3.3-9.2) for SII<1019.6, and 4.3 months (95% CI 3.1-5.4) for SII≥1019.6 (*p=0.086*). Median OS was found to be 17.6 months (95% CI 11.1-24.2) for SII<1019.6 and 11.0 months (95% CI 10.1-11.9) for SII≥1019.6 (*p=0.005*). Kaplan-Meier survival curves according to SII and PIV are shown in Figure I.

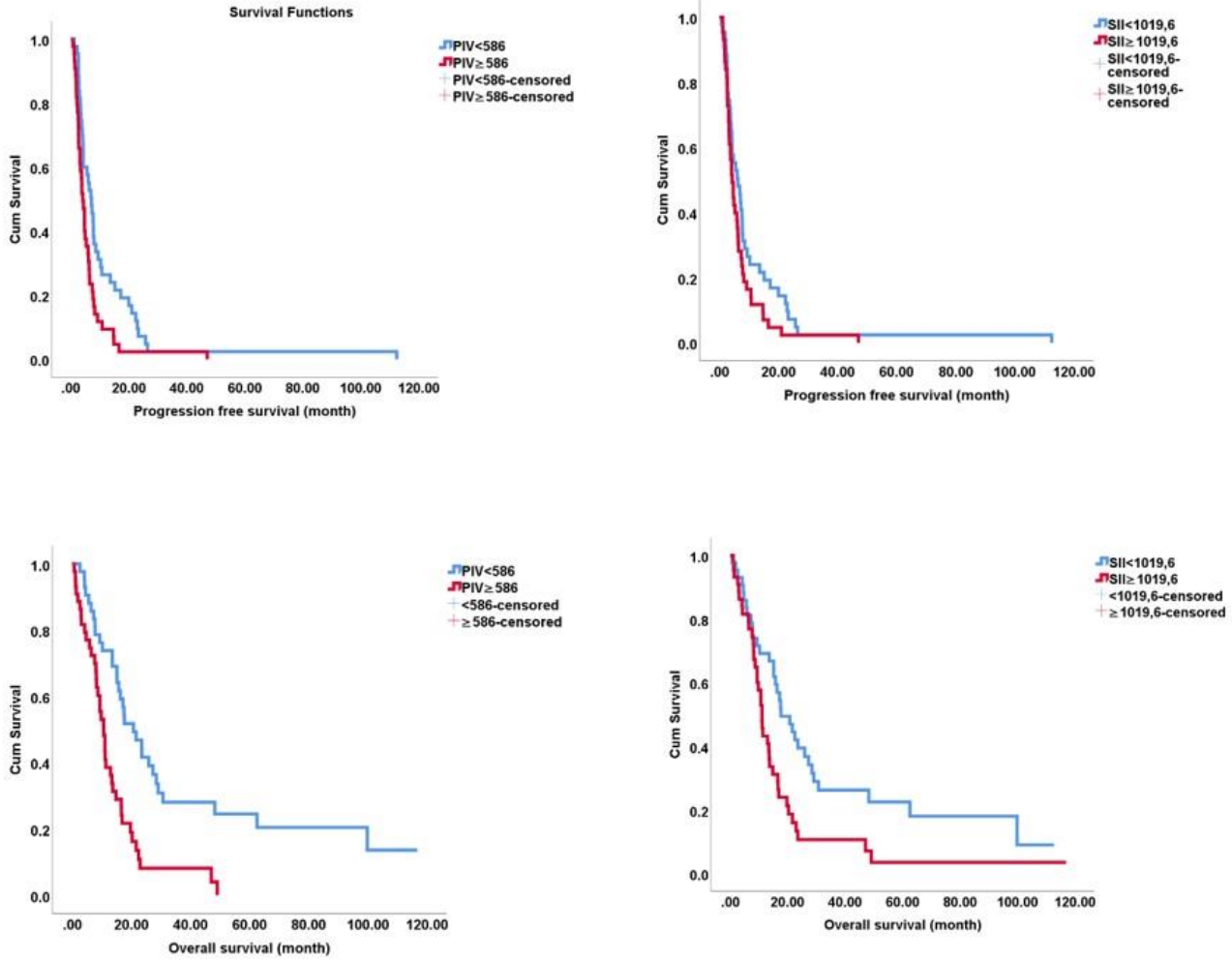


**Figure I.** Kaplan-Meier Survival Curves of Patients

Univariate and multivariate Cox-regression analysis performed for prognostic factors affecting OS and PFS. Univariate analysis for OS revealed that the PIV and SII parameters reached statistical significance, and these parameters were included in the multivariate analysis. PIV value was found to be an independent prognostic factor for decreased OS (Table II and III).

**Table II.** Cox Regression Analysis for Progression-free Survival

| Variable | Univariate Analysis | |
|---|---|---|
| | HR (95% CI) | p |
| **Age (years)** <65 (ref). ≥65 | 0.936 (0.577-1.517) | *0.788* |
| **Gender** Male (ref). female | 1.219 (0.785-1.892) | *0.378* |
| **Metastasis status** De novo (ref). recurrent disease | 0.682 (0.436-1.067) | *0.094* |
| **Tumor location** Extremity (ref). non-extremity | 1.045 (0.670-1.629) | *0.846* |
| **First-line treatment** Anthracycline-based chemotherapy (ref). other treatments (anthracycline-free chemotherapy, pazopanib) | 0.785 (0.487-1.267) | *0.322* |
| **PIV** <586 (ref) ≥586 | 1.808 (1.165-2.806) | ***0.008*** |
| **SII** <1019.6 (ref) ≥1019.6 | 1.460 (0.945-2.256) | *0.088* |

**PIV:** Pan-immune-inflammation value; **SII:** Systemic immune-inflammation index. **Ref:** Reference, **HR:** Hazard ratio

**Table III.** Cox Regression Analysis for Overall Survival

| Variable | Univariate Analysis | | Multivariate Analysis | |
|---|---|---|---|---|
| | HR (95% CI) | p | HR (95% CI) | p |
| **Age (years)** <65 (ref). ≥65 | 0.922 (0.545-1.560) | *0.761* | - | - |
| **Gender** Male (ref). female | 0.891 (0.559-1.420) | *0.626* | - | - |
| **Metastasis status** De novo (ref). recurrent disease | 0.691 (0.430-1.110) | *0.126* | - | - |
| **Tumor location** Extremity (ref). non-extremity | 0.927 (0.576-1.491) | *0.755* | - | - |
| **First-line treatment** Anthracycline-based chemotherapy (ref). other treatments (anthracycline-free chemotherapy, pazopanib) | 1.365 (0.830-2.244) | *0.220* | - | - |
| **PIV** <586 (ref) ≥586 | 2.572 (1.574-4.204) | ***<0.001*** | 2.511 (1.259-5.010) | **0.009** |
| **SII** <1019.6 (ref) ≥1019.6 | 1.944 (1.207-3.130) | ***0.006*** | 1.034 (0.525-2.037) | 0.923 |

**PIV:** Pan-immune-inflammation value; **SII:** Systemic immune-inflammation index. **Ref:** Reference, **HR:** Hazard ratio

## Discussion

In our study, the prognostic significance of the SII and PIV indices in patients diagnosed with metastatic STS was investigated. A high PIV was associated with decreased OS and PFS, and a high SII value was associated with decreased OS. Moreover, PIV was an independent prognostic factor for decreased OS.

Cancer cells and immune system cells, such as macrophages, lymphocytes, and dendritic cells, infiltrate the tumor microenvironment and interact with cytokines via various mechanisms. This relationship plays a critical role in the pathogenesis of cancer (8). As a result of chronic inflammation, proliferation, angiogenesis, and metastasis are triggered in cancer cells. These conditions, which develop due to chronic inflammation, cause a decrease in the systemic treatment response (5).

Neutrophils, which constitute the highest percentage of leukocytes, cause tumor proliferation and angiogenesis through complex mechanisms. Matrix metallopeptidase 9 (MMP-9), which is secreted from neutrophils, and vascular endothelial growth factor (VEGF) play important roles in angiogenesis. In addition, neutrophils are involved in DNA damage and tumorigenesis via the production of reactive oxygen species (ROS). As a result of interactions between tumor cells and neutrophils, the lifespan of cancer cells in the peripheral blood is prolonged (9-11). On the other hand, lymphocytes, unlike neutrophils, platelets, and monocytes, have antitumor effects on the cytokines they secrete and inhibit the proliferation of tumor cells (12). Platelets form a fibrinogen shield around tumor cells in the bloodstream, preventing cancer cells from being cytolyzed by leukocytes (13). Platelets in the tumor tissue form microthrombi, triggering local inflammation and the resulting macrophage response. Thus, the process of carcinogenesis and metastasis development is accelerated (14,15).

As a reflection of the interactions between cancer cells and immune system cells, there is variability in blood neutrophil, lymphocyte, platelet, and monocyte values. On the basis of these proportional and quantitative changes, many inflammatory indices have been developed, and their prognostic importance in different types of cancer has been investigated. The SII and PIV are also inflammatory indices developed in this way. Studies have shown that these indices can be used as prognostic biomarkers in many types of cancer (16-18).

There are a limited number of studies on the prognostic importance of the SII in patients with different histological subtypes of STS and there are limited number of studies evaluating PIV in patients diagnosed with STS. In a study investigating the prognostic significance of preoperative inflammatory indices in patients with osteosarcoma, OS was found to be lower in patients with high SII values in the preoperative period. In the same study, the preoperative SII was shown to be a prognostic factor for OS (19). Another study evaluating head and neck STS revealed that a high SII value before treatment had no prognostic effect on PFS or OS. However, in the abovementioned study, the proportion of patients in the metastatic stage was only 17%. Given that all the patients were at the metastatic stage in our study, we believe that the findings would not be suitable for comparison (20).

In another study involving different histological subtypes, pretreatment high SII values were associated with decreased PFS in patients with STS who had received at least two lines of treatment. However, there was no significant difference in OS between patients with high and low SII values (21). We found that although patients with high SII values had decreased PFS, this difference did not reach statistical significance, but patients with low SII values were found to have prolonged OS. In our study, most patients were high-risk patients with de novo metastasis, high histological grade, and visceral metastasis, possibly caused this difference. The main differences of our study compared to the aforementioned studies are considered to be the inclusion of only patients with metastatic stage disease and the representation of various sarcoma subtypes at different patient numbers.

Our study included different histological subtypes due to the nature of STS, was designed retrospectively, and was a single-center experience. These factors were considered limitations of the study.

In conclusion, high SII and PIV were found to be associated with decreased survival times in patients diagnosed with metastatic STS. Our study has the potential to serve as a data for more comprehensive research investigating the relationship between SII and PIV indices and metastatic soft tissue sarcomas. We believe that larger-scale studies with increased patient numbers could more clearly define the prognostic value of both SII and PIV indices in metastatic soft tissue sarcoma.

## References

1. Hui JY. Epidemiology and Etiology of Sarcomas. Surgical Clinics of North America 2016;96:901-914.

2. Judson I, Verweij J, Gelderblom H, et al. European Organization and Treatment of Cancer Soft Tissue and Bone Sarcoma Group. Doxorubicin alone versus intensified doxorubicin plus ifosfamide for first-line treatment of advanced or metastatic soft-tissue sarcoma: a randomized controlled phase 3 trial. The Lancet Oncology 2014;15:415-423.

3. Ramanathan RC, A'Hern R, Fisher C, Thomas JM. Modified staging system for extremity soft tissue sarcomas. Annals of Surgical Oncology 1999;6:57-69.

4. Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. Cell 2010;19:883-899.

5. Zhao H, Wu L, Yan G, et al. Inflammation and tumor progression: signaling pathways and targeted intervention. Signal Transduction and Targeted Therapy 2021;6:263.

6. Hu B, Yang XR, Xu Y, et al. Systemic immune-inflammation index predicts prognosis of patients after curative resection for hepatocellular carcinoma. Clin Cancer Research 2014; 20:6212-6222.

7. Fucà G, Guarini V, Antoniotti C, et al. The Pan-Immune-Inflammation Value is a new prognostic biomarker in metastatic colorectal cancer: results from a pooled-analysis of the Valentino and TRIBE first-line trials. British Journal of Cancer 2020;123:403-409.

8. Binnewies M, Roberts EW, Kersten K, et al. Understanding the tumor immune microenvironment (TIME) for effective therapy. Nature Medicine 2018;24:541-550.

9. Christoffersson G, Vågesjö E, Vandooren J, et al. VEGF-A recruits a proangiogenic MMP-9-delivering neutrophil subset that induces angiogenesis in transplanted hypoxic tissue. Blood 2012;120:4653-4662.

10. Timaxian C, Vogel CFA, Orcel C, et al. Pivotal Role for Cxcr2 in Regulating Tumor-Associated Neutrophil in Breast Cancer. Cancers (Basel) 2021;13:2584.

11. Xiong S, Dong L, Cheng L. Neutrophils in cancer carcinogenesis and metastasis. European Journal of Haematology 2021;14:173.

12. Singh N, Baby D, Rajguru JP, et al. Thakkannavar SS, Pujari VB. Inflammation and cancer. Annals of African Medicine 2019;18:121-126.

13. Nieswandt B, Hafner M, Echtenacher B, et al. Lysis of tumor cells by natural killer cells in mice is impeded by platelets. Cancer Research 1999;59:1295-1300.

14. Queiroz KC, Shi K, Duitman J, et al. Protease-activated receptor-1 drives pancreatic cancer progression and chemoresistance. International Journal of Cancer 2014;135: 2294-2304.

15. Ward Y, Lake R, Faraji F, et al. Platelets Promote Metastasis via Binding Tumor CD97 Leading to Bidirectional Signaling that Coordinates Transendothelial Migration. Cell Reports 2018;23:808-822.

16. Tian BW, Yang YF, Yang CC, et al. Systemic immune-inflammation index predicts prognosis of cancer immunotherapy: systemic review and meta-analysis. Immunotherapy 2022;14:1481-1496.

17. Zhu M, Chen L, Kong X, et al. The Systemic Immune-Inflammation Index is an Independent Predictor of Survival in Breast Cancer Patients. Cancer Management and Research 2022;14:775-820.

18. Qi X, Qiao B, Song T, et al. Clinical utility of the pan-immune-inflammation value in breast cancer patients. Frontiers in Oncology 2023;13:1223786.

19. Ma C, Yu R, Li J, et al. Preoperative prognostic nutritional index and systemic immune-inflammation index predict survival outcomes in osteosarcoma: A comparison between young and elderly patients. Journal of Surgical Oncology 2022;125:754-765.

20. Chen L, Zeng H, Du Z, et al. Nomogram based on pretreatment inflammatory biomarkers predicting survival in patients with head and neck soft tissue sarcoma. Cancer Biomarkers 2020;291:151-161.

21. Fausti V, De Vita A, Vanni S, et al. Systemic Inflammatory Indices in Second-Line Soft Tissue Sarcoma Patients: Focus on Lymphocyte/Monocyte Ratio and Trabectedin. Cancers (Basel) 2023;15:1080.