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# THE RELATION BETWEEN MODIFIED SYSTEMIC INFLAMMATION SCORE AND PROGNOSTIC MARKERS OF GASTROINTESTINAL STROMAL TUMORS

## MODİFİYE SİSTEMİK İNFLAMASYON SKORU İLE GASTROİNTESTİNAL STROMAL TÜMÖRLERİN PROGNOSTİK GÖSTERGELERİ ARASINDAKİ İLİŞKİ

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## Öz

### Amaç
Gastrointestinal stromal tümörler, gastrointestinal sistem boyunca yerleşebilen mezenkimal kökenli tümörlerdir. Bu çalışmada Modifiye sistemik inflamasyon skorunun (mSIS) bu tümörlerin prognozunu öngörmedeki rolü araştırıldı.

### Gereç ve Yöntem
1 Haziran 2019 ile 1 Aralık 2022 tarihleri arasında Ankara Şehir Hastanesi'nde ameliyat edilen Gastrointestinal Stromal Tümör (GIST) tanısı alan 115 hasta incelendi. Tümörün lokalizasyonu, boyutu, rüptür-kanama-nekroz varlığı, ki-67 düzeyi, mitotik indeks ve ameliyat öncesi albümin, lenfosit ve monosit düzeyleri değerlendirildi. mSIS skoru 0, 1 ve 2 olarak gruplandırıldı. mSIS ile Ki-67 indeksi, rüptür, nekroz ve kanama varlığı ile ilişkisi araştırıldı.

### Bulgular
115 hastanın 68'i (% 59) erkek, 47'si (% 41) kadın olup yaş ortalaması 62,5 (± 12,67) idi. Tümör lokasyonları: mide (% 64,3), ince bağırsak (% 26), kolon (% 5,2), yemek borusu (% 1,8), pankreas (% 1,8) ve yumurtalık (% 0,9). 25'inde (% 30,7) nekroz, 67'sinde (% 58,7) kanama, 19'unda (% 16,8) rüptür vardı ve ortalama Ki-67 düzeyi 9,09 (± 10,64) idi. Hastaların 63'ünde (% 54,8) mSIS 0, 29'unda (% 25,2) mSIS 1 ve 23'ünde (% 20) mSIS 2 vardı. İstatistiksel analizlerde, mSIS ile nekroz mevcudiyeti arasında anlamlı bir korelasyon bulundu.

### Sonuç
mSIS skoru vücuttaki inflamasyonu gösteren değerli bir skordur ve birçok malignitenin prognozu ile ilişkili olduğu gösterilmiştir. Çalışmamızda tümörde nekroz varlığı mSIS skoru ile ilişkili bulunmuştur. Bu sonuç tek başına prognozu tahmin etmek için yeterli olmasa da yeni çalışmalara kapı açabilecek bir konu olduğu düşünülmektedir.

**Anahtar Kelimeler:** Gastrointestinal stromal tümör, Modifiye sistemik inflamasyon skoru, Prognoz, Tümör nekrozu

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## Abstract

**Objective**
Gastrointestinal stromal tumours are tumours of mesenchymal origin that can be located along the gastrointestinal tract. In this study, the role of Modified systemic inflammation score in predicting the prognosis of these tumours was investigated.

**Material and Method**
115 patients diagnosed with Gastrointestinal Stromal Tumor (GIST) who underwent surgery at Ankara City Hospital between June 1, 2019 and December 1, 2022 were examined. Tumor location, size, presence of rupture-bleeding-necrosis, Ki-67 level, mitotic index and preoperative albumin, lymphocyte and monocyte levels were evaluated. mSIS score was grouped as 0, 1 and 2. The relationship between mSIS and Ki-67 index and the presence of rupture, necrosis and bleeding was investigated.

**Results**
Out of 115 patients, 68 (59 %) were male, 47 (41 %) were female, with an average age of 62.5 (± 12.67) years. Tumor locations: stomach (64.3 %), small intestine (26 %), colon (5.2 %), esophagus (1.8 %), pancreas (1.8 %), and ovary (0.9 %). Necrosis was in 25 (30.7 %), hemorrhage in 67 (58.7 %), rupture in 19 (16.8 %), and the mean Ki-67 level was 9.09 (± 10.64). 63 (54.8 %) patients had mSIS 0, 29 (25.2 %) had mSIS 1, and 23 (20 %) had mSIS 2. Statistical analysis found a significant correlation between mSIS and necrosis, but not with other parameters.

**Conclusion**
The mSIS score is a valuable score showing inflammation in the body and has been shown to be associated with the prognosis of many malignancies. In our study, the presence of necrosis in the tumour was found to be associated with the mSIS score. Although this result alone is not sufficient to predict the prognosis, it is thought to be an issue that may open the door to new studies.


**Keywords:** Gastrointestinal stromal tumour, Modified systemic inflammation score, Prognosis, Tumour necrosis

## Introduction

Gastrointestinal stromal tumors (GIST) are mesenchymal-derived neoplasias that can be located along the gastrointestinal tract, have an incidence of 0.43-2.2/100000, and are seen equally in both genders. It is found to originate from Cajal cells associated with intestinal motility and it is observed to express CD-117 (C-kit) antigen at the molecular level (1). The most common location of GISTs is the stomach with a rate of up to 70%. This is followed by the small intestines and colon (2). Rarely (<5%), GISTs may also be seen in structures outside the gastrointestinal tract (mesentery, omentum, retroperitoneum, pancreas, spleen, falsiform ligament, hepatogastric ligament, mediastinum, pelvis, etc.) and these GISTs are called Extragastrointestinal Stromal Tumors (EGIST) (3). In 20% of cases, metastasis is detected at the time of diagnosis, and the primary treatment method is curative resection (4).

The most important factors in GIST prognosis are tumor localization, tumor size and mitotic index. These parameters also have an important role in shaping the treatment (5). In addition, age, presence of necrosis and hemorrhage in the tumor, and the Ki-67 index are other factors that affect prognosis (5, 6). In the preoperative period, prognostic determinants such as tumor location, size and age of the patient can be determined, but critical parameters such as mitotic index, Ki-67, presence of necrosis or hemorrhage can only be learned after surgical resection. The determination of these parameters before surgery may change the treatment method.

The relationship between systemic inflammation, cancer pathogenesis and prognosis has long been recognized. This subject, which was first addressed by Rudolf Virchow in 1863, has been examined in various ways since then (7, 8). This relationship has been supported by indicators such as Glasgow Prognostic Index and Modified systemic inflammation score (mSIS) (9, 10). The mSIS; it is a parameter created by albumin and lymphocyte-monocyte ratio (LMR), and its relationship with the prognosis of some malignancies such as stomach and thyroid cancer has been shown in the literature (11, 12).

In our study, we aimed to evaluate the relationship between mSIS, which has not been investigated before in the literature, and prognostic indicators of GISTs; and to investigate whether the result will have an impact on the treatment decision made in the preoperative period in patients with GISTs.

## Material and Method

The study included 115 patients with a final pathological diagnosis of GIST who underwent surgery at Ankara City Hospital between June 1, 2019 and December 1, 2022. Clinical information of the patients was obtained from the hospital data recording system. Demographic data, tumor localization and size, presence of tumor rupture-hemorrhage-necrosis, Ki-67 level, mitotic index, preoperative albumin, lymphocyte and monocyte levels were analyzed.

The mSIS score was calculated using albumin and LMR. If Albumin ≥ 4 g / dL and LMR ≥ 3.4 mSIS score were considered 0; if albumin < 4 g / dL or LMR < 3.4 mSIS score was considered 1; if albumin <4 g / dL and LMR <3.4 mSIS score was considered 2. Patients were divided into 3 groups according to mSIS score (0-1-2). The relationship between these groups and Ki67 index, presence of rupture, presence of necrosis, and presence of hemorrhage was investigated.

### Statistical Analysis

Categorical variables were expressed as number of patients (frequency) and percentage (%). Statistical differences between mSIS score and the presence of rupture, necrosis and bleeding were analyzed with the Chi Square test. Firstly, the Kolmogorov-Smirnov test was performed for the relationship between the mSIS score and Ki-67. Since the data were not normally distributed, Kruskal-Wallis test was used. All analyzes were performed with the SPSS v25 package program. P value < 0.05 was considered significant.

## Results

A total of 115 patients were included in the study. 68 (59 %) of these patients were male and 47 (41 %) were female. The average age of the patients was 62.5 (± 12.67). The tumor was located in the stomach in 74 (64.3 %), small intestine in 30 (26 %), colon in 6 (5.2 %), esophagus in 2 (1.8 %), pancreas in 2 (1.8 %) and ovary in 1 (0.9 %) of the patients. Necrosis was detected in 25 (30.7 %), hemorrhage in 67(58.7 %), rupture in 19 (16.8 %) of the patients and the mean Ki-67 level was calculated as 9.09 (± 10.64). It was observed that 63 (54.8 %) patients had mSIS 0, 29 (25.2 %) had mSIS 1, and 23 (20 %) had mSIS 2. Statistical analysis revealed a statistically significant correlation between mSIS and necrosis development, but no statistically significant correlation was found between mSIS and other parameters (Table 1, 2).

**Table 1** Demographic and tumoral characteristics

| Variables | | Count |
|---|---|---|
| **Gender** | Male | 68 (%59) |
| | Female | 47 (%41) |
| **Tumor Localization** | Gastric | 74 (%64,3) |
| | Intestinal | 30 (%26) |
| | Colonic | 6 (%5,2) |
| | Esophageal | 2 (%1,8) |
| | Pancreatic | 2 (%1,8) |
| | Ovarian | 1 (%0,9) |
| **Histopathologic Characteristics** | Rupture | 19 (%16,8) |
| | Necrosis | 25 (%30,7) |
| | Hemorrhage | 67 (%58,7) |
| **mSIS*** | 0 | 63 (%54,8) |
| | 1 | 29 (%25,2) |
| | 2 | 23 (%20) |

*mSIS: Modified Systemic Inflammation Score

**Table 2** Correlation between mSIS and prognostic markers

| | mSIS 0 | mSIS 1 | mSIS 2 | p |
|---|---|---|---|---|
| **Rupture** | 7 | 4 | 8 | 0,069 |
| **Necrosis** | 7 | 9 | 9 | 0,008 |
| **Hemorrhage** | 34 | 18 | 15 | 0,57 |

## Discussion

GIST is a rare pathology with a broad-spectrum prognosis. Important prognostic factors such as Ki-67 and presence of necrosis-rupture-hemorrhage in the tumor can only be learned after surgical resection (5). Finding a preoperative prognostic marker as valuable as postoperative markers may be effective in treatment planning and increasing disease-free survival. For this purpose, the relationship between mSIS score and prognostic parameters for GIST was evaluated in our study.

In studies on GIST prognosis, high Ki-67 levels and the presence of necrosis, hemorrhage and rupture in the tumor were found to be among the poor prognostic factors. A study of 114 patients showed that the presence of necrosis in the tumor was an independent risk factor for poor prognosis. In a study examining only gastric-located GISTs, it was found that the presence of necrosis in the tumor reduced the 5-year disease-free survival from 94.9 % to 71.6 % (13-16). In our study, a significant relationship was found between mSIS and only tumor necrosis among the prognostic parameters of GIST.

## Conclusion

The mSIS score is a valuable indicator of inflammation in the body. Many studies have shown a correlation with the presence of malignancy and prognosis, but in our study, a correlation was found only with the presence of tumor necrosis. We believe that more comprehensive studies are needed, as the results will not be effective in predicting prognosis and determining treatment in the preoperative period.

**Conflict of Interest Statement**
The authors have no conflicts of interest to declare.

**Ethical Approval**
This study was conducted in accordance with the Declaration of Helsinki with the approval of Ankara City Hospital Clinical Research Ethics Committee No. 1 dated 07.06.2023 and numbered E1-23-3649.

**Consent to Participate and Publish**
Written informed consent to participate and publish was not obtained due to retrospective nature of the study.

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**Authors Contributions**
F.C: Conceptualization; Investigation; Methodology; Writing-original draft

S.O: Conceptualization; Methodology; Writing-review & editing.

C.C: Investigation; Data curation; Formal analysis; Validation

A.G: Formal Analysis; Research; Data curation

İ.G: Supervision; Writing-review & editing.

S.G.T: Conceptualization, Writing-review & editing.

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