Tepecik Eğit. ve Araşt. Hast. Dergisi 2019;29(2):148-156
doi:10.5222/terh.2019.65668

# Effectiveness of Radiological Findings of Gastrointestinal Stromal Tumors in the Prediction of High-Risk Potential for Malignancy

## *Gastrointestinal Stromal Tümörlerin Radyolojik Bulgularının Malignite Potansiyelini Öngörmedeki Etkinliği*

Özgün Araştırma
*Research Article*

**Fatma Ceren Sarioglu, Dilek Oncel, Orkun Sarioglu, Asli Irmak Biranci, Gulden Diniz**

**ABSTRACT**

***Objective:*** *The purpose of our study was to investigate the effectiveness of radiological findings in the prediction of malignancy potential in gastrointestinal stromal tumors according to the National Institutes of Health and the Armed Forces Institute of Pathology criteria.*
***Methods:*** *In our study 50 patients who were diagnosed pathologically as gastrointestinal stromal tumors between January 2010 and January 2018 were evaluated retrospectively. Twenty-seven patients were excluded from the study because their preoperative computed tomography results could not be reached. We evaluated preoperative computed tomography examinations of 23 patients included in the study with gastrointestinal stromal tumors according to size, contour, central hypoattenuation, homogeneity, contrast enhancement, growth pattern, mesenteric heterogeneity, local invasion to surrounding tissues, cavitation, concomitant presence of lymphadenopathy larger than 1 cm, fluid collection and metastasis. Radiological findings were compared with histopathologic findings, and the effectiveness of radiological findings on the prediction of malignancy potential was evaluated according to the National Institutes of Health and the Armed Forces Institute of Pathology criteria. Univariate and multivariate logistic regression analyses were used and p<0.05 was accepted as the level of statistical significance.*
***Results:*** *Tumor size (p=0.023) and central hypodensity (p=0.036) were found to be statistically significant for risk stratification according to the National Institutes of Health criteria. Contour irregularity (p=0.036, p=0.026) and mesenteric heterogeneity (p=0.021, p=0.005) were found to be statistically significant in decreasing importance in the evaluation of high risk potential according to the National Institutes of Health and the Armed Forces Institute of Pathology criteria, respectively.*
***Conclusion:*** *Contour irregularity and mesenteric heterogeneity may be useful to predict the high risk potential according to the both criteria. Tumor size and central hypodensity may provide risk stratification according to the NIH criteria.*

***Keywords:*** *Gastrointestinal stromal tumor, computed tomography, malignant, benign*

**ÖZ**

***Amaç:*** *Çalışmamızın amacı gastrointestinal stromal tümörlerin radyolojik bulgularının malignite potansiyelini öngörmedeki etkinliğinin National Institutes of Health ve Armed Forces Institute of Pathology kritlerine göre araştırılmasıdır.*
***Yöntem:*** *Çalışmamızda Ocak 2010-Ocak 2016 tarihleri arasında patolojik olarak gastrointestinal stromal tümör tanısı almış 50 hasta rerospektif olarak incelenmiştir. Yirmi yedi hasta preoperatif bilgisayarlı tomografi tetkiklerine ulaşılamadığından çalışma dışı bırakılmıştır. Çalışmaya dahil olan 23 hastanın preoperatif bilgisayarlı tomografi tetkiklerinde tümörler boyut, kontur özellikleri, homojenite, kontrastla boyanma şekli, santral hipoatenüasyon varlığı, büyüme paterni, mezenterik heterojenite, çevre dokulara invazyon, kavitasyon, eşlik eden batın içi serbest sıvı, eşlik eden karaciğer metastazı ve 1 cm'den büyük lenf nodunun varlığı açısından değerlendirilmiştir. Radyolojik bulgular histopatolojik bulgular ile kıyaslanmış ve radyolojik bulguların malignite potansiyelini öngörmedeki etkinlikleri araştırılmıştır. Tek değişkenli ve çok değişkenli lojistik regresyon analizleri kullanılmış ve p<0,05 olması anlamlı kabul edilmiştir.*
***Bulgular:*** *Yirmi üç hasta ile yaptığımız çalışmamızda tümör boyutu (p=0,023) ve santral hipodansite varlığı (p=0,036) National Institutes of Health kriterlerine göre risk grubunu belirlemede anlamlı bulundu. Kontur düzensizliği (p=0,036, p=0,026) ve mezenterik heterojenite (p=0,021, p=0,005) ise sırasıyla hem National Institutes of Health hem de Armed Forces Institute of Pathology kritelerine göre yüksek risk varlığını belirlemede anlamlı olarak bulundu.*
***Sonuç:*** *Sonuç olarak, kontur düzensizliği ve mezenterik heterojenite yüksek risk varlığını ön görmede yol gösterici olabilmektedir. Tümörlerin radyolojik olarak benign ve malign olma özellikleri tedavi ve takip sürecinde hastalar için önemli farklar yarattığından, çalışmamızın bu süreçlerde önemli yarar sağlayacağını düşünmekteyiz.*

***Anahtar kelimeler:*** *Gastrointestinal stromal tümör, bilgisayarlı tomografi, malign, benign*

**Alındığı tarih:** 05.01.2019
**Kabul tarihi:** 10.01.2019
**Online Yayın tarihi:** 29.08.2019

**Fatma Ceren Sarioglu**
*Dokuz Eylul Üniversitesi*
*Tıp Fakültesi,*
*Radyoloji Anabilim Dalı,*
*Izmir - Türkiye*
drcerenunal@gmail.com
**ORCİD:** 0000-0002-6714-2367

**D. Oncel** 0000-0001-5341-5558
**O. Sarioglu** 0000-0003-1173-8046
**A.I. Biranci** 0000-0002-6262-1799
*SBÜ İzmir Tepecik Eğitim ve*
*Araştırma Hastanesi,*
*Radyoloji Anabilim Dalı,*
*İzmir, Türkiye*

**G. Diniz** 0000-0003-1512-7584
*SBÜ İzmir Tepecik Eğitim ve*
*Araştırma Hastanesi,*
*Patoloji Anabilim Dalı,*
*İzmir, Türkiye*

**Cite as:** Sarioglu FC, Oncel D, Sarioglu O, Biranci AI, Diniz G. Effectiveness of radiological findings of gastrointestinal stromal tumors in the prediction of high-risk potential for malignancy. Tepecik Eğit. ve Araşt. Hast. Dergisi. 2019;29(2):148-56.

© Telif hakkı T.C. Sağlık Bakanlığı İzmir Tepecik Eğit. ve Araşt. Hastanesi. Logos Tıp Yayıncılık tarafından yayınlanmaktadır. Bu dergide yayınlanan bütün makaleler Creative Commons Atıf-GayriTicari 4.0 Uluslararası Lisansı ile lisanslanmıştır.

© Copyright Association of Publication of the T.C. Ministry of Health İzmir Tepecik Education and Research Hospital. This journal published by Logos Medical Publishing.
Licenced by Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0)

## INTRODUCTION

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal tumors of the gastrointestinal (GI) tract [1]. GISTs originate from interstitial cells of Cajal localized in muscularis propria of the GI tract [2,3]. GISTs are usually seen in the middle-aged and older adults [2]. They occur anywhere along the GI tract but are most commonly seen in the stomach and small bowel [4]. Colon, rectum, and esophagus are less frequently affected [4,5]. Furthermore, there are areas of extra-GI tract, especially the mesentery, omentum and retroperitoneum [6]. GISTs are often located in muscularis propria; therefore routine endoscopic technique can be inadequate to show this type of tumor. Computed tomography (CT), magnetic resonance imaging, and endoscopic ultrasonography are useful to detect GISTs [7,8]. Imaging techniques play an important role to show the relationship between the tumoral mass and adjacent structure, to determine the metastatic lesions and to evaluate the potential of recurrence in post-treatment period.

The definite identification and risk stratification of GISTs are essential since the unresectable or metastatic GISTs can be treated with a specific molecular therapy that is chosen according to the genetic defect [9]. There are great differences between the group of very low risk and high risk groups regarding treatment and follow-up. In the literature, there are two major classifications; the National Institutes of Health (NIH) criteria and the Armed Forces Institute of Pathology (AFIP) criteria, to stratify risk groups, linking them to a higher or lower risk of tumor recurrence and distant metastasis [10,11]. Tumor recurrence and distant metastasis are accepted as malign behaviors. According to these criteria, the malignancy risk of GISTs has been categorized as very low, low, moderate, and high. In 2002, based on the NIH criteria, the risk of recurrence has been estimated according to tumor size and mitotic activity [11]. The anatomical localization is not taken into account in this study. In 2006, AFIP criteria presented by Miettinen et al. [10], suggested a new modified risk stratification that evaluates the size, mitotic activity and also anatomical localization. Comparison of the NIH and AFIP criteria is important when a GIST is stratified into the moderate risk group according to NIH criteria, because a differentiation occurs in terms of tumor location according to AFIP criteria. For instance, a GIST localized at stomach may be stratified into the moderate risk group while it may be in the high-risk group at small intestine. Several studies in the literature concerned about the prediction of malignancy potential in GISTs with CT findings [5,12,13]. However, to our knowledge, the prediction of high-risk potential for malignancy in GISTs by using CT and comparison of relationships between risk groups for malignancy and CT findings according to the NIH and AFIP criteria have not been evaluated together.

The purpose of our study was to identify the prediction of malignancy potential in GISTs by using CT findings and comparison of relationships between risk groups for malignancy and CT findings according to the NIH and AFIP criteria.

## MATERIALS and METHODS

### Patient selection

This retrospective study included 50 patients who were operated and had a histopathological confirmation between January 2010 and January 2016. However, 27 patients were excluded from the study because we could not reach their preoperative radiologic examinations. For the remaining 23 patients, preoperative radiologic examinations and pathology reports were obtained from our picture archiving and communication system (PACS) archive. Additionally, these 23 patients also did not receive neoadjuvant tyrosine kinase inhibitors to provide the accurately mitotic count in the final resection. The study was approved by the Human Research Ethics Committee of our institution. Informed consent was obtained from all the patients.

**Imaging acquisition**

CT examinations were performed by using a 128-slice system (Somatom Definition AS; Siemens, Munich, Germany) and 64-slice system (Aquilion; Toshiba Medical Systems, Tochigi, Japan). Routine abdominal CT examinations were obtained from the xiphoid process to the symphysis pubis as well as the inguinal canal orifices. The parameters of 128-slice system CT were following: 0.6 mm × 128 detector rows, tube current modulation at 120 kV, rotation time 0.5 sec, field of view of 360 mm, and 5-mm thickness with 5 mm interval for image reconstruction. The parameters of 64-slice system CT were following: 0.5 mm × 64 detector row, tube current modulation at 120 kV, rotation time 0.5 sec, field of view of 360 mm, and 5-mm thickness with 5 mm interval for image reconstruction. Nonionic contrast material was used for all the patients. The images were performed after the administration of 1 ml/kg of 350 mgI/ml iodized non-ionic venous contrast material (Xenetix, 350 mg Iodine/mL, Guerbet, Istanbul, Turkey) by an automatic injector at a rate of 3 mL/s. Oral contrast-enhanced CT was performed in some of patients. Remainders were not excluded since using orally administered contrast material is not essential to determine all of the features of GISTs. All the scans, including axial slices, coronal and sagittal reformatted images were obtained.

**Imaging interpretation**

We evaluated the tumors retrospectively with CT scan, according to size, contour characteristics, central hypodense area, grade of contrast enhancement, growth pattern, mesenteric heterogeneity, local invasion, mucosal ulceration, intraabdominal fluid collection, metastasis and presence of regional lymphadenopathy. The greatest dimension which was evaluated in both 3-planes was considered for the measurement of the tumor size as they were classified into three groups, as <5 cm, 5-10 cm, and >10 cm. Contour characteristics were classified as regular and irregular. To evaluate the central hypodense area, which contained necrosis, ulceration, or hemorrhage, we were looked for a hypoattenuated area within the tumor. For determining the grade of contrast enhancement, circular region-of-interest (ROI) cursors were placed over the tumor, liver parenchyma and paravertebral muscles on a commercially available workstation using PACS. The ROI circle was made as 1 cm. The Hounsfield units were measured and compared. There were three subgroups classified based on densities of paravertebral muscles and liver as follows: poor (the density of tumor is equal or lower than paravertebral muscles), moderate (the density of tumor is between paravertebral muscles and liver parenchyma), and good (the density of tumor is equal or higher than liver parenchyma). The growth pattern was classified as intraluminal, extraluminal and mixed. Striations in fatty tissue adjacent to tumor were considered as mesenteric heterogeneity. The relationship between the tumor and adjacent structures was considered for the evaluation of local invasion. An ulceration on the luminal site which was filled with air and fluid was accepted as a mucosal ulceration. Regional lymphadenopathy was considered as positive if it was greater than 1 cm in short-axis dimension.

All of the images were evaluated by two radiologists (F.C.S., A.I.B.) who had four- and three years of experience, respectively. The readers were unaware of the operation findings and tumors' risk groups. The readers evaluated the CT images and recorded the findings. In cases of the disagreement between the two radiologists, the images were reevaluated and the final decision was reached by consensus. Besides, a third radiologist (D. O.) who had twenty years of experience reanalyzed the imaging data, and the majority opinion was accepted.

These findings were correlated with histopathologic findings, and their relevance for the prediction of malignancy potential was evaluated.

**Assessment of risk groups for malignancy**

All of the patients underwent various methods of

surgical resection such as stomach wedge resection, intestinal resection, and subtotal gastrectomy. An expert pathologist confirmed the diagnosis of GIST and calculated their mitotic index that was determined by counting the number of mitotic figures per 50 high-power fields (HPFs). We classified these tumors according to the NIH and AFIP criteria separately. Tables 1 and 2 summarize the risk stratifications according to the NIH and AFIP criteria, respectively. Also, for both groups, we evaluated the tumors if they have a high-risk potential for malignancy.

### Statistical analysis

All statistical analyses were performed with SPSS software, version 22.0 (IBM corp., Armonk, NY, USA). A univariate and chi-square analysis of the following factors was performed; size, contour characteristics, central hypodense area, grade of contrast enhancement, growth pattern, mesenteric heterogeneity, local invasion, mucosal ulceration, intraabdominal fluid collection, metastasis and presence of regional lymphadenopathy anticipated to be associated with high-risk potential for malignancy. Differences were considered significant when p values were less than 0.05.

**Table 1. Risk stratification according to the NIH criteria [11].**

| Risk | Tumor size (cm) | Mitotic count (n/50 HPF) |
|---|---|---|
| Very low | <2 | <5 |
| Low | 2-5 | <5 |
| Moderate | <5 | 6-10 |
| | 5-10 | <5 |
| High | >5 | >5 |
| | >10 | Any mitotic rate |
| | Any size | >10 |

*NIH: National Institutes of Health, HPF: High-power field*

## RESULTS

Of the 23 patients with GISTs, 11 were male (47.8%) and 12 were female (52.2%). The age range of the patients was 39-85 (mean age, 62.7). Tumors were located in stomach (n=15; 65.2%), duodenum (n=3; 13.1%), jejenum/ileum (n=5; 21.7%). No GIST detected in esophagus, colon, anorectum, or extra-GI tract.

According to the NIH criteria, tumors were classified in low (n=4 :17.3%), intermediate (n=4:17.3%), and high-risk (n=15:65.2%) groups, and none of them were in very low-risk group. According to the AFIP criteria, 2 (8.6%), and the tumors were classified in very low (n=2: 8.6%), low5 (21.7%), intermediate (n=3:13%), and high-risk (n=13: 56.5%) groups. Table 3 summarizes the CT characteristics of GISTs and the relationship between CT findings and risk stratification according to the NIH and AFIP criteria. GISTs size ranged from 2 to 25 cm. Tumor size (p=0.023) and central hypodensity (p=0.036) were found as the

**Table 2. Risk stratification according to the AFIP criteria [10].**

| Risk | Stomach<br>Tumor size (x)<br>and mitotic count (n/50 HPF) | Duodenum<br>Tumor size (x) and mitotic<br>count (n/50 HPF) | Jejunum/ileum<br>Tumor size (x) and mitotic<br>count (n/50 HPF) | Rectum<br>Tumor size (x) and mitotic<br>count (n/50 HPF) |
|---|---|---|---|---|
| None | x≤2 cm and ≤5<br>x≤2 cm and >5* | x≤2 cm and ≤5 | x≤2 cm and ≤5 | x≤2 cm and ≤5 |
| Very low | 2<x≤5 cm and ≤5 | ** | ** | ** |
| Low | 5<x≤10 cm and ≤5 | 2<x≤5 cm and ≤5 | 2<x≤5 cm and ≤5 | 2<x≤5 cm and ≤5 |
| Moderate | x>10 cm and ≤5<br>2<x≤5 cm and >5 | ** | 5<x≤10 cm and ≤5 | ** |
| High | 5<x≤10 cm and >5<br>>10 cm and >5 | x>10 cm and ≤5<br>2<x≤5 cm and >5<br>>10 cm and >5 | x>10 cm and ≤5<br>2<x≤5 cm and >5<br>5<x≤10 cm and >5<br>>10 cm and >5 | x>10 cm and ≤5*<br>x≤2 cm and >5<br>2<x≤5 cm and >5<br>>10 cm and >5 |

** Category with small number of cases, ** Category with insufficient number of cases for prediction of malignant potential, AFIP: Armed Forces Institute of Pathology, HPF: High-power field*

**Table 3. Risk stratification by using the CT characteristics according to the NIH and AFIP criteria.**

| Characteristic | Very low risk (NIH/AFIP) | Low risk (NIH/AFIP) | Moderate risk (NIH/AFIP) | High risk (NIH/AFIP) | Total (n=23) | P value (NIH/AFIP) |
|---|---|---|---|---|---|---|
| **Tumor size** | | | | | | 0.023/ 0.083 |
| <5 cm | 0 / 2 | 3 / 1 | 0 / 1 | 2 / 1 | 5 | |
| 5-10 cm | 0 / 0 | 1 / 4 | 4 / 1 | 8 / 8 | 13 | |
| >10 cm | 0 / 0 | 0 / 0 | 0 / 1 | 5 / 4 | 5 | |
| **Contour** | | | | | | 0.095/ 0.063 |
| Irregular | 0 / 0 | 1 / 2 | 2 / 2 | 12 / 11 | 15 | |
| Regular | 0 / 2 | 3 / 3 | 2 / 1 | 3 / 2 | 8 | |
| **Central hypodensity** | | | | | | 0.036/ 0.085 |
| Absent | 0 / 2 | 3 / 1 | 0 / 1 | 3 / 2 | 6 | |
| Present | 0 / 0 | 1 / 4 | 4 / 2 | 12 / 11 | 17 | |
| **Grade of contrast enhancement** | | | | | | 0.093/ 0.974 |
| Poor | 0 / 1 | 3 / 2 | 0 / 1 | 7 / 6 | 10 | |
| Moderate | 0 / 1 | 1 / 3 | 4 / 2 | 8 / 7 | 13 | |
| Good | 0 / 0 | 0 / 0 | 0 / 0 | 0 / 0 | 0 | |
| **Growth pattern** | | | | | | 0.861/ 0.516 |
| Intraluminal | 0 / 0 | 1 / 1 | 0 / 1 | 2 / 1 | 3 | |
| Extraluminal | 0 / 2 | 2 / 1 | 2 / 1 | 7 / 7 | 11 | |
| Mixed | 0 / 0 | 1 / 3 | 2 / 1 | 6 / 5 | 9 | |
| **Mesenteric heterogeneity** | | | | | | 0.068/ 0.052 |
| Absent | 0 / 2 | 4 / 5 | 4 / 3 | 8 / 6 | 16 | |
| Present | 0 / 0 | 0 / 0 | 0 / 0 | 7 / 7 | 7 | |
| **Local invasion** | | | | | | 0.584/ 0.087 |
| Absent | 0 / 2 | 4 / 5 | 3 / 1 | 12 / 11 | 19 | |
| Present | 0 / 0 | 0 / 0 | 1 / 2 | 3 / 2 | 4 | |
| **Mucosal ulceration** | | | | | | 0.738/ 0.157 |
| Absent | 0 / 2 | 2 / 1 | 2 / 2 | 10 / 9 | 14 | |
| Present | 0 / 0 | 2 / 4 | 2 / 1 | 5 / 4 | 9 | |
| **Intraabdominal fluid collection** | | | | | | 0.558/ 0.640 |
| Absent | 0 / 2 | 4 / 5 | 4 / 3 | 13 / 11 | 21 | |
| Present | 0 / 0 | 0 / 0 | 0 /0 | 2 / 2 | 2 | |
| **Metastasis** | | | | | | 0.757/ 0.848 |
| Absent | 0 / 2 | 4 / 5 | 4 / 3 | 14 / 12 | 22 | |
| Present | 0 / 0 | 0 / 0 | 0 / 0 | 1 / 1 | 1 | |
| **Regional lymhadenopathy** | | | | | | 0.399/ 0.448 |
| Absent | 0 / 2 | 4 / 5 | 4 / 3 | 12 / 10 | 20 | |
| Present | 0 / 0 | 0 / 0 | 0 / 0 | 3 / 3 | 3 | |

*CT: Computed Tomography, AFIP: Armed Forces Institute of Pathology, NIH: National Institutes of Health*

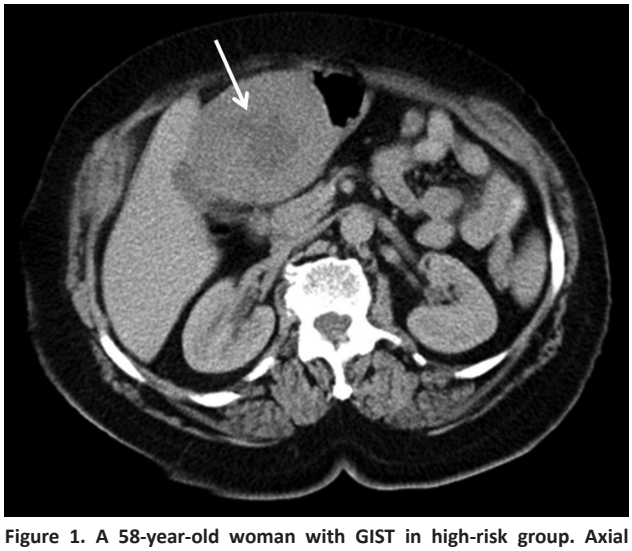


**Figure 1. A 58-year-old woman with GIST in high-risk group. Axial contrast-enhanced scan shows central hypodensity (arrow) of gastric tumor.**

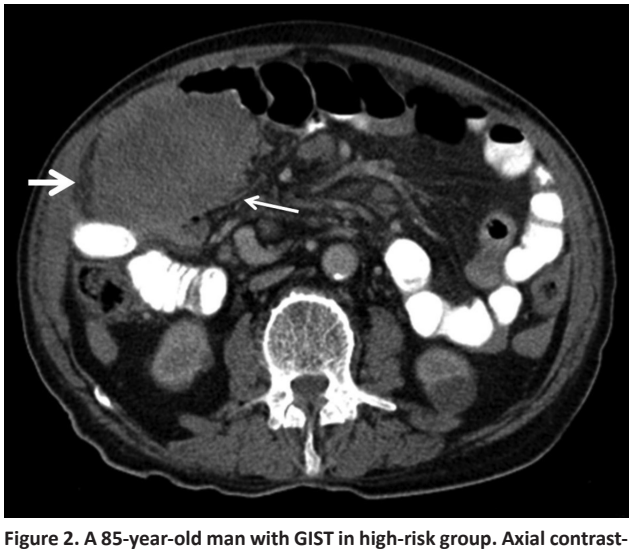


**Figure 2. A 85-year-old man with GIST in high-risk group. Axial contrast-enhanced CT scan shows mesenteric heterogeneity (thick arrow) and irregular contour (thin arrow) of ileal tumor.**

**Table 4. CT findings associated with high risk potential for malignancy according to the NIH and AFIP criteria.**

| Characteristic | Absence of high risk potential (NIH/AFIP) | Presence of high risk potential (NIH/AFIP) | Total (n=23) | P value (NIH/AFIP) |
|---|---|---|---|---|
| **Tumor size** | | | | 0.126/ 0.137 |
| <5 cm | 3 / 4 | 2 / 1 | 5 | |
| 5-10 cm | 5 / 5 | 8 / 8 | 13 | |
| >10 cm | 0 / 1 | 5 / 4 | 5 | |
| **Contour** | | | | 0.042/ 0.026 |
| Irregular | 3 / 4 | 12 / 11 | 15 | |
| Regular | 5 / 6 | 3 / 2 | 8 | |
| **Central hypodensity** | | | | 0.363/ 0.183 |
| Absent | 3 / 4 | 3 / 2 | 6 | |
| Present | 5 / 6 | 12 / 11 | 17 | |
| **Grade of contrast enhancement** | | | | 0.673/ 0.768 |
| Poor | 3 / 4 | 7 / 6 | 10 | |
| Moderate | 5 / 6 | 8 / 7 | 13 | |
| Good | 0 / 0 | 0 / 0 | 0 | |
| **Growth pattern** | | | | 0.988/ 0.642 |
| Intraluminal | 1 / 2 | 2 / 1 | 3 | |
| Extraluminal | 4 / 4 | 7 / 7 | 11 | |
| Mixed | 3 / 4 | 6 / 5 | 9 | |
| **Mesenteric heterogeneity** | | | | 0.021/ 0.005 |
| Absent | 8 / 10 | 8 / 6 | 16 | |
| Present | 0 / 0 | 7 / 7 | 7 | |
| **Local invasion** | | | | 0.651/ 0.772 |
| Absent | 7 / 8 | 12 / 11 | 19 | |
| Present | 1 / 2 | 3 / 2 | 4 | |
| **Mucosal ulceration** | | | | 0.435/ 0.349 |
| Absent | 4 / 5 | 10 / 9 | 14 | |
| Present | 4 / 5 | 5 / 4 | 9 | |
| **Intraabdominal fluid collection** | | | | 0.280/ 0.194 |
| Absent | 8 / 10 | 13 / 11 | 21 | |
| Present | 0 / 0 | 2 / 2 | 2 | |
| **Metastasis** | | | | 0.455/ 0.370 |
| Absent | 8 / 10 | 14 / 12 | 22 | |
| Present | 0 / 0 | 1 / 1 | 1 | |
| **Regional lymhadenopathy** | | | | 0.175/ 0.103 |
| Absent | 8 / 10 | 12 / 10 | 20 | |
| Present | 0 / 0 | 3 / 3 | 3 | |

*CT: Computed Tomography, AFIP: Armed Forces Institute of Pathology, NIH: National Institutes of Health*

most significant CT findings concerning risk stratification according to the NIH criteria. Central hypodensity was shown in Figure 1. Five of 23 tumors >10 cm in size were in the high-risk group. Seventeen of the 23 tumors with central hypodensity were in the low (n=1; 5.9%) , intermediate (n=4: 23.5%), high risk (n=12: 70.5%) groups. Any significant difference was not found between CT findings and risk stratification according to the AFIP criteria.

Table 4 summarizes the CT findings associated with the presence or absence of high-risk potential for malignancy according to the NIH and AFIP criteria. The statistical analysis demonstrated that contour (p=0.04 vs p=0.026) and mesenteric heterogeneity (p=0.021 vs p=0.005) were significant for high risk potential according to NIH, and AFIP criteria. respectively. Mesenteric heterogeneity and irregular contour were shown in Figure 2. According to NIH criteria 12 (80%) out of 15, and to AFIP criteria 11 (73.3%) tumors with irregular contours were associated with high-risk potential. Seven tumors with mesenteric heterogeneity belonged to the high-risk group according to both of two criteria. Additionally, according to the NIH and AFIP criteria, 8 (50%) and 10 (62.5%) of 16 tumors without mesenteric heterogeneity did not have high-risk potential, respectively.

## DISCUSSION

In this study, we found that tumor size and presence of central hypodensity were statistically significant for determination of risk stratification according to the NIH criteria. Furthermore, contour characteristics and mesenteric heterogeneity were the most significant features for the prediction of high-risk potential in GISTs according to both NIH and AFIP criteria.

There were numerous prognostication systems for the risk stratification of GISTs and many studies investigated the most accurate system [14]. The parameters vary in these systems. The most common variables include tumor size, mitotic rate, and location. The results of the prediction of high-risk potential for malignancy in GISTs by using CT findings also vary in the literature. Tateishi et al. [15] found the following significant features for prediction of high risk potential in GIST tumors, which are tumor larger than 11.1 cm (median + 1 SD), irregular surface, indistinct contours, presence of invasion, heterogeneous enhancement, hepatic metastasis, and peritoneal dissemination. Yang et al. [13] found large tumor size (≥ 5 cm) and old age were correlated with high-risk potential in GISTs.

GISTs occur at a median age of 60 years in most series [8,12,16,17]. In our study, GISTs have no gender predilection like some other studies [5,13,15]; however, a male predominance has been shown in the literature [18,19]. In our series, GISTs were commonly located in the stomach followed by the small bowel which is compatible with previous studies [10,13]. We did not have any patients with GISTs in large bowel, esophagus, or extra GI tract [1,4,6]. In the literature, there are some studies limited to gastric GISTs [5,12,20,21]. In a study of O'Neill et al. [21], which assessed the metastatic risk of gastric GISTs by CT features according to the AFIP criteria, they found that tumor size >10 cm, an irregular/lobulated margin and the presence of a solid enhancing component were independently associated with an increased risk of metastatic disease, a higher mitotic count and worse survival. Similar to our study, Pelandre et al. [12]. included only gastric GISTs in their study, and found a statistically significant correlation between irregular morphology, mesenteric heterogeneity and high mitotic index. Necrosis, ulceration, or hemorrhage are more likely to be seen as the tumor size increases [1]. Therefore, central hypodensity and tumoral heterogeneity may occur at CT images. Some studies have shown a correlation between the central hypodensity and high mitotic rate [20,22]. On the other hand, Miettinen et al. [3] had shown that ulceration could also be found in both very low risk and high risk GISTs. In our study, there was statistical significance between central hypodensity and risk group stratification according to the NIH criteria. However, there was no correlation between central hypodensity and determination of risk groups because of inhomogeneity of tumor distribution by localization and small patients group.

Mesenteric heterogeneity is a finding that demonstrates the aggressive behavior of the tumors due to the fatty tissue infiltration. Our study found a correlation between mesenteric heterogeneity and high risk potential similarly with some studies [5].

Liver and periton are the most common metastatic sites of GISTs [23]. Some studies reported that the presence of metastasis is associated with a high risk potential [2,3,18]. Although liver metastases are apparently hypodense when compared with liver parenchyma in a portal venous phase [18], small metastases may also be hypervascular [24], so they may be missed on a single venous phase CT. Therefore, it would be useful to include the arterial phase in the CT protocol in order not to overlook metastases. In our study, CT scan was performed only in a portal venous phase and was detected in one patient with a metastatic liver lesion. We thought some liver metastasis might have been missed due to not using the arterial phase imaging similar to other studies.

Metastatic lymphadenopathy is an uncommon finding in GISTs [1]. In a study of Kim et al. [5], 1 of 2 tumors which were accompanied with regional lymphadenopathy has been determined as having a malignant potential. However, the results of histopathological evaluation of these lymph nodes was not mentioned in this study. In our cases, 3 patients who had regional lymphadenopathy were in the high-risk group, but tumoral infiltration was not found in the histopathological analysis.

Our study had several limitations. First, the study was performed retrospectively and we could not follow-up prognosis of our patients. Second, our patient population was small. In light of the data from the small number of patients, histopathological analyses will have to be conducted to show the relation of these results to the prognosis. Third, tumor distribution was inhomogeneous, and we had no patients with GISTs in esophagus, colon, or anorectum. This limitation may have led to a statistically insignificant result in determining risk stratification according to the AFIP criteria. However, no study has shown the relation between CT findings and the prediction of high-risk potential for malignancy according to both NIH and AFIP criteria. Fourth, CT scans were performed only in a portal venous phase so that some liver metastasis might have been missed. Fifth, mutational analysis was not performed. Therefore, we are going to increase the number of patients and continue with this series with optimal CT protocols in the future.

In conclusion, CT imaging may be useful in distinguishing between high-risk groups and very low-risk groups in GISTs. The presence of irregular contour or mesenteric heterogeneity has shown the highest sensitivity for predicting the high-risk potential for malignancy according to NIH and AFIP criteria. Besides, according to the NIH criteria, tumor size and central hypodensity were statistically significant for risk stratification.

**Ethics Committee Approval:** T.C. Ministry of Health, Public Hospitals Authority Turkey Izmir North Public Hospital Association General Secretariat of the Tepecik Training and Research Hospital Ethics Committee approval has been received (2016/8).
**Conflict of Interest:** The authors have no conflict of interest.
**Funding:** None.

**Etik Kurul Onayı:** T.C. Sağlık Bakanlığı Türkiye Kamu Hastaneleri Kurumu İzmir Kuzey Kamu Hastaneleri Birliği Genel Sekreterliği Tepecik Eğitim ve Araştırma Hastanesi Etik Kurul onayı alınmıştır (2016/8).
**Çıkar Çatışması:** Yok.
**Finansal Destek:** Yok.

## REFERENCES

1. Levy AD, Remotti HE, Thompson WM, Sobin LH, Miettinen M. Gastrointestinal stromal tumors: radiologic features with pathologic correlation. Radiographics. 2003;23(2):283-304. [CrossRef]
2. Hasegawa T, Matsuno Y, Shimoda T, Hirohashi S. Gastrointestinal stromal tumor: consistent CD117 immunostaining for diagnosis, and prognosticclassification based on tumor size and MIB-1 grade. Hum Pathol. 2002;33(6):669-76. [CrossRef]
3. Miettinen M, El-Rifai W, H L Sobin L, Lasota J. Evaluation of malignancy and prognosis of gastrointestinal stromal tumors: a review. Hum Pathol. 2002;33(5):478-83. [CrossRef]
4. Miettinen M, Sarlomo-Rikala M, Lasota J. Gastrointestinal stromal tumors: recent advances in understanding of their biology. Hum Pathol. 1999;30(10):1213-20. [CrossRef]
5. Kim HC, Lee JM, Kim KW, Park SH, Kim SH, Lee JY, et al. Gastrointestinal stromal tumors of the stomach: CT findings and prediction of malignancy. AJR Am J Roentgenol. 2004;183(4):893-8. [CrossRef]
6. Miettinen M, Monihan JM, Sarlomo-Rikala M, Kovatich AJ, Carr NJ, Emory TS, et al. Gastrointestinal stromal tumors/smooth muscle tumors (GISTs) primary in the omentum and mesentery: clinicopathologic and immunohistochemical study of 26 cases. Am J Surg Pathol. 1999;23(9):1109-18. [CrossRef]
7. Chourmouzi D, Sinakos E, Papalavrentios L, Akriviadis E, Drevelegas A. Gastrointestinal stromal tumors: a pictorial review. J Gastrointestin Liver Dis. 2009;18(3):379-83.
8. Kim MN, Kang SJ, Kim SG, Im JP, Kim JS, Jung HC, et al. Prediction of risk of malignancy of gastrointestinal stromal tumors by endoscopic ultrasonography. Gut Liver. 2013;7(6):642-7. [CrossRef]
9. Mei L, Smith SC, Faber AC, Trent J, Trent J, Grossman SR, et al. Gastrointestinal Stromal Tumors: The GIST of Precision Medicine. Trends Cancer. 2018;4(1):74-91. [CrossRef]
10. Miettinen M, Lasota J. Gastrointestinal stromal tumors: pathology and prognosis at different sites. Semin Diagn Pathol. 2006;23(2):70-83. [CrossRef]
11. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J,

Longley BJ, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. Hum Pathol. 2002;33(5):459-65. [CrossRef]
12. Pelandré GL, Djahjah MC, Gasparetto EL, Nacif MS, Marchiori E, Mello EL. Tomographic findings of gastric gastrointestinal stromal tumor and correlation with the mitotic index. Arq Gastroenterol. 2013;50(4):244-50. [CrossRef]
13. Yang TH, Hwang JI, Yang MS, Hung SW, Chan SW, Wang J, et al. Gastrointestinal stromal tumors: computed tomographic features and prediction of malignantrisk from computed tomographic imaging. J Chin Med Assoc. 2007;70(9):367-73. [CrossRef]
14. Khoo CY, Chai X, Quek R, Teo MCC, Goh BKP. Systematic review of current prognostication systems for primary gastrointestinal stromal tumors. Eur J Surg Oncol. 2018;44(4):388-94. [CrossRef]
15. Tateishi U, Hasegawa T, Satake M, Moriyama N. Gastrointestinal stromal tumor. Correlation of computed tomography findings with tumor grade and mortality. J Comput Assist Tomogr. 2003;27(5):792-8. [CrossRef]
16. King DM. The radiology of gastrointestinal stromal tumours (GIST). Cancer Imaging. 2005;5:150-6. [CrossRef]
17. Blay JY, Bonvalot S, Casali P, Choi H, Debiec-Richter M, Dei Tos AP, et al. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20-21 March 2004, under the auspices of ESMO. Ann Oncol. 2005;16(4):566-78. [CrossRef]
18. Burkill GJ, Badran M, Al-Muderis O, Meirion Thomas J, Judson IR, Fisher C, et al. Malignant gastrointestinal stromal tumor: distribution, imaging features, and pattern of metastatic spread. Radiology. 2003;226:527-32. [CrossRef]
19. Ghanem N, Altehoefer C, Furtwangler A, Winterer J, Schäfer O, Springer O, et al. Computed tomography in gastrointestinal stromal tumors. Eur Radiol. 2003;13:1669-78. [CrossRef]
20. Miettinen M, Sobin LH, Lasota J. Gastrointestinal stromal tumors of the stomach: a clinicopathologic, immunohistochemical, and molecular genetic study of 1765 cases with long-term follow-up. Am J Surg Pathol. 2005;29(1):52-68. [CrossRef]
21. O'Neill AC, Shinagare AB, Kurra V, Tirumani SH, Jagannathan JP, Baheti AD, et al. Assessment of metastatic risk of gastric GIST based on treatment-naïve CT features. Eur J Surg Oncol. 2016;42(8):1222-8. [CrossRef]
22. Brainard JA, Goldblum JR. Stromal tumors of the jejunum and ileum: a clinicopathologic study of 39 cases. Am J Surg Pathol. 1997;21(4):407-16. [CrossRef]
23. Ulusan S, Koc Z. Radiologic findings in malignant gastrointestinal stromal tumors. Diagn Interv Radiol. 2009;15:121-6.
24. Sandrasegaran K, Rajesh A, Rydberg J, Rushing DA, Akisik FM, Henley JD. Gastrointestinal stromal tumors: clinical, radiologic, and pathologic features. AJR Am J Roentgenol. 2005;184(3):803-11. [CrossRef]