Original Article

Mol Imaging Radionucl Ther 2026;35(1):19-27 **DOI:***10.4274/mirt.galenos.2025.19052*

The Prognostic Significance of Preoperative Staging ^{18}F-FDG PET/MRI Findings in Gastric Cancer Patients Undergoing Gastrectomy

Gastrektomi Yapılan Mide Kanseri Hastalarında Preoperatif Evreleme ^{18}F-FDG PET/MRG Bulgularının Prognostik Önemi

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Abstract

Objective: The aim of this retrospective study was to investigate the prognostic value of preoperative findings on ^{18}F-fluorodeoxyglucose positron emission tomography/magnetic resonance imaging (^{18}F-FDG PET/MRI) in gastric cancer (GC) patients who underwent total or subtotal gastrectomy.

Methods: Patients with GC who underwent pretreatment staging with ^{18}F-FDG PET/MRI and subsequently underwent total or subtotal gastrectomy were included in the study. Demographic and clinicopathologic features of patients were recorded. The maximum wall thickness of gastric tumors, the minimum apparent diffusion coefficient (ADC_{min}), the total number and maximum standard uptake values (SUV_{max}) of ^{18}F-FDG-positive lymph nodes, the short-axis diameter of the largest lymph node, and the tumor SUV_{max}-to-liver SUV_{mean} ratio on ^{18}F-FDG PET/MRI were recorded. Predictors of mortality were evaluated using Cox proportional hazards regression models. Survival analysis was conducted using the Kaplan-Meier method.

Results: Seventy-eight patients with GC who underwent gastrectomy were included in the study. The median follow-up duration was 23.9 months (interquartile range: 33.4); 39 patients (50.0%) died during follow-up. In the multivariate analysis, the tumor SUV_{max}/liver SUV_{mean} ratio (p=0.002) and tumor histopathologic group (p<0.001) were identified as independent predictors of overall survival. The mean overall survival was 42.7 months [95% confidence interval (CI): 35.8-49.6]. The mean overall survival in the signet-ring cell carcinoma/other subtypes group (31.4 months; 95% CI: 22.3-40.4) was significantly shorter than that in the adenocarcinoma group (49.2 months; 95% CI: 40.3-58.2) (p=0.019). Patients with a tumor SUV_{max}/liver SUV_{mean} ratio greater than 2.6 on ^{18}F-FDG PET/MRI (35.7 months; 95% CI: 27.6-43.7) had a shorter overall survival than those with a ratio lower than 2.6 (57.1 months; 95% CI: 46.5-67.7) (p=0.005).

Conclusion: The tumor SUV_{max}-to-liver SUV_{mean} ratio may serve as a robust imaging biomarker for prognosis and for determining histopathologic subtype in GC patients who underwent total or subtotal gastrectomy.

Keywords: Gastric cancer, ^{18}F-FDG PET/MRI, prognosis, overall survival

Öz

Amaç: Bu retrospektif çalışmanın amacı, total veya subtotal gastrektomi uygulanan mide kanseri (GC) tanılı hastalarda preoperatif ^{18}F-florodeoksiglukoz pozitron emisyon tomografisi/manyetik rezonans görüntüleme (^{18}F-FDG PET/MRG) bulgularının prognostik değerini araştırmaktır.

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Received: 04.07.2025 **Accepted:** 26.10.2025 **Epub:** 28.11.2025 **Publication Date:** 03.02.2026

Cite this article as: Gülbahar Ateş Seda, Aydos U, Kalkan R, Akdemir ÜÖ, Atay LÖ. The prognostic significance of preoperative staging ^{18}F-FDG PET/MRI findings in gastric cancer patients undergoing gastrectomy. Mol Imaging Radionucl Ther. 2026;35(1):19-27.

Yöntem: Tedavi öncesi evreleme amacıyla ^{18}F-FDG PET/MRG çekilmiş ve ardından total veya subtotal gastrektomi uygulanmış GC tanılı hastalar çalışmaya dahil edilmiştir. Hastaların demografik ve klinikopatolojik özellikleri kaydedilmiştir. ^{18}F-FDG PET/MRG görüntülemesinde mide tümörlerinin maksimum duvar kalınlığı, minimum görünen difüzyon katsayısı (ADC_{min}) değeri, ^{18}F-FDG pozitif lenf nodu sayısı ve bu lenf nodlarının maksimum standart tutulum değeri (SUV_{maks}) değeri, en büyük lenf nodunun kısa eksen çapı ve tümör SUV_{maks}/karaciğer $SUV_{ortalama}$ oranı değerlendirilmiştir. Mortaliteyi ön gören faktörleri belirlemek amacıyla Cox regresyon analizi yapılmıştır. Sağkalım analizi Kaplan-Meier yöntemiyle değerlendirilmiştir.

Bulgular: Çalışmaya gastrektomi uygulanmış 78 hasta dahil edildi. Medyan takip süresi 23,9 (çeyrekler açıklığı: 33,4) ay olarak hesaplandı ve takip sürecinde 39 (%50,0) hastada mortalite izlendi. Çok değişkenli analizde tümör SUV_{maks}/karaciğer $SUV_{ortalama}$ oranı (p=0,002) ve tümörün histopatolojik grubu (p<0,001) genel sağkalımın bağımsız belirleyicileri olarak saptandı. Ortalama genel sağkalım 42,7 ay [%95 güven aralığı (GA): 35,8-49,6] idi. Taşlı yüzük hücreli karsinom/diğer alt tipler grubunda ortanca sağkalım süresi (31,4 ay, %95 GA: 22,3-40,4), adenokarsinom grubuna kıyasla (49,2 ay, %95 GA: 40,3-58,2) anlamlı derecede daha kısaydı (p=0,019).^{18}F-FDG PET/MRG'de tümör SUV_{maks}/karaciğer $SUV_{ortalama}$ oranı 2,6'dan yüksek olan hastalarda sağkalım (35,7 ay, %95 GA: 27,6-43,7), bu oranın 2,6'dan düşük olduğu hastalara kıyasla daha kısa bulundu (57,1 ay, %95 GA: 46,5-67,7) (p=0,005).

Sonuç: Total veya subtotal gastrektomi uygulanmış GC hastalarında tümör SUV_{maks}/karaciğer $SUV_{ortalama}$ oranı, histopatolojik alt tip ile birlikte, prognostik bir görüntüleme biyobelirteci olarak öne çıkmaktadır.

Anahtar Kelimeler: Mide kanseri, ^{18}F-FDG PET/MRG, prognoz, genel sağkalım

Introduction

Gastric cancer (GC) is the fifth most common cancer worldwide in both incidence and cancer-related mortality (1). It is a global health problem characterized by various risk factors, aggressive clinical behavior, and typically late-stage diagnosis. GC is a heterogeneous disease comprising multiple histopathologic subtypes and molecular features (2).

The appropriate management of GC patients is based on accurate staging. Computed tomography (CT) is the gold-standard imaging modality for staging GC. Moreover, in current clinical practice, when endoscopic ultrasound is performed to evaluate early-stage non-metastatic disease, especially in candidates for endoscopic resection, diagnostic laparoscopy can be used to identify radiologically occult peritoneal disease. ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) is increasingly used for staging GC to assess lymph node involvement and distant metastases, despite ongoing debate about its routine use in GC (2,3,4). It can provide various image-derived semiquantitative parameters, including maximum standardized uptake value (SUV_{max}), and qualitative diagnostic data. ^{18}F-FDG PET/CT has been shown to change treatment management in 3%-29% of GC patients (5). The use of these modalities improves staging accuracy and thus therapeutic management of GC.

The standard treatment for GC is surgery, with the primary goal of complete resection with negative margins (3). However, locoregional recurrence and cancer-related mortality can occur even after a curative surgical approach (6,7,8,9). Therefore, in the era of personalized medicine, predicting prognosis in GC patients who have undergone curative surgery may alter therapeutic management and ultimately improve patient outcomes. The prognostic significance of ^{18}F-FDG PET/CT parameters in GC has been investigated in various studies, although most included heterogeneous patient populations with respect to therapeutic approach (10,11). A limited number of studies have focused specifically on operated GC. Moreover, to the best of our knowledge, despite a few studies on ^{18}F-FDG PET/ PET/magnetic resonance imaging (MRI) in GC patients (12,13,14,15), no study has evaluated its prognostic value in this population. The MRI component of PET/MRI may enhance the prognostic value of ^{18}F-FDG PET in GC patients by providing functional information and superior soft-tissue contrast. Accordingly, the aim of the present study was to evaluate the prognostic value of preoperative ^{18}F-FDG PET/MRI staging findings in GC patients who underwent total or subtotal gastrectomy.

Material and Methods

Patient Population

This retrospective study was approved by Gazi University President's Office Ethics Commission (number: 2025-1103, date: 17.06.2025). The requirement for informed consent was waived. Patients with GC who underwent pretreatment staging with ^{18}F-FDG PET/MRI and subsequently underwent total or subtotal gastrectomy between 2018 and 2024 were included in the present study. Patients who had distant metastases on ^{18}F-FDG PET/MRI or a second primary malignancy were excluded from the study.

Clinicopathologic Features

Demographic and clinicopathologic features of patients were assessed using the hospital information system. Patients' ages, gender, and body mass index; history of chemotherapy and radiotherapy; type of gastrectomy (proximal, distal, or total); and extent of lymph node

dissection (D1 or D1+, D2 or D2+) were recorded. Tumor histopathologic subtype and Lauren classification, the location and diameter of primary gastric tumors, the total number of dissected lymph nodes and the number of metastatic lymph nodes, the diameter of the largest metastatic lymph node, and pathological T (pT) and N (pN) stages according to the 8th tumor–node–metastasis (TNM) staging system were obtained from the pathology reports. The status of human epidermal growth factor receptor 2 (HER_2/neu), the presence of lymphovascular and perineural invasion, and the positivity of surgical margins and peritoneal lavage fluid were recorded. Patients' follow-up was determined from medical records and continued until death, loss to follow-up, or the last documented medical visit. Follow-up duration and overall survival were calculated from the date of PET/MRI acquisition until the date of death or last clinical follow-up.

PET/MRI Acquisition

^{18}F-FDG PET/MRI images were acquired on an integrated 3-T PET/MRI scanner (GE Signa PET/MRI, GE Healthcare, Waukesha, Wisconsin, USA) equipped with a time-of-flight (TOF) PET detector in our department. Patients fasted for at least 4 hours before ^{18}F-FDG PET/MRI. The serum glucose levels measured at the time of ^{18}F-FDG injection were less than 200 mg/dL. ^{18}F-FDG was intravenously administered at a dose of 1.85 MBq/kg body weight. Whole-body ^{18}F-FDG PET/MRI was performed from the vertex of the skull to the upper thigh 60 min after the ^{18}F-FDG injection. ^{18}F-FDG PET/MRI acquisition included axial T1-weighted and coronal T2-weighted MRI sequences, axial diffusion-weighted imaging (DWI) (DWI; b-values of 50 and 800 s/mm^2), and apparent diffusion coefficient (ADC) images, acquired with five or six bed positions. PET scans were obtained using MRI sequences, and the acquisition time per bed position was 4 minutes. The other construction parameters were: the ordered subsets expectation maximization algorithm with TOF technique; field of view= 60 cm × 60 cm; matrix= 256 × 256; filter cut-off= 5.0 mm; subsets= 28; iterations= 2. Attenuation correction was performed by the Dixon-based segmentation method.

Image Analysis

PET images were evaluated using GE Healthcare Volume Share 5 software (Advantage Workstation 4.6, Buc, France). ^{18}F-FDG PET/MRI scans were evaluated simultaneously by two nuclear medicine physicians, who reached consensus. The maximum wall thickness of primary gastric tumors was measured on T1W MRI, and the SUV_{max} of primary gastric tumors was recorded. The minimum ADC (ADC_{min}) values of primary gastric tumors were measured on ADC images. Lymph nodes demonstrating higher ^{18}F-FDG uptake than background activity were considered positive. The total number of ^{18}F-FDG-positive lymph nodes, the SUV_{max} of ^{18}F-FDG-positive lymph nodes, and the short-axis diameter of the largest lymph node were recorded. The SUV_{mean} of the liver was calculated using a spherical region of interest with a 3-cm diameter placed within normal parenchyma of the right hepatic lobe. The ratios of primary tumor SUV_{max} to liver SUV_{mean}, lymph node SUV_{max} to tumor SUV_{max}, and lymph node SUV_{max} to liver SUV_{mean} were calculated.

Statistical Analysis

Statistical analyses were conducted using the SPSS software version 27. The distributions of the variables were assessed using visual methods (histograms and probability plots) and analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Descriptive statistics were presented as frequencies for ordinal/nominal variables, medians and interquartile ranges (IQRs) for non-normally distributed variables, and mean ± standard deviation for normally distributed variables. The Mann-Whitney U test and the Kruskal-Wallis test were used to compare the histopathological groups and ^{18}F-FDG PET/MRI findings. Optimal cut-off values for continuous variables were determined using the Youden index (sensitivity + specificity - 1) obtained from ROC curve analyses. Cox regression analyses were performed to identify predictors of mortality using univariate and multivariate models with backward selection. A sensitivity analysis was also performed to assess the robustness of the results after excluding rare non-adenocarcinoma pathologies from the signet ring cell carcinoma group. Survival analysis was performed using the Kaplan-Meier method. An overall Type I error rate of 5% was used to determine statistical significance.

Results

A total of 78 patients with GC who underwent gastrectomy were included in the present study. The clinicopathological characteristics of the patients are summarized in Table 1. The mean age of the patients was 65.4±13.9 years; 47 (60.3%) were male. Of the 78 patients, 46 (59.0%) were assigned to the adenocarcinoma group, including 28 with well- to moderately differentiated adenocarcinoma, 15 with poorly differentiated adenocarcinoma, and 3 with adenocarcinoma of undefined subtype. The remaining 32 patients (41.0%) were included in the signet-ring cell carcinoma and other subtypes group, comprising 28 patients with signet-ring cell carcinoma and 4 patients with rare non-adenocarcinoma pathologies (2 with lymphoepithelioma-like carcinomas, 1 with mixed adenoneuroendocrine carcinoma, and 1 with large-cell neuroendocrine carcinoma).

Table 1. The patients' clinicopathologic characteristics		
Clinicopathologic features		**Mean ± standard deviation median (interquartile range), n (%)**
Age		65.4±13.9
Gender	Male	47 (60.3%)
	Female	31 (39.7%)
Body mass index		26.2±4.6
Type of gastrectomy	Proximal gastrectomy	14 (17.9%)
	Distal gastrectomy	27 (34.6%)
	Total gastrectomy	37 (47.4%)
Lymph node dissection	D1 and D1+ dissection	4 (5.1%)
	D2 and D2+ dissection	74 (94.9%)
Tumor histopathologic group	Adenocarcinoma group	46 (59%)
	Signet ring cell carcinoma/other subtypes group	32 (41%)
Location primary gastric tumor	Cardia	14 (17.9%)
	Corpus	21 (26.9%)
	Antrum	26 (33.3%)
	More than one region	17 (21.8%)
pT stage (n=69)	pT1-2	12 (17.4%)
	pT3	23 (33.3%)
	pT4	34 (49.3%)
pN stage (n=78)	pN0	22 (28.2%)
	pN1-2	26 (33.2%)
	pN3	30 (38.5%)
Diameter of primary gastric tumors (cm)		5.0 (3.8)
The total number of dissected lymph nodes		26.4±12.0
The total number of metastatic lymph nodes		4.0 (10.0)
The diameter of the largest metastatic lymph node (cm) (n=16)		2.2±0.9
Lauren classification (n=53)	Intestinal type	24 (45.3%)
	Diffuse/signet ring cell carcinoma type	26 (49.1%)
	Other pathologies	3 (5.7%)
Her_2neu (n=68)	Positive	9 (13.2%)
	Negative	59 (86.8%)
Lymphovascular invasion (n=62)	Positive	17 (27.4%)
	Negative	45 (72.6%)
Perineural invasion (n=57)	Positive	18 (31.6%)
	Negative	39 (68.4%)
The positivity of surgical margins (n=73)	Positive	12 (16.4%)
	Negative	61 (83.6%)
The positivity of peritoneal lavage fluid (n=35)	Positive	6 (17.1%)
	Negative	29 (82.9%)
The history of chemotherapy	None	21 (26.9%)
	Pre-operative neoadjuvant chemotherapy	28 (35.9%)
	Post-operative adjuvant chemotherapy	29 (37.2%)
The history of post-operative radiotherapy		13 (16.7%)
Mortality	Positive	39 (50.0%)
	Negative	39 (50.0%)
Follow-up duration (months)		23.9 (33.4)

Table 2. The findings of ^{18}F-FDG PET/MRI

Features	Median (interquartile range)			p value
	All patients (n=78)	Adenocarcinoma group	Signet ring cell carcinoma/ other subtypes group	
The maximum wall thickness of primary tumors (mm)	19.0 (14.5)	21.9 (13.1)	17.4 (11.3)	p=0.044
Tumor SUV_{max}	10.2 (12.3)	16.4 (13.9)	6.6 (6.6)	p<0.001
Tumor ADC_{min} ($x10^{-6}mm^2/sec$)	778.0 (282.0)	755.0 (292.0)	876.0 (318.0)	p=0.105
Total number of ^{18}F-FDG positive lymph nodes	0 (5.0)	1.0 (5.0)	0 (5.0)	p=0.332
Lymph node SUV_{max}	6.3 (6.2)	6.8 (5.3)	4.7 (5.7)	p=0.136
The short axis diameter of the largest lymph node (mm)	7.1 (7.8)	8.4 (8.0)	6.4 (6.1)	p=0.025
Tumor SUV_{max}/liver SUV_{mean} ratio	4.3 (4.9)	6.0 (6.2)	2.9 (3.3)	p<0.001
Lymph node SUV_{max}/tumor SUV_{max} ratio	0.47 (0.34)	0.46 (0.33)	0.48 (0.32)	p=0.332
Lymph node SUV_{max}/liver SUV_{mean} ratio	2.6 (2.5)	2.9 (2.7)	2.4 (2.4)	p=0.569

SUV_{max}: Maximum standardized uptake value, ADC_{min}: Minimum apparent diffusion coefficient, SUV_{mean}: Mean standardized uptake value, ^{18}F-FDG PET/MRI: ^{18}F-fluorodeoxyglucose positron emission tomography/magnetic resonance imaging

The numbers of patients who underwent proximal, distal, and total gastrectomy were 14 (17.9%), 27 (34.6%), and 37 (47.4%), respectively. Furthermore, most patients (94.9%) underwent D2 or D2+ lymph node dissection (Table 1).

The findings from ^{18}F-FDG PET/MRI are shown in Table 2. The maximum wall thickness of primary tumors (p=0.044), tumor SUV_{max} (p<0.001), the ratio of tumor SUV_{max} to liver SUV_{mean} (p<0.001), and the short-axis diameter of the largest lymph node (p=0.025) were significantly higher in the adenocarcinoma group compared with the signet-ring cell carcinoma and other subtypes group (Table 2).

The median follow-up duration was 23.9 (IQR: 33.4) months and 39 (50.0%) patients died during the follow-up. The results of univariate and multivariate analyses for predicting overall survival in GC patients who underwent gastrectomy are shown in Table 3. In the univariate analysis, the type of gastrectomy (p=0.002), tumor histopathologic group (p=0.021), pT stage (p=0.025), pN stage (p=0.004), the presence of lymphovascular (p=0.013) and perineural (p=0.017) invasion, tumor ADC_{min} (p=0.023), the maximum wall thickness of primary tumors (p=0.031), the total number of ^{18}F-FDG positive lymph nodes (p=0.027), the short axis diameter of the largest lymph node (p=0.007), and the tumor SUV_{max}/liver SUV_{mean} ratio (p=0.008) were significantly associated with mortality in GC patients who underwent total or subtotal gastrectomy (Table 3). However, no statistically significant differences were found between mortality and other clinicopathological features presented in Table 1 or PET/MRI findings presented in Table 2 (all p>0.05).

In the multivariate analysis, the tumor SUV_{max}-to-liver SUV_{mean} ratio on pre-treatment ^{18}F-FDG PET/MRI (p=0.002) and the tumor histopathologic group (p<0.001) were identified as independent predictors of overall survival in GC patients who underwent total or subtotal gastrectomy (Table 3). A tumor SUV_{max}/liver SUV_{mean} ratio greater than 2.6 on staging ^{18}F-FDG PET/MRI was significantly associated with an approximately 4.4-fold increased risk of mortality during follow-up among GC patients who underwent total or subtotal gastrectomy. Additionally, the signet ring cell carcinoma/other subtypes group was associated with an approximately 5.9-fold higher risk of mortality during follow-up within the same patient cohort.

In a sensitivity analysis excluding four rare non-adenocarcinoma pathologies (two with lymphoepithelioma-like carcinoma, one with mixed adenoneuroendocrine carcinoma, and one with large-cell neuroendocrine carcinoma) from the signet ring cell carcinoma group, the same independent predictors, the tumor histopathologic group [p<0.001, odds ratio (OR): 5.42, 95% confidence interval (CI): 2.14-13.75] and the tumor SUV_{max}-to-SUV_{mean} ratio (p<0.001, OR: 7.18, 95% CI: 2.27-22.69), remained statistically significant in the multivariate analysis. These findings confirm that the Cox regression model remained robust after exclusion of rare non-adenocarcinoma pathologies.

Table 3. The results of univariate and multivariate analyses for predicting overall survival in gastric cancer patients			
Univariate analysis			
	OR	**95% CI**	**p value**
Type of gastrectomy (proximal, distal, total) (ref. proximal)			0.002
Type of gastrectomy (1)	1.128	0.339-3.753	0.844
Type of gastrectomy (2)	3.812	1.327-10.948	0.013
Tumor histopathologic type (ref. adenocarcinoma group)	2.097	1.116-3.941	**0.021**
pT stage (ref. pT1-2)			**0.025**
pT stage (1)	2.777	0.599-12.863	0.192
pT stage (2)	5.585	1.309-23.829	0.020
pN stage (ref. pN0)			**0.004**
pN stage (1)	3.654	1.185-11.271	0.024
pN stage (2)	5.974	2.028-17.597	0.001
Lymphovascular invasion (ref. negative)	4.542	1.382-14.931	**0.013**
Perineural invasion (ref. negative)	3.622	1.253-10.471	**0.017**
Tumor ADC_{min} (≤94, >94) (ref. ≤94)	0.365	0.153-0.873	**0.023**
The maximum wall thickness of primary tumors (≤13.6,>13.6 mm) (ref. ≤13.6)	2.622	1.092-6.300	**0.031**
Total number of ^{18}F-FDG positive lymph nodes (4, >4) (ref. ≤4)	2.058	1.087-3.897	**0.027**
The short axis diameter of the largest lymph node (≤8.7, >8.7 mm) (ref. ≤8.7)	2.435	1.281-4.627	**0.007**
Tumor SUV_{max}/liver SUV_{mean} ratio (≤2.6, >2.6) (ref. ≤2.6)	3.256	1.355-7.826	**0.008**
Multivariate analysis (backward-wald method)			
	OR	**95% CI**	**p value**
Tumor SUV_{max}/liver SUV_{mean} ratio (≤2.6, >2.6) (ref. ≤2.6)	4.361	1.256-15.147	**0.020**
Tumor histopathologic type (ref. adenocarcinoma group)	5.859	2.229-15.397	**<0.001**

*Statistically significant parameters were shown in the table.
Ref: Reference category, SUV_{max}: Maximum standardized uptake value, ADC_{min}: Minimum apparent diffusion coefficient, SUV_{mean}: Mean standardized uptake value, OR: Odds ratio, CI: Confidence interval, ^{18}F-FDG: ^{18}F-fluorodeoxyglucose

Mean and median overall survival were 42.7 months (95% CI: 35.8-49.6) and 37.4 months (95% CI: 9.04-65.87), respectively, among GC patients who underwent total or subtotal gastrectomy. The estimated overall survival rates at 12, 24, and 36 months were 77.5%, 53.5%, and 48.5%, respectively. During the follow-up period, The median overall survival was not reached in the adenocarcinoma group and in patients with a tumor SUV_{max}/liver SUV_{mean} ratio lower than 2.6. Therefore, mean overall survival times were reported. The mean overall survival in the signet-ring cell carcinoma/other subtypes group (31.4 months, 95% CI: 22.3-40.4) was significantly shorter than that in the adenocarcinoma group (49.2 months, 95% CI: 40.3-58.2) (p=0.019, Figure 1A). Moreover, the patients with a tumor SUV_{max}/liver SUV_{mean} ratio greater than 2.6 (35.7 months, 95% CI: 27.6-43.7) on staging ^{18}F-FDG PET/MRI had a shorter overall survival than those with a ratio lower than 2.6 (57.1 months, 95% CI: 46.5-67.7) (p=0.005, Figure 1B).

Discussion

In the era of precision medicine, stratifying oncology patients based on survival outcomes may alter treatment approaches and ultimately improve patient management. Therefore, identifying prognostic biomarkers plays a pivotal role in the transition to individualized treatment in oncology. Therefore, ^{18}F-FDG PET/MRI is a unique modality that can provide multiparametric imaging biomarkers in different malignancies. In this study investigating the prognostic value of pretreatment ^{18}F-FDG PET/MRI in GC patients who underwent total or subtotal gastrectomy, the tumor SUV_{max}-to-liver SUV_{mean} ratio and the tumor histopathologic group were found to be independent predictors of overall survival. Although the tumor ADC_{min} on pretreatment ^{18}F-FDG PET/MRI was significantly associated with overall survival in the univariate analysis, it did not remain an independent predictor in the multivariate analysis.

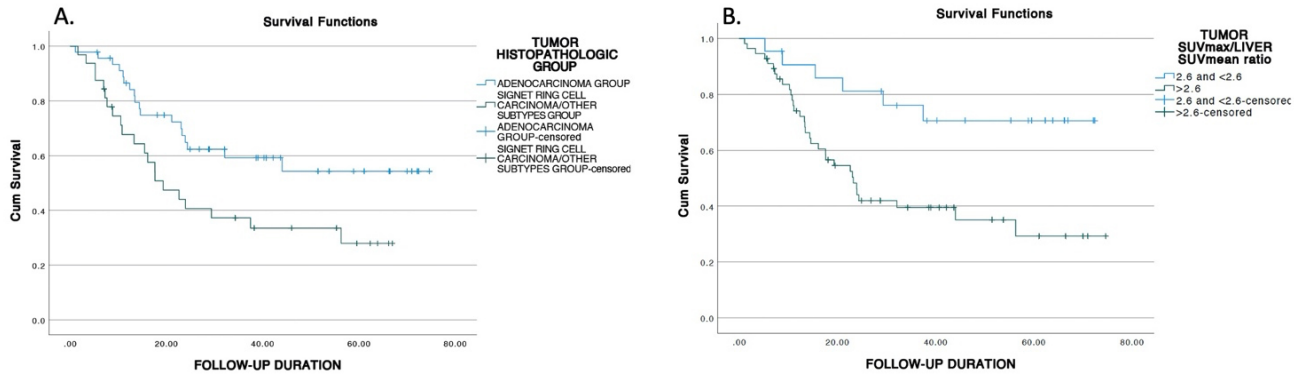

Figure 1. Kaplan-Meier survival analysis according to the tumor histopathologic group (A) and the tumor SUV_{max}/liver SUV_{mean} ratio (B)
SUV_{max}: Maximum standardized uptake value, SUV_{mean}: Mean standardized uptake value

In the present study, the tumor SUV_{max} was not a significant prognostic factor for overall survival in GC patients who underwent total or subtotal gastrectomy. The prognostic value of the semi-quantitative parameters derived from ^{18}F-FDG PET, especially SUV_{max}, has been evaluated in GC patients. Contrary to our results, several studies have demonstrated that a higher SUV_{max} on pretreatment ^{18}F-FDG PET was associated with poorer recurrence-free survival and overall survival in GC patients who underwent total or subtotal gastrectomy (16,17,18,19). On the other hand, similar to our study, some studies have reported no significant association between SUV_{max} and prognosis in GC patients who underwent total or subtotal gastrectomy (20,21). Therefore, these discrepancies among the studies could be attributed to differences in patient populations and in the distribution of histopathological subtypes, since histopathological subtypes of GC may exhibit distinct metabolic characteristics and tumor behaviors. In the study investigating the predictive impact of SUV_{max} by histologic subtype, although the primary tumor SUV_{max} was an independent predictor of overall survival in patients with poorly differentiated adenocarcinoma or signet-ring cell GC, it was not significant in patients with well- to moderately differentiated adenocarcinoma (22). Thus, the prognostic value of the tumor SUV_{max} may be influenced by the histopathologic subtypes in GC patients, which may account for conflicting results among studies with different patient populations.

In this study, unlike tumor SUV_{max}, the tumor SUV_{max}/liver SUV_{mean} ratio was identified as an independent predictor of overall survival in GC patients. This ratio represents the normalized glycolytic activity of the primary gastric tumor relative to that of the liver. Since SUV_{max} can be influenced by several parameters, such as acquisition time, blood glucose level, and other physiological or technical factors, a normalized metric of tumor metabolic activity, such as the tumor SUV_{max}/liver SUV_{mean} ratio, might provide a more reliable and consistent measurement. However, in contrast to our results, the studies by Kwon et al. (17) and Liu et al. (21) demonstrated no significant relationship between the tumor SUV_{max}/liver SUV_{mean} ratio and either overall survival or progression-free survival in advanced GC patients. These inconsistencies among studies may be due to differences in therapeutic approaches, including neoadjuvant therapies, across patient populations. Despite discrepancies among studies, our findings underscore the potential prognostic utility of the tumor SUV_{max}/liver SUV_{mean} ratio in GC patients undergoing total or subtotal gastrectomy.

PET/MRI is a promising modality that offers higher soft-tissue contrast, functional imaging, and multiparametric imaging biomarkers (15). The integration of functional MR sequences, such as DWI and ADC images, into the standard PET/MRI protocol may enhance its diagnostic and prognostic capabilities across different malignancies. DWI reflects the mobility of water protons in tissues, while ADC is a quantitative imaging biomarker that measures the mobility of water molecules in tissues. As a result of the higher cellularity and decreased extracellular space in tumors, water diffusion is restricted, and ADC values decrease (23). The potential prognostic role of ADC value in various cancers has been shown in previous studies (24,25,26,27). To the best of our knowledge, no u^{18}F-FDG PET/MRI study has investigated its prognostic value in GC; however, a limited number of studies have examined the

prognostic value of ADC and DWI MRI in GC (26,27). The study by Giganti et al. (27) demonstrated that a lower ADC value was an independent predictor of poorer prognosis in GC patients who underwent gastrectomy with or without neoadjuvant chemotherapy. Furthermore, Giganti et al. (26) reported that ADC values were associated with TNM stage and overall survival in GC patients who underwent gastrectomy without neoadjuvant chemotherapy. Since these two studies used DWI-ADC MRI and did not incorporate metabolic data from ^{18}F-FDG PET in their analyses, these results must be compared with our results cautiously. In our study, although the tumor ADC_{min} on pre-treatment ^{18}F-FDG PET/MRI was significantly associated with overall survival in GC patients, it was not found to be an independent predictor in the multivariate analysis. The tumor SUV_{max}/liver SUV_{mean} ratio and tumor histopathologic group may be more robust prognostic biomarkers than ADC_{min} in GC patients.

In the present study, the tumor histopathologic group was identified as an independent predictor of overall survival in GC patients. The overall survival in the signet-ring-cell carcinoma group was significantly lower than in the adenocarcinoma group. Consistent with our results, the relationship between signet ring cell carcinoma and poor prognosis has been demonstrated by several studies (28,29). Recent studies indicate that the prognostic impact of signet ring cell pathology depends on the stage of GC, being favorable in early tumor stages but adverse in advanced tumor stages (28,30,31). In our study, the signet ring cell carcinoma group had a worse prognosis than the adenocarcinoma group among GC patients who underwent gastrectomy, further supporting its prognostic relevance even in early-stage disease. Moreover, consistent with the literature, the histopathologic features, such as the pT stage, pN stage, the presence of lymphovascular and perineural invasion, as well as PET/MRI findings, including the maximum wall thickness of primary tumors, the total number of ^{18}F-FDG-positive lymph nodes, and the short-axis diameter of the largest lymph node, were significantly associated with overall survival in GC patients (19,20,32,33). Nevertheless, the tumor histopathologic group and the tumor SUV_{max}/liver SUV_{mean} ratio on pretreatment ^{18}F-FDG PET/MRI were found to be more robust prognostic factors than other histopathologic features and PET/MRI findings.

Study Limitations

The present study has some limitations. First, this study is retrospective and single-center, with a limited sample size. Due to its retrospective nature, the patient population was heterogeneous with respect to neoadjuvant therapy. Moreover, complete histopathological data were not available for all patients. Therefore, multicenter prospective studies with larger cohorts are needed to validate and expand upon these findings.

Conclusion

The tumor SUV_{max}/liver SUV_{mean} ratio, a normalized metric of tumor metabolic activity relative to liver metabolic activity, may serve as a robust imaging biomarker for prognosis and for histopathologic subtype classification in GC patients who underwent total or subtotal gastrectomy. Furthermore, multiparametric data derived from ^{18}F-FDG PET/MRI may offer a comprehensive approach to prognostic evaluation in GC patients. ^{18}F-FDG PET/MRI may emerge not only as a diagnostic tool but also as a valuable prognostic modality in the management of GC.

Ethics

Ethics Committee Approval: This retrospective study was approved by Gazi University President's Office Ethics Commission (number: 2025-1103, date: 17.06.2025).

Informed Consent: This retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.G.A., U.A., R.K., Ü.Ö.A., L.Ö.A., Concept: S.G.A., U.A., Design: S.G.A., U.A., R.K., Ü.Ö.A., L.Ö.A., Data Collection or Processing: S.G.A., U.A., R.K., Ü.Ö.A., Analysis or Interpretation: S.G.A., U.A., Ü.Ö.A., L.Ö.A., Literature Search: G.A., Writing: S.G.A., U.A., Ü.Ö.A., L.Ö.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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