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Inoperability decision in GIS malignancies: How sufficient is CT alone?

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Abstract

The prognosis in gastrointestinal system malignancies is directly correlated with the stage of the disease at the time of presentation. There are debates and variations in the preferred methods for staging (3,4). Despite being part of the recommendations of international associations in preoperative staging, the adequacy of CT is controversial. In our study, we aimed to investigate the effectiveness of CT in the decision of inoperability based on our case series of patients who were admitted to our clinic with a preliminary diagnosis of gastrointestinal system malignancy and deemed inoperable. At the General Surgery Clinic of - University Training and Research Hospital, demographic data of patients with intraoperatively detected inoperable gastrointestinal malignancies between 2018 and 2023, preoperative CT and endoscopy findings, surgical reports, and neoadjuvant treatment applications were retrospectively analyzed. Preoperative endoscopic and cross-sectional imaging findings were compared with intraoperative findings. The study included 91 patients. The sensitivity of preoperative endoscopy was found to be 80.2%, while the sensitivity of preoperative CT was 69.2%. When comparing organ-based intraoperative findings with the distant invasion signs findings detected in preoperative treatment was examined, no statistically significant relationship was found in the statistical analysis. In our study, the sensitivity and specificity of CT were found within ranges consistent with the literature. However, the adequacy of CT in invasive and metastatic disease was again found to be low, in line with the literature. Therefore, to prevent misinterpretation, we believe that adding advanced imaging modalities (MRI, PET, EUS) during the preoperative period in addition to CT may help reduce unnecessary laparotomies.

Keywords: computed tomography, gastrointestinal malignancies, surgical, oncology

1. Introduction

The prognosis in gastrointestinal system malignancies is directly associated with the stage of the disease at the time of presentation. In localized disease, surgical resection is often sufficient for treatment (1,2). However, in metastatic disease, treatment modalities vary. Therefore, staging of the disease holds a crucial place in treatment protocols. There are debates and variations in the preferred methods for staging (3,4). Although computed tomography (CT), magnetic resonance imaging (MRI), gastroscopy, and colonoscopy are routinely used in preoperative staging, advanced investigations may be required for determining local recurrence, the extent of surgical resection, and the need for adjuvant and neoadjuvant therapy (5,6). Despite being part of the recommendations of international associations in preoperative staging, the adequacy of CT is controversial. It is known to be useful, especially in the presence of synchronous tumors, metastatic disease, and invasion of adjacent organs (7,8). In our study, we aimed to clarify the adequacy of preoperative CT in the decision-making process for inoperability by investigating the effectiveness of CT in determining inoperability in a series of patients who presented to our clinic with a preliminary diagnosis of gastrointestinal system malignancy and were deemed inoperable after laparotomy

2. Materials and Methods

In this retrospective study, 91 patients who underwent elective surgery with a preliminary diagnosis of gastrointestinal malignancy at the General Surgery Clinic of Samsun University Training and Research Hospital between January 1, 2018, and September 1, 2023, and were found to have inoperable gastrointestinal malignancy during surgery were included. Palliative operations such as tube gastrostomy, tube jejunostomy, gastroenterostomy, ileostomy, and colostomy were performed. Patients aged 18-90 years without a history of previous surgery for gastrointestinal malignancy, not referred to our center with laboratory and imaging findings, and undergoing elective surgery were included in the study. Data regarding patients' age, gender, preoperative endoscopy, preoperative imaging, neoadjuvant therapy, and surgical procedures were obtained from the archives. Preoperative endoscopic findings, CT findings including organ invasion and distant organ metastasis, whether preoperative neoadjuvant therapy was received, intraoperative procedures and duration, and intraoperative findings were recorded. Preoperative CT findings such as para-aortic lymph nodes, liver metastasis, lung metastasis, pancreatic invasion, peritoneal invasion, major vessel invasion, and bladder invasion were generally

considered as distant invasion signs of malignancy. The effectiveness of neoadjuvant therapy, preoperative endoscopic and CT findings, and the distant invasion signs on CT were compared with intraoperative findings. The study was approved by the - University Clinical Research Ethics Committee on January 31, 2024, with protocol number -. Descriptive statistics were performed to provide information about the general characteristics of the study groups. Data for quantitative variables were described using mean and standard deviation, while data for qualitative variables were described using number (n) and percentage (%). Differences between groups for qualitative variables were evaluated using the Chisquare test. Agreement between two different times in evaluating categorical items was calculated using the Kappa statistic. The effectiveness of the diagnostic methods was evaluated using the True Positive Rate (Sensitivity) and True Negative Rate (Specificity). Statistical software (IBM SPSS Statistics 22, SPSS Inc., an IBM Co., Somers, NY) was used for calculations.

3. Results

Between January 1, 2018, and December 31, 2022, a total of 237 patients who underwent elective surgery with a preliminary diagnosis of gastrointestinal malignancy and were considered inoperable, subsequently undergoing palliative operations such as tube gastrostomy, tube jejunostomy, gastroenterostomy, ileostomy, and colostomy were identified. However, 18 patients were excluded due to pancreaticobiliary malignancy, 43 patients due to missing data, 23 patients due to previous malignancy operation history, and 62 patients due to emergency surgery. Consequently, 91 patients were included in the study (Fig. 1). Of these patients, 65 were female and 26 were male. The median age was found to be 66.44 years. The mean surgical duration was calculated as 100.87 minutes (Table 1). Upon examination of preoperative endoscopic findings, gastric malignancy was most commonly observed in 29 patients, followed by rectal malignancy in 14 patients. Analysis of the performed surgical procedures revealed that the most common procedure was feeding jejunostomy, performed in 30 patients, mostly in gastric malignancies (16, 55.2%), followed by esophageal malignancies (11, 78.6%); colostomy was performed in 22 patients, mostly in rectal malignancies (12, 75%); finally, enterotomy/enterostomy was performed in the right colon malignancies of 5 patients (83%) (Table 2).

Table 2. Preoperative gastroscopy/colonoscopy - surgery analysis

Preoperative CT findings revealed that in 13 patients (68.4%), organ-based diagnosis could not be established, and the distant invasion signs could not be predicted, while in 6 patients, although organ-based diagnosis could not be established, the distant invasion signs was predicted; in 18 patients (64.3%), gastric malignancy was suspected, but the distant invasion signs could not be predicted, and in 10 patients, distant invasion signs was detected. Liver metastasis was predicted in 5 of these patients (Table 3).

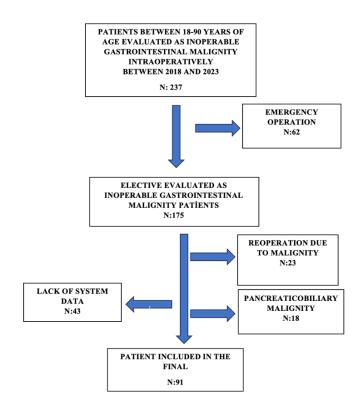


Fig. 1. Included and excluded patients

 Table 1. Age, gender and operation duration

•	0	•		
	Mean	Standard Deviation	Minimum	Maximum
Age	66.44	14.81	26.00	97.00
Operation Duration (min)	100.87	46.86	30.00	235.00
		n	(%
Gender	Female	65	7	1.4
	Male	26	28.6	

		Operation									
		Tube jejunostomy (30)	Gastroenterosto my (15)	Tube gastrostomy (Surgery) (7)	İleostomy (17)	Colostomy (22)					
ve olo	Normal	-	1(100.0)	-	-	-					
ativ /Col	Stomach	16(55.2)	10(34.5)	2(6.9)	-	1(3.4)					
ers py/	Sigmoid colon	-	-	-	4(50.0)	4(50.0)					
reoper: roscopy noscopy	Esophagus	11(78.6)	-	3(21.4)	-	-					
Pre Gastros nos	Rectum	-	-	-	4(25.0)	12(75.0)					
	Left colon	-	-	-	-	1(100.0)					
6	Transverse colon	-	-	-	2(100.0)	-					

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Right colon	-	-	-	5(83.3)	1(16.7)
Duodenum	-	3(100.0)	-	-	-
Stomach+Esophagus	2(40.0)	-	2(40.0)	1(20.0)	-
Sigmoid colon+Rectum	-	-	-	-	2(100.0)
Sigmoid colon+Left colon	-	-	-	1(100.0)	-
Stomach+Transverse colon	1(100.0)	-	-	-	-
Stomach+Duodenum	-	1(100.0)	-	-	-
Right colon+Duodenum	-	-	-	-	1(100.0)
Left colon+Sigmoid Colon+ Rektum	-	-	-	-	-

Table 3. Preoperative CT findings - distant invasion signs analysis

					Dista	nt Invasion S	igns		
		None	Paraaortic Lymph Node	Liver	Lung	Pancreas	Peritoneum	Major Vessel Invasion	Bladder
	Normal	13(68.4)	1(5.3)	2(10.5)	2(10.5)	1(5.3)	-	-	-
	Stomach	18(64.3)	1(3.6)	5(17.9)	-	-	4(14.3)	-	-
operative	Sigmoid colon	2(40)	-	3(60)	-	-	-	-	-
rat	Esophagus	2(28.6)	1(14.3)	-	4(57.1)	-	-	-	-
ope	Rectum	6(75)	2(25)	-	-	-	-	-	-
cv rec	P Left colon	1(100)	-	-	-	-	-	-	-
- F	Transverse colon	2(100)	-	-	-	-	-	-	-
tive CT Maligna	Right colon	3(42.9)	-	3(42.9)	-	1(14.3)	-	-	-
/e (Ial	Duodenum	-	-	-	-	1(50)	-	1(50)	-
N ati	Stomac+Esophagus	1(100)	-	-	-	-	-	-	-
era	Sigmoid colon+Rectum	4(57.1)	-	1(14.3)	-	-	1(14.3)	-	1(14.3)
Preoperative Ma	Sigmoid colon+Left Colon	1(50)	-	-	1(50)	-	-	-	-
	Left Colon+Sigmoid colon +Rectum	-	-	-	-	-	1(100)	-	-

When comparing the organ-based agreement between preoperative endoscopy, preoperative CT, and intraoperative findings: the agreement between preoperative endoscopy and intraoperative findings (kappa: 0.761) (p<0.001) was found to be more significant compared to the agreement between preoperative CT and intraoperative findings (kappa: 0.625) (p<0.001). The sensitivity of preoperative endoscopy was found to be 80.2%, while the sensitivity of preoperative CT was 69.2% (Tables 4, 5). All patients were evaluated as inoperable intraoperatively. When comparing organ-based intraoperative findings with the signs of distant invasion on preoperative CT, no proportionally high signs of distant invasion were observed in gastric malignancies in 21 patients (63.6%), rectal malignancies in 7 patients (77.8%), and sigmoid colon and rectal malignancies in 6 patients (66.7%); however, proportionally high signs of distant invasion were observed in esophageal malignancies in 9 patients (69.2%), and no significant difference was found (p=0.332) (Table 6). When correlating the organ-based evaluation of intraoperative inoperable and distant invasion accepted findings with preoperative treatment, it was found that in gastric malignancies, the majority of patients (57.6%) received neoadjuvant treatment, in esophageal malignancies, 69.2% received neoadjuvant treatment; in sigmoid colon and rectal malignancies, 55.6% received neoadjuvant treatment, while in rectal malignancies, 6 (66.7%), transverse colon malignancies, 2 (100%), and right colon malignancies, 6 (85.6%) patients did not receive neoadjuvant treatment despite the presence of inoperable and distant invasion accepted findings. Statistical

analysis revealed no significant relationship (p=0.126) (Table 6). Detailed analysis of preoperative CT signs of distant invasion and preoperative neoadjuvant treatment revealed that in the group not receiving neoadjuvant treatment, signs of involvement were not predominantly observed in preoperative CT in 27 patients (62.8%); in the group receiving neoadjuvant treatment, signs of distant invasion were not predominantly observed in preoperative observed in preoperative CT in 26 patients (54.2%), and no significant difference was observed (p=0.535) (Table 7).

4. Discussion

In gastrointestinal malignancies, accurate diagnosis and staging are crucial for treatment selection. Endoscopy with diagnostic biopsy is the gold standard for diagnosis. CT is used for TNM staging, which evaluates tumor size, depth of invasion, extent of the tumor (T), metastasis (M), lymph nodes (N), and ascites. Controversial aspects of CT include local tumor invasion, normal-sized metastatic lymph nodes, and peritoneal invasion (9). In our study of patients operated on due to GI malignancy and intraoperatively found to be inoperable, preoperative CT findings showed normal CT findings in 14 (15.38%) out of 91 patients and signs of distant invasion in 37 (40.65%) patients, indicating that CT sensitivity for local invasion or distant organ metastasis was consistent with the literature (Table 3). For these reasons, although the role of CT in preoperative evaluation remains debatable, CT, positron emission tomography (PET), endoscopy, and endoscopic ultrasonography (EUS) are commonly used preoperative staging imaging procedures for gastrointestinal malignancies (10-11).

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	Intraoperative Malignancy														
		Stomach	Sigmoid Colon	Esophagus	Rectum	Left colon	Transverse Colon	Right Colon	Duodenum	Stomach+ Esophagus	Sigmoid Colon+ Rektum	Sigmoid Colon+ Left colon	Left colon+ Rektum	Stomach+ Left colon+ Sigmoid Colon+ Rectum	Total
	Normal	1	0	0	0	0	0	0	0	0	0	0	0	0	1
	Stomach	28	0	0	0	0	0	0	0	1	0	0	0	0	29
	Sigmoid Colon kolon	0	5	0	0	0	0	0	0	0	1	1	0	1	8
d	Esophagus	0	0	13	0	0	0	0	0	1	0	0	0	0	14
sce	Rectum	0	0	0	9	0	0	0	0	0	6	0	1	0	16
ono	Left colon	0	0	0	0	1	0	0	0	0	0	0	0	0	1
/ Col	Transverse Colon	0	0	0	0	0	2	0	0	0	0	0	0	0	2
b.	Right Colon	0	0	0	0	0	0	6	0	0	0	0	0	0	6
[00]	Duodenum	0	0	0	0	0	0	0	3	0	0	0	0	0	3
astros	Stomach+ Esophagus	2	0	0	0	0	0	0	0	3	0	0	0	0	5
ive G	Sigmoid Colon+ Rektum	0	0	0	0	0	0	0	0	0	2	0	0	0	2
Preoperative Gastroscopy / Colonoscopy	Sigmoid Colon+ Left Colon	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Preol	Stomach+ Transverse Colon	1	0	0	0	0	0	0	0	0	0	0	0	0	1
	Stomach+ Duodenum	1	0	0	0	0	0	0	0	0	0	0	0	0	1
	Right Colon+ Duodenum	0	0	0	0	0	0	1	0	0	0	0	0	0	1

Table 4. Preoperative gastroscopy / colonoscopy - intraoperative malignancy compatibility

Kappa: 0.761; p < 0.001*

(The Kappa test value ranges from -1 to +1. As it approaches -1, there is no agreement between the observations. A value of 0 indicates that the agreement is due to chance. As the value approaches +1, the agreement between observers increases.)

There was a significant ($p \le 0.001$) and positively substantial agreement between Preoperative Gastroscopy / Colonoscopy and Intraoperative Malignancy organbased findings (Kappa: 0.761, according to Landis and Koch's Kappa Classification).

Sensitivity = 80.2%

Table 5. Preoperative CT findings - intraoperative malignancy compatibility

]	Intrao	perati	ve Ma	lignan	ey				0 t
	Normal	6	1	6	1	0	0	1	1	1	2	0	0	0	19
	Stomach	25	0	0	0	0	0	0	0	3	0	0	0	0	28
×.	Sigmoid Colon kolon	0	4	0	1	0	0	0	0	0	0	0	0	0	5
Findings	Esophagus	0	0	7	0	0	0	0	0	0	0	0	0	0	7
pu	Rectum	1	0	0	6	0	0	0	0	0	1	0	0	0	8
	Left colon	0	0	0	0	1	0	0	0	0	0	0	0	0	1
CT	Transverse Colon	0	0	0	0	0	2	0	0	0	0	0	0	0	2
	Right Colon	1	0	0	0	0	0	6	0	0	0	0	0	0	7
ati	Duodenum	0	0	0	0	0	0	0	2	0	0	0	0	0	2
Preoperative	Stomach+ Esophagus	0	0	0	0	0	0	0	0	1	0	0	0	0	1
Pr	Sigmoid Colon+ Rektum	0	0	0	1	0	0	0	0	0	6	0	0	0	7
	Sigmoid Colon+ Left colon	0	0	0	0	0	0	0	0	0	0	2	0	0	2
	Left Colon+ Sigmoid Colon+ Rectum	0	0	0	0	0	0	0	0	0	0	0	1	1	2
]	Fotal	33	5	13	9	1	2	7	3	5	9	2	1	1	91

Kappa: 0.625; $p < 0.001^*$ (The Kappa test value ranges from -1 to +1. As it approaches -1, there is no agreement between the observations. A value of 0 indicates that the agreement is due to chance. As the value approaches +1, the agreement between observers increases.) There was a significant (p < 0.001) and moderately positive agreement between Preoperative CT and Intraoperative Malignancy organ-based findings (Kappa: 0.625, according to Landis and Koch's Kappa Classification).

Sensitivity = 69.2%

According to McHugh's Kappa Classification (2012):

0.00-0.20: No Agreement 0.21-0.39: Minimal Agreement 0.40-0.59: Weak Agreement 0.60-0.79: Moderate Agreement 0.80-0.90: Strong Agreement 0.90< : Excellent Agreement

According to Landis and Koch's Kappa Classification (1977):

<0.00 : Poor Agreement 0.00-0.20: Slight Agreement 0.21-0.40: Fair Agreement 0.41-0.60: Moderate Agreement 0.61-0.80: Substantial Agreement 0.81< : Almost Perfect Agreement

Table 6. Intraoperative malignancy - distant invasion signs - treatment

			asion Signs ,332)	Trea	atment
		Absent (n=53)	Available (n=38)	Absent(n=43)	Neoadjuvant Therapy(n=48)
	Stomach	21(63,6)	12(36,4)	14(42,4)	19(57,6)
A	Sigmoid Colon	2(40)	3(60)	3(60)	2(40)
Malignancy	Esophagus	4(30,8)	9(69,2)	4(30,8)	9(69,2)
gna	Rectum	7(77,8)	2(22,2)	6(66,7)	3(33,3)
alig	Left Colon	1(100)	-	1(100)	0(0)
Ŵ	Transverse Colon	2(100)	-	2(100)	0(0)
ive	Rİght Colon	4(57,1)	3(42,9)	6(85,7)	1(14,3)
rati	Duodenum	1(33,3)	2(66,7)	2(66,7)	1(33,3)
bei	Stomach+Esophagus	4(80)	1(20)	0(0)	5(100)
.30	Sigmoid Colon+Rectum	6(66,7)	3(33,3)	4(44,4)	5(55,6)
Intraoperative	Sigmoid Colon+Left Colon	1(50)	1(50)	1(50)	1(50)
-	Left Colon+Rectum	-	1(100)	0(0)	1(100)
	Stomach+Left Colon+Sigmoid Colon+Rectum	-	1(100)	0(0)	1(100)
The day	ta are presented as $n(\%)$				

The data are presented as n(%).

p: Chi-square Test

There was no significant difference between intraoperative malignancy organ-based findings and preoperative CT signs of distant invasion (p=0.332)

Table 7. Distant invasion signs - treatment

		Preoperatif N	eoadjuvan Treatment	
		Absent	Available	þ
Distant Invesion Simo	Absent	27(62,8)	26(54,2)	0.525
Distant Invasion Signs	Available	16(37,2)	22(45,8)	0,535
T1 1 (0/)				

The data are presented as n(%).

p: Chi-square Test

The preoperative treatment status did not show a significant difference with the preoperative CT signs of distant invasion . (p=0.535)

When we compared the organ-based findings of preoperative endoscopies with intraoperative organ-based findings of patients identified as intraoperatively inoperable, a high level of concordance was observed, especially in gastric malignancies, followed by esophageal and rectal malignancies. According to kappa analysis, significant agreement was found (kappa: 0.761, p<0.001) (Table 4). The sensitivity rate of endoscopic examination in gastrointestinal malignancies in the literature ranges from 78% to 98% (14). In our study, the sensitivity rate of the endoscopic procedure was found to be 80.2%, consistent with the literature. When we examined the intraoperative organ-based findings of patients identified as intraoperatively inoperable and compared them with preoperative CT organ-based findings, it was observed that in 19 patients, preoperative CT findings were reported as normal, but malignancy was intraoperatively detected in all of these patients, most of whom had gastric malignancy. Upon further examination of the remaining patients, a high level of concordance was observed between the preoperative CT organ-based findings and intraoperative organ-based findings, especially in gastric malignancies, with 25 patients, followed by esophageal, rectal, and right colon malignancies. According to kappa analysis, significant agreement was found (kappa: 0.625, p<0.001) (Table 5). Minami et al. found the accuracy of abdominal CT in diagnosing early and advanced gastric cancer patients to be between 53% and 92% (15). Leufkens et al. determined the staging and accuracy rate of CT in colorectal cancers to be between 67% and 77% (16). In our study, the sensitivity of preoperative CT was found to be 69.2%, which is close to the literature.

In advanced stage and inoperable gastrointestinal malignancies, unnecessary laparotomies increase the risk of mortality and morbidity, and over the past 20 years, there have been numerous developments in diagnosis and staging to reduce unnecessary laparotomies. Many studies indicate that CT, MRI, Transrectal USG, Intraoperative USG, and EUS examinations are valuable methods for operability (12-13). Kwee et al. reported in a systematic review that the sensitivity of CT in detecting lymph node metastasis ranged from 62.5% to 91.9%, and its specificity ranged from 50.0% to 87.9% (17). The widespread use of CT during imaging for distant metastases in the pelvis, abdomen, and thorax simultaneously is a significant reason. In one study, the sensitivity and specificity of CT in detecting distant metastases in gastric malignancies were reported to be 14.3%-59.1% and 93.3%-99.8%, respectively (18). The detection of peritoneal metastasis with CT can be challenging, with a reported sensitivity of 28.3% and specificity of 93.3%-99.8% (19).

While distant organ metastasis plays a crucial role in determining treatment protocols, in cases where visceral metastatic disease is detected by CT, alternative methods such as colonic stenting can be used instead of laparotomy. There are also studies in the literature showing that CT has high sensitivity in detecting metastases (20). In our study, when organ-based findings were examined along with preoperative CT findings of distant invasion, preoperative CT did not find distant invasion signs in a high percentage of patients, especially in gastric malignancies (63.6%) and rectal malignancies (77.8%). A high rate of distant invasion sign findings (69.2%) was found in esophageal malignancies. There was no statistically significant relationship between organbased findings and preoperative CT distant invasion sign findings (p: 0.332). The sensitivity of CT regarding distant organ metastases is consistent with controversial results in the literature. Neoadjuvant therapy before surgery for gastric, esophageal, and rectal malignancies is a commonly standardized method nowadays for tumor regression. In the EORTC 22921 study on rectal malignancies, tumor regression was found to be significant in patients receiving preoperative chemotherapy and radiotherapy, with rates of 14% and 5.3%, respectively (p<0.001) (21). In another Polish study, complete response rates with preoperative chemotherapy and short-term radiotherapy were shown to be 16% and 1%, respectively (p<0.0001) (22). When intraoperative malignancy findings were examined in patients considered inoperable intraoperatively, with preoperative neoadjuvant therapy, it was found that in 57.6% of patients with gastric malignancies, 69.2% of patients with esophageal malignancies, and 33.3% of patients with rectal malignancies, significant responses were not achieved despite preoperative neoadjuvant therapy, and they were evaluated as inoperable intraoperatively. In the statistical analysis of preoperative CT findings of distant invasion signs and preoperative neoadjuvant therapy, in the group not receiving neoadjuvant therapy, patients without distant invasion signs on preoperative CT account for a high percentage (62.8%), whereas in the group receiving neoadjuvant therapy, patients without distant invasion signs on CT account for 54.2%. Although the group without distant invasion sign findings was more frequently observed in the group not receiving treatment, there was no statistically significant difference between the groups (p: 0.535).

The data in our study were collected from the hospital database. The main limitations include limited access to certain patient data, selection of a limited number of patients with specifically gastrointestinal system malignancies, and the single-center, retrospective study design.

In advanced stage and inoperable gastrointestinal malignancies, unnecessary laparotomies increase the risk of mortality and morbidity. Although preoperative CT is the preferred imaging method due to its relatively high accuracy and widespread availability, we believe that adding advanced imaging modalities (MRI, PET, EUS) during the preoperative period may help reduce unnecessary laparotomies by preventing misinterpretation of distant organ metastasis and distant invasion sign findings.

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: M.A.A, C.A. Design: M.A.A, M.G.B. Data Collection or Processing: Ö.F.B., M.G.B. Analysis or Interpretation: C.A, Ö.F.B., Literature Search: Ö.F.B., C.A. Writing: M.A.A., M.G.B.

Ethical Statement

Approval was obtained from Samsun University Non-invasive Clinical Research Ethics Committee, the study started. The ethics committee decision date is 31/01/2024 and the number of ethical committee decisions is 2024/3/1.

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