VIA MEDICA

ORIGINAL ARTICLE

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Comparison of clinical, pathological, and prognostic features of small bowel tumors

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Oncology in Clinical Practice
DOI: 10.5603/ocp.102621

ISSN 2450–1654
e-ISSN 2450–6478

ABSTRACT

Introduction. Although approximately 75% of the digestive system's length and almost 90% of its surface area consists of the small intestine, small bowel tumors are rare. In this study, we aimed to compare the clinical, pathological and prognostic features of small bowel tumors.

Material and methods. 107 patients diagnosed with small bowel tumor were evaluated retrospectively. Their clinical and pathological features were examined. The effects of the evaluated parameters on survival were analyzed, and overall survival rates were determined.

Results. Of the 107 patients diagnosed with small bowel malignancy included in the study, 44 (41%) were diagnosed with adenocarcinoma, 27 (25%) were diagnosed with GIST, 22 (20.6%) were diagnosed with NHL, and 14 (13.1%) were diagnosed with NET. Distant metastases were more common at diagnosis in adenocarcinoma patients [22 patients (50%)] than in GIST [5 patients (18.5%)] and NHL patients [3 patients (13.6%)] ($p = 0.011$, $p = 0.006$, respectively). The median OS in the adenocarcinoma group was 1.1 (min–max = 0.7–1.6) years, in the NET group it was 8.8 (min–max = 3.5–14.2) years, in the NHL group it was 10.7 (min–max = 1.9–19.6) years, but in the GIST group the median OS was could not be reached. OS differences between adenocarcinoma and other groups were statistically significant ($p < 0.001$).

Conclusions. The overall survival of adenocarcinoma was significantly lower than other small bowel tumor subgroups.

Keywords: small bowel tumors, GIST, NHL, NET, adenocarcinoma

Oncol Clin Pract

Introduction

Although the small intestine accounts for approximately 90 percent of the total surface area of the gastrointestinal (GI) tract, small intestine tumors are rare. They represent about 3–6 percent of all GI neoplasms, less than 5 percent of GI malignancies, and approximately 0.6 percent of all cancers in the United States [1]. The etiology of most small bowel tumors remains unknown, although several risk factors and predisposing conditions have been identified. These include advanced age, cystic fibrosis, inflammatory bowel diseases, celiac disease, hereditary syndromes, dietary factors (such as consumption of alcohol, refined sugar, red meat, and salt-cured or smoked foods), and obesity. Diagnosis of small bowel tumors is often challenging because these lesions are rare, and the presenting signs and symptoms are nonspecific. As a result, delays in diagnosis are common, which may lead to poor treatment outcomes [2, 3]. Malignant tumors of the small bowel include adenocarcinomas, neuroendocrine tumors (NETs), stromal tumors, and lymphomas; they account for 93% of small bowel tumors [4].

The distribution of histological types of malignant small bowel tumors has been changing, primarily due to the rising incidence of NETs. Over the past 20 years,

Received: 16.09.2024 Accepted: 10.01.2025 Early publication: 07.02.2025

the number of NET cases has increased fourfold. As a result, NETs have surpassed adenocarcinomas as the most common small bowel tumor reported in the National Cancer Database. By 2005, the proportion of patients with NETs increased from 28 percent to 44 percent, while the proportion of those with adenocarcinomas decreased from 42 percent to 33 percent. The incidence of stromal tumors and lymphomas was reported at 17 percent and 8 percent, respectively [5].

In this study, we aimed to describe the epidemiological and clinical characteristics, diagnostic methods, and survival outcomes for patients with small bowel malignancies who were treated at our clinic, as well as to identify prognostic factors that influence survival.

Material and methods

The present study was conducted at Ankara City Hospital, a multidisciplinary tertiary referral center in Turkey, and was designed as a single-center, retrospective, descriptive study.

Four distinct study groups were formed, including 107 adult patients (> 18 years old) who visited the Oncology Department of Ankara City Hospital at least once between January 1, 2002, and December 31, 2023, and who were diagnosed with one of the following subtypes of small bowel tumors: adenocarcinoma, NETs, non-Hodgkin lymphoma (NHL), or gastrointestinal stromal tumors (GISTs). Tumors of the periampullary region and ampulla of Vater were excluded. Demographic, clinical, pathological, and follow-up data were retrospectively analyzed.

The staging of NHL patients was performed using the Ann-Arbor Staging System. Staging for patients with NETs, adenocarcinomas, and GISTs was conducted using the 9th edition of the American Joint Committee on Cancer (AJCC) Staging System. The Eastern Cooperative Oncology Group (ECOG) performance scale was used to assess the patients' performance status [6].

Patient data and medical history (age, sex, presenting symptoms, smoking, tumor size, tumor location, surgical margin, diagnostic method, obstruction, perforation, and ECOG performance status) were retrieved from the hospital's records and death notification database.

Progression data were available for all patients, while overall survival (OS) data were available for 97 patients. Overall survival was defined as the time from the date of diagnosis to death or the last follow-up, with the follow-up period for living patients extended until the most recent update of their information at the end of the study.

Approval for this study was obtained from the Ethics Committee of Ankara City Hospital.

Statistical analysis

Data were analyzed using the SPSS Statistical Package for the Social Sciences, version 25.0 (IBM Corp., Armonk, NY, US). Continuous variables were expressed as medians (ranges), while categorical variables were presented as percentages. The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. In comparisons between four groups, the Kruskal-Wallis test was used for data that did not follow normal distribution. If significance was found, subgroup analyses were performed using the Mann-Whitney U test. The Chi^2 test was used to compare categorical variables. Survival analysis was conducted using the Kaplan-Meier method. A p-value of < 0.05 was considered statistically significant.

Results

The characteristics of the patients based on tumor subtypes are presented in Table 1. A total of 107 patients with small bowel tumors were included in the study. Seventy-six (71%) of the patients were male, and thirty-one (29%) were female. The most common histological subtype was adenocarcinoma, affecting 44 (41.2%) patients. Twenty-seven (25%) patients were diagnosed with GISTs, 22 (20.6%) with NHLs, and 14 (13.1%) with NETs.

The most common presenting symptom was abdominal pain, observed in 58.9% of patients. Distant metastases were detected at the time of diagnosis in 33 (30.9%) of all patients with small bowel tumors. Distant metastases were found in 22 (50%) patients in the adenocarcinoma group, 3 (21.4%) in the NET group, 5 (18.5%) in the GIST group, and 3 (13.6%) in the NHL group. Distant metastases were more frequently detected at the time of diagnosis in the adenocarcinoma group compared to other groups ($p < 0.05$).

Adenocarcinomas were mostly located in the duodenum, affecting 33 patients (75.0%). Neuroendocrine tumors were most frequently located in the jejunum (5 patients, 35.7%) and ileum (5 patients, 35.7%). GISTs were most commonly found in the jejunum (11 patients, 40.7%), while NHLs were usually localized in the jejunum (9 patients, 40.9%). Differences in tumor locations between adenocarcinoma patients and other tumor groups were statistically significant ($p < 0.001$).

The ECOG performance status of all patients in the NET and GIST groups was between 0–2. In contrast, 37 (84%) patients in the adenocarcinoma group had an ECOG performance status of 0–2, while 7 (16%) patients had an ECOG performance status of ≥ 3. These differences were statistically significant ($p < 0.001$) (Tab. 1).

Table 1. Comparison of clinical, pathological, and prognostic features of small bowel tumors according to subtypes

	Adeno-carcinoma (n = 44)	NET (n = 14)	GIST (n = 27)	NHL (n = 22)	p-value
Age [year], median (minimum–maximum)	61 (22–85)	63 (45–83)	57 (24–77)	53 (18–89)	0.094
	n (%)	n (%)	n (%)	n (%)	
Sex					
Male	30 (68.2%)	12 (85.7%)	17 (63.0%)	17 (77.2%)	0.487
Female	14 (31.8%)	2(14.3%)	10 (37.0%)	5 (22.8%)	
Smoking					
No	24 (54.5%)	9 (64.3%)	19 (70.4%)	14 (63.6%)	0.596
Yes	20 (45.5%)	5 (35.7%)	8 (29.6%)	8 (36.4%)	
ECOG PS					
0–2	37 (84%)	14 (100%)	14 (100%)	19 (86%	**< 0.001**
3–4	7 (16)	0 (0%)	0 (0%)	3 (14%)	
Presenting symptoms					
Weakness	6 (13.6%)	2 (14.3%)	5 (18.5%)	2 (9.1%)	0.500
Abdominal pain	27 (61.4%)	9 (64.3)	17 (63%)	10 (45.5%)	
Other	11 (25%)	3 (21.4%)	5 (18.5%)	10 (45.5%)	
Tumor localization					
Duodenum	33 (75.0%)	2 (14.3%)	4 (14.8%)	4 (18.2%)	
Jejenum	8 (18.2%)	5 (35.7%)	11 (40.7%)	9 (40.9%)	**< 0.001**
İlleum	2 (4,5%)	5 (35.7%)	4 (14.8%)	3 (13.6%)	
Unknown	1 (2.3%)	2 (14.3%)	8 (29.6%)	6 (27.3%)	
Distant metastases at diagnosis					
Yes	22 (50%)	3 (21.4%)	5 (18.5%)	3 (13.6%)	**0.004**
No	22 (50%)	11 (78.6%)	22 (81.5%)	19 (86.4%)	
Relapse or progression[1]					
Yes	38 (86.4%)	8 (57.1%)	7 (25.9%)	13 (59.1%)	**< 0.001**
No	6 (13.6%)	6 (42.9%)	20 (74.1%)	9 (40.9%)	
Survival[2]					
Exitus	35 (79.6%)	7 (50%)	4 (14.8%)	9 (40.9%)	**< 0.001**
Alive	7 (15.9%)	6 (42.9%)	23 (85.2%)	6 (27.3%)	
Not known	2 (4.5%)	1 (7.1%)	0 (0%)	7 (31.8%)	

[1]Any occurrence of progression or relapse at any time after diagnosis; [2]The patient's condition at the last follow-up; ECOG PS — Eastern Cooperative Oncology Group performance scale; GIST — gastrointestinal stromal tumor; NET — neuroendocrine tumor; NHL — non-Hodgkin lymphoma

A total of 38 (86.3%) adenocarcinoma patients received chemotherapy. Of these, 20 patients (45.5%) received adjuvant chemotherapy, while 18 patients (40.9%) received palliative chemotherapy. Among the 18 patients who underwent chemotherapy and had data on response evaluation available, 2 patients (11.1%) achieved a complete response, 9 patients (50%) had stable disease, 2 patients (11.1%) had a partial response, and 5 patients (27.8%) experienced disease progression.

Four patients (28.6%) in the NET group received chemotherapy; however, data on treatment response was unavailable.

In the GIST group, all patients (100%) were treated with imatinib. However, data on treatment response were unavailable.

In the NHL group, 15 patients (68.2%) received chemotherapy. Among the 4 patients with available response evaluation data, 3 (75.0%) achieved a complete response, and 1 (25.0%) had stable disease.

Overall survival data were available for 97 patients. Median OS in the adenocarcinoma group was 1.1 years (range = 0.7–1.6 years). In the NET group, the median OS rate was 8.8 years (range = 3.5–14.2 years), and in the NHL group, median OS was 10.7 years (range = 1.9–19.6 years). Median OS was not reached in the GIST group. The median OS rate in the adenocarcinoma group was significantly lower than that in both the NHL and NET groups ($p = 0.019$ and $p = 0.015$, respectively) (Fig. 1).

Discussion

Malignancies involving the small intestine are rare, they account for only 2 percent of all gastrointestinal

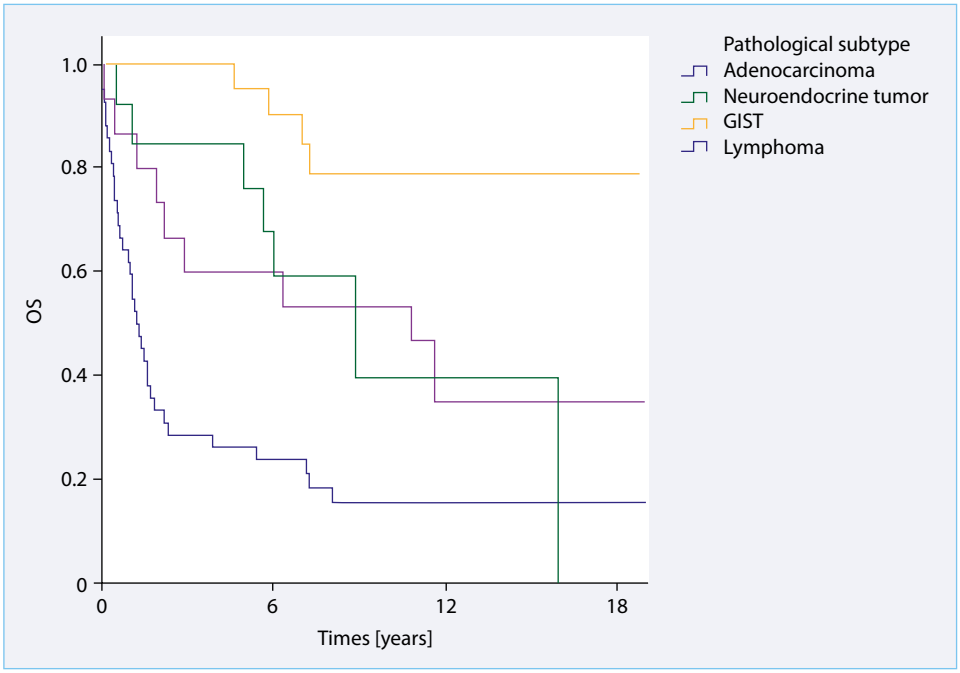

Figure 1. Overall survival analysis according to subtypes of small bowel tumors; GIST — gastrointestinal stromal tumor; OS — overall survival

tract neoplasms and less than 0.6 percent of all cancers in the United States. The most common symptom of small intestine tumors is abdominal pain, which is typically intermittent and crampy. Other symptoms include nausea, vomiting, weight loss, intestinal obstruction, and gastrointestinal bleeding [7–10]. In our patients, the most common symptom was abdominal pain, consistent with previous reports.

In our study, the proportion of males was higher across all small bowel cancer subtypes. The literature generally reports a slight male predominance (male-to-female ratio of 1.5:1), with several studies noting a higher incidence in Black patients compared to White patients. In the study by Haselkorn et al. [11], men had higher rates of small bowel cancer than women. Similarly, in a study of 80 patients, Koç et al. [12] found that 55 patients were male, with the number of male patients being 2.2 times higher than female patients.

The most common histological subtype of small bowel tumors in our study was adenocarcinoma. According to population-based registry data from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program, obtained in 1987, the most common histological subtype of malignant small bowel tumors was adenocarcinoma, which accounted for 45% of cases. The second most common subtype was NET, at 29% [13]. However, the incidence of NET has significantly increased in recent years. According to the National Cancer Data Base (NCDB), NET is now the most common type of small bowel tumor [5]. In a recent study by Silva et al. [14], which included 104 patients with small bowel tumors, NET was similarly the most common histological subtype, affecting 43.7% of patients (n = 38). The relatively high frequency of adenocarcinoma in our study can be attributed to several factors, including the small sample size, geographic and dietary factors, and potential differences in smoking and alcohol consumption patterns. Additionally, the lower referral rate of NET patients to oncology centers after surgery in surgical clinics may have led to an underestimation of the true frequency of these tumors. Given that in our study patients were included from 2002 onward, this may also help explain the higher observed frequency of adenocarcinoma.

In this study, adenocarcinomas were most commonly located in the duodenum, while NETs were predominantly found in the jejunum and ileum, and both GISTs and NHLs were most frequently located in the jejunum. In the study by Dabaja et al. [15], the duodenum was the most common location for adenocarcinoma, found in 113 (52%) of patients. Similarly, Halfdanarson et al. [16] reported that the duodenum was the most frequent tumor site in patients with adenocarcinoma (57%). In a retrospective observational study conducted between 2007 and 2021 in a university hospital in Chile, GISTs were more common in the duodenum (50%; n = 12), while NETs were predominantly located in the ileum (65.8%; n = 25) [14]. Moreover, in line with the literature, NETs are most commonly found in the ileum, while GISTs are typically located in the jejunum and ileum, which is consistent with our findings [7, 17].

In this study, distant metastases were more frequently observed at the time of diagnosis in the adenocarcinoma group compared to other tumor subtypes, and patients in this group had a worse ECOG performance status. Additionally, the histological subtype of the tumor was found to have a statistically significant impact on OS. The median OS rate in the adenocarcinoma group was 1.1 years (min–max = 0.7–1.6 years), which was the shortest among the small bowel tumor subtypes. Furthermore, after adjusting for age and sex, both NETs and GISTs were independently associated with better survival compared to adenocarcinoma.

In the literature, adenocarcinoma has been shown to have a negative impact on survival compared to other histological subtypes. Nodal involvement, in particular, is considered one of the most important prognostic factors in adenocarcinomas. Meijer et al. [18] reported that the five-year survival rate for node-positive disease was approximately 40% lower than for node-negative disease. Additionally, the presence of distant metastases significantly increases the mortality rate, thereby further reducing the five-year survival prognosis [18]. Consistent with the existing literature, studies by Koç et al. [12] also demonstrated that the presence of distant metastasis in patients with small bowel tumors negatively impacts survival, similar to our findings.

In patients with GISTs, the five-year survival rate is approximately 80% for resectable lesions. The prognosis for NETs is generally more complex compared to other gastrointestinal malignancies. Neuroendocrine tumors without evidence of carcinoid syndrome are associated with high survival rates, sometimes exceeding 90%. For NETs, resectable lesions are typically linked to favorable outcomes. Similarly, in patients with NHLs, resectable lesions are associated with high survival rates. However, resection in NHL patients is generally reserved for selected cases aimed at symptom palliation, with systemic therapy being the primary treatment modality. The initial treatment of NHLs is determined by the histological subtype and disease stage. Treatment options include chemotherapy, immunotherapy, radiation therapy, or a combination of these modalities. A subset of patients may receive high-dose chemotherapy followed by stem cell support, such as autologous hematopoietic cell transplantation [19].

Conclusions

Overall survival in patients with small intestine adenocarcinoma was significantly lower compared to other small bowel tumor subgroups. Factors such as tumor stage, ECOG performance status, tumor type, and the presence of distant metastases were found to significantly impact OS. Prospective studies involving larger patient cohorts are required to more clearly identify and validate the prognostic factors influencing survival.

Article Information and Declarations

Data availability statement

The patients' data were included in the study with ethics committee approval. It is not suitable for sharing.

Ethics statement

Ethics committee approval was received.

Author contributions

M.K.: contributed to the conception, revising, final approval of the version to be published, and agreed to be accountable for all aspects of the work; S.A.E.: contributed to the drafting the work, final approval of the version to be published, and agreed to be accountable for all aspects of the work; F.T.K.: contributed to the drafting the work, final approval of the version to be published, and agreed to be accountable for all aspects of the work; B.C.: contributed to the drafting the work, final approval of the version to be published, and agreed to be accountable for all aspects of the work; D.U.: contributed to the drafting the work, final approval of the version to be published, and agreed to be accountable for all aspects of the work.

Funding

None.

Acknowledgments

None.

Conflict of interest

The authors have no conflicts of interest to disclose.

Supplementary material

None.

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