

Evaluation of Prognostic Factors and Adjuvant Chemotherapy in Patients With Small Bowel Adenocarcinoma Who Underwent Curative Resection

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Abstract

This is a multicenter study to assess the prognostic factors and adjuvant chemotherapy in patients with small bowel adenocarcinoma (SBA). A total of 78 patients with SBA diagnosed with completely resected SBA were involved in the study. Only status of surgical margin was determined to be an independent prognostic factor in patients with SBA who underwent curative resection. Neither disease-free survival nor overall survival was found to be significantly improved by the adjuvant chemotherapy

Background: Small bowel adenocarcinoma (SBA) is a rare tumor of the gastrointestinal system with poor prognosis. Because these are rarely encountered tumors, the aim of this multicenter study was evaluation of prognostic factors and adjuvant chemotherapy in patients with curatively resected SBA. **Materials and Methods:** A total of 78 patients diagnosed with curatively resected SBA were involved in the retrospective study. Forty-eight patients received 1 of 3 different chemotherapy regimens, whereas 30 patients did not receive any adjuvant treatment. No adjuvant and adjuvant chemotherapy cohorts were matched (1:1) by propensity scores based on the likelihood of receiving chemotherapy or the survival hazard from Cox modeling. Overall survival (OS) was compared with Kaplan-Meier estimates. **Results:** Median age of 78 patients with curatively resected SBA was 58, and 59% of these were men. According to TNM classification, 8 (10%) of the patients were at stage I, 26 (34%) were at stage II, and 44 (56%) were at stage III. Median follow-up duration was 29 months. Three-year median disease-free survival (DFS) and OS were

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62.5% and 67.0%, respectively. In univariate analysis, presence of vascular invasion, perineural invasion, lymph node involvement, and presence of positive surgical margin were significant predictors of poor survival. Multivariate analysis showed that the only adverse prognostic factor independently related with OS was the presence of positive surgical margin (hazard ratio, 0.37; 95% confidence interval, 0.11-1.26; $P = .01$). Neither DFS nor OS was found to be significantly improved by the adjuvant chemotherapy in both matched and unmatched cohorts. **Conclusions:** Only status of surgical margin was determined to be an independent prognostic factor in patients with SBA who underwent curative resection.

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Introduction

Malignant tumors of the small bowel are relatively rare tumors of the gastrointestinal system. Although the small bowel constitutes a large part of the gastrointestinal tract length and surface area, only approximately 3% of all gastrointestinal tumors derive from small bowel.^{1,2} Along with adenocarcinoma, carcinoid tumor, stromal tumor, and lymphoma are the most common malignant tumors of the small intestine.³ Adenocarcinoma accounts for approximately one-third of small bowel tumors.² Small bowel adenocarcinoma (SBA) predominantly arises in the duodenum (57%-65%) with a decline in frequency toward the distal parts.^{4,5}

The average diagnostic age is between 50 and 70 years, and there is a slight male predominance.⁶ Although the definitive etiologies of small bowel tumors are unknown, various risk factors and predisposing conditions, such as genetic diseases that are accompanied by gastrointestinal polyps and chronic inflammatory bowel diseases, have been defined.^{2,7-9}

Symptoms of patients with SBA are usually nonspecific, with nearly half of the patients presenting with abdominal pain.⁵ As the disease is rarely seen and the signs and symptoms observed are not specific, the course of diagnosis is troublesome.^{10,11} Because of delays in recognition of correct diagnosis, approximately 60% of patients are at stage III-IV when diagnosed.¹² This situation decreases survival and negatively influences the response to treatment. As in most malignancies, early diagnosis and surgical resection are the only chance for cure in SBA¹⁰; whereas 5-year disease-specific survival is 65% in stage I, it decreases up to 4% in stage IV.¹² Along with advanced stage, duodenal primary site, lymph node invasion, pT4, and surgical margin positivity have been described as poor risk factors.^{2,13-17}

In curatively resected small bowel adenocancers, recurrence pattern is usually as distant metastasis, rather than as local recurrence. Relapse pattern is the liver, peritoneum, locoregional recurrence, and abdominal wall involvement in order of frequency.⁴

Although poor risk factors have been described, data regarding the role of adjuvant chemotherapy and radiotherapy in operated small bowel cancers are limited and insufficient. Because these are rarely seen tumors, there is no prospective study for any adjuvant chemotherapy. In most of the oncology clinics and the participating institutions involved in our study, although there is not a standardized treatment protocol, planning of adjuvant chemotherapy based on studies regarding adjuvant chemotherapy in colorectal cancers is being carried out. There is a significant space left regarding adjuvant chemotherapy in SBA. We, therefore, aimed to

describe clinicopathological features of our patients who are diagnosed with curatively resected small bowel adenocancers and to determine effect of adjuvant chemotherapy on overall survival (OS) and disease-free survival (DFS) and potential prognostic factors.

Material and Methods

A total of 118 patients diagnosed with SBA in 18 different institutions in Turkey between August 2003 and May 2013 were evaluated retrospectively. Adenocarcinomas derived from duodenum, ileum, and jejunum were included in the study, whereas patients with tumor of ampulla of Vater and accompanying second malignant neoplasm were excluded. Patients who were at advanced stage at the time of diagnosis also were excluded. Thus, 78 patients diagnosed with curatively resected SBA were included in the study. Patients were categorized according to whether they received adjuvant chemotherapy or not. Clinical information, such as age, gender, Eastern Cooperative Oncology Group (ECOG) performance score of patients, localization of the tumor, margin of resection, histopathological grade, vascular invasion, perineural invasion, lymph node involvement, pT stage, TNM stage, treatments, chemotherapeutic toxicity, status of recurrence, pattern of recurrence, and survey were obtained from patient records. Staging of the patients was performed according to available pathologic, clinical, and radiological findings at the time of diagnosis by using the 2010 7th edition of American Joint Committee on Cancer system.¹⁸

Follow-Up Schedule

During follow-up of patients, medical histories and physical examinations were carried out once every 3 months in the first 2 years, every 6 months for the next 3 to 5 years, and annually after 5 years. In controls of the patients, along with complete blood counts and biochemistry panels, tumor markers (carcinoembryonic antigen, cancer antigen 19-9) also were evaluated. Chest radiographs and abdominal computed tomography scans were performed every 3 months in the first year, every 6 months in the second postoperative year, and annually thereafter for 5 years.

Statistical Analysis

The data were analyzed to determine the clinical characteristics, treatment patterns, outcomes, and prognostic factors of SBA. Statistical calculations were performed using the SPSS 22.0 statistical program (SPSS Inc, Chicago, IL). Descriptive analyses were presented using means and standard deviations for normally distributed variables. The significance of the differences among the means was

Prognosis and Adjuvant Chemotherapy in SBA

determined by the Mann-Whitney U test. Differences in the distribution of ordinal variables were evaluated with the χ^2 test or Fisher's exact test. Survival analysis and curves were compared using the log-rank test by the Kaplan-Meier method. DFS was defined as the time from curative surgery to disease progression or recurrence, or to the date of death or lost to follow-up. OS was described as the time interval from diagnosis to the date of the patient's death or lost to follow-up. Univariate and multivariate analyses (Cox proportional hazards model) were used to calculate hazard ratios (HRs) with 95% confidence intervals (CI). A 2-sided $P < .05$ was considered to indicate a statistically significant difference. To minimize selection bias between patients who received adjuvant chemotherapy and those who did not, propensity scores were used. No adjuvant and adjuvant chemotherapy cohorts were matched (1:1) by propensity scores based on the likelihood of receiving chemotherapy or the survival hazard from Cox modeling. According to adjustment, which was made with propensity scores, 10 patients for each group were selected.

Adjuvant Chemotherapy

Whereas 30 (38%) patients did not receive adjuvant chemotherapy, 48 (62%) patients received 1 of the 3 different chemotherapy regimens as an adjuvant chemotherapy. Among the patients who were delivered adjuvant chemotherapy, 19 (40%) patients received bolus leucovorin-5 fluorouracil (LV-5FU) regimen (5FU 425 mg/m² plus LV 20 mg/m², each given days 1 to 5, every 4 weeks), 23 (48%) patients received a modified FOLFOX 6 regimen (oxaliplatin 85 mg/m² day 1, leucovorin 400 mg total dose over 2 hours day 1, FU 400 mg/m² bolus day 1, followed by 2400 mg/m² over 46 hours, cycled every 14 days), and 6 (12%) patients received cisplatin-5FU regimen (cisplatin 75 mg/m² day 1, FU 750 mg/m² intravenous continuous infusion over 24 hours daily on days 1-4, cycled every 21 days).

Results

Patient Analysis

Median age of 78 patients with curatively resected SBA was 58 (range 18-74) and 59% of these were men. ECOG performance status of all patients was 0 to 1. In 70% of the patients, the primary location of the tumor was the duodenum, in 18% the location was jejunum, and in 10% it was ileum. The surgical procedure was wide segmental resection, which involves resection of the primary, investing mesentery, and lymph nodes, in 59% of patients, whereas 41% of patients underwent pancreaticoduodenectomy, all of whom had duodenum-originated tumors. Whereas most of the patients had well- and moderately differentiated tumors, in half of them vascular or perineural invasion was present. In 6 (8%) patients, R1 surgical margin positivity was present. According to TNM classification, pT stages of patients were as follows: 2 (3%) pT1, 12 (15%) pT2, 30 (38%) pT3, and 34 (44%) pT4, respectively. Whereas in 34 (44%) of the patients there was no lymph node involvement, in 44 (56%) of the patients (39% N1, 17% N2), lymph node involvement was present. According to TNM classification, 8 (10%) of the patients were at stage I, 26 (34%) were at stage II, and 44 (56%) were at stage III. Whereas 48 (62%) patients received 1 of 3 different chemotherapy regimens as an adjuvant treatment, 30 (38%) patients did not receive any adjuvant treatment. In the group that received chemotherapy, the median chemotherapy cycles were 6 (range 2-12). Six patients who received

adjuvant chemotherapy and had surgical margin positivity received adjuvant radiotherapy (45.0-50.4 Gy). Clinical and histopathologic features of 2 groups were balanced except that vascular invasion, perineural invasion, lymph node involvement, and number of patients with higher TNM stages were significantly more in the group that received adjuvant chemotherapy compared with the group that did not. Baseline characteristics of the patients are detailed in Table 1. During follow-up, relapse occurred in 30 (38%) patients. Relapsing patterns were as liver metastases in 15 patients, peritoneal metastases in 7 patients, local mass in 4 patients, pulmonary metastases in 3 patients, and bone metastasis in 1 patient. Whereas curative surgery was performed for none of the patients who developed relapse, 22 of them received palliative chemotherapy (mostly regimens based on platin or irinotecan).

Toxicity

Patients were evaluated in terms of toxicity related to adjuvant chemotherapy. In LV-5FU ($n = 19$), FOLFOX ($n = 23$), and cisplatin-5FU ($n = 6$) regimens, grade 3 to 4 toxicity was observed in 5, 4, and 2 patients, respectively. Most of the grade 3 to 4 toxicities were hematological. Hematological toxicities were predominantly neutropenia (72%) and thrombocytopenia (18%). One patient who received cisplatin experienced nephrotoxicity and in 2 patients who received oxaliplatin, neurotoxicity developed. Toxicity-related death occurred in none of the chemotherapy regimens. Eighty-five percent of the patients were able to complete the scheduled adjuvant chemotherapy. Dose reductions in 15% of the patients and dose delays in 19% of the patients were carried out.

Survival Analyses in the Unmatched Cohort

A total of 78 patients were analyzed in an unmatched cohort. Median follow-up duration was 29 months (range, 6-136 months), and during this period, relapse occurred in 30 patients (38%). Two- and 3-year DFS rates were 70.8% and 62.5%, respectively. Twenty-three patients (29%) died and 2- and 3-year OS rates were 85% and 67%, respectively. When patients were stratified according to status of lymph node involvement, 3-year DFS rate was 80% and 55% ($P = .023$); 3-year OS rate was 78% and 48%, in the lymph node-negative and -positive groups, respectively ($P = .018$). When they were stratified according to status of surgical margin, in patients with negative surgical margin and with positive surgical margin, DFS rate was found to be 68% and 0%, respectively ($P = .0001$) (Figure 1A), and OS rate was found to be 73% and 0%, respectively ($P = .0001$) (Figure 1B). When they were stratified according to receipt of adjuvant chemotherapy, in patients with no adjuvant chemotherapy ($n = 30$) and adjuvant chemotherapy ($n = 48$), DFS rate was found to be 65% and 56%, respectively ($P = .481$) (Figure 2A), and OS rate was found to be 79% and 59%, respectively ($P = .259$) (Figure 2B). According to univariate analysis, presence of vascular invasion, perineural invasion, lymph node involvement, TNM stage, and presence of positive surgical margin were significant predictors of poor survival (Table 2). Multivariate analysis showed that the only adverse prognostic factor independently related with OS was the presence of positive surgical margin (HR, 0.37; 95% CI, 0.11-1.26; $P = .01$) (Table 3). Adjuvant chemotherapy was not a significant prognostic predictor for either DFS or OS according to unmatched cohort analyses.

Table 1 Baseline Characteristics of Patients According to Unmatched and Matched Cohorts

Characteristics	According to Unmatched Cohort			According to Propensity Score-Matched Cohort		
	No Adjuvant Chemotherapy, n = 30	Adjuvant Chemotherapy, n = 48	P	No Adjuvant Chemotherapy, n = 10	Adjuvant Chemotherapy, n = 10	P
	n (%)	n (%)		n (%)	n (%)	
Age			.11			1.00
<60	17 (57)	34 (71)		6 (60)	6 (60)	
>60	13 (43)	14 (29)		4 (40)	4 (40)	
Gender			.28			1.00
Women	12 (40)	20 (42)		3 (30)	3 (30)	
Men	18 (60)	28 (58)		7 (70)	7 (70)	
Localization			.56			1.00
Duodenum	22 (74)	33 (69)		10 (100)	9 (90)	
Jejunum + ileum	7 (23)	15 (31)		0 (0)	1 (10)	
Missing	1 (3)	0 (0)		—	—	
Grade of differentiation			.24			.650
Well	8 (27)	14 (29)		5 (50)	3 (30)	
Moderate + poor and not	20 (67)	28 (59)		5 (50)	7 (70)	
Missing	2 (6)	6 (12)		—	—	
Vascular invasion			.001			1.00
No	20 (67)	10 (21)		8 (80)	8 (80)	
Yes	6 (20)	29 (60)		2 (20)	2 (20)	
Missing	4 (13)	9 (19)		—	—	
Perineural invasion			.004			.93
No	20 (73)	9 (25)		8 (80)	9 (90)	
Yes	5 (10)	27 (50)		2 (20)	1 (10)	
Missing	5 (17)	12 (25)		—	—	
pT stage			.063			1.00
pT 1-3	25 (83)	19 (40)		8 (80)	8 (80)	
pT 4	5 (17)	29 (60)		2 (20)	2 (20)	
Lymph node involvement			.0001			1.00
No	27 (90)	7 (15)		8 (80)	8 (80)	
Yes	3 (10)	41 (85)		2 (20)	2 (20)	
TNM stage			.0001			1.00
I+II	27 (90)	7 (15)		8 (80)	8 (80)	
III	3 (10)	41 (85)		2 (20)	2 (20)	
Surgical margins			.22			1.00
R0	30 (100)	42 (88)		10 (100)	10 (100)	
R1	0 (0)	6 (12)		0 (0)	0 (0)	

Bolded values indicate statistically significant ($P < .05$).

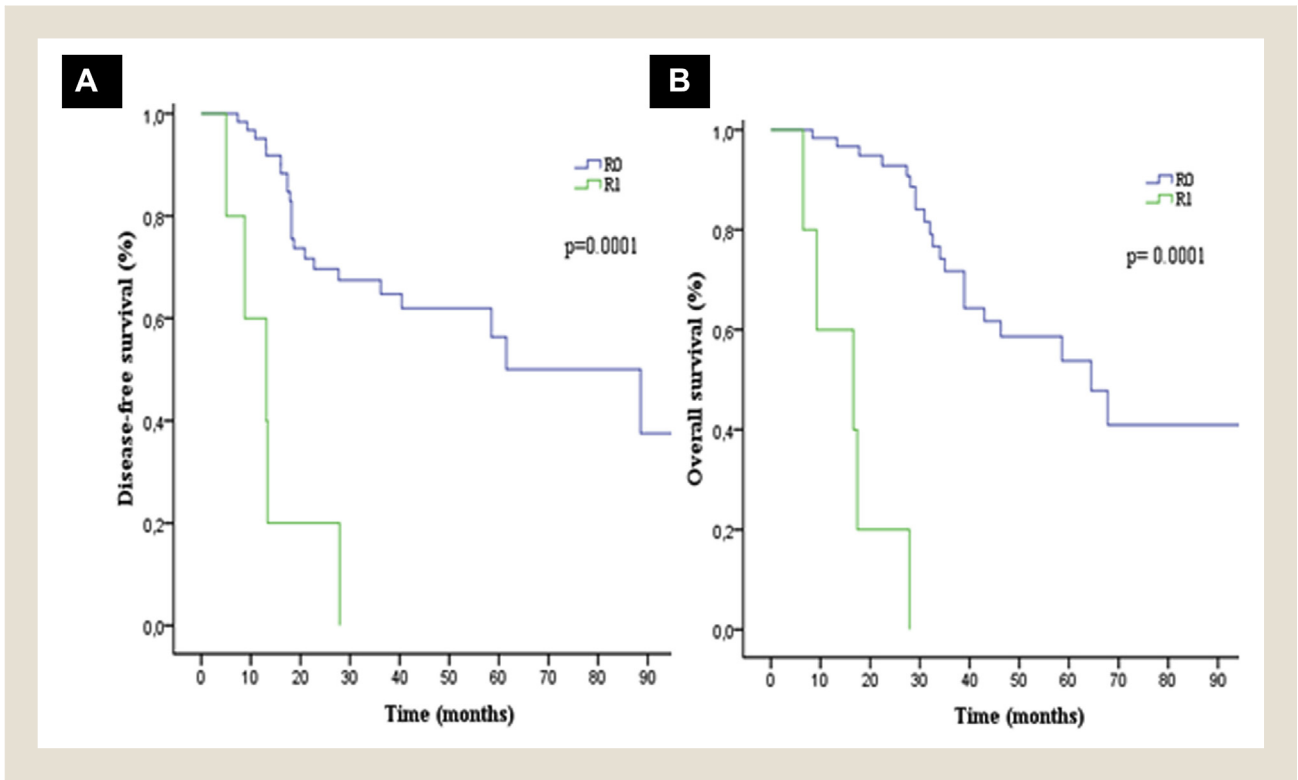
Abbreviations: R0 = microscopic-negative margins; R1 = microscopic-positive margins; RT = radiotherapy; — indicates no data.

Effect of Adjuvant Chemotherapy on Survival in the Propensity Score-Matched Cohort

To exclude selection bias, patients were matched 1:1 according to characteristics in the unmatched cohort that may affect prognosis. The resulting propensity score-matched cohort included 20 patients: 10 (50%) were in the no adjuvant chemotherapy group and the other half was in the adjuvant group. Intergroup variations in the unmatched cohort, such as vascular invasion, perineural

invasion, lymph node involvement, and TNM stage, were balanced following the matching (Table 1). At a median follow-up of 37 months (11-112), the median DFS and OS of the propensity-matched cohort was 49 months (9-92) and 61 months (22-107), respectively. There was no significant DFS (Figure 3A) or OS (Figure 3B) advantage for patients who received adjuvant chemotherapy as compared with those who did not (median DFS 48 vs. 53 months, $P = .41$; median OS 59 vs. 64 months, $P = .57$).

Figure 1 The Survival Curves of DFS (A) and OS (B) According to Surgical Margins



Discussion

Small intestinal carcinoma is a rarely seen tumor. Despite its increased frequency recently, troublesome challenges still exist for

determination of diagnostic methods and treatment.¹⁹ At the time of diagnosis, two-thirds of patients were generally nonmetastatic and candidates for potential resection.¹² Surgical resection is the only

Figure 2 The Curves of DFS (A) and OS (B) According to Adjuvant Treatment in the Unmatched Cohort

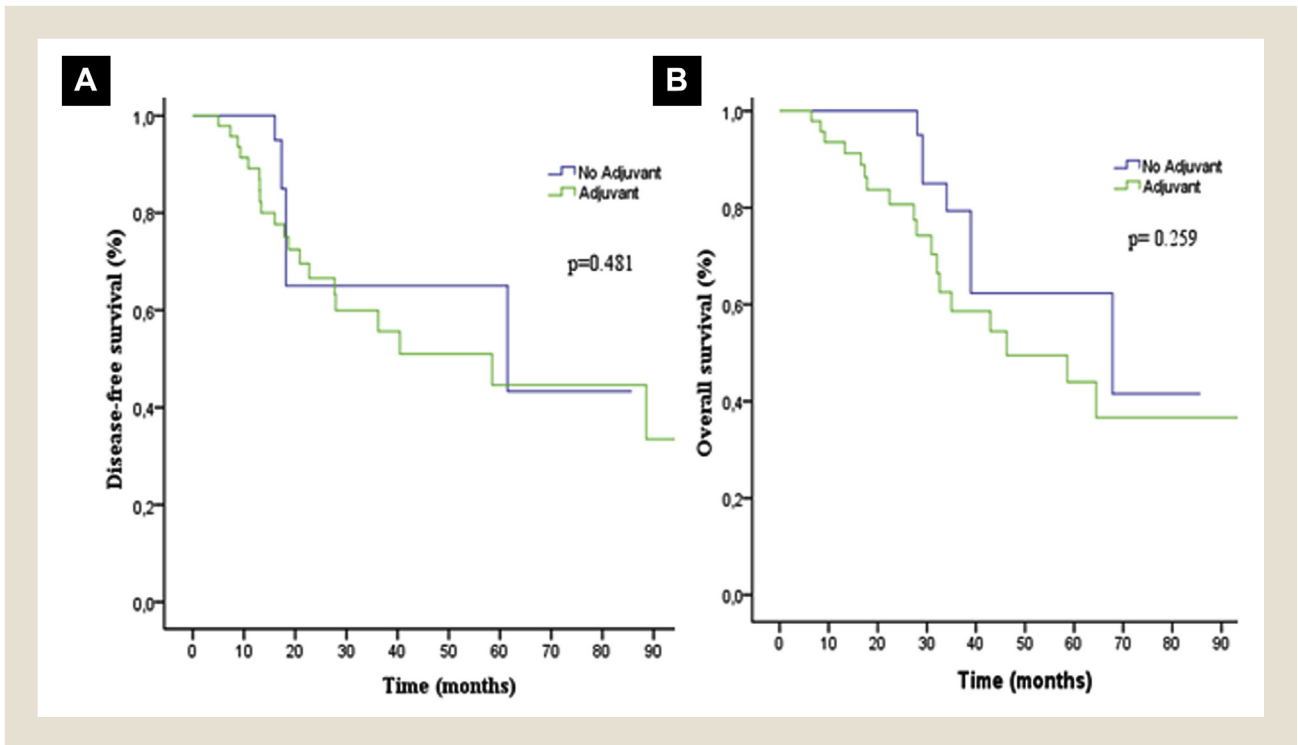


Table 2 Univariate Analyses of Association Among Covariates, DFS, and OS

Variables	Univariate Analyses for DFS			Univariate Analyses for OS		
	HR	95% CI	P	HR	95% CI	P
Age (<60 vs. >60)	1.91	0.73-5.41	.17	2.04	0.75-5.55	.17
Gender (Male vs. female)	0.65	0.27-1.55	.34	0.63	0.26-1.49	.29
Localization (Duodenum vs. others)	2.37	0.70-8.04	.16	2.28	0.67-7.78	.18
Grade of differentiation (Well vs. others)	2.18	0.88-5.38	.08	2.15	0.87-5.33	.09
Vascular invasion (No vs. yes)	0.16	0.05-0.49	.001	0.18	0.06-0.55	.003
Perineural invasion (No vs. yes)	0.18	0.06-0.53	.002	0.18	0.06-0.52	.002
pT stage (pT 1-3 vs. pT4)	0.53	0.23-1.24	.14	0.51	0.21-1.19	.12
Lymph node involvement (No vs. yes)	0.33	0.13-0.86	.023	0.29	0.10-0.80	.018
TNM stage (Stage I-II vs. III)	0.33	0.13-0.86	.023	0.29	0.10-0.80	.018
Surgical margins (R0 vs. R1)	0.10	0.03-0.30	.0001	0.047	0.01-0.16	.0001
Adjuvant chemotherapy (Yes vs. no)	0.45	0.13-1.54	.16	0.38	0.11-1.30	.12

Bolded values indicate statistically significant ($P < .05$).

Abbreviations: CI = confidence interval; DFS = disease-free survival; HR = hazard ratio; OS = overall survival; R0 = microscopic-negative margins; R1 = microscopic-positive margins.

curative method in patients at early stages.¹⁰ Resection of the primary and investing mesentery achieves surgical clearance of both the primary and the regional nodes at risk for metastases. However, in most of the patients, both pT stage and N stage were advanced, due to the nonspecific symptoms and signs and delay in the course of the diagnosis.²⁰⁻²⁴ Nodal involvement is one of the significant predictors of survival.¹² When node-negative patients and node-positive patients were compared in our study, 3-year DFS and OS rates were significantly longer (78% vs. 48% and 80% vs. 55%, respectively) in node-negative patients than in node-positive patients.

Surgical margin was the only independent predictor for OS in the present study. Although the results in our study do not support this, there are studies in the literature that have determined that pT4, poorly differentiated histology, and origin from the duodenum compared with the ileum and jejunum are poor prognostic factors.^{19,21-25}

There are a limited number of retrospective studies reporting no advantage of adjuvant chemotherapy for survival.^{5,23,24,26,27} One of the largest retrospective studies regarding this issue belongs to the Mayo Clinic.⁵ In this retrospective study, 33 of 491 patients diagnosed with SBA received 5FU-based chemotherapy and 40 patients were given adjuvant chemoradiotherapy. Neither of these 2 approaches seemed to provide an additional benefit.

In another study carried out by the M.D. Anderson Cancer Center, 54 patients diagnosed with completely resected SBA were

evaluated retrospectively.²⁷ In this study, 30 patients (56%) received adjuvant therapy consisting of systemic chemotherapy with or without radiation in 28 patients and radiation alone in 2 patients. In consequence of multivariate analysis, improvement in DFS was provided with adjuvant chemotherapy ($P = .05$), whereas it did not provide any statistically significant benefit on OS. However, in the adjuvant chemotherapy group, the number of patients with lymph node involvement and at advanced stages was significantly more than the radiation-alone group.²⁷

In another multicenter retrospective study involving 122 patients diagnosed with duodenal adenocarcinoma, adjuvant chemotherapy was given to 34 patients.²⁴ No significant difference was found between the patients who received adjuvant chemotherapy and those who did not in terms of 5-year survival rates (47% vs. 48%, respectively). Similar to our study, in the group of adjuvant chemotherapy, the number of patients with lymph node involvement and advanced stages was significantly more compared with the group that did not receive adjuvant chemotherapy. In our study, similar to the 3 aforementioned retrospective studies, there was no significant difference between patients who received adjuvant treatment ($n = 48$, 19 patients LV-5FU, 23 patients FOLFOX, 6 patients cisplatin-5FU) and patients who did not ($n = 30$) in terms of 3-year DFS and OS rates. However, in our study, the number of patients with vascular and perineural invasion, lymph node involvement, surgical margin positivity, and higher TNM stage was significantly more in the group that received adjuvant chemotherapy

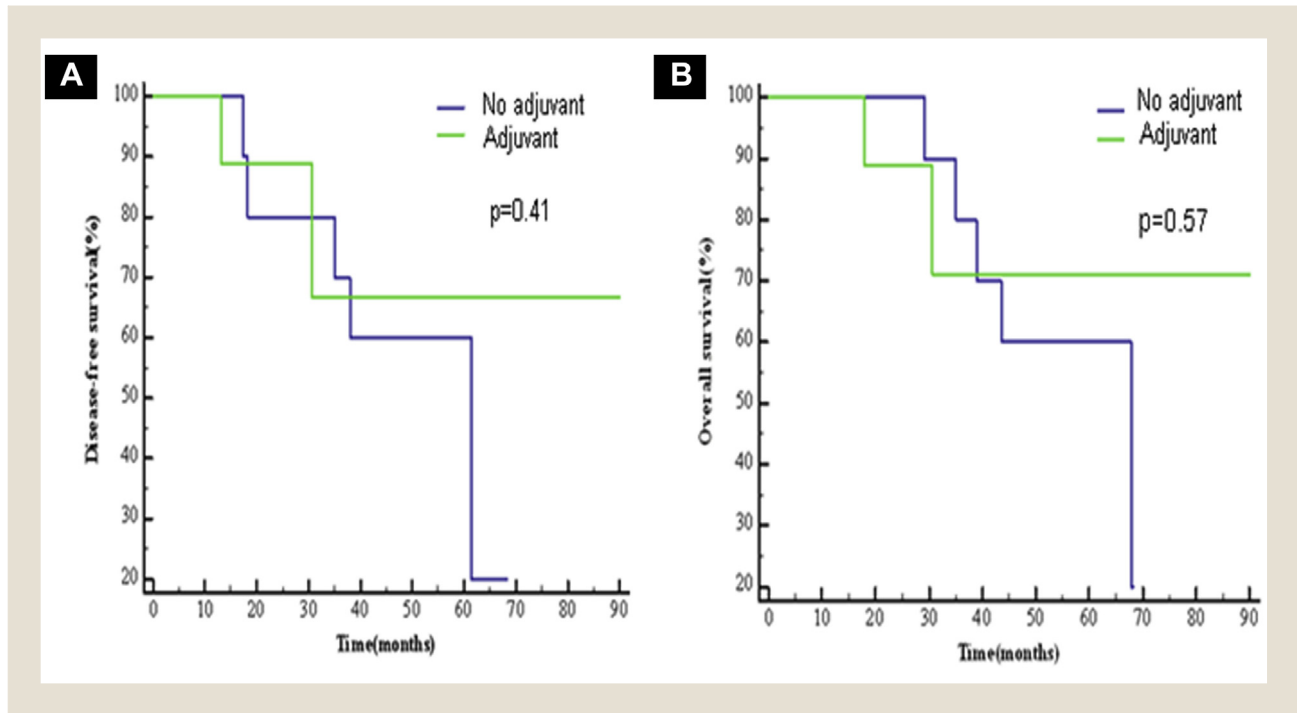
Table 3 Multivariate Analyses of Association Among Covariates, DFS, and OS

Variables	Multivariate Analyses for DFS			Multivariate Analyses for OS		
	HR	95% CI	P	HR	95% CI	P
Vascular invasion (No)	0.31	0.07-1.41	.13	0.39	0.82-1.93	.25
Perineural invasion (No)	0.45	0.08-2.29	.97	0.41	0.07-2.32	.31
Lymph node involvement (No)	0.97	0.23-4.04	.96	0.93	0.21-4.25	.93
Surgical margin (R0)	0.37	0.11-1.26	.11	0.16	0.04-0.65	.01

Bolded value indicates statistically significant ($P < .05$).

Abbreviations: CI = confidence interval; DFS = disease-free survival; HR = hazard ratio; OS = overall survival; R0 = microscopic-negative margins; R1 = microscopic-positive margins.

Figure 3 The Curves of DFS (A) and OS (B) According to Adjuvant Chemotherapy in the Propensity-Matched Cohort



compared with the group that did not. Although differences about vascular invasion, perineural invasion, lymph node involvement, and TNM stage between groups in the unmatched cohort were balanced after matching, adjuvant chemotherapy was still found not to have any prognostic relevance for either DFS or OS. This result probably occurred because the number of patients decreased subsequent to matching, particularly the ones with involved lymph nodes, who are the leading targets.

More recently, the large retrospective study conducted by Ecker et al.²⁸ demonstrated that adjuvant chemotherapy significantly improved survival in patients with stage III SBA according to their propensity score—matched analysis. This is not in keeping with previous trials, and also our study found no survival benefit with contribution of adjuvant chemotherapy. Although not statistically significant, they found a trend toward increased survival time for stage II SBA with positive surgical margins and T4 tumor subclassification. Additionally, their analysis reported that duodenal tumors were associated with worse OS compared with jejunoileal counterparts. However, our study failed to demonstrate the significance of tumor localization as a prognostic factor.

Despite the lack of published data supporting a benefit from adjuvant therapy, in most oncology clinics in our study, adjuvant therapy is given especially to patients with node-positive completely resected small bowel adenocancers. The rationale of adjuvant chemotherapy is basically the MOSAIC study,²⁹ which shows survival advantage of adjuvant chemotherapy given to node-positive colorectal cancers. In oncology clinics participating in our study, for curatively resected, especially node-positive, small intestinal adenocancers, the adjuvant chemotherapy principles applied in colorectal cancers are being carried out. An oxaliplatin-based regimen (ie, FOLFOX) is preferred in patients with node-positive SBA, as it is in node-positive

colon cancers. LV-5FU or capecitabine can be used as an alternative to oxaliplatin-based regimens in node-negative high-risk patients (high grade, vascular and perineural invasion, pT4, poor lymph node dissection, obstruction, perforation).

SBA is a rare but extremely aggressive disease. Due to its rarity and difficulties in diagnosis, studies regarding this issue are limited to retrospective studies carried out with a small number of patients. The power of our study is weak due to its nonrandomized, retrospective nature with low number of patients and nonoptimal homogeneity. Therefore, multicenter prospective studies involving a large number of patients are required to establish optimal adjuvant treatment and determine histopathological prognostic factors.

Conclusions

The presence of vascular invasion, perineural invasion, lymph node involvement, and positive surgical margin were significant predictors of poor survival. The only adverse prognostic factor independently related with OS was the presence of positive surgical margin. Neither DFS nor OS was found to be significantly improved by the adjuvant chemotherapy. However, in our study, the number of patients with vascular and perineural invasion, lymph node involvement, and higher TNM stage were significantly more in the group that received adjuvant chemotherapy compared with the group that did not.

Clinical Practice Points

- Given the infrequent and challenging diagnosis of SBA, trials on both adjuvant chemotherapy and prognostic factors of this entity are rare and a great need exists in the literature concerning the subject.

- In the current study, positive surgical margin was shown to be an independent adverse prognostic factor for OS. Neither DFS nor OS was found to be significantly improved by the adjuvant chemotherapy.
- Regarding the improvement in OS, our findings provide the importance of targeting surgical strategies to achieve tumor-negative surgical margins in patients with local or locally advanced SBA.

Disclosure

The authors have stated that they have no conflicts of interest.

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