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Evaluating the effect of tumor size and sidedness on prognosis in stage 2 colon cancer: a retrospective population study

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Abstract. – OBJECTIVE: In this study, we aimed to evaluate the effect of tumor size and tumor sidedness on prognosis in patients with stage 2 colon cancer.

PATIENTS AND METHODS: Data of 501 patients diagnosed with stage 2 colon cancer were evaluated retrospectively. It was evaluated whether the patients' age, gender, tumor differentiation, tumor node metastasis (TNM) stage, overall survival rate, and disease-free survival rate had any correlation with horizontal tumor diameter and tumor sidedness. In the ROC analysis performed to determine the cut-off value for the tumor diameter, which we think will predict survival, no significant results were obtained with maximum sensitivity and specificity. Therefore, the median value of the tumor diameter, which is 5 cm, was accepted as the cut-off value. Kaplan-Meier method and Cox regression analysis were used for survival analysis and determination of prognostic factors.

RESULTS: When the patients were evaluated in terms of tumor localization, 189 (37.7%) patients had right colon tumors and 312 (62.3%) patients had left colon tumors. There was no statistically significant difference in terms of disease-free survival and overall survival according to tumor localization. When the patients were analyzed by dividing them into two groups according to the horizontal tumor size (<5 cm and ≥5 cm), no statistically significant difference was found between the groups in terms of disease-free survival (DFS) and overall survival (OS) p=0.085, p=0.699, respectively.

CONCLUSIONS: Our results suggest that the management of patients with stage 2 colon cancer requires a better understanding of tumor biology rather than features such as tumor size and localization.

Key Words:
Colon cancer, Tumor size, Tumor sidedness, Prognosis.

Introduction

Colon cancer is the 3rd most common cancer in both women and men, and it is the second most common cause of cancer-related death[1]. In recent years, significant improvements have been achieved in the prognosis of patients with new treatment options such as surgery, chemotherapy, targeted therapies, and immunotherapy[2].

In Stage II and Stage III patients, 5-year overall survival with multidisciplinary treatment is around 70% and 50%, respectively. However, 5-30% of patients develop recurrence and metastasis despite surgical and adjuvant treatment[3,4].

In the 8th version of the American Joint Com-

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mission on Cancer (AJCC) TNM staging system, which is currently used in the staging of colorectal cancers, T stage refers to the depth of tumor invasion in different layers of the intestinal wall of the tumor[5]. Tumor size is defined as the maximal horizontal tumor diameter, and it is included in the TNM staging of many cancers such as breast, lung, and renal cancers and it is used to determine the prognosis[6-9]. Studies[10,11] suggest that tumor size may be an important prognostic factor in gastric cancers. However, the effect of tumor size on the prognosis of colon cancer is still unclear, and there are conflicting results[12-15].

Surgery is the main treatment of early-stage colon cancer, and although the efficacy of adjuvant chemotherapy on survival in patients with stage 3 colon cancer after surgery has been clearly demonstrated, the use of adjuvant therapy in stage 2 patients is still controversial. Today, European (European Society of Medical Oncology ESMO) and American (American Society of Clinical Oncology (ASCO) and National Comprehensive Cancer Network (NCCN) guidelines define high-risk factors and recommend adjuvant treatment in case any of these factors is present[16,17]. These risk factors were determined as pT4 tumor, lymphatic/vascular invasion (LVI), poor differential tumor, perineural invasion (PNI), obstruction, localized perforation, close or positive surgical margin, and fewer than 12 lymph node dissection. However, in some population-based studies, the contribution of adjuvant therapy to survival in all high-risk stage 2 colon cancers has not been demonstrated[18,19]. Again, it is not possible to access molecular markers such as microsatellite instability, which are determined as prognostic factors, in many countries and centers.

Currently, defined risk factors are insufficient in the selection of adjuvant therapy, and additional prognostic factors are needed to be defined in order to effectively manage these patients. Also, tumor size is overlooked in the AJCC TNM staging system. Therefore, in our study, we aimed to evaluate the relationship between tumor size and well-known prognostic factors and tumor localization, and its potential role as a prognostic indicator.

Patients and Methods

The files of 608 patients treated and followed up with the diagnosis of stage II colon cancer between January 2012 and December 2020 were retrospectively reviewed. Five oncology centers from Turkey were included in the study. Patients over the age of 18 who underwent curative surgery and were diagnosed with stage II colon cancer according to the 8th version of the American Joint Commission on Cancer (AJCC) TNM staging system were included in the study. Patients with stage I, stage III and stage IV colon cancer, rectal cancer, palliative surgery, no pathological diagnosis, follow-up data, tumor localization, and tumor diameter unknown were excluded from the study. After excluding patients who were not eligible for the study, the data of the remaining 501 patients were included in the evaluation (Figure 1). Data such as demographic characteristics, tumor localization, tumor diameter, grade, number of lymph nodes removed by dissection, number of metastatic lymph nodes of the patients were obtained through file records or medical records in the hospital information system. The patient's risk factors, adjuvant treatments, recurrence dates, last control dates, or *exitus* dates were recorded. Tumors localized in the anatomical region from the cecum to the distal 2/3 of the transverse colon were defined as right-sided tumors, tumors localized to the 1/3 transverse colon, descending colon, and sigmoid colon was defined as left-sided tumors. Tumor size was defined as the maximum horizontal tumor diameter obtained from formalin-fixed surgical specimens and specified in the pathology report. In the ROC analysis performed to determine the cut-off value for the tumor diameter, which we think will predict survival, no significant results were obtained with maximum sensitivity and specificity, therefore, the median value of the tumor diameter, which is 5 cm, was accepted as the cut-off value, and the tumor sizes were grouped as above 5 cm and below 5 cm (Figure 2).

The primary endpoints were overall survival (OS) and disease-free survival (DFS). OS was defined as the time from diagnosis to death from any cause, and DFS was defined as the time from diagnosis to recurrence, metastasis, or death.

Statistical Analysis

Data analysis was performed by using Statistical Package for Social Science (SPSS-22 for Windows, IBM, Armonk, NY, USA). Whether the variables were normally distributed or not was investigated using visual (histograms, probability plot) and analytical methods (Kolmogorov-Smirnov) categorical variables were interpreted by frequency tables. The chi-square test was used

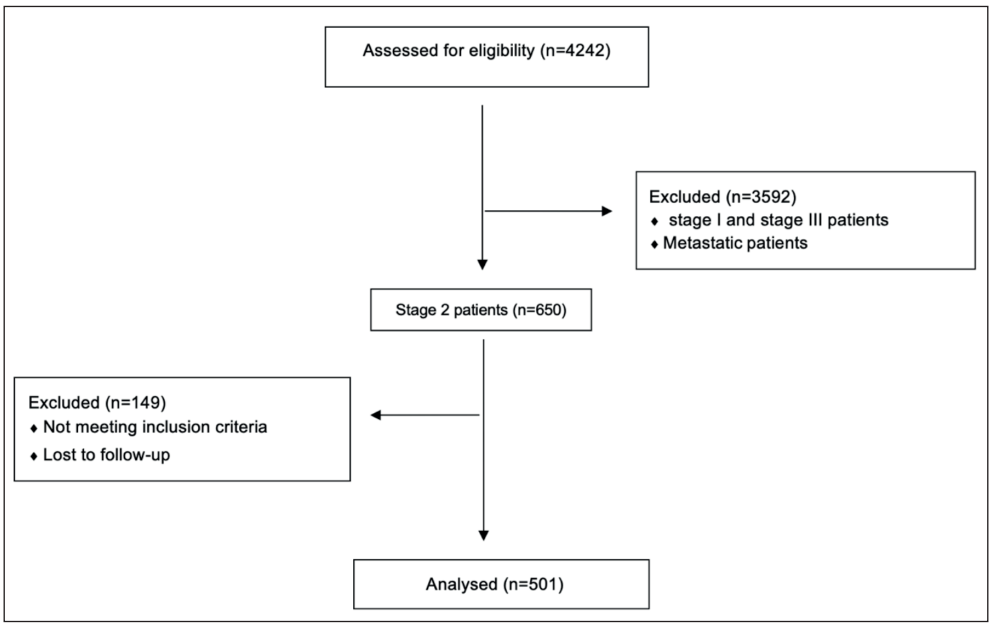

Figure 1. Flowchart of the patients.

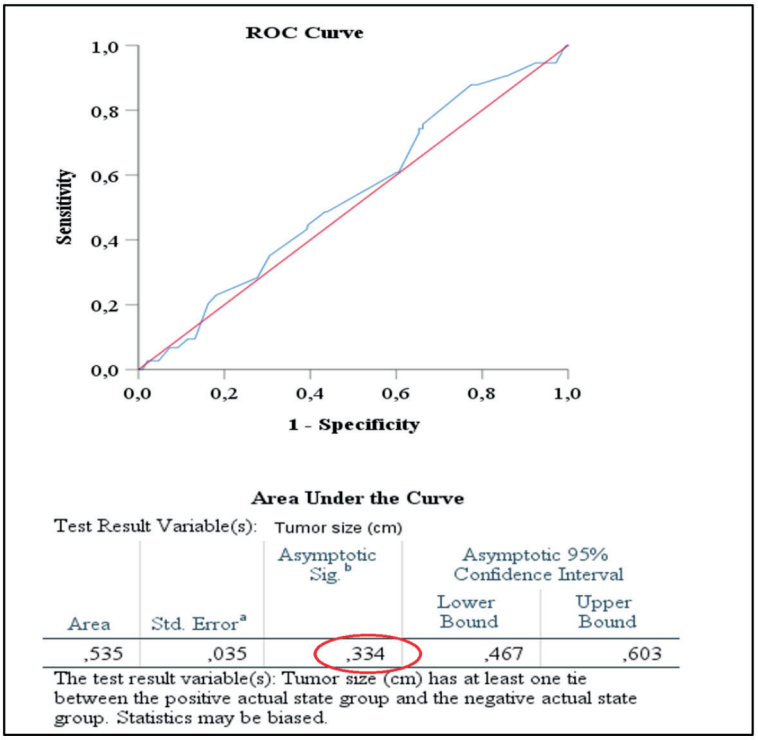

Figure 2. ROC (Receptor operating characteristic) analysis showing the effect of tumor size in predicting mortality.

to determine whether there was any difference between the groups in terms of quality variables. The continuous variables were expressed as mean and Standard deviation or as median and interquartile range, depending on the normality of their distribution. If there is a difference between the groups in terms of numeric variables and if parametric test conditions were fulfilled, the independent groups were examined by *t*-test and, if not, Mann Whitney's U-test was used.

The role of tumor size in predicting mortality was analyzed with the "Receiver Operating Properties (ROC)" curve analysis. While evaluating the area under the curve, a 5% type-1 error level was used to accept a statistically significant predictive value of the test variables. The Kaplan-Meier survival estimates were calculated. The effects of some variables on overall survival and disease-free survival were analyzed using the Log-rank test. Possible factors associated with survival outcomes ($p \leq 0.250$) in univariate analysis were selected for testing in multivariate models. The independent predictors of survival were determined with multivariate Cox regression models. A 5% type-I error level was used to infer statistical significance. The statistically significant two-tailed *p*-value was considered as <0.05.

Results

The median age of 501 patients included in the study was 61 (range 18 to 94). One hundred eighty-eight of the patients (37.5%) were female and 313 (62.5%) were male. The median body mass index (BMI) was 26.8 (range 10.7-39.8). When the patients were evaluated according to the tumor grade, the number of Grade 1/2/3 patients was 150 (29.9%)/294 (58.7%)/25 (5%), respectively. When the patients were evaluated according to the T stage, the number of patients who had T3, and T4 tumors were 373 (74.5%) and 128 (25.5%), respectively. The most common histological subtype was adenocarcinoma, with 446 (89%) patients. Adjuvant chemotherapy was given to 62.3% of the patients and 29.9% of them were chemotherapy regimens containing oxaliplatin. The clinical and pathological features of the patients are given in Table I.

In the ROC analysis performed to determine the cut-off value for the tumor diameter, which we think will predict survival, no significant results were obtained with maximum sensitivity and specificity. Therefore, the median value of the tumor diameter, which is 5 cm, was accepted as the cut-off value. The size of the tumor was less than 5 cm in 199 (39.7%) of the patients, and it was 5 cm and above in 302 (60.3%) patients. There was no significant difference between patients with tumor size ≥5 cm and <5 cm in terms of age, gender, location of the tumor on the right or left side, T stage, grade, LVI, BMI, rates of receiving adjuvant chemotherapy, and use of oxaliplatin in adjuvant therapy. However, there was a significant correlation between PNI and tumor diameter. It was found that as the tumor size increased, the PNI increased. Patients with tumor size ≥5 cm had a significantly higher rate of more than 12 lymph node dissection at surgery ($p<0.001$). There was no significant correlation between tumor diameter and recurrence rate. The recurrence rate was 10.2% in patients with tumor diameter <5 cm and 14.9% in patients with tumor diameter ≥5 cm. There was no significant difference between the groups in terms of MSI status either. The relationship between tumor size and baseline characteristics is given in Table II.

Table I. Baseline characteristics of all stage-2 colon cancer patients.

	Patients (n=501)
Age, years (range)	61 (18-94)
Gender, n (%)	
Male	313 (62.5)
Female	188 (37.5)
BMI, kg/m²	26.8 ± 4.8
Histology, n (%)	
Adenocarcinoma	446 (89.0)
Mucinous adenocarcinoma	52 (10.4)
Signet ring cell carcinoma	1 (0.2)
Undifferentiated carcinoma	2 (0.4)
Tumor location, n (%)	
Right colon	189 (37.7)
Left colon	312 (62.3)
T stage, n (%)	
T3	373 (74.5)
T4	128 (25.5)
Tumor size (cm)	
Median (IQR)	5 (4-7)
≤2, n (%)	16 (3.2)
>2-≤4, n (%)	146 (29.1)
>4-≤6, n (%)	183 (36.5)
>6, n (%)	156 (31.1)
Tumor grade, n (%)	
Unknown	32 (6.4)
Grade 1	150 (29.9)
Grade 2	294 (58.7)
Grade 3	25 (5.0)
Chemotherapy regimens, n (%)	
No	189 (37.7)
FOLFOX-XELOX	93 (18.6)
Fluorouracil-capecitabine	219 (43.7)
Microsatellite instability, n (%)	
Unknown	343 (68.5)
Positive	67 (13.4)
Negative	91 (18.2)

Continuous variables were expressed as means ± Standard deviation, or medians (interquartile ranges). Categorical variables were expressed as the number of cases (percentage in brackets).

There was no statistically significant difference between the groups for tumor size in terms of disease-free survival (DFS) (p=0.085) and overall survival (OS) (p=0.699) (Figure 3).

There were right colon tumors in 189 (37.7%) patients and left colon tumors in 312 (62.3%) patients. There was no difference between the patients with right or left colon tumors in terms of age, gender, T stage, histopathological grade, and the number of lymph node dissections. However, there was a statistically significant difference between right and left colon tumors in terms of BMI (p=0.003), chemotherapy use (p=0.005), and oxaliplatin treatment (p=0.001) (Table III). While BMI was found to be higher in patients with right colon tumors, the use of adjuvant chemotherapy and treatments containing

Table II. Comparison of clinical features and baseline characteristics according to tumor size in stage-2 colon cancer.

	Tumor size		*p*-value
	≥5 cm (n=302)/%	<5 cm (n=199)/%	
Age, years			0.922
≥65	(111) 36.8%	(74) 37.2%	
<65	(191) 63.2%	(125) 62.8%	
T stage			0.101
T3	(217) 71.9%	(156) 78.4%	
T4	(85) 28.1%	(43) 21.6%	
Gender			0.068
Male	(179) 59.3%	(134) 67.3%	
Female	(123) 40.7%	(65) 32.7%	
Tumor location			0.861
Right colon	(113) 37.4%	(76) 38.2%	
Left colon	(189) 62.6%	(123) 61.8%	
BMI, kg/m²			0.846
≥25	(96) 61.9%	(60) 63.2%	
<25	(59) 38.1%	(35) 36.8%	
Tumor grade			**0.040***
Unknown	(25) 8.3%	(7) 3.5%	
Grade 1	(91) 30.1%	(59) 29.6%	
Grade 2	(167) 55.3%	(127) 63.8%	
Grade 3	(19) 6.3%	(6) 3.0%	
Chemotherapy			0.696
Yes	(186) 61.6%	(126) 63.3%	
No	(116) 38.4%	(73) 36.7%	
Chemotherapy regimens (in Chemotherapy, n=312)			0.519
Oxaliplatin	(58) 31.2%	(35) 27.8%	
Others	(128) 68.8%	(91) 72.2%	
Removed lymph node			**<0.001**
≥12	(222) 73.5%	(111) 55.8%	
<12	(80) 26.5%	(88) 44.2%	
Nüks			0.820
Absent	(251) 85.1%	(176) 89.8%	
Present	(44) 14.9%	(20) 10.2%	
Perineural invasion			**0.050**
negative	(205) 68.1%	(132) 67.3%	
positive	(65) 21.6%	(31) 15.8%	
unknown	(31) 10.3%	(33) 16.8%	
Lympho-vascular invasion			0.098
negative	(219) 72.8%	(138) 70.4%	
positive	(64) 21.3%	(36) 18.4%	
unknown	(18) 6.0%	(22) 11.2%	

*The difference is only between the "unknown" categories. BMI, body mass index.

Table III. Comparison of clinical features and baseline characteristics according to tumor localization in stage-2 colon cancer.

	Tumor location		*p*-value
	Right colon (n=189)/ %	Leftcolon (n=312)/ %	
Age, years ≥65 <65	(78) 41.3% (111) 58.7%	(107) 34.3% (205) 65.7%	0.117
T stage T3 T4	(145) 76.7% (44) 23.3%	(228) 73.1% (84) 26.9%	0.365
Gender Male Female	(114) 60.3% (75) 39.7%	(199) 63.8% (113) 36.2%	0.438
BMI, kg/m² ≥25 <25	(73) 73.7% (26) 26.3%	(83) 55.0% (68) 45.0%	**0.003**
Tumor grade Unknown Grade 1 Grade 2 Grade 3	(14) 7.4% (51) 27.0% (111) 58.7% (13) 6.9%	(18) 5.8% (99) 31.7% (183) 58.7% (12) 3.8%	0.314
Chemotherapy Yes No	(103) 54.5% (86) 45.5%	(209) 67.0% (103) 33.0%	**0.005**
Chemotherapy regimens (in Chemotherapy, n=312) Oxaliplatin Others	(21) 20.4% (82) 79.6%	(72) 34.4% (137) 65.6%	**0.011**
Removed lymph node ≥12 <12	(132) 69.8% (57) 30.2%	(201) 64.4% (111) 35.6%	0.213
Recurrens Absent Present	(163) 87.6% (23) 12.4%	(264) 86.6% (41) 13.4%	0.422

oxaliplatin was observed more frequently in patients with left colon tumors. There was no significant relationship between tumor localization and disease-free survival and overall survival (Figure 4).

There was no significant relationship between disease-free survival and age, T stage, number of lymph node dissection, receiving adjuvant chemotherapy, and receiving oxaliplatin therapy. However, the presence of lymphovascular invasion (LVI) and peri-neural invasion had a statistically significant effect on disease-free survival (Figure 5).

Overall survival was significantly worse in patients over 65 years of age ($p<0.001$), with LVI ($p=0.017$), with PNI ($p=0.009$), and without adjuvant chemotherapy ($p<0.001$). Factors such as T stage, a number of lymph nodes dissected, and no oxaliplatin in adjuvant therapy had no significant effect on overall survival (Figure 6). In multivariate analysis, only being over 65 years of age in both groups based on tumor size had a significant effect on mortality (HR:3.38, 95%CI, 1.40-7.13, $p<0.001$) (Table IV).

MSI status was evaluated in only 158 of the patients, and MSI positivity was detected in 67 (13.4%) patients. MSI positivity rate was higher in the right colon tumors (19.6% *vs*. 9.6%). Of the MSI-positive patients, 88.1% had T3 tumors and 11.9% had T4 tumors.

The median follow-up in the entire study population was 50 months. There was no difference in median follow-up time between the groups according to tumor size. For those with tumor size <5 cm, the median follow-up period was 52 months (IQR: 30-84), and for those with ≥5 cm, it was 48.5 months (IQR: 22-84). In the follow-up, 64 patients developed recurrence and 74 patients died.

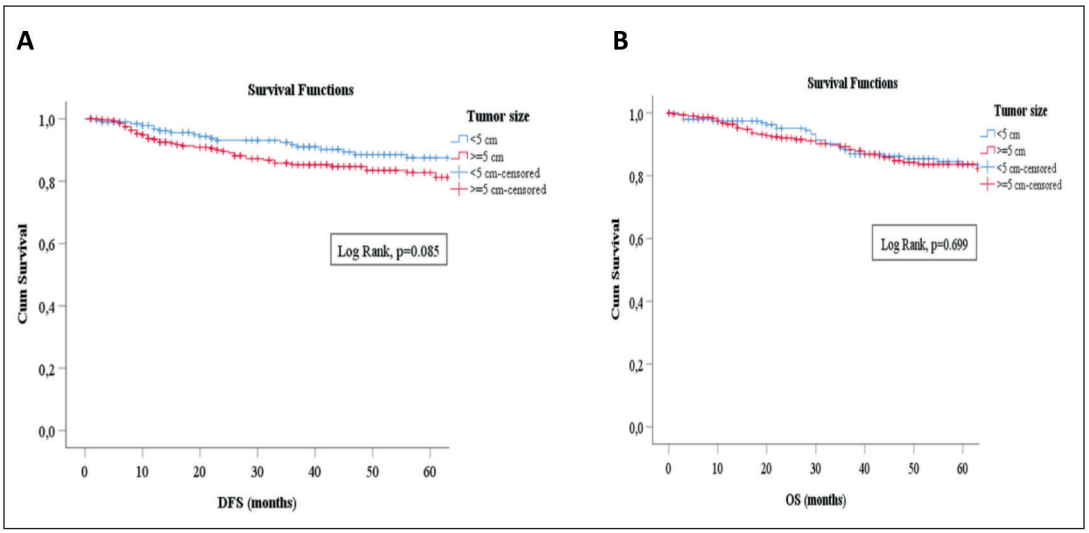

Figure 3. Kaplan-Meier Curve of (**A)** disease free survival in tumor size <5 cm and tumors greater than 5 cm; 5 years DFS for tumor size <5 cm and ≥5 cm: 87.5% *vs.* 82.8 % respectively (p=0.085). **B,** Overall survival in tumor size <5 cm and tumors greater than 5 cm; 5 years OS for tumor size <5 cm and ≥5 cm: 83.5% *vs.* 83.6% (p=0.699).

Table IV. Cox proportional hazards analysis for 60-months mortality.

	Tumor Size					
	<5 cm (n=199)			≥5 cm (n=302)		
	5-year OS (%)	HR (95% CI)	*p*-value	5-year OS (%)	HR (95% CI)	*p*-value
Age, years <65, ref* ≥65	91 70	3.16 (1.40-7.13)	**0.006**	94 65	3.38 (1.74-6.57)	**<0.001**
T stage T3, ref* T4	82 88	0.57 (0.20-1.66)	0.301	82 87	0.89 (0.43-1.82)	0.742
Lymphovascular invasion No, ref* Yes Unknown	83 79 96	1.06 (0.37-3.0) 0.43 (0.04-4.4)	0.916 0.480	87 72 82	2.11 (1.08-4.16) 1.19 (0.26-5.39)	**0.030** 0.820
Perineural invasion No, ref* Yes Unknown	85 72 91	2.96 (1.07-8.19) 0.75 (0.18-3.05)	**0.037** 0.684	86 71 86	1.75 (0.85-3.61) 0.87 (0.23-3.37)	0.129 0.843
Chemotherapy No, ref* Yes	73 89	0.41 (0.17-0.99)	**0.047**	75 89	0.74 (0.39-1.43)	0.377
Chemotherapy regimens Oxaliplatin, ref* Others	90 82	0.94 (0.25-3.58)	0.925	No death 80	-**	-**

The multivariate analysis was adjusted for covariates such as age (under 65 andover), T-stage (T3 and T4), lympho-vascular invasion, perineural invasion, chemotherapy and taking the oxaliplatin regimen or not, for each variable.**ref:* reference category.**The regression hypothesis was not met because the number of events was not sufficient in the group with tumor ≥5 cm.

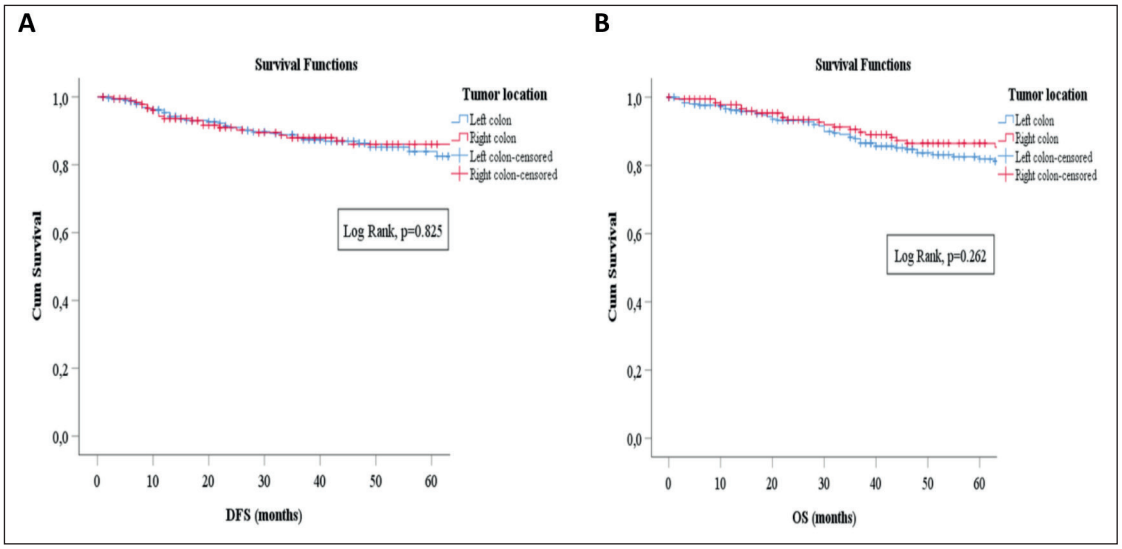

Figure 4. Kaplan-Meier curve of DFS an OS for tumor sidedness. **A,** 5 years DFS for right sided = 86.0% *vs.* left sided= 83.9%; (*p*=0.825). **B,** 5 years OS for right sided = 86.5% *vs.* left sided = 81.9%; (*p*=0.262).

Discussion

There are confusing results in the literature regarding the effect of tumor size on the prognosis in patients with stage 2 colon cancer, and it does not seem possible to reach a clear conclusion. In our study, we found that tumor size did not have a significant effect on disease-free survival and overall survival in stage 2 disease.

Mejri et al[20] found a significant relationship between tumor size and survival and other prognostic factors. In this study, tumor diameter <4 cm predicted better overall survival[20]. However, the study population was heterogeneous and included patients with stage II-III colorectal cancer. In our study, the study population was homogeneous, and only stage II colon cancer patients were included. Therefore, we think that our results are more reliable.

In the study by Sha et al[13] they found a positive correlation between increasing tumor size and prognostic factors and a negative correlation between survival. However, the patient population in this study was also heterogeneous. All stages were included in the study and a clear interpretation of the prognosis cannot be made in early-stage patients.

Li et al[21] reported that smaller tumor size was significantly associated with poorer survival in patients with stage I-III colon cancer undergoing curative surgery, and the survival analyses using propensity score; however, there was no difference in OS, DFS, and cancer-specific survival in groups with tumor size less than or greater than 4 cm.

In our study, a significant correlation was found between tumor size and PNI, among the well-known prognostic factors. However, it could not be shown that tumor size has a predictive value in determining the indication for adjuvant therapy in stage II colon cancer.

The prognostic importance of tumor localization in colon cancers, especially in stage IV patients, is a current issue. Many studies[22-24,28] have shown that there are differences between right and left colon cancers in terms of clinicopathological features and survival. Subgroup analyzes of randomized controlled trials in stage IV patients showed that tumors localized in the right colon had worse treatment response and survival outcomes than those on the left[23,24]. However, the prognostic value of the tumor localization in early-stage patients is a less-discussed issue. There are conflicting results in the literature regarding the tumor localization in the early stage. One of the important results of our study is the demonstration that tumor location is not an independent prognostic factor in stage II colon cancer.

In the study of Weiss et al[25] they showed that there was no difference in 5-year mortality between right and left side tumors in patients with early-stage colon cancer.

In the study of Chan et al[26] in which they included 3281 patients with stage I-III colon cancer, they showed that tumor localization had no effect on survival in all patient population and stage II patients.

In the study of Kennecke et al[27] in which they evaluated 5378 patients with stage I-III colon cancer, they concluded that the right location of the tumor in stage II patients was associated with a better prognosis, but it was not effective on overall survival and relapsed survival in stage III patients. This study also showed a higher detection rate of MSI-H in right colon tumors. In our study, MSI-H detection rates were significantly higher in patients with right colon tumors, similar to the literature.

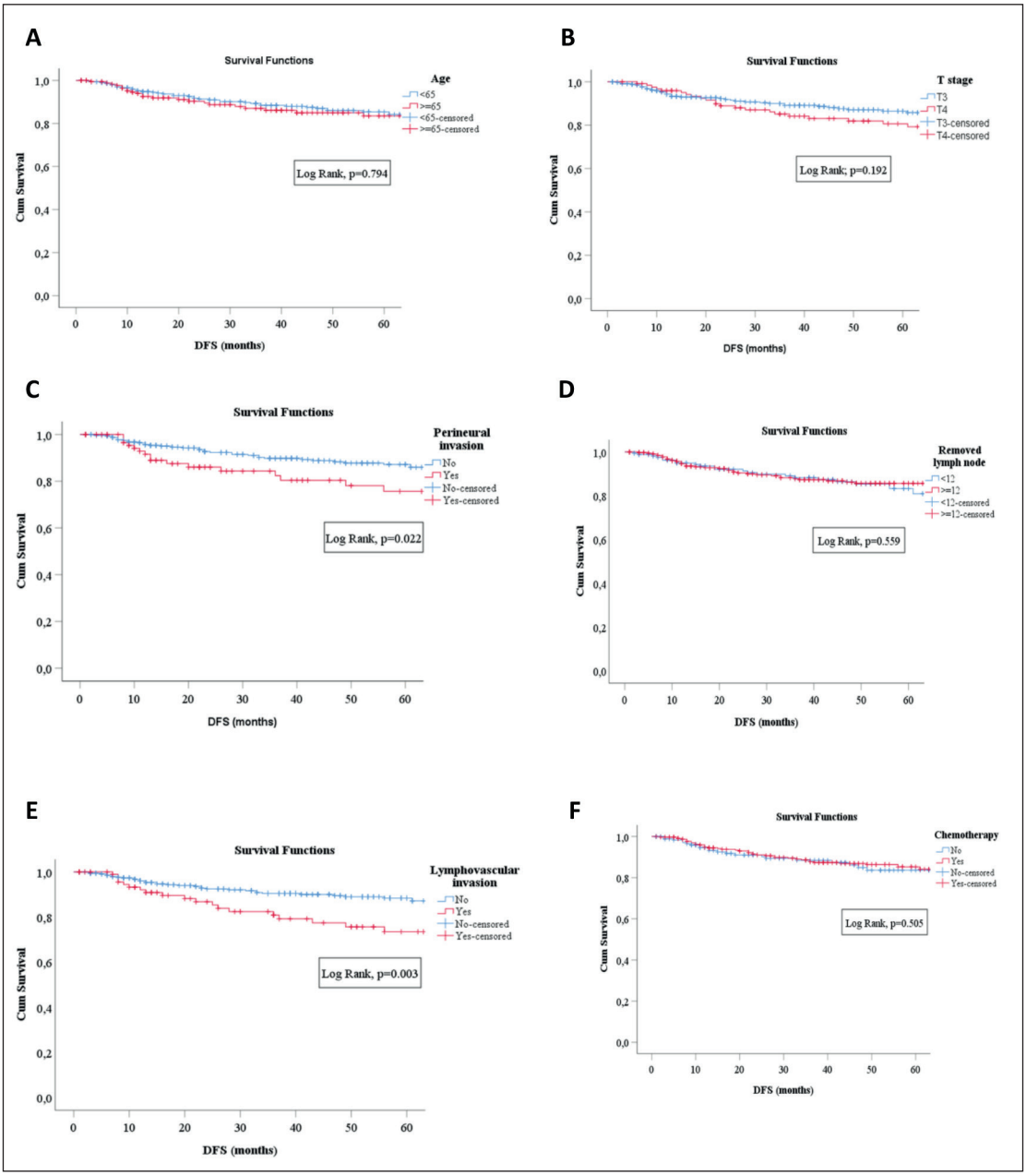

Figure 5. Kaplan-Meier curves of disease free survival (DFS) by some risk factors. **A**, For stage 2 colon cancer according to age patients aged <65 years and ≥65 (p=0.794). **B**, For stage 2 colon cancer according to pT stage: T3 *vs*. T4 (p=0.192). **C**, For stage 2 colon cancer according to PNI status: absent vs present (p=0.22). **D**, For stage 2 colon cancer according to removed lymph node: <12 *vs*. ≥12 (p=0.559). **E,** For stage 2 colon cancer according to LVI status: absent vs present (p=0.003). **F**, For stage 2 colon cancer according to adjuvan chemotherapy: recieved vs not recieved (p=0.505)

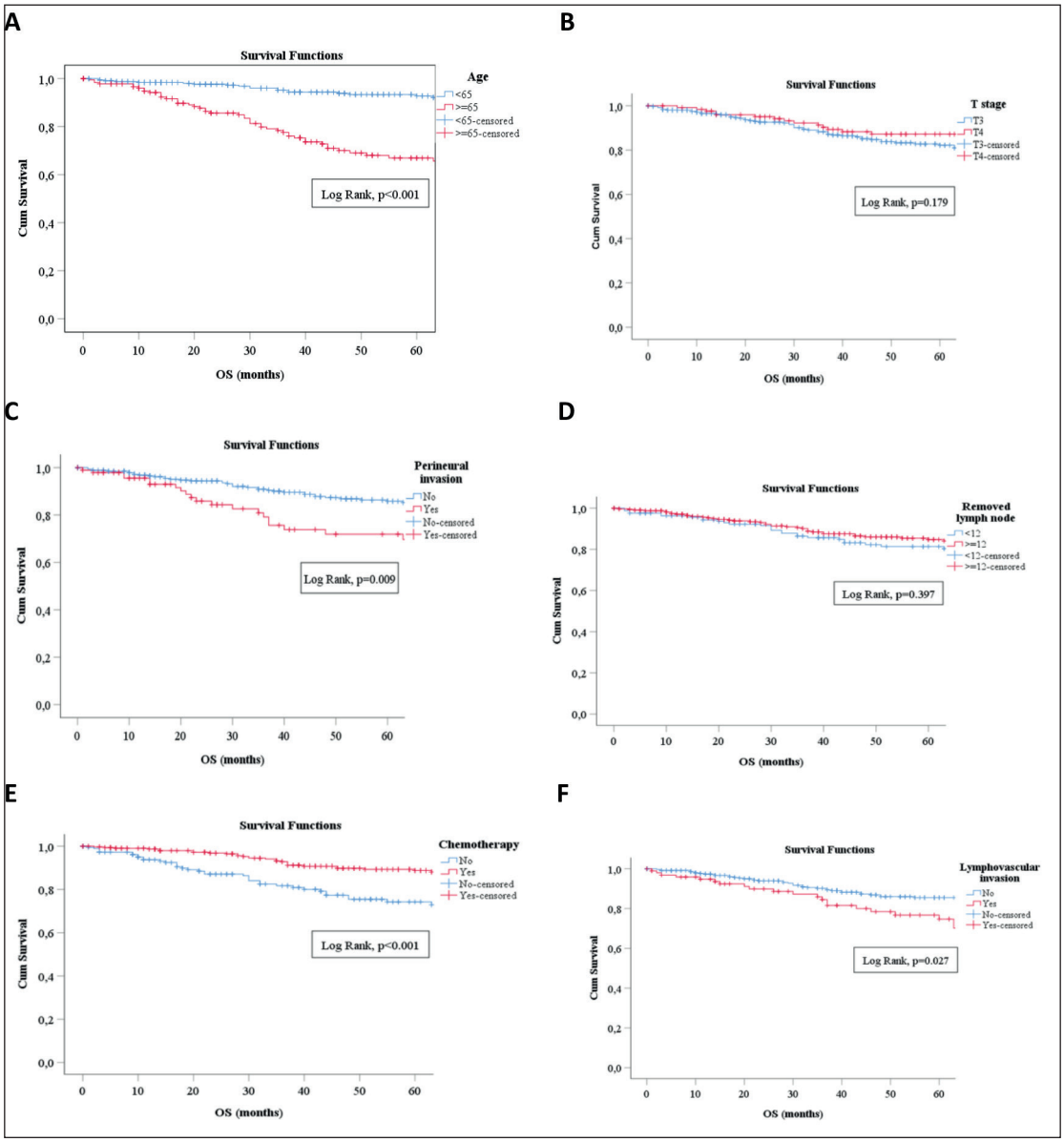

Figure 6. Kaplan-Meier curves of overall survival (OS) by risk factors factors. **A**, For stage 2 colon cancer according to age patients aged <65 years and ≥65 (p<0.001). **B**, For stage 2 colon cancer according to pT stage: T3 *vs.* T4 (p=0.179). **C**, For stage 2 colon cancer according to PNI status: absent vs present (p=0.009). **D**, For stage 2 colon cancer according to removed lymph node: <12 *vs.* ≥12 (p<0.397). **E**, For stage 2 colon cancer according to LVI status: absent vs present (p=0.027) **F,** For stage 2 colon cancer according to adjuvan chemotherapy: recieved vs not recieved (p<0.001)

In the large SEER-based retrospective study of Li et al[28], 5-year cancer-specific survival rates due to colorectal cancer were found to be 88.9% for the right colon in stage I-II patients and 87% for the left colon, and it was statistically significant. In our study, 5-year overall survival and disease-free survival rates were better in right colon tumors than in left colon tumors, but this result was not statistically significant. There was no difference in terms of age, gender, T stage, histopathological grade, LVI, PNI, and tumor size between patients with right and left colon tumors. The reason for the different results regarding the prognosis of right colon tumors in patients with early-stage and advanced-stage colon cancer in previous studies may be the higher rate of MSI-H in right colon tumors[29-31]. In our study group, the rate of

MSI-H was statistically significantly higher in right colon tumors, but there was no difference in survival compared to left colon tumors. This result suggests that the higher rates of adjuvant chemotherapy in patients with left colon tumors may have eliminated the difference in survival.

In previous studies[32-34], it has been demonstrated that clinico-pathological factors such as age, performance status, serum CEA levels, histo-pathological subtype, various molecular factors such as RAS/ B-RAF/ PTEN can affect the prognosis in patients with colon cancer. Our results showed that age is an important prognostic factor in stage II colon cancer.

The limitations of our study are that it is a retrospective study, short follow-up times, and lack of data on prognostic molecular parameters such as MSI, RAS, and BRAF. Despite these limitations, according to our current knowledge, our study is the first study in the literature that evaluates the prognostic role of tumor size and tumor sidedness in a large patient cohort consisting of only stage II patients undergoing curative surgery.

The effects of tumor localization and size on survival in patients with early-stage colon cancer are still controversial. In this regard, well-designed, prospective, randomized studies evaluating the molecular properties of the tumor in detail are needed.

Conclusions

Recurrence in colon cancer is still an important issue. Currently used TNM staging and clinical-pathological factors are insufficient to predict prognosis, especially in stage II disease. We found that tumor size and localization are not markers for predicting survival in patients with completely resected stage II colon cancer. According to our study results, we think that tumor size and localization cannot be a criterion for determining the prognosis, especially for deciding on the indication for adjuvant therapy in stage II disease. Our results suggest that a better understanding of tumor biology rather than features as tumor size and localization is required in the management of stage II patients.

Conflicts of Interest

The authors declare no conflicts of interest.

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Ethics Approval

The study was approved by local Ethics Committee of Afyonkarahisar Health and Science University (Approval no:2021/3 2011 KAEK-2).

Consent for Publication

All Authors have approved the manuscript and gave consent for publication.

Authors' Contributions

Study design: H. Demir; Study Concepts: H. Demir; Statistical analysis: A. Demirci, I. Beypınar; Manuscript preparation: H. Demir; Quality control of data and algorithms: I. Beypınar, M. Baykara, SE. Davarcı, S. Urvay, M. Araz, M. İnanç; Manuscript editing: M. Baykara, M. Aytaç, M. Araz, F. Yıldız, M. İnanç, S. Urvay; Data Collection: H. Demir, D. Çağlayan, Ö. Kaman, SE. Davarcı, S. Urvay.

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