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Prognostic value of lymphovascular and perineural invasion in colorectal cancer

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Ethics Committee Approval
The study was approved by the Hitit University Clinical Research Ethics Committee with the decision numbered 2022-86.
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Lymphovascular and perineural invasion (LVI and PNI, respectively) are associated with poor prognosis in various cancers. We sought to identify clinical variables associated with LVI and PNI in colorectal cancer (CRC) and their effects on survival.
Methods: Our study design is consistent with a retrospective cohort study. Data from 237 patients with documented LVI or PNI who underwent surgery for colorectal cancer between 2017 and 2021 were retrospectively reviewed. Demographic characteristics, surgery and pathology reports, disease-free and overall survival (DFS and OS, respectively) of the patients were examined.
Results: When the DFS duration of the patients were evaluated, The mean DFS of the LVI-negative group was 27.4 (15.09) months, and the mean of the LVI-positive patients was 20.45 (13) months. DFS was longer in the LVI-negative group (P<0.001). DFS was 52.26 (1.89) months in PNI-negative patients and 34.29 (2.71) months in PNI-positive patients. DFS expectation of PNI-positive patients was approximately 18 months less than that of negative patients (P<0.001). When the patients were evaluated in terms of OS duration, no significant difference was observed in LVI-negative and -positive patient groups, while the estimated OS duration was 52.29 (1.84) months in PNI-negative patients, and 40.10 (2.49) months in PNI-positive patients. OS was 12 months shorter in PNI-negative patients (P<0.001).
Conclusion: The use of PNI and LVI together was found to have a significant impact on the survival rates of patients with colorectal cancer. Documenting LVI and PNI status in biopsy specimens can aid in the management, prognosis, and decision-making for treating colorectal tumors.

Keywords: colorectal cancer, lymphovascular invasion, perineural invasion

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Introduction

Colorectal cancer (CRC) is one of the most common cancers and the fifth leading cause of cancer-related death [1]. Despite advances in technology and treatment, recurrence and metastases continue to cause reductions in patient survival [2]. The extent of the disease is important in terms of treatment choices and prognosis of CRC. It is based on the American Joint Committee on Cancer (AJCC) staging. This classification (TNM) includes various histopathological features, such as tumor invasion depth (T), lymph node metastasis (N), and the presence of metastatic disease (M) [3]. However, TNM classification is insufficient to predict the prognosis of CRC as patients with the same TNM stage may experience different survival times and recurrence rates [4,5].

Various risk factors for poor prognosis have been identified: (1) T4 tumor, (2) perforation, (3) obstruction, (4) high-grade tumor, (4) lymphovascular invasion (LVI) or perineural invasion (PNI), (5) positive resection margin, and/or (6) removal of less than 12 lymph nodes [6,7]. Various international guidelines, including those of the American Society of Clinical Oncology (ASCO), the National Comprehensive Cancer Network, and the European Society of Medical Oncology, recommend adjuvant chemotherapy for stage II patients with these risk factors [8–10]. However, no conclusive evidence supporting the efficacy of adjuvant chemotherapy in this patient group has been presented. In addition, several conflicting results have been reported about the benefits of adjuvant chemotherapy even in high-risk patients [11,12].

LVI is the involvement of small lymphatic or blood (typically venous) vessels in the tumor, while PNI is defined as the involvement of nerve cells and the nerve sheath around the organ with the tumor [13,14]. Histopathological identification of LVI has long been considered a potential prognostic indicator and predictor of patient outcomes because of its association with increased lymphatic metastasis [15–17]. PNI has been associated with more aggressive tumor phenotypes and poor prognoses in various cancers [14].

In this study, we aimed to evaluate the prognostic significance of LVI and PNI in patients with CRC.

Materials and methods

Our study was planned as a retrospective cohort study after it was approved by the Hitit University Clinical Research Ethics Committee with the decision numbered 2022-86. Data were collected by examining patient files and computer records.

Between 2017 and 2021, we screened 354 CRC patients who underwent surgery at the Department of General Surgery. Two-hundred thirty-seven patients were included in the study after the study excluded several types of patients: (1) those under the age of 18, (2) those with known hematological and oncological diseases other than colon carcinoma, (3) those with pre-operative metastases, those with post-operative pathology other than adenocarcinoma, and those whose records could not be reached. Patients' age, gender, operation type, operation technique, pathology result, tumor size, number of metastatic lymph nodes, T-and M-stages, length of hospital stay, duration of operation, pre-operative serum lymphocytes, platelets, neutrophils, carcinoembryonic antigen and cancer antigen 19 (CEA and CA 19-9 levels, respectively) presence of lymphovascular and/or perineural invasion in pathology reports, presence of recurrence and/or metastasis during follow-up, disease-free survival (DFS), overall survival (OS) duration, and the presence of cancer-related mortality and all-cause mortality were obtained by retrospectively scanning records from the archive system.

Statistical analysis

IBM SPSS Statistics for Windows program was used for all statistical analysis (version 26; IBM Corp., Armonk, N.Y., USA). For descriptive statistics, numbers and percentages were used for categorical variables, and means (standard deviations [SD]) were used for numerical variables. Normal data distribution was evaluated using the Shapiro–Wilk test. Relationships between variables were investigated with Pearson's or Spearman's correlation coefficient based on data distribution. Comparison of numerical measurements for two independent groups' ages, tumor sizes, number of metastatic lymph nodes, lengths of hospital stay, operation times, pre-operative serum lymphocytes, platelets, neutrophils, CEA and CA19-9 levels, DFS, OS using the Mann–Whitney U test were evaluated.

Categorical variables, such as gender, operation type, operation technique, pathology result, T- and M-stages, presence of lymphovascular invasion in pathology reports, presence of perineural invasion, presence of recurrence and/or metastasis during follow-up, presence of cancer-related mortality, and all-cause mortality frequency and distribution were determined by research groups. Ratio comparisons were evaluated using the chi-squared test. Estimated DFS and OS times of the patients according to LVI and PNI status were determined and compared using the Kaplan–Meier analysis and log-rank test. For the statistical significance level, $P<0.05$ was accepted.

Results

The mean age of the patients in the whole group was 69.84 (10.82) years. Of these patients, 151 (63.71%) were male, and 86 (36.29%) were female (Table 1). No statistical difference in terms of operation type and technique ($P=0.453$ and $P=0.211$, respectively) were found. Of the extracted materials, 59 were well differentiated (24.89%),164 were moderately differentiated (69.20%), and 14 were poorly differentiated (5.91%). The mean tumor diameter was 4.99 (2.12) cm. The mean number of metastatic lymph nodes in the excised material was two.

When the patients were examined in terms of T-stage, nine patients were in T1 (3.80%), 27 patients were in T2 (11.39%),150 patients were in T3 (63.29%), and 51 patients were in T4 (21.52%). One-hundred fifteen patients were N0 (48.52%), 86 (36.29%) N1, and 36 patients were N2 (15.19%). The mean hospital stay of the patients in the whole group was 16.03 (8.85) days, and the mean operation time was 157.51 (53.62) min.

When the laboratory values were examined, the mean lymphocyte count of the patients in the whole group was 1.63 (0.68), the mean platelet count was 271.54 (93.54), and the mean neutrophil count was 5.7 (3.25). The mean of the CEA was 26.49 (175.64) µg/L, and the mean of CA19-9 was 28.56 (79.33) U/mL.

Table 1: Descriptive characteristics and association of both lymphovascular and perineural invasion with clinicopathological features

Variables		All Patients	LVI negative (n=121)	LVI positive (n=116)	*P*-value	PNI negative (n=154)	PNI positive (n=83)	*P*-value
Age		69.84(10.82)	70.2(10.87)	69.38(10.78)	0.354	69.92(10.66)	69.7(11.17)	0.715
Gender	Male	151 (63.71%)	69 (57.02%)	82 (70.69%)	0.029	96 (62.34%)	55 (66.27%)	0.549
	Female	86 (36.29%)	52 (42.98%)	34 (29.31%)		58 (37.66%)	28 (33.73%)	
Operation type	Hemicolectomy, right-sided	72 (30.38%)	34 (28.10%)	38 (32.76%)	0.654	45 (29.22%)	27 (32.53%)	0.453
	Hemicolectomy left-sided	44 (18.57%)	26 (21.49%)	18 (15.52%)		33 (21.43%)	11 (13.25%)	
	Low anterior resection	102 (43.04%)	51 (42.15%)	51 (43.97%)		65 (42.21%)	37 (44.58%)	
	Abdominoperineal resection	19 (8.02%)	10 (8.26%)	9 (7.76%)		11 (7.14%)	8 (9.64%)	
Operation technique	Open	202 (85.23%)	103 (85.12%)	99 (85.34%)	0.962	128 (83.12%)	74 (89.16%)	0.211
	Laparoscopic	35 (14.77%)	18 (14.88%)	17 (14.66%)		26 (16.88%)	9 (10.84%)	
Pathologic type	Adenocarcinoma, well-differentiation	59 (24.89%)	35 (28.93%)	24 (20.69%)	0.010	50 (32.47%)	9 (10.84%)	0.001
	Adenocarcinoma, moderate-differentiation	164 (69.20%)	84 (69.42%)	80 (68.97%)		97 (62.99%)	67 (80.72%)	
	Adenocarcinoma, poor-differentiation	14 (5.91%)	2 (1.65%)	12 (10.34%)		7 (4.55%)	7 (8.43%)	
Tumor size (cm)		4.9(2.12)	4.8(2.27)	5.18(1.93)	0.077	4.7(2.17)	5.38(1.97)	0.011
Metastatic lymph node count (n=120)		2 (1-13)	1 (1-12)	2 (1-13)	0,038	2 (1-12)	2 (1-13)	0.020
T stage	T1	9 (3.80%)	9 (7.44%)	0 (0,00%)	<0.001	9 (5.84%)	0 (0.00%)	<0.001
	T2	27 (11.39%)	23 (19.01%)	4 (3.45%)		25 (16.23%)	2 (2.41%)	
	T3	150 (63.29%)	77 (63.64%)	73 (62.93%)		94 (61.04%)	56 (67.47%)	
	T4	51 (21.52%)	12 (9.92%)	39 (33.62%)		26 (16.88%)	25 (30.12%)	
N stage	N0	115 (48.52%)	97 (80.17%)	18 (15.52%)	<0.001	94 (61.04%)	21 (25.30%)	<0.001
	N1	86 (36.29%)	22 (18.18%)	64 (55.17%)		49 (31.82%)	37 (44.58%)	
	N2	36 (15.19%)	2 (1.65%)	34 (29.31%)		11 (7.14%)	25 (30.12%)	
Hospitalization duration (days)		16.03(8.85)	16.45(8.77)	15.59(8.94)	0.453	15.73(7.99)	16.58(10.29)	0.643
Operation duration (minutes)		157.51(53.62)	153.92(47.51)	161.25(59.31)	0.453	155.86(51.31)	160.5(57.86)	0.580
Lymphocyte count		1.63(0.68)	1.61(0.66)	1.66(0.69)	0.563	1.58(0.6)	1.74(0.78)	0.233
Platelet count		271.54(93.54)	261.07(93.53)	282.47(92.7)	0.086	259.29(85.3)	294.28(103.95)	0.011
Neutrophile count		5.7(3.25)	5.46(3.25)	5.94(3.24)	0.094	5.35(2.94)	6.33(3,69)	0.024
CEA		26.49(175.64)	8.49(22.23)	45.26(249.2)	0.038	25.6(208.25)	28.15(88.7)	0.159
CA19-9		28.56(79.33)	22.49(36.25)	34.88(107.07)	0.813	27.58(92.16)	30.37(47.49)	0.511
Lymphovascular invasion	LVI negative	121 (51.05%)				104 (67.53%)	17 (20.48%)	<0.001
	LVI positive	116 (48.95%)				50 (32.47%)	66 (79.52%)	
Perineural invasion	PNI negative	154 (64.98%)	104 (85.95%)	50 (43.10%)	<0.001			
	PNI positive	83 (35.02%)	17 (14.05%)	66 (56.90%)				
Disease status	Disease-Free	169 (71.3%)	108 (89.3%)	61 (52.6%)	<0.001	128 (83.1%)	41 (49.4%)	<0.001
	Recurrence or Metastasis	68 (28.7%)	13 (10.7%)	55 (47.4%)		26 (16.9%)	42 (50.6%)	
Disease free survival duration (months)		24(14.5)	27.4(15.09)	20.45(13)	<0.001	26.26(15.04)	19.8(12,47)	<0.001
Overall survival (months)		27.97(14.5)	29.02(14.77)	26.89(14.21)	0.237	28.88(14.99)	26.3(13.49)	0.254
Cancer related mortality	No cancer related mortality	204 (86.1%)	111 (91.7%)	93 (80.2%)	0.010	141 (91.6%)	63 (75.9%)	0.001
	Cancer-related Mortality	33 (13.9%)	10 (8.3%)	23 (19.8%)		13 (8.4%)	20 (24.1%)	
All Causes Mortality	Alive	179 (75.53%)	96 (79.34%)	83 (71.55%)	0.163	126 (81.82%)	53 (63.86%)	0,002
	Exitus	58 (24.47%)	25 (20.66%)	33 (28.45%)		28 (18.18%)	30 (36.14%)	

PNI: perineural invasion, LVI: lymphovascular invasion

When the patients were examined in terms of lymphovascular invasion, there were 121 patients with negative LVI (51.05%) and 116 patients with positive LVI (48.95%). Considering PNI, 154 PNI-negative patients (64.98%) and 83 PNI-positive patients (35.02%) were found. In the post-operative follow-up period, 169 (71.3%) patients showed no signs of relapse, but recurrence or metastasis was observed in 68 (28.7%) patients.

The mean DFS of the patients in the study group was 24 (14.5) months, and the mean OS was 27.97 (14.5) months. When the patients were examined in terms of cancer-related mortality, cancer-related mortality was observed in 33 patients (13.9%). When all-cause mortality was evaluated, mortality was observed in 58 patients (24.47%).

Lymphovascular invasion

No statistical significance was found when the patients were compared in terms of age (*P*=0.354). When the gender distribution was examined, the male ratio was higher in LVI-positive patients (*P*=0.029) as shown in Table 1. No statistical significance in terms of the operation type and surgical techniques used for the patients (*P*=0.654 and *P*=0.962, respectively).

When the pathology results were examined, the rate of poorly differentiated carcinoma was higher in the second group (*P*=0.01), and was considered a statistically significant different.

No statistical significance between the two groups in terms of the mean tumor diameter of LVI-negative and positive patients (*P*=0.077) was found. The number of removed metastatic lymph nodes was higher in LVI-positive patients (*P*=0.038).

When the relationship between PNI and LVI was examined, 104 (85.95%) patients in the LVI negative group were PNI negative, 17 (14.05%) were PNI positive, in the LVI positive group 50 (43.10%) patients were PNI negative, and 66 (56.90%) patients were found to be PNI positive. LVI positivity and PNI positivity were more common together, which would be statistically significant (*P*<0.001).

Recurrence or metastasis was observed in only 13 (10.7%) patients in the LVI negative group, this rate increased in the LVI positive group, and recurrence or metastasis was observed in 55 (47.4%) patients, which was statistically significant (*P*<0.001).

When the DFS was evaluated in the patients, the mean of the LVI-negative group was 27.4(15.09) months, and the mean of the LVI-positive patients was 20.45 (13) months. Statistical significance (*P*<0.001) was noted. When OS was examined, the mean survival time of LVI-negative patients was 29.02 (14.77) months, and the mean OS of LVI-positive patients was 26.89 (14.21) months, and no statistically significant difference was found (*P*=0.237).

In the LVI-negative group, mortality was observed in 10 (8.3%) patients due to cancer-related causes. In the LVI-positive group, this rate increased and cancer-related mortality was observed in 23 (19.8%) patients, and a statistically significant difference was observed (*P*=0.01). When compared in terms of overall mortality, 25 (20.66%) patients died in the LVI negative

group, and 33 (28.45%) died in the LVI positive group. Although an increase in the rate was observed; however, statistical significance could not be determined (*P*=0.163).

Perineural invasion

When the patients were compared in terms of age, no statistical significance in terms of age and gender was found (Table 1).

No statistically significant difference was found between the type and surgical technique (*P*=0.453 and *P*=0.211, respectively).

The mean tumor diameter of PNI-negative patients was 4.78 (2.17) cm and that of PNI-positive patients was larger at 5.38 (1.97) cm. A statistically significant difference (*P*=0.011) was found. More metastatic lymph nodes were dissected in PNI-positive patients (*P*=0.02).

A comparison in terms of T-stages is summarized in Table 1. When the mean duration of hospitalization and operation time of PNI-negative and positive patients were compared between the groups, no statistically significant difference was found (*P*=0.643 and *P*=0.580, respectively). Similarly, no statistically significant difference was observed between the serum lymphocyte, CEA, and CA19-9 levels of the patients in the two groups (*P*= 0.233, *P*=0.159, and *P*=0.511, respectively).

The mean platelet count of the patients in the PNI-negative group was 259.29 (85.3), while it was 294.28 (103.95) in the PNI-positive patients. A statistically significant difference (*P*=0.011) was detected. When evaluated in terms of neutrophil count, the mean of PNI-negative patients was 5.35 (2.94) while it was 6.33 (3.69) in PNI-positive patients, and a statistically significant difference was observed (*P*=0.024).

When the relationship between PNI and LVI was in terms of PNI, in the PNI-negative group, 104 (67.53%) patients were LVI negative, and 50 (32.47%) patients were LVI positive. In the PNI positive group, 17 (20.48%) patients were LVI negative, and 66 (79.52%) patients LVI was found to be positive, which was statistically significant. The incidence of LVI positivity increased in PNI positivity (*P*<0.001).

In the PNI-negative group, 128 (83.1%) patients remained disease-free. Recurrence or metastasis was observed in 26 (16.9%) patients in the PNI-negative group, and in 42 (50.6%) patients in the PNI-positive group, which resulted in a significant increase in the recurrence rate (*P*<0.001).

The mean DFS was found to be 26.26 (15.04) months in PNI-negative patients and 19.8 (12.47) months in PNI-positive patients (*P*<0.001). When the OS was examined, the mean OS time of PNI-negative patients was 28.88 (14.99) months and that of PNI-positive patients was 26.3 (13.49) months. No statistical significance between groups was found (*P*=0.254).

In the examination of cancer-related death (CRD) rates, 13 (8.4%) of PNI-negative patients died due to cancer-related causes, while this rate increased in 20 (24.1%) patients in the PNI-positive group, and statistical significance was observed (*P*<0.001). When the patients were evaluated in terms of overall mortality, it was observed that 28 (18.18%) patients died in the PNI-negative group, while the mortality rate in the PNI-positive group increased. A statistically significant difference was found, and 30 (36.14%) patients were passed away (*P*=0.002).

Estimated disease free survival and overall survival analyzes

As a result of the Kaplan–Meier survival analysis and log-rank test to determine the estimated overall survival (OS) of the patients in the study, the mean estimated OS expectation of the whole group was found to be 48.26 (1.60) months (95% confidence interval [CI] 45.120–51.390) as shown in Table 2. The mean estimated OS of LVI-negative patients was 49.09 (1.98) months (95% CI 41.086–50.589) while it was 45.84 (2.42) months (95% CI 45.200–52.977) in LVI-positive patients. No statistically significant difference was observed between the durations (*P*=0.127). When evaluated for PNI, the estimated OS was 52.29 (1.84) months (95% CI 48.690–55.889) in PNI-negative patients and 40.10 (2.49) months (95% CI 35.220–44.971) in PNI-positive patients. PNI positivity shortened OS expectation by 12 months; thus, a statistically significant difference was fond (*P*=0.001) as shown in Figures 1 and 2.

Table 2: Estimated overall survival times of both lymphovascular and perineural invasion

Variables		Estimated OS duration	%95 CI	*P*- value
Lymphovascular invasion	LVI Negative	49.09(1.98)	45.200–52.977	0.127
	LVI Positive	45.84(2.42)	41.086–50.589	
	Estimated OS	48.26(1.60)	45.120–51.390	
Perineural invasion	PNI Negative	52.29(1.84)	48.690–55.889	0.001
	PNI Positive	40.10(2.49)	35.220–44.971	
	Estimated OS	48.26(1.60)	45.120–51.390	

OS: overall survival, PNI: perineural invasion, LVI: lymphovascular invasion, CI: confidence interval

Figure 1: Lymphovascular invasion & overall survival

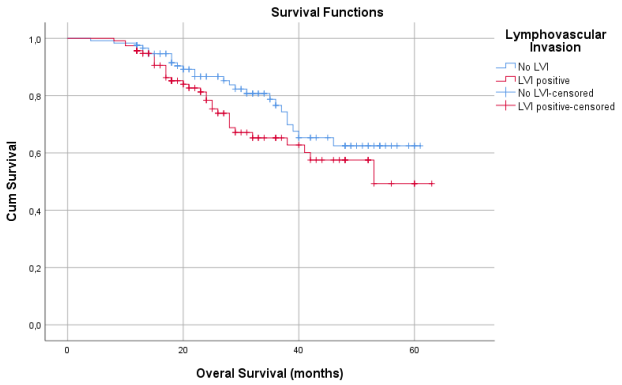
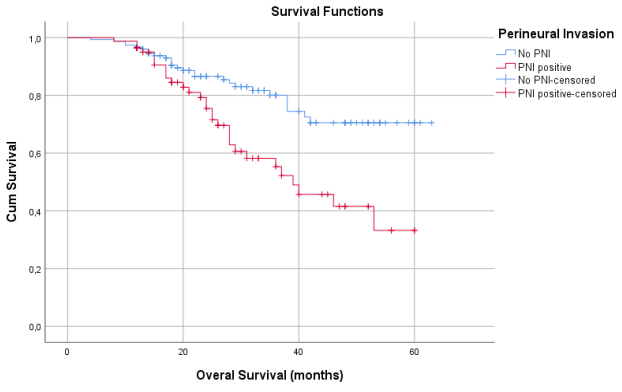


Figure 2: Perineural invasion & overall survival



When evaluated in terms of estimated DFS, the mean estimated DFS expectation of the whole group was found to be 47.34 (1.77) months (95% CI 43.872–50.803). While the mean DFS expectancy of LVI-negative patients was calculated as 48.73 (2.10) months (95% CI 44.608-52.848), it was observed as 44.08 (2.85) months (95% CI 38.493–49.667) in LVI-positive patients with a statistically significant difference (*P*=0.027) as shown in Table 3. The estimated DFS expectancy of PNI-negative patients was calculated as 52.26 (1.89) months (95% CI

48.562–55.954). The estimated DFS expectancy of PNI-positive patients was found to be 34.29 (2.71) months (95% CI 28.986–39.588), and the DFS expectancy of positive patients was approximately 18 months less than negative patients. The difference was considered statistically significant (P<0.001) as shown in Figures 3, and 4.

Table 3: Estimated disease-free survival times of lymphovascular invasion and perineural invasion

		Estimated DFS duration	%95 CI	*P*-value
Lymphovascular invasion	LVI Negative	48.73(2.10)	44.608–52.848	0.027
	LVI Positive	44.08(2.85)	38.493–49.667	
	Estimated DFS	47.34(1.77)	43.872–50.803	
Perineural invasion	PNI Negative	52.26(1.8)	48.562–55.954	<0.001
	PNI Positive	34.29(2.71)	28.986–39.588	
	Estimated DFS	47.34(1.77)	43.872–50.803	

DFS: disease free survival, PNI: perineural invasion, LVI: lymphovascular invasion, CI: confidence interval

Figure 3: Lymphovascular invasion & disease free survival

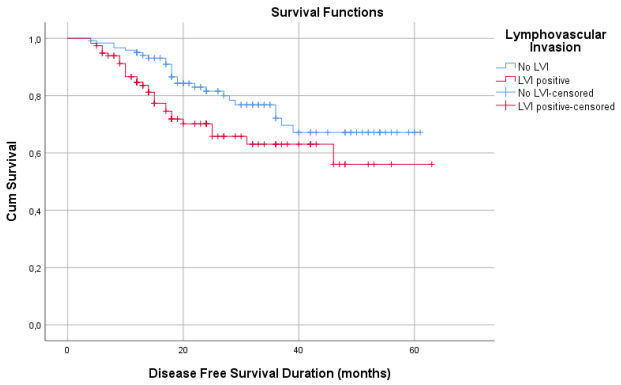
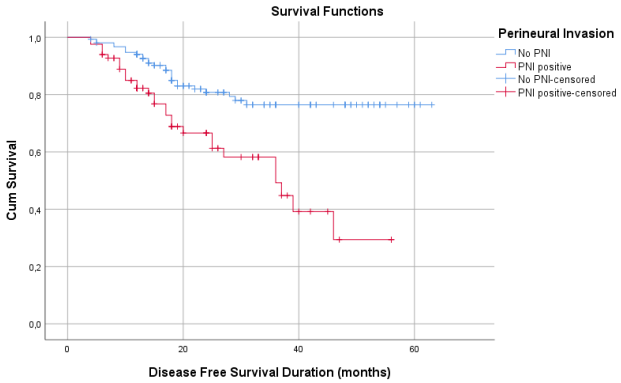


Figure 4: Perineural invasion & disease free survival



Discussion

In this study, it was found that LVI had a prognostic effect on DFS but had no effect on OS in CRC patients. It was observed that PNI affected both DFS and OS, and the DFS expectation was 18 months lower in the patient group with PNI than in the one without PNI.

Metastasis formation pathways in CRC has been investigated in many studies. It has been shown that the first step in metastasis formation is the invasion of vascular and neural structures. PNI represents tumor invasion of the space surrounding a nerve. Many studies have investigated the relationship between PNI and cancers. Beard et al. [18] reported that PNI is associated with recurrence and metastases in patients with prostate cancer. Harnden et al. [19] also reported that PNI leads to an increase in recurrences and is a prognostic marker in prostate cancer patients. Mendenhall [20] showed that PNI is associated with an increase in the risk of regional and distant metastases in head and neck cutaneous squamous cell carcinoma in addition to an increase in the risk of local recurrence, most prominently including recurrences in both the skin and cranial nerves.

In colorectal cancer, the incidence of PNI ranges from <10% to 35% from series to series [14,21,22]. Liebig et al. observed an average of 22% of PNI in stage I–IV colorectal cancer [14] as also found in our study. The incidence of patients with the disease was found to be 35%, which is consistent with reports in the literature. Detection of PNI is important for treatment decisions since PNI is an indicator of poor prognosis in patients with CRC in previous studies [23]. In a series of 269 stages I–IV patients with CRC, 5-year DFS and OS in those with PNI-positive tumors were significantly higher, and PNI proved to be both an overall cancer-specific and an independent prognostic factor for disease [14]. In a study of Sun et al. [24], the risk of poor survival was found to be 4.8 times higher in patients with PNI. In our study, a statistically significant difference was observed in PNI in terms of both DFS and OS, and the DFS expectation was 18 months in the patient group with PNI compared to the patient group without PNI, which was observed to be lower.

LVI is defined as tumor invasion in the vascular and lymphatic structures. Since it is not possible to distinguish between lymphatic and venous vessels histologically, the term LVI is often used to refer to any of these structures [25]. The presence of LVI in the literature ranges from 10% to about 90% [26,27]. Zhong et al. [28] reported the presence of LVI in 20% of patients. However, the results of Yuksel et al. [29] are similar to those in our study in which 48.95% of patients had LVI. Differences in the presence of LVI in studies may be due to the heterogeneity of the study population. Differences may also be due to differences in interpretation of LVI as some authors refer to LVI as lymphatic invasion, angiolymphatic invasion, or venous invasion [13,30].

In many studies it has been reported that LVI is an important prognostic factor for OS and DFS. In a study by Nakamura et al. [31] with a series of 316 patients, they concluded that LVI has a negative effect on OS and DFS and is associated with peritoneal recurrence in stages II and III, and liver metastasis of colon cancer after curative resection. In contrast, Osterman et al. [32] concluded that LVI did not affect OS and DFS in their study. Zhang et al. [33] found that LVI did not affect OS in their study evaluating the effect of adjuvant chemotherapy. No statistically significant difference was observed. The DFS expectancy of LVI-positive patients was approximately four months less than that of negative patients and was statistically significantly different. Our results were similar to those found by Zhang et al. [33].

Limitations

Our study has some limitations. One is the retrospective design, and the fact that some selection bias exists. The sample size was not large enough, and more samples may be needed to further validate our model. In addition, the inability of pathologists to evaluate samples independently may have caused errors in the ratios of PNI and LVI.

Conclusion

As a result, the DFS duration of the patients was longer in the LVI-negative group. The DFS expectancy of PNI-positive

patients was approximately 18 months less than that of negative patients. In addition, no significant difference was observed in LVI-negative and -positive patient groups in terms of OS durations. OS was 12 months shorter in PNI-negative patients than in PNI-positive patients.

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