Research Article

Lymphovascular (LVI) and Perineural Invasion (PNI) in Colorectal Carcinoma and Their Association with Tumor Stages: A Retrospective Study on 250 Cases in Bangabandhu Sheikh Mujib Medical University

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Abstract

Introduction: Colorectal cancer (CRC) is the most prevalent type of cancer and ranks as the fifth leading cause of cancer-related death. Despite advancements in technology and treatment, recurrence and metastases continue to be significant issues, leading to decreased patients' survival. Lymphovascular invasion (LVI) involves small lymphatic or blood (typically venous) vessels within the tumor, while perineural invasion (PNI) is the tumor invasion of the perineural sheath or epineurium. LVI and PNI may be the significant indicators for CRC prognosis and progression. This paper aimed to determine the association between lymphovascular invasion (LVI) and perineural invasion (PNI) with the tumor stages of colorectal carcinoma.

Methods: This retrospective cross-sectional descriptive type of study was conducted at the Department of Pathology in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during January, 2024 to June, 2024. A consecutive sampling technique was used and a series of 250 excised cases of colorectal carcinoma irrespective of age and sex were retrospectively enrolled in this study. The data were analyzed using Statistical Package for Social Sciences (SPSS) software, version-23.0.

Results: A series of 250 excised cases of colorectal carcinoma irrespective of age and sex were enrolled in this study. The mean age of the patients was 47.89±15.71 years. Most cases (143, 57.20%) were males. Ascending colon was the most frequent (74, 29.6%) site of the growth of colorectal carcinoma.The most frequent histologic type of colorectal carcinoma was found to be adenocarcinoma NOS 203 (81.2%). The lymphovascular invasion (LVI) and perineural invasion (PNI) were significantly associated with the tumour stages of colorectal carcinoma (p<0.05).

Conclusion: In conclusion, this study provides valuable insights into the clinicopathological characteristics of CRC in Bangladeshi patients. Lymphovascular invasion (LVI) and perineural invasion (PNI) were significantly associated with tumor stages of colorectal carcinoma which indicates LVI and PNI are the significant prognostic indicators of the CRC disease progression and prognosis

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Keywords: Lymphovascular, Perineural, Invasion, Association, Tumor, Stages

Introduction

Colorectal cancer (CRC) is the most prevalent type of cancer and ranks

as the fifth leading cause of cancer-related death [1]. Despite advancements in technology and treatment, recurrence and metastases continue to be significant issues, leading to decreased patients' survival [2]. The disease's extent, critical for determining treatment options and prognosis, is categorized using the American Joint Committee on Cancer (AJCC) staging system. This TNM classification considers various histopathological features: tumor invasion depth (T), lymph node metastasis (N), and the presence of metastatic disease (M) [3]. However, the TNM classification alone is insufficient for predicting CRC prognosis, as patients with the same TNM stage may have different survival times and recurrence rates [4.]. Several risk factors for poor prognosis have been identified, including the stage T4 tumor, perforation, obstruction, high-grade tumor, lymphovascular invasion (LVI) or perineural invasion (PNI), positive resection margin, and/or removal of fewer than 12 lymph nodes [5,6]. Various international guidelines, such as those from 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 [7]. However, conclusive evidence supporting the efficacy of adjuvant chemotherapy in this patient group is lacking, and conflicting results have been reported regarding its benefits even in high-risk patients [8,9]. Lymphovascular invasion (LVI) involves small lymphatic or blood (typically venous) vessels within the tumor, while PNI is defined as the tumor invasion of the perineural sheath or epineurium. [10, 11]. Histopathological identification of lymphovascular invasion (LVI) has long been considered a potential prognostic indicator due to its association with increased lymphatic metastasis .Similarly, PNI has been linked to more aggressive tumor phenotypes and poor prognoses in various cancers [12-14]. However, there are very few studies and limited data on lymphovascular (LVI) and perineural invasion (PNI) in colorectal carcinoma and their association with tumor stages in Bangladesh context. This study aimed to determine the lymphovascular (LVI) and perineural invasion (PNI) in colorectal carcinoma and their association with tumor stages of the excised cases attended in Bangabandhu Sheikh Mujin Medical University (BSMMU), Dhaka, Bangladesh.

Methods

This retrospective cross-sectional descriptive type of study was conducted at the Department of Pathology in Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during January, 2024 to June, 2024. A consecutive sampling technique was used and a series of 250 excised cases of colorectal carcinoma irrespective of age and sex were retrospectively enrolled in this study. The tumors were classified following World Health Organization

(WHO) Classification of tumours of the Digestive System [15] and grading of tumor was classified by using Canadian Cancer Society (CCS) specified two-tiered grading system [16]. Staging was performed following TNM Classification of Colorectal Carcinoma of American Cancer Society, 2020[17].The data were collected using Excel data sheet from the registry of Pathology Department of Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. The collected data were methodically ordered, edited and coded for computer entry. The data were analyzed using Statistical Package for Social Sciences (SPSS) software, version-23.0. Descriptive statistical analysis were performed and the results were presented in tables and charts. Chi-square tests were performed to assess the association between lymphovascular and perineural invasion with the tumor stages of colorectal carcinoma, where P<0.05 considered as the level of significance with 95% CI. During the assessment of association between LVI and PNI with the tumor stages, the undetermined cases were excluded.

Table 1: Demographic characteristics of the study patients (N=250)

Demographic characteristics	Frequency N	Percent
Age(years)		
<20	2	0.8
21-40	76	30.4
41-60	116	46.4
61-80	54	21.6
>81	2	0.8
Total	250	100
Mean age (years)	47.89±15.71	
Median	43	
Mode	44	
Sex		
Male	143	57.2
Female	107	42.8
Total		

Table 1: shows the Demographic characteristics of the study patients. The most frequent age group was 41-60years which includes 116(46.4%) patients followed by 21-40 years, 76(30.4%), 61-80years, 54(21.6%) both <20 and>81 years includes the same 2(0.8%) patients. The mean age was (47.89±15.71) years, with the age of median 43byears and mode of 44 years. The most cases 143(57.20%) were males and 107(42.805) were females.

Table 2: Site distribution of colorectal growth with the study patients (N=250).

Sites	Frequency	
	N	%
Anal canal	2	0.8
Mesorecturm	2	0.8
Rectum	23	9.2
Recto sigmoid	21	8.4
Sigmoid	64	25.6
Mesocolon	2	0.8
Descending colon	5	2
Transverse colon	5	2
Ascending colon	74	29.6
Ileocaecal	2	0.8
Colon not specified	50	20
Total	250	100

Table 2 shows the site distribution of the growth of colorectal carcinoma with the study patients. The most frequent site of the growth of the colorectal carcinoma was observed at ascending colon in 74(29.6%) patients followed sigmoid colon in 64(25.6%), colon not specified in 50(20%), rectum region in 23(9.2%), recto sigmoid in 21(8.4%), descending colon in 5(2.00%) ,transverse colon in 5(2.00%),Ileocaecal region in 2(0.8%), mesorectum in 2(0.8%) and anal canal in only 2(0.8%).

Table 3: Distribution of histologic type of colorectal carcinoma (N=250).

Histologic type of colorectal carcinoma	Frequency	
	N	%
Adenocarcinoma NOS	203	81.2
Mucinous Adenocarcinoma	45	18
Papillary Adenocarcinoma	2	0.8
Total	250	100

Table 3 shows the distribution of histologic type of colorectal carcinoma with the study patients. The most frequent histologic type of colorectal carcinoma was adenocarcinoma NOS found in 203(81.2%) patients followed mucinous adenocarcinoma 45(18%), papillary adenocarcinoma in only 2(0.8%).

Table 4: Grade distribution of observed colorectal carcinoma (N=250).

Histologic Grade of Colorectal Carcinoma	Frequency	
	N	%
Low grade	207	82.8
High grade	43	17.2
Total	250	100

Table 4 shows the grade distribution of observed colorectal carcinoma. The most frequent grade of colorectal carcinoma was observed low grade in 207(82.8%) and 43(17.2%) cases were high grade.

Table 5: Lymphovascular and perineural invasion counted in total colorectal carcinoma cases (N=250).

LVI and PNI count	Frequency	
	N	%
Both LVI and PNI invasion	21	8.4
Omly LVI invasion	23	9.2
Only PNI invasion	18	7.2
Undetermined	188	75.2
Total	250	100

Table 5 shows the lymphovascular and perineural invasion counting in total colorectal carcinoma cases. Among 250 colorectal carcinoma cases, both lymphovascular and perineural invasion were counted in 21 (8.4%) patients, only lymphovascular invasion was counted in 23(9.2%) patients , only perineural invasion was found in (7.2%) patients and 188(75.2%) patients remained undetermined of lymphovascular and perineural invasion.

Table 6: Association between lymphovascular invasion and stages of colorectal carcinoma (n=23).

Stages(T)	Lymphovascular Invasion of colorectal carcinoma		P-value
	Present	Absent	
	N	N	
pT0	1	0	
pT1	2	1	
pT2	5	3	
pT3	7	2	
pT4	0	0	
Stages (N)			
pNx	3	1	
pN0	5	1	
pN1	0	0	0.005
pN1a	0	0	
pN1b	0	0	
pN1c	0	0	
pN2	0	0	
pNa	0	0	
pN2b	0	0	

Absent cases (62-23) = 39, of them, in only 8 cases T and N stages were observed.

Table-6: Presents data on the lymphovascular invasion (LVI) of colorectal carcinoma, segmented by tumor stages (T) and nodal stages (N). In the tumor stages (T), the presence of LVI was observed in 1 case of pT0 (4.34%), 2 cases of pT1 (8.69%), 5 cases of pT2 (21.73%), and 7 cases of pT3 (30.43%). No LVI was observed in pT4. In contrast, LVI was absent in 0 cases of pT0, 1 case of pT1 (2.56%), 3 cases of pT2 (13.04%), 2 cases of pT3 (8.69%), and 0 cases of pT4. For the nodal stages (N), LVI was present in 3 cases of pNx (13.04%) and 5 cases of pN0 (21.73%), but absent in 1 case of pNx (2.56%) and 1 case of pN0 (2.56%). No LVI was observed in any other nodal stages (pN1, pN1a, pN1b, pN1c, pN2, pNa, pN2b). The p-value for the association between LVI and tumor stages (T) and nodal stages (N) is indicating a statistically significant association (p= 0.005).

Table 7: Association between perineural invasion and stages of colorectal carcinoma (n=18).

Stages(T)	Perineural Invasion of colorectal carcinoma		P-value
	Present	Absent	
	N	N	
pT0	0	0	
pT1	1	0	
pT2	8	1	
pT3	3	2	
pT4	0	0	
Stages (N)			0.012
pNx	2	1	
pN0	4	3	
pN1	0	0	
pN1a	0	0	
pN1b	0	0	
pN1c	0	0	
pN2	0	0	
pNa	0	0	
pN2b	0	0	

Table-7: Presents data on perineural invasion (PNI) of colorectal carcinoma, segmented by tumor stages (T) and nodal stages (N). In the tumor stages (T), the presence of PNI was observed in 1 cases of pT1 (5.55%), 8 cases of pT2 (44.44%), and 3 cases of pT3 (16.66%). In contrast, PNI was absent in 1 cases of pT2 (5.55%), 2 cases of pT3 (11.11%). For the nodal stages (N), PNI was present in 2 cases of pNx (11.11%) and 4 cases of pN0 (22.22%), but absent in 1 case of pNx (5.55%) and 3 case of pN0 (16.66%). No PNI was observed in any other nodal stages (pN1, pN1a, pN1b, pN1c, pN2, pNa, pN2b). The p-value for the association between PNI and tumor stages (T) and nodal stages (N) indicates a statistically significant association (p = 0.012).

Discussion

This retrospective study at Bangabandhu Sheikh Mujib Medical University (BSMMU) investigated the lymphovascular (LVI) and perineural invasion (PNI) in colorectal carcinoma in 250 cases and their association with tumor stages. The average patient age was 47.89 years, with the highest incidence (46.4%) occurring in the 41-60 age group. These findings suggest a higher prevalence in middle and older adults, almost similar to a study in Indonesia with a mean age of 53.2 years [18]. However, our study observed a higher proportion of cases under 50 years old (compared to 38.1% in the Indonesian study). This difference might be due to variations in lifestyle, diet, or environmental factors between the populations. Males were more likely to be diagnosed with CRC (57.20%) compared to females. This could be associated with smoking, alcohol consumption, or a more westernized lifestyle among males. These findings are consistent with a study in Iran [19] that reported 50.9% male patients. The most frequent tumor locations were the ascending colon (29.6%) and sigmoid colon (25.6%). This distribution differs from a study conducted in Bangladesh[20] which found the rectum to be the most common site (36.7%), followed by the sigmoid colon (33.3%). These variations highlight the need for further research on geographical disparities in CRC presentation. Adenocarcinoma NOS (81.2%) was the predominant histological type, followed by mucinous adenocarcinoma (18%). These findings partially align with a study in Poland [21] where adenocarcinoma NOS constituted 87% of cases. Low-grade tumors (82.8%) were more prevalent than high-grade tumors (17.2%). In our stud, we found a strong association between lymphovascular invasion (LVI) and both tumor and lymph node stages in colorectal carcinoma (p=0.005), which indicates its potential value as a significant prognostic indicator in the disease's progression. In our study, we also observed an acute association between perineural invasion (PNI) and both tumor stages and lymph node involvement in colorectal carcinoma (p=<0.012), which also highlights the potential significance of perineural invasion (PNI) in disease progression and prognosis. Another study found PNI is a common feature in various malignancies and is associated with tumor invasion, metastasis, cancer-related pain, and unfavorable clinical outcomes [22].

Conclusion

In conclusion, this study provides valuable insights into the clinicopathological characteristics of CRC in Bangladeshi patients. Lymphovascular invasion (LVI) and perineural invasion (PNI) were significantly associated with tumor stages of colorectal carcinoma which indicates LVI and PNI are the significant prognostic indicators of CRC disease progression and prognosis.

Limitations of the Study

This study was conducted in a single center with a limited consecutive sampling technique. Therefore, the results of this study may not reflect the representative scenario of the whole country. Hence a multi-center study may be conducted across the country with an adequate sample size.

Recommendations

Comprehensive policies should be adopted to promote awareness about the growth of colorectal cancer especially among the adult population in Bangladesh to promote colorectal health care at an early stage, screening program, affordable treatment and better prognosis.

Conflict of Interest: None declared

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