https://doi.org/10.15218/zjms.2017.041

The relationship between lymph node metastasis and some clinicopathologic variables in mucinous and non mucinous colorectal adenocarcinoma

Received: 26/6/2016 Accepted: 10/10/2016

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Abstract

Background and objective: Involvement of lymph nodes is an important prognostic factor in most cancers, including colorectal cancer in which lymph node status is the strongest pathologic predictor of patient outcome. This study aimed to find any relationship between lymph node metastasis and associated clinicopathologic variables in colorectal carcinoma.

Methods: In this retrospective study, 136 cases of colorectal cancer were reviewed from Rizgary Teaching Hospital and some private labs in Erbil, Kurdistan region, Iraq during the period between August 2010 and December 2015. All cases were surgically treated with total colectomy or hemi colectomy.

Results: A total of 136 cases of colorectal cancer were included in this study; 53% presented with one or more lymph node metastasis, 47% were between 40 and 60 years of age and 68% were male. There was no statistically significant relationship between lymph node status and any of the studied clinicopathologic variables.

Conclusion: In colorectal adenocarcinoma, there was no statistically significant correlation between lymph node involvement and any of the studied clinicopathologic variables including tumor size, anatomic location, differentiation and histologic type, depth of invasion or patient gender and age.

Keywords: Colorectal; carcinoma; Lymph node; Metastasis.

Introduction

Colorectal cancer is the commonest malignancy in the gastrointestinal tract.[1] Every year, nearly one million people worldwide develop colorectal cancer, of which 50% die within five years.[2] A multidisciplinary approach has been established for the management of colorectal cancer, The pathologist has an important role, especially in diagnosis and tumor staging. The quality of the histopathology report in colorectal cancer is vital in predicting prognosis and the need for adjuvant chemotherapy and radiotherapy.[3,4] Gross description, including tumor size, microscopic features, invasiveness and tumor staging are essential information obtained from a histopathology report, the involvement of resection margin by cancer is a considerable factor for recurrence. Nodal involvement by cancer has a significant implication on prognosis and outcome. The distance to the dentate line in an abdominoperineal resection (APR) specimen is important to predict internal sphincter involvement.[5,6] According to the tumor, node, metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC), the designation "T" refers to the local extent of the untreated primary tumor at the time of diagnosis and initial work-up at its deepest point of invasion, the designation "N" refers to the metastatic status of the regional (draining) lymph nodes, and "M" refers to distant metastatic disease at this time.[7] The TNM staging system is the international language of colorectal cancer staging in all disciplines. It has many advantages over other staging systems.[8]

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The presence of lymph node metastases is one of the most important prognostic factors in colorectal cancer for which adjuvant systemic chemotherapy is generally recommended. Patients with curatively resected stage I and II colorectal cancer without nodal tumor involvement do not receive adjuvant systemic therapy since only small improvements in survival have been shown.[9] However, 10–30% of these node-negative patients will develop loco-regional recurrence or distant metastases.[9] This study aimed to highlight the importance of lymph node metastasis in colorectal carcinoma by studying its association with some clinicopathological variables.

Methods

In this retrospective study, 136 cases of colorectal cancer were assembled from archived material in Rizgary Teaching Hospital and some private labs in Erbil, Kurdistan region-Iraq during the period between August 2010 and December 2015. Cases of all ages and both sexes were included. All cases surgically treated by total colectomy or hemi colectomy for removal of the tumor. The minimum number of examined lymph nodes necessary for adequate staging is 12 according to both the International Union Against Cancer and the American Joint Committee on Cancer.[10,11] Patients divided into three age groups (below 40 years, between 40 and 60 years, and above 60 years). Cases were classified into those located in proximal colon and those found in distal colorectal area. This anatomic categorization was done according to International Classification of Diseases for Oncology, third edition (ICD-O-3).[12] Based on microscopic examination of colorectal cancer slides we separated them into mucinous and non-mucinous types according to the recommendation of WHO.[13] According to the recommendations of College of American Pathologists (CAP), well and moderately differentiated conventional adenocarcinomas were grouped together and called low grade malignancy, while poorly differentiated and undifferentiated conventional adenocarcinomas and non-mucinous adenocarcinomas were called high grade malignancy. Low grade: ≥50% gland forming (Well differentiated: >95% gland forming, moderately differentiated: 50-95% gland forming). High grade: <50% gland forming (Poorly differentiated: 0-49% gland forming).[14] The tumors were segregated into two main groups: those equal or less than 5 cm in diameter, and those which are more than 5 cm. Finally, the American Joint Committee on Cancer (AJCC) TNM system was used for assessing depth of invasion (T), dividing it into T1: tumor invades submucosa, T2: tumor invades muscularis propria, T3: tumor invades pericolorectal tissue and T4: tumor that penetrates visceral peritoneum or directly adherent or invades other organs.[15]

Statistical Analysis: Results were expressed as frequency and percentages. Data analyzed using statistical package for the social sciences (version 19) computer software. A *P* value of ≤0.05 was regarded statistically significant. Cross tables and associations between different variables were measured by using Chi-square and Fisher exact tests.

Results

A total of 136 cases of colorectal cancer were included in this study. Lymph node involvement not found in 64 cases (47%), while the remained 72 cases (53%) presented with one or more positive lymph nodes. Most of the patients were males [(92/136) (68%)], while [(44/136) (32%)] of them were females. Positive lymph node involvement occurs more in female patients [(25/44) (57%)] than male patients [(47/92) (51%)], but the relationship between the gender and lymph node involvement was statistically not significant (*P* = 0.583). The studied patients were divided into three age groups (<40y, 40-60 y, and >60y). Most of the patients [(64 (47%)] were in

https://doi.org/10.15218/zjms.2017.041

the age group 40-60 yr., but lymph node positivity was more in patients > 60 years of age [(21/38) (55%)]. The relationship between lymph node involvement and age distribution was not significant (*P* = 0.937). Majority of colorectal cancer cases [(86 (63%)] were found in the distal colorectal area, only 50 cases (37%) were located in the proximal colon. The lymph node positivity occur more in colorectal cancer of the distal colorectal area [(50/86) (58%)], but no significant relationship was observed between lymph node involvement and site of colorectal cancer (*P* = 0.153). Among the 136 cases, the majority were of non-mucinous histologic type [(110/136) (81%)] (Figure 1), and only [(26 /136) (19%)] of cases were of mucinous type (Figure 2).

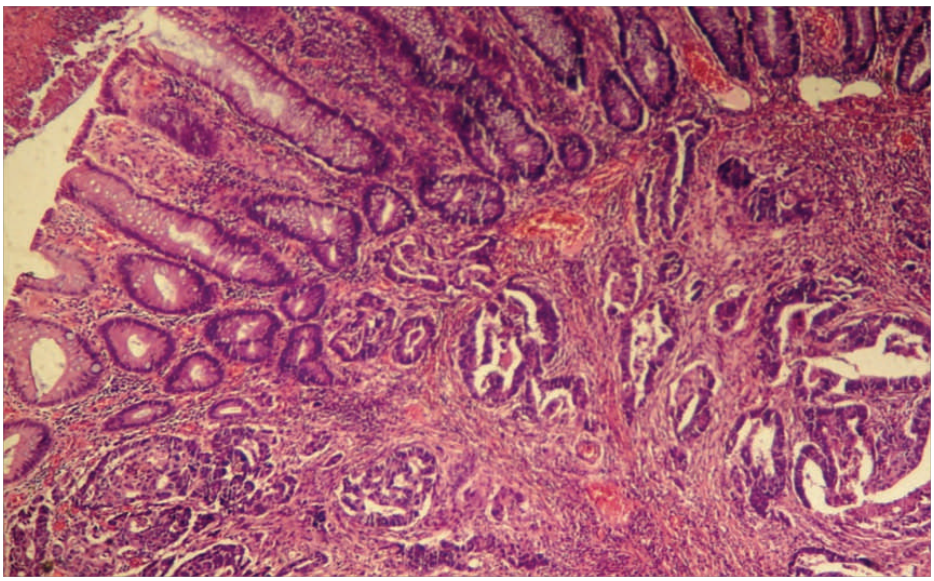

Figure 1: Low grade colorectal adenocarcinoma H&E (x200).

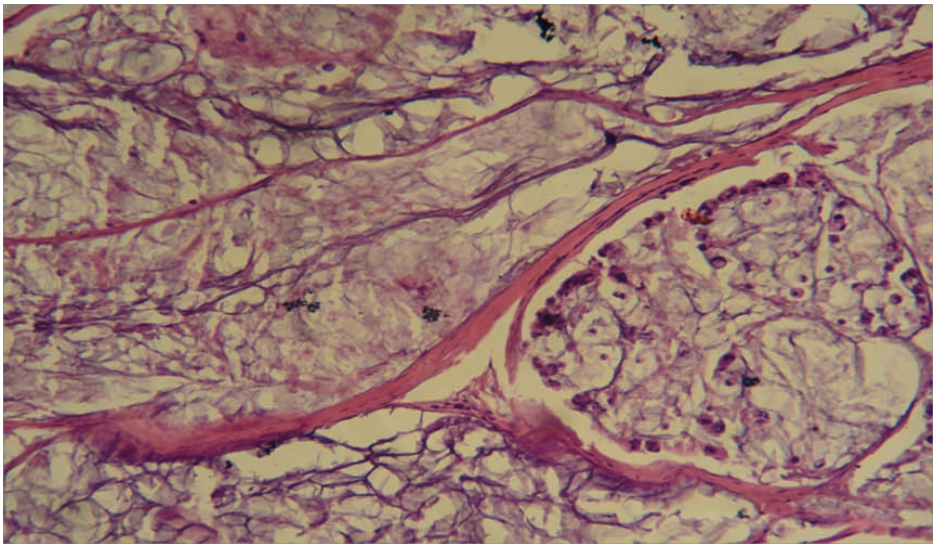

Figure 2: High grade Mucinous colorectal adenocarcinoma H&E (x400).

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Lymph node involvement by colorectal cancer was seen more in mucinous type [(15/26) (58%)], but the relationship between histologic type and lymph node involvement was not significant (*P* = 0.665). The majority of cases were low grade [(100/136) (74%)], while only 36 cases (26%) were high grade. Most of the high grade malignant cases [(22/36) (61%)] showed positive lymph node involvement. Also, the relationship between the grading and lymph node involvement was not significant (*P* = 0.33). Most colorectal cancer cases were ≤ 5cm in diameter [(78/136) (57%)], only 58 cases (43%) were > 5cm in diameter. The Positive lymph nodes were found more in tumors of ≤ 5cm in diameter [(42/78) (54%)], Tumor size showed a nonsignificant relationship to lymph node involvement (*P* = 0.862) (Table1). Regarding tumor invasion, 54 cases (39.7%) presented with tumor that invades pericolorectal tissue (T3), followed by 35 cases (25.7%) which invade muscularis propria (T2), 24 cases (17.6%) penetrate visceral peritoneum or directly adherent or invade other organs (T4), and only 23 cases (17%) invade submucosa (T1), but still the relationship was not significant (*P* = 0.098). Table 1 shows the comparison between lymph node metastasis and different clinicopathologic variables in colorectal carcinoma.

Table 1: Comparison between lymph node metastasis and different clinicopathologic variables in colorectal carcinoma.

Clinicopathologic variables		No. (%)	Lymph node involvement		*P* value
			Negative (%)	Positive (%)	
Gender	Female	44 (32)	19 (43)	25 (57)	0.583
	Male	92 (68)	45 (49)	47 (51)	
Age (years)	<40 Y	34 (25)	16 (47)	18 (53)	0.937
	40-60 Y	64 (47)	31 (48)	33 (52)	
	>60Y	38 (28)	17 (45)	21 (55)	
Site	Proximal colon	50 (37)	28 (56)	22 (44)	0.153
	Distal colorectal	86 (63)	36 (42)	50 (58)	
Histological type	Mucinous	26 (19)	11 (42)	15 (58)	0.665
	Non mucinous	110 (81)	53 (48)	57 (52)	
Grading	Low	100 (74)	50 (50)	50 (50)	0.33
	High	36 (26)	14 (39)	22 (61)	
Tumour size	≤ 5cm	78 (57)	36 (46)	42 (54)	0.862
	> 5cm	58 (43)	28 (48)	30 (52)	
Depth of invasion	T1	23(17)	12(52)	11(48)	0.098
	T2	35(25.7)	11(31)	24(69)	
	T3	54(39.7)	31(57)	23(43)	
	T4	24(17.6)	10(42)	14(58)	

P ≤0.05 considered statistically significant
T1: tumor invades submucosa
T2: tumor invades muscularis propria
T3: tumor invades pericolorectal tissue
T4: tumor penetrates visceral peritoneum, or adherent or invades other organs.

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Discussion

In this retrospective study of 136 patients with colorectal carcinoma most of our cases were present with lymph node metastasis at the time of diagnosis in that 64 cases (47%) showed no lymph node involvement, while 72 cases (53%) presented with one or more positive lymph nodes. This is mostly due to delayed presentation and lack of screening programs for colorectal cancer in our locality as also shown in two other studies.[16,17] Tumor size (as 57% were ≤ 5cm) showed non-significant correlation with lymph node metastasis in concordance with other studies.[18-20] In the current study, colorectal carcinomas were more common in male (68%) than female (32%). Several other studies were agreed with us that there is male predominance,[17,21,22] this may be due to chance or more likely from a complex interplay of genetic, hormonal and environmental risk factors. Although 57% of female patients were present with positive lymph node involvement and 43% with negative lymph node involvement compared to nearly equal percentage of lymph node status in male patients, the statistical relation was non-significant, other two studies reached to the same result.[18,20] Most cases were in the age group 40-60 years (47%), this is in agreement with several others.[17,21,23] These findings may be due to the short life span of our population or due to more percentages of undiagnosed hereditary colorectal cancer in our areas. The relation between patient age and lymph node involvement was non-significant, that was in concordance with other studies.[18,20] Majority of the tumors [(86 cases) (63%)] of the study samples were located in the distal colon and rectum. Most other studies showed the same anatomic distribution,[17,21,24] among which 36 cases (42%) had no lymph node metastasis and 50 cases (58%) presented with lymph node metastasis at diagnosis. On the other hand, 50 cases (37%) were located in the proximal colon, among which 28 cases (56%) had negative lymph node at the time of surgery and the remaining 22 cases (44%) presented with involved lymph node, but the relationship was not significant. Another research done by (Nasser et al.) had reached to the same result.[18] Most tumors were low grade (74%). Although high grade tumors showed more lymph node involvement, this was statistically non-significant. Two other studies showed the same results.[19,25] Regarding depth of invasion fifty four cases (39.7%) were invading pericolorectal tissue (T3) followed by 35 cases (25.7%) invading muscularis propria (T2), another 24 cases (17.6%) were penetrating visceral peritoneum or directly adherent or invade other organs (T4), while only 23 cases (17%) were invading submucosa (T1), the same results obtained by many others.[9,16,26] The relation between depth of invasion and lymph node involvement was in agreement with other studies which was statistically nonsignificant.[18]

Conclusion

Lymph node involvement in colorectal adenocarcinoma showed non-significant correlation with studied clinicopathologic factors including tumor size, anatomic location, differentiation and histologic type, depth of invasion, and patient gender and age. We recommend future works carried out in this field to use more samples and multicenter studies to confirm our results.

Conflicts of interest

The authors report no conflicts of interest.

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