ORIGINAL ARTICLE

A REVIEW OF RELATIONSHIP BETWEEN PRESENTING SYMPTOMS AND TUMOUR LOCATION IN COLORECTAL CARCINOMA IN TERTIARY CENTRE HOSPITAL

Zaid Maad Ahmed Samem[1], Micheal Wong Pak Kai[1], Firdaus Hayati[2], Nik Amin Sahid[2], Nornazirah Azizan[3], Wan Zainira Wan Zain[1] and Andee Dzulkarnaen Zakaria[1]

[1]Department of Surgery, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, Kelantan, Malaysia
[2]Department of Surgery, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia
[3]Department of Pathobiology and Medical Diagnostic, Faculty of Medicine and Health Sciences, Universiti Malaysia Sabah, Sabah, Malaysia

Corresponding author:
Firdaus Hayati
Email: firdaushayati@gmail.com

ABSTRACT

Colorectal cancer is ranked as the most common cancer for men and the second most common cancer for women according to the Malaysian National Cancer Registry Report (MNCR) 2007-2011. However, delay in the diagnosis of colorectal cancer is still common partly attributable due to late presentation and incorrect diagnosis by the general practitioners. The aim of this study is to determine the relationship between presenting symptoms of colorectal cancer to the location of the tumour in order to prevent delay in diagnosis of colorectal cancer. Between 1996 until 2009, a total of 212 patient data from Hospital Universiti Sains Malaysia were retrospectively analyzed. The demographic and surgical data were obtained. We studied the relationship of the presenting symptoms of colorectal cancer to the location of the tumour. The age of candidate included in this study range from 16 to 93 years old with mean age was 56 and male predominance. In this study, there is a strong relationship between presenting symptoms and the location of the colorectal cancer but no significant relationship between age and sex to the anatomical location of the tumour. The study showed the presenting symptoms of rectal bleeding, change in bowel habit and tenesmus were significantly associated with rectal tumor, intestinal obstruction with left sided tumors and anemia and abdominal mass with right sided tumors (p-value <0.05). However abdominal pain does not follow this role as it is mostly associated with other presenting symptoms and it has no significant relation to the anatomical location of the tumor.

***Keywords**: Colorectal cancer; Symptom assessment; Neoplasms by site*

INTRODUCTION

Colorectal cancer (CRC) is one of the most common gastrointestinal malignancies worldwide with annual incidence of 1.4 million cases per year and an annual mortality of more than 694,000[1]. In a report by the Malaysian National Cancer Registry Report (MNCR) 2007-2011, CRC is ranked as the most common cancer for men and the second most common cancer for women with age-standardized rate of 14.6 and 11.1 incidences per 100,000 population respectively[2]. The incidence of CRC is continually increasing. Despite significant improvement in the screening programs and diagnostic methods, delay in the diagnosis of colorectal cancer is still common. Delay in the diagnosis of colorectal cancer is still common partly due to late presentation and incorrect diagnosis by the general practitioners or clinicians, but delay due to lack of awareness by the patients themselves[3].

Majority of the patients complained of change of bowel habit, rectal bleeding and anemia as the predominant presenting symptoms of CRC[4,5]. Other symptoms include abdominal pain, loss of weight and appetite, and abdominal mass[4]. Tumours of the right colon are often clinically silent and the only possible sign is anemia. Occult bleeding from the large bowel is widely believed to be the most common cause of iron deficiency anemia in patients without an obvious source of blood loss[6,7]. Right sided colon tumour tends to be bulky and exophytic, growing into the colon lumen[8]. Conversely, tumour on the left side can present with fresh rectal bleeding, change of bowel habit and intestinal obstruction due to its constricting nature[8]. In addition, distal disease can cause tenesmus in certain patients. However, the value of symptoms to predict CRC is still poor in certain condition[9]. The aim of this study is to determine and analyze the relationship between presenting symptoms of colorectal cancer to the location of the tumour in order to prevent delay in diagnosis of colorectal cancer.

METHODOLOGY

This was a retrospective observational study on a total of 212 patients data performed from July 2014

to October 2015. The study protocol was approved by the USM Ethic and Research Committee before embankment. Inclusion criteria applied to all patients who were diagnosed as colorectal cancer from January 1996 to December 2009. The patients with lost or incomplete data of the medical records were excluded. The data were collected by tracing and reviewing the medical records of patients and recorded in a standard form. The first presenting symptoms obtained from the data were rectal bleeding, change of bowel habit, intestinal obstruction, anemia and abdominal pain.

They were divided into 4 main categories according to the age group namely age of 49 and less, 50 to 59 years old, 60 to 69 years old and age of 70 and above. The tumours were grouped into right-sided (caecum to proximal two-thirds of transverse colon), left sided (from the distal third of transverse colon up to end of sigmoid), and rectal tumours. Subsequently, they were compared with the presenting symptoms obtained to look for the statistical significance. All evaluated data were analyzed using SPSS software (Version 18). The descriptive analysis was evaluated by using Pearson chi-square test or Fisher's exact test. Statistical significance was set at P-value <0.05.

RESULTS

During the initial phase of study period, data from a total number of 255 patients were selected but 43 patients were excluded. The remaining 212 patients' data were chosen into this study. There were 125 male (59%) and 87 female (41%) patients. The mean age was 56 with range from 16 to 93 years old. Of 212 patients, majority were rectal tumour which account for 92 (43.4%) cases followed by left sided tumours of 80 (37.7%) cases and the right sided tumour of 40 (18.9%) cases. A cross analysis was performed between 4 age groups and the location of the tumour (Table 1). The result showed that there was no significant difference between age group and the location of the tumours in which all three tumor locations were identified mainly in those with age group of 49 and less.

Table 1: A relation between location of tumours and different age groups

Location of the tumour	Age group ≤49 (%)	Age group 50-59 (%)	Age group 60-69 (%)	Age group ≥ 70 (%)	p-value
Right side	15 (7.1)	8 (4.2)	9 (4.2)	8 (3.8)	0.97
Left side	24 (11.3)	19 (9.0)	22 (10.4)	15 (7.1)	
Rectal	28 (13.2)	21 (9.9)	22 (10.4)	21 (9.9)	

Another comparison was done to establish the association between gender and location of the tumour (Table 2). Out of 212 cases, rectal tumour was more common in both male and female group, 54 and 38 cases respectively compared to left and right sided tumours. However, there was no significant relation between the gender and the location of the tumour.

Table 2: A relation between location of tumours and gender

Location of the tumour	Male	Female	p-value
Right side	22	18	0.43
Left side	49	31	
Rectal	54	38	

The seven most common presenting symptoms that were seen in 212 patients with colorectal cancer presented to Hospital Universiti Sains Malaysia from 1996 to 2009 were rectal bleeding, change of bowel habit, intestinal obstruction, anemia, abdominal pain, abdominal mass and tenesmus (Table 3). From the study, 137 cases complained of change of bowel habit and 97 cases had rectal bleeding. Furthermore 32, 53 and 80 cases presented with intestinal obstruction, anemia and abdominal pain respectively. Other symptoms were abdominal mass and tenesmus with 34 and 21 cases respectively.

Table 3: Presenting symptoms to Hospital Universiti Sains Malaysia

Presenting Symptoms	Number of Cases
Rectal bleeding	97
Change of bowel habit	137
Intestinal obstruction	32
Anemia	53
Abdominal pain	80
Abdominal mass	34
Tenesmus	21

A comparison analysis between presentation of rectal bleeding and location of the tumour revealed 72 (34%) cases are rectal tumour, while origin from the left and right side, only 3 (1.4%) and 22 (10.4%) cases respectively (Table 4). There was a significant relation between rectal bleeding symptom and the location of the tumour (p value <0.001).

Table 4: A relation between location of tumours and presenting symptoms

	Presenting Symptoms		
Location of the tumours	**Rectal bleeding (%)**	**No rectal bleeding (%)**	**p-value**
Right side	3 (1.4)	37 (17.5)	0.00001*
Left side	22 (10.4)	58 (27.4)	
Rectal	72 (34)	20 (9.3)	
	Change of bowel habit (%)	No change of bowel habit (%)	
Right side	21 (9.9)	19 (9)	0.034*
Left side	48 (22.6)	32 (15.1)	
Rectal	68 (32)	24 (11.3)	
	Intestinal obstruction (%)	No Intestinal obstruction (%)	
Right side	2 (0.9)	38 (17.9)	0.00001*
Left side	24 (11.3)	56 (26.4)	
Rectal	6 (2.8)	86 (40.6)	
	Anemia (%)	No anemia (%)	
Right side	32 (15.1)	8 (3.8)	0.00001*
Left side	8 (3.8)	72 (34)	
Rectal	13 (6.1)	79 (37.3)	
	Abdominal pain (%)	No abdominal pain (%)	
Right side	16 (7.5)	24 (11.3)	0.07
Left side	37 (17.5)	43 (20.3)	
Rectal	27 (12.7)	65 (30.7)	
	Abdominal mass (%)	No abdominal mass (%)	
Right side	16 (7.5)	24 (11.3)	0.00001*
Left side	11 (5.2)	69 (32.5)	
Rectal	7 (3.3)	85 (40.1)	
	Tenesmus (%)	No tenesmus (%)	
Right side	0 (0)	40 (18.9)	0.002*
Left side	5 (2.3)	76 (35.8)	
Rectal	16 (7.5)	75 (35)	

** indicates that p-value <0.05 and it is statistically significant*

Majority of the CRC cases presented with change of bowel habit such as spurious diarrhea and/or chronic constipation. In this study a comparison was done between change of bowel habit and location of the tumour (Table 4). From 137 (64.6%) cases presented with change of bowel habit, majority of them were rectal tumour with 68 (32%) cases, while 21 (9.9%) and 48 (22.6%) cases are right and left tumour respectively. There was a statistically significant difference between change of bowel habit and location of the tumour (p-value <0.05).

In this study, a comparison was done between intestinal obstruction and location of the tumour (Table 4). From 32 (15.1) cases with intestinal obstruction, 24 (11.3%) cases were left sided tumours, while 2 (0.9%) and 6 (2.8%) cases were right sided and rectal tumours respectively. There was a significant relation between intestinal obstruction and the location of the tumour (p-value <0.001).

In this study a comparison was done between anemia symptom and the location of the tumour (Table 4). The current national guideline defines anemia as when Hb less than 10 g/dl in females and Hb less than 11 g/dl in males[10]. From 53 (25%) cases presented with anemia, 32 (15.1%) cases are right side tumour, which represent the majority of cases, while 8 (3.8%) and 13 (6.1%) cases presented with this symptom are left side and rectal tumour respectively. There was a significant relation between anemic symptom and location of the tumour (p-value <0.001).

Abdominal pain is nonspecific symptom that may occur in many cases of abdominal pathology. However, it is one of the important presenting symptoms for colorectal cancer disease. In this study a comparison was done between abdominal pain symptom and the location of the tumour (Table 4). From 80 (37.3%) cases with abdominal pain, 37 (17.5%) cases are left side tumour, while 27 (12.7%) and 16 (7.5%) cases are rectal and left side tumour respectively. However, using Pearson chi-square, there was no relation between abdominal pain symptom and the location of the tumour (p-value >0.05).

When comparing between abdominal mass and location of the tumour, we noticed that most of the cases (7.5%) presented with this symptom are those with right side tumour, while only 3.3% of rectal tumor are presented with abdominal mass (Table 4). There was a significant relation between abdominal mass and the location of the tumour (p value < 0.001).

Tenesmus was recorded in 21 (9.9%) cases with colorectal cancer, where the most common cases presented with this symptom are those with rectal tumour 17 (8%), while no case presented with tenesmus on the right side tumour cases in this study. However, as shown in Table 4 using Pearson Chi-square, there was a significant relation between tenesmus and the location of the tumour (p-value <0.05).

DISCUSSION

Colorectal cancers are growing in Malaysia. The overall incidence rate of CRC was 21.32 cases per 100, 000[11]. Data from the National Cancer Patient Registry-Colorectal Cancer, 2008 to 2013 indicated that overall mortality rate was 9.79 in 100,000 population[11]. The mean age of CRC in this study was 56 years old and majority of the cases were 50 years old and more which mirrored the study by University of Malaya[12]. In other series, majority of cases were in the age group more than 70 years old[13]. This indicates that sporadic CRC is a disease of the elderly. This delay is attributable to a variety of causes which involve the healthcare systems, managing clinicians as well as patients. In Malaysia setting, there is no official screening cancer program for CRC until now even though the incidence and prevalence are climbing up. Hence, the population awareness is low towards CRC. It is time to start proper CRC screening in country.

This study showed that there was no significant different between the age group and the location of the tumour but there was an increment of distal tumour in older age group. This finding was consistent with another study by Fazeli et al[14]. Another study which was done in South Korea, also revealed that the patients with proximal tumours prone to be slightly older in age[8]. The possible explanation for this variation in the results is due to a higher incidence of microsatellite instability (MSI)-high CRC that was seen more in elderly[15]. Based on an animal study, MSI-high CRC carries loxP sites flanking exon 14 of adenomatous polyposis coli (Apc) gene regulated by CDX2 promoter and a long mononucleotide tract (CDX2P9.5-G22Cre;Apcflox/flox)[15].

The sex distribution was studied and revealed there was male predominance, 60%:40% with male:female ratio of 3:2. However there was no significant relation between gender and anatomical site of the tumour. This result was similar to the study which was done at University of Malaya, showing a male predominance[12,16]. It was hypothesized that hormonal factors were responsible for the differing rates of CRC in men and women[17].

Hayne et al studied the anatomical site distribution of CRC and found that the most common site was the rectal tumour (37%) cases followed by left side tumours (35%) and right side tumours (26%)[17]. These findings were consistent with our current study. In ours, majority of the cases were rectal tumours 43.4%, followed by 37.7% and 18.9% for left and right side tumour respectively. The clinical implication of these findings is when choosing of the best screening methods for high risk group of the population whereas flexible sigmoidoscopy and faecal occult blood test may be more cost effective compared with other screening methods.

Rectal bleeding was the commonest presenting symptom of CRC[18]. Based on our study, there were 97 cases of rectal bleeding, second after change of bowel habit. However, when they were compared with the location of tumour, 34% of total cases were rectal in origin and there were statistically significant. The UK Referral Guidelines for Suspected Colorectal Cancer came out with 2 important criteria or symptoms, those are rectal bleeding and change in bowel habit[19]. When rectal bleeding presented along with change of bowel

habit and abdominal pain, these three majority symptoms were prone to rectal cancer[18].

In this study, change of bowel habit has strong relation with the anatomical location of colorectal cancer (p value < 0.05). These results were similar to the study done by Kent et al., who found that Change in bowel habit (diarrhea and constipation) was significantly more common in rectal cancers and is not specific to left and right-sided cancers[20].

CRC causes approximately 50% of symptoms of intestinal obstruction, while more benign pathology including volvulus, diverticular stricture, hernia and fecal impaction account for the remaining 50% of cases[21]. Mulcahy HE et al has reported that bowel obstruction has strong relation to the anatomical site of colorectal cancer, and 34% of cases with this emergency presentation, presented at the left side and 25% at right side tumour, while it is less common symptom for rectal cancer cases[22]. Intestinal obstruction is common emergency presentation on the left side colon cancer and presented in 24 patients. Meanwhile, right sided tumour only presented in two patients. This is most probably related to the difference in the morphology of the tumour on both sides, as the lesions tend to be infiltrating and constricting on the left side giving obstructive symptom, beside the feces is more in solid form in left sided tumour[8].

Anemia was elicited more frequently in those with right-sided colon cancer compared to the left sided and rectal tumours[10]. The most common error was failure to initiate or complete the investigation of anaemia[24]. It is recommended to examine both the upper and lower gastro-intestinal tract for the adequate investigation of anemia to rule out benign causes as well as malignant upper gastro-intestinal tumours. In this study, the haemoglobin levels were significantly lower for right sided lesions as compared to left and rectal cancer cases (p-value <0.001). This finding was due to the difference in the macroscopic variety of the tumour, in which it tends to be ulcerative or cauliflower lesions for the right side, which tend to bleed causing this anemic symptom[18].

Abdominal pain is a vague and non-specific symptom of colorectal cancer. Hamilton et al. reported that abdominal pain is a difficult problem for the doctor in primary care and it is a very common symptom, and still associated with colorectal cancer[23]. Furthermore, abdominal pain retained their association with the cancer 180 days before diagnosis, so serious consideration should be given to the possibility of cancer with this symptom[23]. It was revealed from this study, that abdominal pain mostly associated with other presenting symptoms like intestinal obstruction or abdominal mass rather than be mono-symptomatic for colon cancer. Otherwise this symptom has no significant relation to the anatomical location of the tumour (p-value >0.05). These results was similar to the study which is done at Karolinska Hospital, Stockholm, Sweden, who found that abdominal pain was most common on right and left colon cancer more than rectal cancer[24]. In this study, abdominal mass was significantly higher in patients with right-sided than in those with left-sided colon cancer. These results were similar to the results which by Nawa at al., at Okayama University in Japan, who revealed that abdominal mass presentation is common on right side than on left side colon tumour[25].

Tenesmus is a painful straining to empty the bowel without resultant evacuation. This is a very important presenting symptom for colorectal cancer mostly related to locally advanced tumour[26]. Though the sample size to study the relation of this symptom to the location of the tumour is not enough, but we found that tenesmus is mostly associated with rectal tumours (17%), while no case was reported clinically to have tenesmus in right sided tumour. These finding was similar to other study done by Saidi et al, who reported that tenesmus presented commonly in rectal cancer cases (30%)[18]. The explanation of high percentage of tenesmus in rectal site related to the pathophysiology of this symptom, as this clinical symptom result from continuous stimulation of the defective reflexes, these stimuli may be normal passage of feces, or abnormal, arising from either continued stimulation of stretched receptors probably due to obstruction caused by the tumour itself or mucosal irritation after infiltration of the tumour to the mucosal layer.

Part of the main limitations of this study is due to the nature of retrospective and a single-centered study. There were deficit in data and documentation and non-professional history taking from the patients and this is due to lack of knowledge regarding this disease especially in our trainee doctors. The second limitation is the small size of our study population to appreciate significant differences between groups, although the sample size was achieved in this study. Furthermore we noted that there were number of patients who were excluded from this study are first treated in other centers and admitted to our hospital for chemotherapy only which made it difficult to obtain the data that are needed in this study. Creation of well-organized reference record system for colorectal cancer cases, will facilitate the tracing of information. Beside a well-developed functional department of colorectal surgery may be the solution.

CONCLUSION

Rectal cancer represents the highest percentage of all anatomical location of colorectal cancer in this study, followed by left sided tumour. Alteration in bowel habit is the most frequent presenting symptom, reported in more than half of our cases with colorectal cancer. There is strong relationship between the presenting symptoms and the location of the colorectal cancer. This study will be helpful in our clinical practice by choosing the appropriate investigation method for our patients for diagnosis and screening of high risk groups, which may be cost effective and less time consuming, preventing any delay in management process. We would like to suggest to start proper CRC screening program in Malaysia for better prognosis and survival in future.

ACKNOWLEDGEMENTS

The authors wish to thank the staffs of the Medical Record Unit, Hospital Universiti Sains Malaysia for the assistance in searching for the data in this study.

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