

RESEARCH COMMUNICATION

Colorectal Cancer Patients in a Tertiary Referral Centre in Malaysia: a Five Year Follow-up Review

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Abstract

Background: Colorectal cancer (CRC) is one of the major malignancies in the world. In Malaysia, CRC is fast becoming the commonest cause of cancer death. Its etiology is complex, involving both environmental and genetic factors. This study looked at the profile and outcome of five-year follow-up of patients with CRC. **Materials and Methods:** Retrospective case review study done on CRC patients at Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur, Malaysia. Patients' socio-demographic characteristics, modalities of treatment, cancer characteristics and outcome at 5-year follow up were extracted from the case records. **Results:** A total of 107 case records of patients were analyzed. Peak age of CRC presentation was 40-69 years (71.1%). Male to female ratio was 1.2:1 with Chinese predominance (52.3%). Anaemia and its related symptoms including per rectal bleeding was the commonest clinical presentation. The median duration of clinical presentation was 13 weeks (IQR 21.8). More than two-thirds presented as non-emergency cases (69.2%). Most patients presented with Dukes C stage (40.2%). The overall 5-year survival rate was 40% with local recurrence rate of 19.6%. Metastasis after curative-intend treatment (surgery with adjuvant therapy) developed in 26% of patients. Lower recurrence ($p = 0.016$, OR = 0.205) and metastatic disease ($p = 0.02$, OR = 0.24) found among the Chinese patients. Almost half of the patients defaulted follow up care (43%), most often within the first year of treatment (22.4%) and the Chinese were the least likely to default ($p = 0.04$, OR = 0.45). **Conclusion:** Socio-demographic profile of CRC patients in UKMMC is comparable to Asia pacific region. Apparent delay in seeking treatment gives rise to poor overall survival and local recurrence rates.

Key Words: Colorectal cancer - rectal bleeding - delay in treatment - survival

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Introduction

Colorectal cancer (CRC) is one of the major malignancies afflicting both western and eastern world society. It is the third commonest cause of cancer death in Malaysia, contributing to admission rates from 8.1 percent in 1987 to 11.9 percent in 1995 with an incidence of 22.5 per 100,000 of the population (Ministry of Health, 1999; Ahmedin et al., 2004)

Environmental and genetic mechanism interplay with each other and contribute to the etiology of CRC. Recently significant proportion of cases are found to have developed from genetic mutation in which adenoma will ultimately become carcinoma over 10-20 years (Volgestein et al., 1988; Dove-Edwin and Thomas, 2001). Up to 15% of all colorectal cancer cases have a genetic predisposition, including those with familial adenomatous polyposis and hereditary non-polyposis colorectal cancer (Cannon-Albright et al., 1988; Houlston et al., 1992).

Clinical manifestations of CRC are not specific. They are usually the consequence of narrowing of lumen

producing obstruction or by loss of blood or mucus from the tumor surface resulting in change in bowel habit. Per rectal bleeding is one of the alarming symptoms of colorectal cancer and may be regarded as one of the pathognomonic sign of CRC (Yan and Tan et al., 2002). In combination with change in bowel habit or loose stool occurring over 6 weeks, it is a sensitive indication for further investigation of CRC. Secondary effects include severe iron deficiency anemia and a clear sign of intestinal obstruction.

Population screening has been shown to reduce mortality from colorectal cancer (Mandel et al., 1993; Hardcastle et al., 1996; Kronborg et al., 1996). However, mass screening is not yet available in Malaysia. Hence, many cancer cases are diagnosed from symptomatic patients and delayed diagnosis is a major obstacle to favorable outcome. Nonetheless, we do practice opportunistic screening program using various methods including fecal occult blood test (FOBT), flexible sigmoidoscopy and colonoscopy. Another major problem in managing cancers in Malaysia is the tendency of

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patients defaulting follow up. Combining this with the prevalence of delayed diagnosis may contribute to poor overall outcome for several cancer treatments in this country.

We here studied the profile of presentation, socio-demographic characteristics and outcome of five-year follow-up of patients with colorectal cancer in Universiti Kebangsaan Malaysia Medical Centre (UKMMC) Kuala Lumpur, Malaysia. This hospital is one of the tertiary referral centers that serve a multi-racial population of approximately 1 million people.

Patients and Methods

We reviewed 107 complete 5 year follow-up case records of patients treated for CRC from September 1997 to December 2000. Patients' socio-demographic characteristics, cancer characteristics, modalities of treatment, and outcome of 5-year follow up were analyzed. We defined delayed presentation as the duration of 2 weeks or more from first classical symptom of CRC to consultation. Defaulters were those whose record showed failure to follow treatment plan and clinic follow up. Mortality outcome from defaulters were determined from telephone interview of their close relatives focusing on the time and reason for death. Statistical analysis was performed using SPSS version 12, Chicago Illinois. Findings were considered significant when the p value was less than 0.05.

Results

A total of 59 males and 48 females were treated for colorectal cancers over the 4-year study period. The mean age was 57.5 ± 14 years. The youngest patient was a 21-year old male. The age distribution among the rectal and colon cancers were similar (55.5 years versus 59.7 years, $p=0.117$). However, we observed significantly more male patients being treated for rectal cancers (64.3 percent versus 35.7 percent, $p=0.04$). The ethnicity distribution was 52.3 percent Chinese, 43 percent Malay, 2.8 percent Indian and 1.9 percent others. Cancer sites were distributed evenly within the colon and the rectum in each race.

Common clinical presentation are listed in Table 1 which showed main symptoms characteristics CRC among the studied population. Symptomatic anaemia, significant weight loss, abdominal pain, anorexia, altered bowel habit and per rectal bleeding were the main presenting features of colorectal cancers. Although the majority of these symptoms occurring in combination, individual analysis of symptoms showed a more than 50 percent of colorectal presenting features. Per rectal bleeding was also found predominant among patients with rectal cancers. In addition, only 19 patients presented with features of large bowel obstruction and the majority of these were left sided tumors. Cardiovascular co-morbid factors such as hypertension, ischaemic heart disease, stroke and diabetes mellitus were the common concomitant illness among the patients. There was a trend of delayed presentation with an average duration of 13 weeks to consultation from the first noticeable symptoms.

Table 1. Common Clinical Presenting Symptoms

Symptom	Colon (51) No. (%)	Rectum (56) No. (%)	Total (107) No. (%)
Anaemia	36 (70.6)	31 (55.3)	67 (62.6)
Weight Loss	26 (50.9)	34 (60.7)	60 (56.0)
Abdominal Pain	32 (62.7)	24 (42.8)	56 (52.3)
Anorexia	27 (52.9)	29 (51.7)	56 (52.3)
PR Bleeding	14 (27.0)	38 (67.8)	52 (48.5)
Altered Bowel Habit	19 (37.2)	33 (58.9)	52 (48.5)
Constipation	13 (25.4)	18 (32.1)	31 (28.9)
Diarrhoea	9 (17.6)	16 (28.5)	25 (23.3)
Tenesmus	5 (9.8)	20 (35.7)	25 (23.3)
Mucus in the Stool	7 (13.7)	17 (30.3)	24 (22.4)
Nausea and Vomiting	9 (17.6)	11 (17.9)	20 (18.7)
Obstruction	11 (21.5)	8 (14.3)	19 (17.7)
Fatigue	8 (15.7)	10 (17.9)	18 (16.8)
Positive FOB	3 (5.8)	1 (1.78)	4 (3.7)

FOB, Faecal Occult Blood

Table 2. Duke's staging at Initial Presentation/Diagnosis

Stage	Colon (51) No. (%)	Rectum (56) No. (%)	Total (107) No. (%)
A	1 (2.0)	2 (3.6)	3 (2.8)
B	17 (33.3)	21 (37.5)	38 (35.5)
C	20 (39.2)	23 (41.1)	43 (40.2)
D	13 (25.5)	10 (17.9)	23 (21.5)

More than two third of patients presented as out patients (non-emergency) and the majority of emergency interventions were those with colonic cancers ($p=0.02$) (Table 5). Final histopathological staging using Dukes classification showed more than 75 percent belong to Duke stage B and C and only 21.5 percent were categorized to have metastatic disease at presentation. These metastases were significantly higher among the younger colonic cancer patients. In addition, less than 3 percent of patients had early cancers (Duke A) (Table 2).

More than half of patients defaulted conventional follow up treatment over 5-years. Unfortunately, this happened more often (67.2 percent) during the first two critical years of follow up and the defaulters were predominantly less among the Chinese.

In UKMMC, between 1997 to 2000, adjuvant chemotherapy and/or radiotherapy were given to Duke stage C patients and to those where insufficient margin clearance of rectal carcinoma were detected after a curative intent surgery. It was found that during this period the local recurrence at follow up were 9.7 percent and 19.6 percent for early and locally advanced cancers respectively. Indeed these were mainly the rectal cancers and there was no age and gender preponderance to this. However, there was a predilection of local recurrence occurring significantly more among races other than the Chinese ($p=0.01$). Furthermore, metastatic recurrence developed in 26 percent of patients who had received adjuvant treatments compared to 6 percent in those who had surgery alone (OR=0.20). This again occurred significantly less in the Chinese patients ($p=0.02$, OR=0.24)

The overall survival at 5-year follow up was 40 percent. More than 70 percent of Duke stage B and C

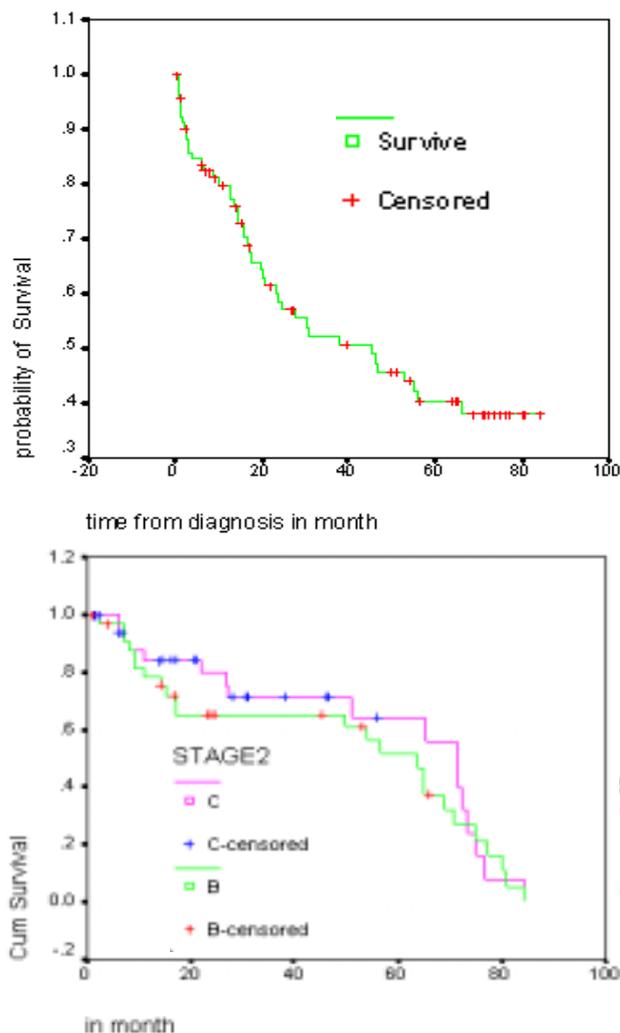


Figure 1. Kaplan-Meier Curves for Survival Probability. a) Overall; b) Stratified by stage at presentation B and C

patients were alive at 2-years and this dropped abruptly afterwards with more Duke stage B patients contribute to the overall mortality (Figure 1).

Discussion

Universiti Kebangsaan Malaysia Medical Centre (UKMMC) in Kuala Lumpur started its tertiary referral services in 1997. The colorectal unit began in the same year and the treatment for colorectal cancers follows the standard universal multi-disciplinary approach. It caters to an estimated number of 1 million city population of predominantly Chinese and Malay race. Over the first 4 years of service, UKMMC saw a similar trend of patients diagnosed to have colorectal cancers to other parts of Malaysia (Selvaratnam et al., 2005) and the world which mainly involved patients' older than 55 years of age (Jessup et al., 1996; Majumdar et al., 1999). There was also no gender preponderance for this disease in the study population but the prevalence among the Chinese elderly is exceptionally prominent. Despite its location in the centre of a city population, our data showed a worrying 13 week delayed of presentation to consultation trend. Knowledge from several biological studies signified that this duration is long enough for progression of stage to

occur which in turn may affect the overall optimal outcome. The delay may have contributed to the distribution of more than 95 percent of patients having locally advanced and metastatic disease with less than 3 percent early cancers detected at presentation. Unfortunately, the reasons for the delay is beyond the scope of this study but since population screening for CRC is yet available in Malaysia, it will be pertinent to use this evidence to initiate one. Perhaps this is an invaluable strategy to pursue considering the global increasing trend of CRC incidence.

Our study have also prevailed that CRC is a disease manifested by several judicious symptoms. The combination of symptomatic anemia, weight loss with anorexia and altered bowel habit should alarm the attending physician towards the diagnosis, which then mandates a thorough lower gastrointestinal assessment like colonoscopy. In addition, the detection of blood at defecation in elderly individuals should call for a more urgent role for the physicians (Toit et al., 2006). Our study has revealed an estimated 13-week delay for consultation after the first symptoms. Although the age factor may play a role in this phenomenon, the fact that the study was conducted from a city population may signify problems with knowledge dissemination of CRC. This may urge for a more effective campaign to raise knowledge that will enhance medical or health seeking behavior. The campaign must also provide information to the tools available for both diagnosis and treatment. On the other hand, this study has also revealed a significant defaulter trend among the non-Chinese races. This occurred mainly during the first 2 years of treatment follow up which is vital for disease progression screening and the local recurrence detection.

Fear and anxiety of chemotherapy, prolonged depression and adjustment disorder and thinking that the disease has been removed could be the answers to this defaulter trend. However no study has been done to elucidate these reasons. Again, dissemination of knowledge is greatly important to be delivered not only to patients who survived surgical procedures but their care givers as well.

With regard to the overall survival at 5 years follow-up, our findings were similar to those in other studies (Hobler, 1986; McLeish et al., 2002; McArdle et al., 2005). Ironically, stage Dukes B has contributed more to the overall mortality despite active intervention. This could be explained by the wrong staging at diagnosis, inadequate lymph nodes excision and inefficient circumferential margin clearance during surgical exploration and resection. The Chinese patients in our study tended to have better outcome in terms of local recurrence and metastatic disease at 5-year follow up. In addition, this ethnicity has significant less defaulter trend among all of the different ethnicities in Malaysia.

In conclusion, similar socio-demographic profile is seen among the CRC patients in UKMMC compared to other areas of the country (Talens et al., 1993; Jessup et al., 1996; Ministry of Health, 1999; Ahmedin et al., 2004). Most patients present late with an apparent delay of treatment seeking of 13 weeks that gives rise to poor overall survival and local recurrence rates.

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