Applied Medical Research

Original Research

DOI: doi.org/10.47363/AMR/2015(1)111

Clinicopathological characteristics of colorectal cancers at KHMC

Ahmad Telfah[1], Mohammad Obeidat[2], Ayman Abu-Kamar[2], Ahmad Bawa'neh[2], Abdulmajeed Arabeiat[2], Hani Al-Kafaween[3], Luna Fayyad[4]

[1]Department of Medicine, Head of Division of Medical Oncology, King Hussein Medical Centre, Royal Medical Services, Amman, Jordan, [2]Department of Medicine, Division of Medical Oncology, Medical Oncologist, King Hussein Medical Centre, Royal Medical Services, Amman, Jordan, [3]Department of surgery, King Hussein Medical Centre, Royal Medical Services, Amman, Jordan, [4]Department of pathology, King Hussein Medical Centre, Royal Medical Services, Amman, Jordan

Address for correspondence: Mohammad Obeidat, Department of Medicine, Division of Medical Oncology, Medical Oncologist, King Hussein Medical Centre, Royal Medical Services, Amman, Jordan. E-mail: mohamadobedat@gmail.com

Received: January 16, 2015
Accepted: January 26, 2015
Published: February 11, 2015

ABSTRACT

Background: Colorectal cancer (CRC) is a common malignancy in Jordan, it was the third most common cancer in male and female, it is curable if detected in early stage. **Objectives:** The objective was to study the epidemiological, clinical, and pathological features of CRC patients and analyzed the prognosis of this disease among our Jordanian patients in King Hussein medical city at Amman - Jordan. **Materials and Methods:** Retrospective cross-sectional study done at KHMC. Totally, 500 patients with proven diagnosed of CRC included in our study. A detailed clinical history was taken. And physical examination was performed. Clinicopathological data were collected and analyzed; histopathology report, management, and prognosis of these patients were also studied. **Results:** About 70% was colon cancer and 30% was rectal cancer, the mean age was 61 years, 55% were male, and 45 % were females, most common presenting symptom was abdominal pain. Only in 24 (2%) of patients diagnosed by routine screening program of CRC. In 90 patients (18%), they presented with metastatic disease, most common sites of metastasis was liver in 90%. The most common histopathology was adenocarcinoma. Adjuvant chemotherapy or chemoradiotherapy given in 320 patients, Median follow-up of patients post surgery was 45 months, during this period most of the patients developed recurrence of disease. **Conclusion:** we demonstrate advanced stage of presentation of this type of cancer, high probability of recurrence, and it significantly correlated with poor survival. Further investigation is required to fully understand pathology and prognosis of CRC.

KEY WORDS: Colorectal cancer, clinicopathological, Jordan

INTRODUCTION

Colorectal cancers (CRC) are common malignancy in Jordan; it was the third most common cancer in male and female after bronchogenic and prostate in male and lung and breast cancers in females [1]. Surgery is the only curative treatment for CRC [2]. About half of CRC patients develop metastatic disease with no curative treatment except in the minority of patients [3]. Which mean that resistance to conventional adjuvant treatment [4]. Survival can be improved with palliative chemotherapy regimens [5]. Outcomes can be improved with early diagnosis and proper management [6]. CRC is a disease of elderly with about 80% of patients aged more than 60 years [7]. And the incidence is 50 times greater in above age of 60 years olds than people younger than 40 [8]. Adjuvant chemotherapy post surgery improves survival especially in Stage II and III [9]. Delay to start adjuvant treatment affects the outcome [10]. Screening of CRC with fecal occult blood (FOBT) and colonoscopy after age of 50 years decreases CRC incidence and mortality [11]. Diagnosis of CRC was done by

endoscopic biopsy [12]. Adenocarcinoma is the most common histopathology [13]. Staging of CRC depend preoperatively on CTscan, a clinical stage in rectal cancer showed which patients benefit from neoadjuvant chemoradiotherapy [14]. Furthermore, CT scan has high sensitivity of distant metastasis, and to identify involvement of nodal disease [15]. In this retrospective study, we documented the epidemiological, clinical, and pathological features of CRC and analyzed the prognosis of this disease among our Jordanian patients in King Hussein medical city at Amman – Jordan.

MATERIALS AND METHODS

It was a retrospective cross-sectional study done at single referral oncology center in Amman - Jordan. Totally, 500 patients who diagnosed and histopathology proven CRC included in our study. Study period was 5 years between January 2009 and January 2014. All patients were referred to our oncology clinic after proven diagnosis and underwent colonoscopy, or during emergency laparotomy because of obstruction or perforation. A detailed clinical history was taken. And physical examination was performed. The following demographics and clinicopathological data were collected from the records of patients and analyzed: Age, sex of patients, presenting and duration of symptoms of disease, mode of diagnosis, colonoscopy results, site of tumor, preoperative diagnostic investigation, presence of distant metastasis prior surgery, and histopathology report which included: Location, size and grade of tumor, depth of invasion, lymph vascular invasion, perineural Invasion, lymph nodes involvement, presence of synchronous cancer, margin status. Staging of disease is based on Joint Committee of Cancer tumor, lymph node, and metastases classification. Neoadjuvant chemoradiotherapy given in rectal tumors where it indicated, details of adjuvant treatment included. Follow-up of patients consisted of laboratory tests and computed tomography (CT). Recurrence pattern and time of recurrence documented. Management of patients with CRC done according to multidisciplinary clinic guidelines, our study was approved by the ethical committee. Statistical analysis was performed using SPSS, version 19.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Among the 500 patients with confirmed CRC diagnosis by histopathology whom included in our study, 70% (350 patients) was colon cancer and 30% (150) was rectal cancer, the mean age was 61 years (range from 24 to 85 years old), 55% of patients were male and 45 % were females, most common presenting symptoms were abdominal pain in 15% of patients, bleeding per rectum in 12%, intestinal obstruction in 10%,anemic symptoms in 8%, weight loss, constipation, altered bowel motion, diarrhea, jaundice, anorexia, and tenesmus were the most common presenting symptoms in the rest of patients. Only in 24 (2%) of patients was diagnosed in routine screening program of CRC whether by FOBT or sigmoidoscopy and colonoscopy. In 8 patients, there was a history inflammatory bowel disease, mean duration of presenting symptom was 90 days (range from 1 day to 2 years. In 90 patients (18%), they presented with metastatic disease, most common sites of metastasis were live in 90%, bone and lung in 15 and 12%, respectively. Most of CRC was located in cecum in 25%, right colon in 12% left colon in 13%, sigmoid in 10% and rectal in 20%. The mean Size of tumor was 5 cm range from 1 and 20 cm. The most common histopathology was adenocarcinoma in 95%, squamous cell, Small cell, medullary carcinoma, and undifferentiated carcinoma in minority of patients. More histopathology details are shown in Table 1. Staging of disease is shown in Table 2. Neodjuvant concurrent chemoradiotherapy is indicated in lower rectal cancer, in clinically T3, T4 tumors, and node-positive disease. It was given in 38 patients complete response was noted in 5 patients, and no tumor documented in histopathology report post surgery.Adjuvant chemotherapy or chemoradiotherapy given in 320 patients, FOLFOX or 5FU +Leucovorin protocols given in nonmetastatic, FOLFIRI or IFL with or without bevacizumab in metastatic disease. Except in 25 of patients with stage them not given chemotherapy, and in 35 patients with Stage II who had no high risk features like poorly differentiated tumors, lympho or vascular invasion, bowel obstruction, inadequate lymph nodes or positive margin. Median follow-up of patients' post surgery was 45 months and done with colonoscopy and CT scan. During this period, most of the patients developed recurrence of disease whether local or distant metastasis, especially in firs three years. In about 70% who underwent curative surgery, especially in T4 tumors and most of the patients with recurrent disease died within few years of recurrence. The main sites of recurrence were lymph nodes, liver, lung, and bones. In 10% of patients developed local recurrence at site of resection.

DISCUSSION

CRC is one of the most common cancers and a leading cause of cancer-related death [16]. It is also curable if detected in early stage [17]. The present data indicate that most of CRC is elderly around age of 60 years, and some patients are young age, few patients in the second decade of life, this finding similar to worldwide [18-20]. Which indicates that CRC is disease of the elderly, it is somewhat more common in male patient 55%

Table 1: Histopathology report of CRC patients

Differentiation	%	*n*
Grade I	7.4	37
Grade II	56	280
Grade III	36.6	138
Total	100	107

CRC: Colorectal cancer

Table 2: AJCC stage staging of all patients

Stage	No. of patients
Stage I	25
Stage II	85
Stage IIIa	102
Stage IIIb	100
Stage IIIc	98
Stage IV	90
Total	500

AJCC: American Joint Committee on Cancer

versus 45% in male and female, respectively. In 30% of patients, the tumor was located in the rectum, and 25% in cecum, this distribution of tumor is similar to many other studies done in Europe and USA [21,22]. Most of our patients were symptomatic at diagnosis; most of the patients were complained of abdominal pain and bleeding. Emergency surgery due to acute surgical abdomen done in 15% and these patients had a poor prognosis and given chemotherapy even the tumor was in early stage. FOBT screening able to detect CRC at early stage thus improve clinical outcome and reduce mortality by 15% [23]. In minority of our patients, only in 2% diagnosed by screening programs, this pattern of diagnosis was differ from many countries whom patients with CRC was mostly diagnosed during screening, and diagnosed at early stages, thus carry a good prognosis [24,26]. Survival of patients with CRC related to the stage of disease at diagnosis, being excellent at early stages, with 5-year survival ≥95%, and the poor in advanced disease [27,28]. The mean duration of symptoms before diagnosis was about three months because the symptoms of CRC were non-specific and attributed to irritable bowel syndrome; these findings related that most of the tumors at diagnosis was advanced stages. In about 20% of our patients was metastatic disease at presentation, this finding was similar to many studies in other countries [29,30]. Most common site of metastasis was the liver, as expected finding because of lymphatic drainage of colon, with more lung metastasis with rectal cancer because of blood supply of rectal tumor with a systemic circulation. Most of CRC histopathology type in our patient was adenocarcinoma, it was documented in 95%, and it was the most common histopathology subtype worldwide, except in minority of patients, squamous, small cell, and undifferentiated carcinoma documented [31,33]. The mean size of the tumor at histopathology report post surgery was about 5 cm which somewhat similar to many other studies in other countries [33]. Most of the tumors in our patients were moderately to high grade that mean aggressive of this type of tumor and the need of adjuvant treatment after surgery. And only a few tumors were well-differentiated or grade 1 tumor. This finding is related partially to late presentation of patients with CRC and delay of diagnosis [34]. Like this finding, most of our patients included in this study were presented with high stage of disease, only in the minority of patients presented with stage one in about 5%. Since 1990 adjuvant chemotherapy was indicated for Stage III colon cancer and Stage II/III of rectal cancer [35,36]. Randomized clinical trials demonstrated that neodjuvant chemoradiotherapy reduces local recurrence in lower rectal cancer [37]. It was given in 38 patients of these 5 patients developed complete response at histopathology report. There is no doubt that adjuvant chemotherapy prolongs time to disease progression and overall survival when compared to best supportive care [38,39], adjuvant chemotherapy was given in most of non-metastatic CRC and palliative chemotherapy was given in also most of patients with metastatic disease. Except in the minority of patients with early stage and for poor performance status in adjuvant and metastatic settings, respectively. All patients with non-metastatic CRC were kept on regular follow-up at oncology clinic and included, carcinoembryonic antigen levels, abdominal and pelvic CT scan; about 70% of patients on regular follow up developed recurrence of disease, most common sites of recurrence were lymph nodes, liver, and lungs, which were the same common sites of metastasis at presentation. High rate of recurrence was in T4 lesion and poorly differentiated tumors. The recurrence patterns of colon cancer and rectal cancer are quite different with more lung metastasis in rectal cancer. This finding is similar to recent studies in USA [30].

CONCLUSION

We demonstrate a high prevalence of CRC among our patients, advance stage of presentation of this type of cancer, high probability of recurrence, and it significantly correlated with poor survival. Further investigation is required to fully understand pathology and prognosis of CRC.

Ethical Standards

This study was approved by Ethical Committee at Royal Medical

ACKNOWLEDGMENTS

We would like to thank nursing, radiology, and pathology stuffs in our hospital.

REFERENCES

1. Alexander J, Watanabe T, Wu TT, Rashid A, Li S, Hamilton SR. Histopathological identification of colon cancer with microsatellite instability. Am J Pathol 2001;158:527-35.
2. Benatti P, Gafà R, Barana D, Marino M, Scarselli A, Pedroni M, *et al*. Microsatellite instability and colorectal cancer prognosis. Clin Cancer Res 2005;11:8332-40.
3. Ogura Y, Bonen DK, Inohara N, Nicolae DL, Chen FF, Ramos R, *et al*. A frameshift mutation in NOD2 associated with susceptibility to Crohn's disease. Nature 2001;411:603-6.
4. Hampe J, Cuthbert A, Croucher PJ, Mirza MM, Mascheretti S, Fisher S, *et al*. Association between insertion mutation in NOD2 gene and Crohn's disease in German and British populations. Lancet 2001;357:1925-8.
5. Pistoia V, Morandi F, Wang X, Ferrone S. Soluble HLA-G: Are they clinically relevant? Semin Cancer Biol 2007;17:469-79.
6. Faure M, Long EO. KIR2DL4 (CD158d), an NK cell-activating receptor with inhibitory potential. J Immunol 2002;168:6208-14.
7. Braud V, Jones EY, McMichael A. The human major histocompatibility complex class Ib molecule HLA-E binds signal sequence-derived peptides with primary anchor residues at positions 2 and 9. Eur J Immunol 1997;27:1164-9.
8. Sanoff HK, Carpenter WR, Stürmer T, Goldberg RM, Martin CF, Fine JP, *et al*. Effect of adjuvant chemotherapy on survival of patients with Stage III colon cancer diagnosed after age 75 years. J Clin Oncol 2012;30:2624-34.
9. Sanoff HK, Carpenter WR, Martin CF, Sargent DJ, Meyerhardt JA, Stürmer T, *et al*. Comparative effectiveness of oxaliplatin vs non-oxaliplatin-containing adjuvant chemotherapy for Stage III colon cancer. J Natl Cancer Inst 2012;104:211-27.
10. Armitage P, Doll R. A two-Stage theory of carcinogenesis in relation to the age distribution of human cancer. Br J Cancer 1957;11:161-9.
11. Easton D. Breast cancer – not just whether but when? Nat Genet 2000;26:390-1.
12. Peto J, Mack TM. High constant incidence in twins and other relatives of women with breast cancer. Nat Genet 2000;26:411-4.
13. Working Group Report. International rules for multiple primary cancers (ICD-0 third edition). Eur J Cancer Prev 2005;14:307-8.
14. Levi F, Delachaux A, Junod B, Wietlisbach V. Cancer incidence in Vaud, Switzerland (1975-1977). In: Waterhouse J, Muir C, Shanmugaratnam K, Powell J, editors. Cancer Incidence in Five Continents. IARC Scientific Publications No 42. Vol. IV. Lyon: IARC; 1982. p. 546-9.
15. World Health Organization. International Classification of Diseases for

Oncology, ICD-O. Geneva: World Health Organization; 1976. p. 131.
16. World Health Organization. International Classification of Diseases for Oncology. 3rd ed. Geneva: World Health Organization; 2000. p. 240.
17. Jeong SY, Shin KH, Shin JH, Ku JL, Shin YK, Park SY, *et al*. Microsatellite instability and mutations in DNA mismatch repair genes in sporadic colorectal cancers. Dis Colon Rectum 2003;46:1069-77.
18. Jernvall P, Mäkinen MJ, Karttunen TJ, Mäkelä J, Vihko P. Microsatellite instability: Impact on cancer progression in proximal and distal colorectal cancers. Eur J Cancer 1999;35:197-201.
19. Twelves C, Wong A, Nowacki MP, Abt M, Burris H rd, Carrato A, *et al*. Capecitabine as adjuvant treatment for Stage III colon cancer. N Engl J Med 2005;352:2696-704.
20. Lembersky BC, Wieand HS, Petrelli NJ, O'Connell MJ, Colangelo LH, Smith RE, *et al*. Oral uracil and tegafur plus leucovorin compared with intravenous fluorouracil and leucovorin in Stage II and III carcinoma of the colon: Results from National Surgical Adjuvant Breast and Bowel Project Protocol C-06. J Clin Oncol 2006;24:2059-64.
21. Nakanishi R, Harada J, Tuul M, Zhao Y, Ando K, Saeki H, *et al*. Prognostic relevance of KRAS and BRAF mutations in Japanese patients with colorectal cancer. Int J Clin Oncol 2013;18:1042-8.
22. Parsons MT, Buchanan DD, Thompson B, Young JP, Spurdle AB. Correlation of tumour BRAF mutations and MLH1 methylation with germline mismatch repair (MMR) gene mutation status: A literature review assessing utility of tumour features for MMR variant classification. J Med Genet 2012;49:151-7.
23. Adebamowo CA, Adeyi O, Pyatt R, Prior TW, Chadwick RB, de la Chapelle A. Case report on hereditary non-polyposis colon cancer (HNPCC) in Nigeria. Afr J Med Med Sci 2000;29:71-3.
24. Chew MH, Yeo SA, Ng ZP, Lim KH, Koh PK, Ng KH, *et al*. Critical analysis of mucin and signet ring cell as prognostic factors in an Asian population of 2,764 sporadic colorectal cancers. Int J Colorectal Dis 2010;25:1221-9.
25. Adekunle OO, Ajao GO. Colorectal cancer in adolescent Nigerians. Scand J Gastroenterol Suppl 1986;124:183-6.
26. Shia J. Immunohistochemistry versus microsatellite instability testing for screening colorectal cancer patients at risk for hereditary nonpolyposis colorectal cancer syndrome. Part I. The utility of immunohistochemistry. J Mol Diagn 2008;10:293-300.
27. Lochhead P, Kuchiba A, Imamura Y, Liao X, Yamauchi M, Nishihara R, *et al*. Microsatellite instability and BRAF mutation testing in colorectal cancer prognostication. J Natl Cancer Inst 2013;105:1151-6.
28. Ward RL, Cheong K, Ku SL, Meagher A, O'Connor T, Hawkins NJ. Adverse prognostic effect of methylation in colorectal cancer is reversed by microsatellite instability. J Clin Oncol 2003;21:3729-36.
29. Sanchez JA, Krumroy L, Plummer S, Aung P, Merkulova A, Skacel M, *et al*. Genetic and epigenetic classifications define clinical phenotypes and determine patient outcomes in colorectal cancer. Br J Surg 2009;96:1196-204.
30. Sargent DJ, Goldberg RM, Jacobson SD, Macdonald JS, Labianca R, Haller DG, *et al*. A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. N Engl J Med 2001;345:1091-7.
31. Schrag D, Cramer LD, Bach PB, Begg CB. Age and adjuvant chemotherapy use after surgery for Stage III colon cancer. J Natl Cancer Inst 2001;93:850-7.
32. Comparison of fluorouracil with additional levamisole, higher-dose folinic acid, or both, as adjuvant chemotherapy for colorectal cancer: A randomised trial. QUASAR Collaborative Group. Lancet 2000;355:1588-96.
33. Moertel CG, Fleming TR, Macdonald JS, Haller DG, Laurie JA, Tangen CM, *et al*. Fluorouracil plus levamisole as effective adjuvant therapy after resection of Stage III colon carcinoma: a final report. Ann Intern Med 1995;122:321-6.
34. Marsoni S. Efficacy of adjuvant fluorouracil and leucovorin in Stage B2 and C colon cancer. International multicenter pooled analysis of colon cancer trials investigators. Semin Oncol 2001;28:14-9.
35. Moertel CG, Fleming TR, Macdonald JS, Haller DG, Laurie JA, Goodman PJ, *et al*. Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. N Engl J Med 1990;322:352-8.
36. Wolmark N, Colangelo L, Wieand S. National Surgical Adjuvant Breast and Bowel Project trials in colon cancer. Semin Oncol 2001;28:9-13.
37. Graham RA, Wang S, Catalano PJ, Haller DG. Postsurgical surveillance of colon cancer: Preliminary cost analysis of physician examination, carcinoembryonic antigen testing, chest x-ray, and colonoscopy. Ann Surg 1998;228:59-63.
38. Buyse M, Piedbois P. Should Dukes' B patients receive adjuvant therapy? A statistical perspective. Semin Oncol 2001;28:20-4.
39. O'Connell MJ, Mailliard JA, Kahn MJ, Macdonald JS, Haller DG, Mayer RJ, *et al*. Controlled trial of fluorouracil and low-dose leucovorin given for 6 months as postoperative adjuvant therapy for colon cancer. J Clin Oncol 1997;15:246-50.

Source of Support: Nil, Conflict of Interest: None declared.