

RESEARCH ARTICLE

Clinicopathological Features of Colon Adenocarcinoma in Qazvin, Iran: A 16 Year Study

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Abstract

Background: Colorectal cancer (CRC) was the fourth most commonly diagnosed cancer in Iran between 2000 and 2009, with adenocarcinoma (AC) as the most common histological type. Demographic, topographic and histological variables are important in the epidemiology and biology of cancer. The aim of this study was to investigate clinicopathological features of colon adenocarcinomas in Qazvin, Iran. **Materials and Methods:** With a retrospective design, patient records of two pathology wards from March 1997 to March 2013 were studied with regard to anatomical location and histological classification. A broader anatomical grouping was also used including distal vs proximal regions and right sided vs left sided tumors. Data were analyzed using T-test and chi-square test. **Results:** 118 (50.9%) male and 114 (49.1%) female patients were included in the study. Mean age was 57.3±14.7 years, with 29.2% under 50 years. There was no significant gender difference for age at diagnosis. The rectum (56%) and sigmoid colon (25%) were the most frequent anatomical locations. Proximal cases accounted for 18.6% in males and 8.8% in females (p=0.02). AC was more prevalent than other usual types in younger patients. The proportion of proximal cancer was 1.7% in first eight years of the study period vs 12.1% in the second one (p=0.005). A similar trend was also seen in right sided colon cancers (p=0.018). **Conclusions:** Young people are also at risk for the cancer with poor prognosis. Screening programs and weight loss in obese individuals can reduce incidence and complications of CRC.

Keywords: Colorectal cancer - adenocarcinoma - colonoscopy - anatomical location

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Introduction

Colorectal cancer (CRC) is the third most common diagnosed cancer in men and the second most in women (Jamal A, 2011). It constitutes about 12% of all cancers. Nevertheless, it doesn't have equal geographical distribution. High risk areas have 20 times more likelihood to develop CRC compared to low risk areas (Redstone Mark and Odze RD, 2009). Moreover, the trend of prevalence of CRC changes with time. For instance, incidence and mortality of CRC decreased significantly in the USA which is one of the high risk countries, because of early diagnosis (Jamal et al., 2011). On the other hand, rapid increase of colorectal cancer has been observed in areas that had been recognized as low risk areas previously (Hosseini et al., 2004; Khuhaprema and Srivatanakul, 2008; Safaee et al., 2012). Iran is known as low risk country for CRC (Jamal et al., 2011).

Study of Sajadi (2007) showed that this cancer is the third common cancer in men and the fourth common diagnosed cancer in women in Iran. Also, the national

cancer registry has revealed that this cancer has been the fourth most common diagnosed cancer in Iran between 2000 and 2009 (Kolahdoozan et al., 2010).

Higher incidence of this cancer in young people and positive family history in considerable proportion of the patients are two distinct features among Iranian patients who have had CRC (Mahdavinia et al., 2005; Moghimi-Dehkordi et al., 2008; Malekzadeh et al., 2009; Kolahdoozan et al., 2010).

National Cancer registry was begun from 2000 in Iran. Its results have yielded an important resource for cancer study. According to the acquired data, there is obvious difference in incidences of colorectal cancer in different parts of Iran. For example, Teheran and Northern provinces are high risk areas. There was higher incidence of CRC in Qazvin province compared to other parts, especially in women. Demographic, topographic and histological data are important in study of epidemiology and biology of cancer, but these data are not documented completely or uniformly in National Cancer registry. We aimed to conduct a long term study in Buali-sina Hospital,

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a university referral center on patients with CRC to find more complete characteristics in CRC, to compare them with similar studies.

Materials and Methods

Data was obtained from patient's records of two pathology wards which were receiving colon samples sent by endoscopy ward of the hospital. The request forms, endoscopy and pathology reports were evaluated in details. Inclusion criteria were sampling of a colorectal tumor by colonoscopy and confirmation of malignancy by pathology report. Only malignant neoplasms with glandular origin were included in the study and other types such as malignant melanoma were excluded.

Exclusion criteria were lack of data about anatomical location of the cancer, positive history of inflammatory bowel disease (IBD), presence of other histological types of neoplasm, presence or history of polyposis.

We considered four histological types for CRC: 1- adenocarcinoma (AC): usual type, including AC with or without adenoma (polyp) as precursor lesion. it was characterized by obvious gland formation and well, moderate or poorly differentiation according to the references (Redstone Mark, Odze RD ,2009); 2- mucinous AC or mucin producing AC: characterized by abundant extra cellular mucin secretion; 3-signet ring carcinoma: distinguished by presence of signet ring cells as predominant cellular morphology; and 4- undifferentiated carcinoma: characterized by epithelial differentiation without obvious gland formation or only small component of glands (less than 5%). We use this categorization, because histological types have prognostic importance (Kang et al., 2005; Makino et al., 2006; Maksimović, 2007; Song et al., 2009).

The histological reports and their pertinent slides were reviewed by a pathologist for histological classification.

Details of endoscopy reports were reviewed for determination of anatomical location of the cancer. Anatomical location of the cancer was determined directly by physician who had been performed endoscopy or was deduced from data about distance of the tumor from anal verge. We compared these distances with reference Table for tumor site determination (SEER Training Website). We considered few cases of anal canal tumor as rectal cancer and few cases of recto sigmoid junction tumor as sigmoid cancer.

In addition to anatomical location (rectum, sigmoid, descending colon, splenic flexure, transverse colon, liver flexure, ascending colon, and cecum), we also use more broad anatomical grouping ;including distal region (rectum, sigmoid, descending colon, and splenic flexure) vs proximal region (transverse colon, liver flexure, ascending colon, and cecum) and right sided tumors (including transverse colon, liver flexure, ascending colon, and cecum) vs left sided tumors (including sigmoid, descending colon, and splenic flexure).

Our study was included records of 16 years; from 21th March 1997 to 21th March 2013. For evaluation of time trends we divided this time period to two eight years sequential intervals.

Data were presented as frequency and mean plus or minus standard deviation were appropriate. Chi square test and independent samples T-test were performed to examine relationship between different categorical and numerical variables. p-values less than 0.05 were considered as statistically significant.

Results

Two hundred thirty two cases were included in present study .14 cases were excluded from the study because inadequate information, presence of IBD, involvement by other histological types, and presence of polyposis.

118 patients were male (50.9%) and 114 were female (49.1%). The youngest and oldest patients were 20 and 90 years old, respectively .Mean age was 57.3±14.7 years and median was 58 years. The most prevalent age decade was 50-59 years which comprised 24.1% of cases. 12% and 29.2% of patients were under forty and fifty years old respectively. 25.2% and 5.2% of patients were higher than 70 and 80 years old respectively.

There was no significant difference between males and females in age at diagnosis; males mean age was 57.7±14.5 years vs females which was 56.6±15.0 (p>0.05). Number of patients younger than 40 was equal in males and females. Age distribution was shown in Figure 1. Indications for colonoscopy are shown in Figure 2.

There was not consistency in description of tumor by different clinicians, but generally the tumors had been described as large fungating mass with severe intestinal lumen obstruction approximately in 90% of cases, or ulcerative -infiltrative lesions in the remainders.

Rectum and sigmoid were the most frequent locations

Table 1. Histological Subtypes and Anatomical Subsites of Colorectal Adenocarcinoma

Anatomic subsites	Adenocarinoma, Usual type		Mucinous carcinoma		Undifferentiated carcinoma		Signet ring carcinoma		Total	
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Rectum	55 (82.1)	55 (87.3)	10(14.9)	4(6.3)	2(3.0)	2(3.2)	0	2(3.2)	67(56.8)	63(55.3)
Sigmoid	22(100)	30 (83.3)	0	3(8.3)	0	3(8.3)	0	0	22(18.6)	36(31.6)
Descending Colon	5(100)	2(100)	0	0	0	0	0	0	5(4.2)	2(1.8)
Splenic flexure	2(100)	3(100)	0	0	0	0	0	0	2(1.7)	3(2.3)
Transverse Colon	5(100)	2(100)	0	0	0	0	0	0	5(4.2)	2(1.8)
Liver flexure	4(100)	2(100)	0	0	0	0	0	0	4(3.4)	2(1.8)
Ascending Colon	4(100)	4(100)	0	0	0	0	0	0	4(3.4)	4(3.5)
Cecum	6 (66.7)	2(100)	2(22.2)	0	1(11.1)	0	0	0	9(7.6)	2(1.8)
Total	103 (87.3)	100 (87.7)	12(10.2)	7(6.1)	3(2.5)	5(4.4)	0	2(1.8)	118(100)	114(100)

seen in right sided colon cancers ($p=0.018$).

Discussion

Mean age of our patients was slightly lower than study of Safaee performed on CRC in Iran (Safaee et al., 2012), but higher than other studies conducted in Tehran city (Fazeli et al., 2007; Omranipour et al., 2012). These minor variations are acceptable considering different material and methods of the studies. Mean age of the patients in this study was close to some related studies in Asia (Rashid et al., 2009; Shaikh et al., 2009).

Proportions of under forty and fifty years old patients in current study were close to other studies in Iran (Ansari et al., 2006; Safaee et al., 2012), but were in contrast with the studies performed in high risk countries. A study on CRC in USA showed 50% the patients were older than 70 and 24.3% were older than 80 (Stewart et al., 2006).

We didn't observe considerable difference between male/female proportions in CRC prevalence. Male/female ratio in our study was close to similar studies in Iran (Fazeli et al., 2007; Omranipour et al., 2012), but was lower than that has reported by Safaee (Safaee et al., 2012), a study based on national CRC registration in whole Iran. Male predominance has also been reported by other studies in Asia (Rashid et al., 2009; Shaikh et al., 2009).

Rectal cancer comprised 56% of the patients and the remaining was colon cancer in present study but the proportions were 21.9% and 78.9% respectively in study of Safaee (2012). This difference may be probably originated from different interpretation of not specified topographic codes in cancer registration system. Colon NOS topographic code doesn't always mean non-rectal cancer and may be used at the time of cancer registration when there isn't any information about anatomic location. A study on CRC in Japan showed that these nonspecific codes have been used in about 20% of CRC cases (Toyoda et al., 2009). Another reason for this notable difference is method of the present study. Colon cancers may be firstly diagnosed and register as colon cancer by diagnostic methods other than colonoscopy such as surgery or imaging studies, particularly cancers of right side of colon. Such types of cancers were not included in our study.

Proximal and distal colon cancer constituted 13.7% and 80.3% of patients in present study, respectively. It is comparable to study of Fazeli MS (2007).

AC constituted 97.9% of CRC in our study. This high percentage was similar to other studies (Fazeli et al., 2007; Haghdoost et al., 2011; Stewart et al., 2006), but it can be mentioned that colonoscopy is not ideal method for diagnosis of all CRC. In present study, proportions of other types of CRC; mucinous and signet ring carcinoma were comparable to other studies (Song et al., 2009; Safaee et al., 2012). Percentage of undifferentiated carcinoma in our study was higher than that reported by other studies (Stewart et al., 2006; Redstone and Odze, 2009). Immunohistochemistry (IHC) study was not performed in present study and sizes of the biopsied samples were small. Therefore, diagnosis of other rare forms of carcinomas such as poorly differentiated adeno-squamous carcinoma or medullary carcinoma was not possible. Undifferentiated

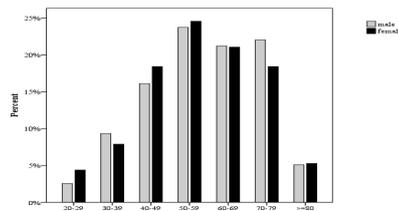


Figure 1. Age Distribution of Colorectal Adenocarcinoma in Male and Female

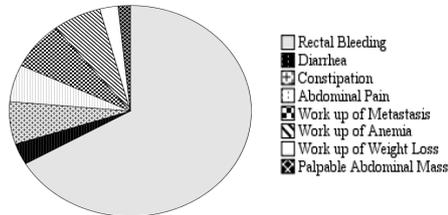


Figure 2. Indications for Colonoscopy in Patients with Colorectal Adenocarcinoma

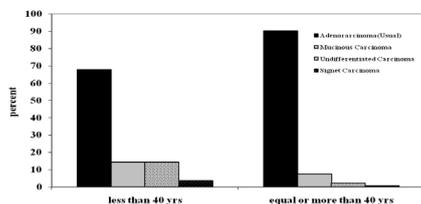


Figure 3. Comparison of Adenocarcinoma Subtypes Distribution with 40yrs Cut off

of the tumor and constituted 56% and 25% of cases respectively. Rectal cancer had been reported in 130 cases and non rectal cancer had been seen in 102 cases; included 32 cases in right side and 70 cases in left side colon (Table 1).

There was not statistically significant difference between anatomical locations of the cancer and age or gender and or histological types ($p>0.05$).

There was a significant difference in sex and anatomical location of the cancer, if it was grouped as proximal or distal part. Proximal cases was 18.6% in males, whereas only 8.8% in females ($p=0.02$).

AC, the usual type of the cancer was most frequent type (203 cases, 87.5%). Other histological type were mucinous (19 cases, 8.5%), undifferentiated carcinoma (8 cases, 3.4%) and signet ring carcinoma (2 cases, 0.9%). There was no significant difference between sex and histological type ($p>0.05$); but there was statistically significant relationship between histological type and age with forty years cut off point ($p=0.001$).

The proportion of AC, usual type was 67.9% and 90.2% in patients under and higher than forty, respectively (Figure 3).

There was not statistically significant relationship between anatomical location of the cancer and its histological types.

The number of cases has significantly increased in the second 8 years (34.9% vs 65.1%). Mean age of patient has slightly increased too (54 year vs 58 year, $p=0.049$). No gender or histological trends were seen. An anatomical trend was seen in proximal- distal grouping. The proportion of proximal cancer was 1.7% in first eight years vs 12.1% in the second ($p=0.005$). A trend was also

carcinoma may be also seen concomitant with other carcinomas. Its presence in a tumor increases probability that the tumor contains DNA mismatch repair deficiency. It is clinically important (Redstone Mark et al 2009).

There was statistically significant relationship between patients' age and histological type of the cancer. AC other than usual type was more prevalent in younger patients. It is comparable to other studies (Fazeli et al., 2007; Redstone and Odze, 2009; Song et al., 2009).

Studies performed in western countries (Redstone and Odze, 2009) and Japan (Toyoda et al., 2009) showed that the trend of CRC is toward right side of colon, but this trend has not been seen in some studies in Iran (Hosseini et al., 2004; Omranipour et al., 2012). However, the trend was seen in present study.

Mean age of our patients was higher in the second 8 years of present study. It is in contrast with a study performed in Iran (Hosseini et al., 2004).

Unfortunately, we couldn't evaluate CRC risk factors because of retrospective nature of the study. However, by comparing our data with other studies, we are able to guess importance of some of known risk factors. Known risk factors of CRC are smoking, physical inactivity, overweight, obesity, alcohol use, and consumption of red or processed meat (Jamal et al., 2011). Relationship between obesity, metabolic syndrome (Kaneko et al., 2010; Forootan et al., 2012) and even waist circumference (Kaneko et al., 2010) with CRC have been suggested.

Incidence of CRC in Qazvin province is higher than some parts of Iran, particularly in women. This is concordant with high prevalence of metabolic syndrome and diabetes in this province (Mirzazadeh et al., 2009; Esmailzadehha et al., 2013). It has showed that one out of 5 adults in Qazvin city suffer from diabetes mellitus or impaired glucose tolerance test (Larijani et al., 2003).

A meta- analysis about obesity showed significant variations in prevalence of obesity in different cities or provinces of Iran. The highest prevalence of obesity in adult women has been reported in areas such as Tehran, Gillan, Mazandaran and Semnan provinces, while the lowest prevalence has been observed in areas like Sistan& baluchestan and Hormozghan Provinces (Mirzazadeh et al., 2009). These variations in prevalence of obesity are comparable to variations in prevalence of CRC in these areas, as reported by Mahaki (Mahaki B, 2011). Significantly higher prevalence of obesity in women of Qazvin city, as reported by Mirzazadeh may explain higher prevalence of CRC in women of present study which is in contrast with other studies (Rashid et al., 2009; Jemal et al., 2011; Safaee et al., 2012).

Smoking is another risk factor for CRC. Prevalence of smoking is low among Iranian women. We would expect that this fact would increase M/F ratio in our study. However, we didn't observe this finding. A study in Kerman province which has high rate of tobacco and opioids consumption showed lower prevalence of CRC in comparison with other provinces. This paradox may be explained by low prevalence of diabetes and obesity in this province (Haghdoost et al., 2011). These finding suggest that obesity is probably more important than other risk factors for development of CRC.

We had some limitations in present study. Our study was retrospective in nature and this matter may reduce reliability of some findings which were obtained based on information of pathology request form. We couldn't evaluate frequency CRC risk factors or familial forms in our patients. With didn't do IHC study. So, undifferentiated carcinomas in our study were probably a mixture of different poorly differentiated carcinomas. Nevertheless, current study found some valuable information about anatomical locations and histological classification of CRC.

In conclusion, present study showed that despite higher prevalent of CRC among old patients, young people are also at risk for the cancer. Unfortunately, histological types with poor prognosis were more prevalent among them. Colonoscopy indications and description of the tumors on endoscopy reports showed that most cancers have been diagnosed at late stage of the disease. This is an important determinant of lower survival of CRC among Iranian people in comparison with countries with advanced health care system or community based screening program (Moradi et al., 2009). Present study showed that CRC mostly is located in rectum and sigmoid. Therefore, it can be readily diagnosed by rectosigmoidoscopy. It seems that obesity is a major risk factor for CRC. Screening programs and weight loss in obese individuals can reduce incidence and complication of CRC.

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