

RESEARCH COMMUNICATION

Anatomical Distribution of Colorectal Carcinoma in Iran: A Retrospective 15-yr Study to Evaluate Rightward Shift

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Abstract

Background: Although more than two third of colorectal cancers are localized on the left side, recent studies suggest a right ward shift in anatomical distribution with increase in proximal colon cancers. The aim of the present study was to determine the anatomical distribution of colorectal cancer in a referral center over a 15 year period. **Method:** Records of patients who underwent colectomy in the Cancer Institute of Iran from 1994 to 2009 were retrieved. Data including anatomical localization, year of diagnosis, patient age and gender, tumor histology and differentiation, and disease stage were extracted. Tumors located from the cecum to the distal transverse colon were classified as right side and those occurring from the splenic flexure to the descending colon as left-sided. Cancer of rectum and recto-sigmoid junction were considered as rectal cancers. **Results:** A total of 442 patients including 220 (49/8%) men and 222 (50/2%) women with mean age 53 were included. Most patients were in stage II & III (47.1% and 33% respectively). There were 157 (35.5 %) colon cancers and 285 (64.5%) rectal cancers. 43.3% of the colon cancers were right sided and 56.7% were left sided. There was no statistically significant increase in right sided cancer during the period of the study. There were no significant differences in age at diagnosis, gender, grade and stage of tumor between the right and the left sided cancers. **Conclusion:** No proximal shift over time was identified in our study.

Keywords: Colorectal cancer - subsite - lack of rightward shift - Iran

Asian Pacific J Cancer Prev, 13, 279-282

Introduction

Colorectal cancer remains one of the most common cancer-related morbidity and mortality in the world. Although left sided colon cancer are still more common, several studies were done about changes in anatomical distribution of this cancer in recent years. Proximal right ward shift was proven in some of these studies (Sariego et al., 1992; Cady et al., 1993; Nazarian et al., 1993; Cheng et al., 2001) and was not observed in others (Lanier et al., 1973; Vobecky et al., 1984; Crerand et al., 1991). Some believe that the rightward shift result from an absolute decrease in left sided cancer rather than true increase in incidence rate of right-sided colorectal cancer (Saltzstein et al., 1998; Cress et al., 2000; Rabeneck et al., 2003). The aim of this study was to evaluate the time trend of anatomical distribution of colorectal cancer in our patient in Cancer Institute of Tehran University of Medical Science over a 15- years period.

Materials and Methods

Data of all colorectal cancers that had been undergone colectomy in cancer Institute of Iran from 1994 to 2009 were retrospectively reviewed. The informative collected included date of colectomy, patient demographics (gender, age), tumor histology and differentiation, tumor

location and stage (TNM) of cases. All patients were referred after endoscopic biopsy and had proven diagnosis of colorectal cancer.

There were no screening-detected colorectal cancers. Only patient with histologic diagnosis of adenocarcinoma and mucinous or signet ring carcinoma were included and cases of lymphoma and melanoma and carcinoid and sarcoma were excluded. Patient with more than one site of colorectal cancers with synchronous two or more tumors in different locations were excluded. All patients who were inoperable and who had not been undergone resection and only surgeons' note mention the anatomical site of tumor were excluded.

In order to better definition of location we determine the location by both surgeon's note and pathologist note of tumor site. Cancer locating in cecum, ascending colon hepatic flexure, transverse colon were classified as right sided colorectal cancer and cancer in splenic flexure and descending colon and sigmoid were classified as left sided colorectal cancer. Cancer of rectum and rectosigmoid junction was classified separately as rectal cancers. TNM systems were used for tumors staging. Age at diagnosis was subdivided in four classes: 14-40, 41-50, 51-60 and 61-88.

Anatomical location of the cancers was determined for each year during the 15 year period and logistic regression analysis was done for determining the change of

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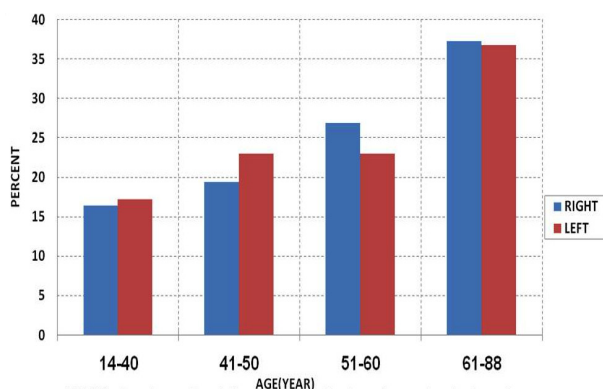


Figure 1. Age by Anatomic Location in Patients Undergoing Colectomy in the Cancer Institute of Iran 1994-2008

anatomical location of the tumor. The association between gender, age and stage, grade and anatomical distribution was assessed by, chi squared and / or Fisher exact tests.

All data were recorded in a standard data form and the statistical analysis were done by the Statistical Package for the Social Sciences for windows version 11.5 (Spss Inc , Chicago, IL). Significance was set at $P < 0.05$. This study was approved by the research ethics committee of the university to which the performing institution is affiliated.

Results

During the study period, a total of 442 cases of primary colorectal cancers were identified. There were 220 (46.8%) males and 222 (50.2%) females with mean ages of 53 years (range 14-88). Stage II was most common representing 47.7% of all cases. Stage III cancers accounted for 33% of the cases, whereas 7.7% presented with stage I, and another 2% were stage 0. 3.6% were metastatic at the time of initial diagnosis. Most of tumors were well and moderately differentiated (32.3% and 48.7%). Seven percent were poorly differentiated and 0.9% were undifferentiated. The most primary site of tumors was in rectum (288 cases) versus colon (157 cases).

There were 68 cases of right sided (43.3%) and 89 cases (56.7%) of left sided colon cancers. In the group of patients with right sided cancers mean age was 55.4years. Forty-four patients (64.7%) were males and 24 patients (35.5%) were females. In the group of left sided colon cancers mean age was 54.5 years, there were 39 (43.8%) males and 50 (56.2%) females. There was no statistical difference between the age at diagnosis in the right and left sided cancers ($p=0.4$) (Figure 1). There were modest differences in anatomical distribution between the sexes with a slightly higher proportion of females diagnosed with left sided colon cancers ($p=0.009$).

Stage 0, I, II, III, IV were seen in 2.9%, 1.5%, 60.3%, 26.5%, 8.8% of patients in right sided colon cancers respectively and in 2.2%, 6.7%, 51.7%, 22.5%, 16.9% of patients in left sided colon cancer respectively. Analysis revealed no statistically significant association between pathologic stages and anatomical distribution of colorectal cancer during 15 years period ($p=0.2$) (Figure 2).

Most of left sided colon cancers were well and moderate differentiated (43.8% and 51.3%), the same as

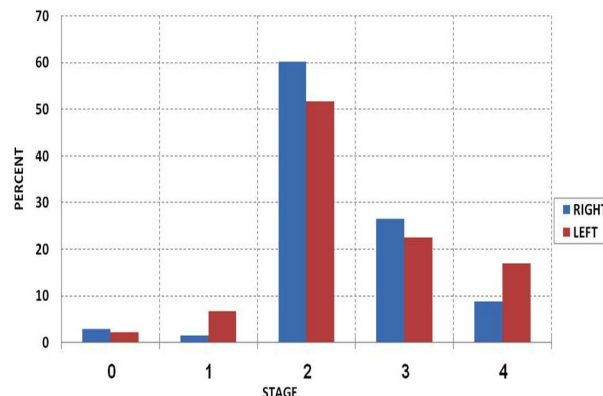


Figure 2. Staging of Colon Carcinoma by Anatomic Location in Patients Undergoing Colectomy in the Cancer Institute of Iran 1994-2008

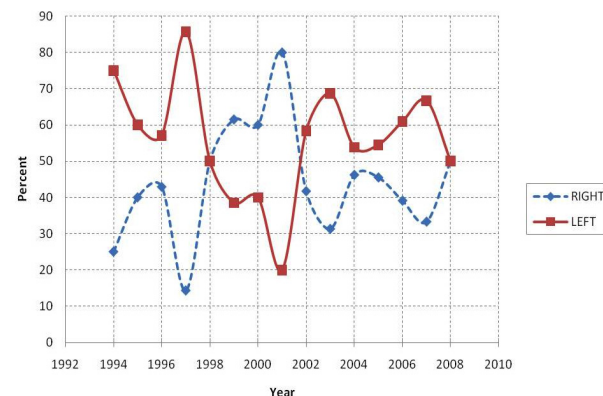


Figure 3. Changes in the Anatomical Distribution of Colon Cancer among Patients Undergoing Colectomy in the Cancer Institute of Iran 1994-2008

right sided colon cancers (33.3% and 56.7%) and there was no statistical difference in grade between right and left sided colon cancers.

A total of 15.38% of all colorectal cancers were right sided over the 15 years study period. There was no significant trends in subsite of colon cancer from left to right side ($p=0.77$). Figure 3 demonstrates the ratio of right to left colon cancers for the patients who were operated over the 15 years. There was no statistically significant difference between the times periods in the right sided colon cancers patients.

Discussion

Change in anatomical distribution of colorectal cancer and rightward shift was confirmed in the statistical data from various countries in recent decades (Kee et al., 1992; Devesa et al, 1993; Obrand et al,1998; Wakefield et al., 1998; Cucino et al., 2002; Larsen et al., 2010). This shift may have an important implication in the screening program and current practice and diagnostic methods used for evaluating high risk individual and symptomatic patients. While some others studies (Jass, 1991; Griffin et al., 1991; Sharma et al., 2000; Gomes et al., 2004) had not confirmed rightward shift, we purposed to determined the pattern of subsite distribution of colorectal cancer over a 15-year period in a referral cancer center in Iran.

In this study we were unable to establish a significant increase in proportions of right sided cancers. The

incidence of colorectal cancer in various subsite was increased in the period of study but there was no proximal or rightward shift. There were no significant relationship between age at diagnosis, tumors grade and stage and anatomic distribution of colorectal cancer. Only there was a slight rightward shift in females in this study.

This controversy may be partially due to lack of agreement on the most appropriate division of the colorectum into anatomical subsite (Nelson, 1998). Right colon was considered the part of colon extending from cecum to the splenic flexure in our study and the part of colon extending from cecum to the descending colon in the several studies which confirmed proximal shift.

Tumours located at the splenic flexure were defined as right sided colorectal cancers in some studies (Cucino et al., 2002; Gomes et al., 2004; Ponz de leon, 2004; Wu et al., 2006; Efremidou et al., 2008; Toyoda et al., 2008; Larsen et al., 2010), and left sided in others (Rabeneck et al., 2003; Gupta et al., 2005). While some authors suggested proximal colon included all subsite above the sigmoid (Cress et al., 2000). Some believe that another important reason of these conflicting results is studying small populations over short periods of time.

The data of our colorectal patients was not accessible before 1994, so we have to select a 15-years period of time, but larger studies over a longer period of time were unable to show a definite increase of right sided tumours. Studies of Crerand et al. (1991) evaluating the anatomical distribution of colorectal cancer in 1553 Irish patients over a 30 years period, Lanier et al (1973) over a 25 year period and Vobecky et al. (1984) over 13 year period all showed a relatively stable rate of proximal lesions. Odigie et al. (2009) studied the clinicopathologic characteristic of colorectal cancer in the Guinea Savannal region between 1981-2005, they found no shift in distribution subsite in (1981-1990) and (1991-2005). Gomez et al. (2004) found no evidence of a shift towards proximal colon by studying of 763 patients during one decade in a district general hospital. Parkash. (1974) in a study of 60000 autopsies carried out between 1928 and 1972 showed an increase of colorectal cancer in all segments of large bowel. Similarly in 2004 Pons de Leon et al from North Italy showed an increase of tumour incidence in all colonic segments more than a shift to the right colon.

The only two published studies (Jalali, 2002; Hosseini, 2004) about shift in colorectal cancer in Iranian populations failed to show a left to right shift in Iran. Hosseini et al (2004) found no change in anatomic distribution of colorectal cancer comparing two period of (1970-1980) and (1990-2000) in Shiraz in Iran. Jalalis studied anatomic distribution of colorectal cancer in some university hospital in Tehran. The right colon accounted for 27% of tumours in the period 1990-2000.

There was an increase incidence of left sided colon cancer over 15 years in our study but some authors (Saltzstein et al., 1998; Cress et al., 2000; Rabeneck et al., 2003) confirmed that proximal migration of colorectal cancer overtime is not attributed to a true increase in incidence of right colorectal cancer and it is explained by a decrease in the incidence of distal colorectal cancer coupled with the aging of the population.

Cress et al. (2000) showed an overall decline in all stages of colorectal in California especially for tumours in the rectum and sigmoid colon. Gupta et al. (2005) in a study of 889 colorectal cancer in 1980-1999 showed a 40% reduction in left sided cancer but the incidence of right colon cancers remained unchanged, only the proportion of right sided cancers increased from 46% to 58%. In a study by Mensink et al. (2002) the proportion of proximal tumors had increased from 25 to 37 percent during 15 years. Some studies (Crerand et al,1991; Sharma et al, 2000) have shown that proximal cancer were more often observed in female but others (Hayne et al., 2001; Cucino et al., 2002; Gomes et al., 2004) have not confirmed this association.

In our study most of right sided colon cancer patients were male but the proportion of the female with right sided cancer was increased during the period of the study. In the study of Fazeli (2007) on colorectal cancer patients in Emam Khomeini complex including Cancer Institute males constituted the majority of patients with proximal tumors (62.5%). There was no significant difference in gender between right and left sided cancers in our study. Although some studies (Lichtman et al., 1994; Rabeneck et al.,2003) have suggested that right sided colon cancer are diagnosed in the older age groups compared with left sided colorectal cancers but our study and others (Gomes et al., 2004). Wu et al. (2006) revealed higher incidence of proximal cancer among white males and females in the low-poverty countries relative to the high-poverty countries.

Most of our patients were from low socioeconomic class and these can be one of our studies limitations, but the main limitation of our study is its small sample size. The data of colorectal cancers included a statistical number of colorectal cancer cases without subsite information so we had to included only patients who had been undergone colectomy to precise our subsite information. Another limitation of our study is that Cancer Institute is a referral center, so patients with distal cancers especially low lying rectal cancer were referred more often than proximal cancers and considering this bias we had to separate rectal cancers from left sided colorectal cancers in statistical analysis.

Access to screening modalities may influence the relative prevalence of proximal and distal cancers. There were no screen detected colorectal cancer in our patients so the higher proportion of distal cancers in our study may be explained by their presentation by rectorrhagia, tenesmus and change of bowel habit which made patients underwent diagnostic evaluation. Although evaluation of shift in our country needs data from a population based cancer registry in the future, the present limited data did not provide any evidence for a rightward shift in our colorectal cancer patients.

Acknowledgements

This research has been supported by Tehran University of Medical Sciences & Health Services grant 87-02-51-7375. The authors declare that they have no competing interests.

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