RESEARCH COMMUNICATION

Four years Incidence Rate of Colorectal Cancer in Iran: A Survey of National Cancer Registry Data - Implications for Screening

Azadeh Safaee[1], Seyed Reza Fatemi[1], Sara Ashtari[1], Mohsen Vahedi[2], Bijan Moghimi-Dehkordi[1]*, Mohammad Reza Zali[1]

Abstract

Introduction: Design and implementation of screening programs in each country must be based on epidemiological data. Despite the relatively high incidence of CRC, there is no nationwide comprehensive program for screening in Iran. This study was designed to investigate national CRC data and help to determine guidelines for screening. Methods: Incidence data used in this study were obtained from Iranian annual of National Cancer Registration report. Age standardized rates (ASR)were calculated using world standard population and were categorized by age, sex, anatomic subsite and morphology of tumor. Data were analyzed using SPSS.V.13 and Open Source Epidemiologic Statistics for Public Health software (OpenEpi v.2.3.1). Results: A quarter of cases were less than 50 years of age. The majority of tumors were detected in the colon. The overall ASR in the four years period was 38.0 per 100000 and was higher for men compared women (P<0.05). Incidence rate of colorectal cancer increased with age. Conclusion: Results of present study indicated that incidence of colorectal cancer is relatively high in Iran. Incidence of CRC in people under 50 years and in rectum were reported higher than other countries that related etiologic factors should be investigate in further studies. According to the increasing of ASR after age 50 years, it seems that onset of screening at age 50 would be appropriate.

Keywords: Colorectal cancer - age standardized rate - anatomic subsite - epidemiology - Iran

Asian Pacific J Cancer Prev, **13**, 2695-2698

Introduction

Colorectal cancer (CRC) is one of the most common cancers (Azadeh et al., 2008; Haggar & Boushey, 2009) accounting for one million new cases each year and 500,000 deaths annually worldwide (Boyle & Leon, 2002). The incidence of CRC is high in North America, Australia and New Zealand, Europe and Japan and low in South America, Asia and a big part of Africa (Faivre et al., 2002).However many Asian countries, particularly in the developed or more westernized nations, have also experienced increasing incidence rates similar to other developed nations (Yee et al., 2009).

Screening is a strategy involves the detection of precancerous polyps and cancers in asymptomatic individuals can prevent the subsequent development of CRC(Jackson et al., 2006; Chong et al., 2009). Studies showed through the use of screening that at least 60% of death from CRC could be prevented (Jackson et al., 2006; Pahlavan & Kanthan, 2006). Reports indicated that the implementation of screening program of CRC in United States has decreased the mortality rate (Chong et al., 2009).Current guidelines recommend screening beginning at age of 50 for average-risk persons and at an earlier age for persons at higher risk (Jackson et al., 2006; Rim et al., 2009), but design and implementation of screening programs in each country will largely depend on basic epidemiological information including; evaluating the magnitude of the problem, identifying average and high risk populations, determination of the most common site of tumor and distribution of age at diagnosis (Rozen et al., 2012).

Recent studies have shown that there is a rapid increase in the incidence of CRC cancer in Iran (Azadeh et al., 2008; Moghimi et al., 2008). According to Iranian annual of National Cancer Registration report, CRC is the fourth most common cancer after skin, breast and gastric cancer. But despite the relatively high incidence of CRC, there is no nationwide comprehensive program for screening in Iran. Only in recent years a pilot screening has been performed on individuals at high risk of familial CRC by the Research Institute for Gastroenterology and Liver Disease, Shahid Beheshti University of Medical Science (Fatemi et al., 2010).

[1]Gastroenterology and Liver Diseases Research Center, Shahid Beheshti University of Medical Science, [2]Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Science, Tehran, Iran
**For correspondence: b_moghimi_de@yahoo.com*

For this reason, this study was designed to investigate national CRC data and help to determining guidelines for screening and identifying strategies for reduction of burden of CRC in Iran.

Materials and Methods

Incidence data used in this study, was derived from Iranian annual of National Cancer Registration report from 2005 to 2009 (Islamic repulic of Iran. Ministry of Health and Medical Education. Center for Disease Control & prevention. Noncommunicable Deputy. Cancer Office, 2008-2009).These patients have been diagnosed by more than 750 private or public pathology centers from the through out of the country and have been reported to Iranian National Cancer Registration System (INCRS). INCRS have covered approximately 89% of the Iran population over the 4 years period. The population denominator data for calculating incidence rates were extracted from the 2006 Iran census. Age Standardized Rates (ASR) were calculated using world standard population (Rozen et al., 2012) and were categorized by age, sex, anatomic subsite and morphology of tumor. Age was stratified into four groups: <40, 40-50, 50-60 and >60 years.

Anatomic subsite was categorized as colon (C18.0-18.9), rectosigmoid junction (C19.9), rectum (C20.9), anus and anal canal (C21.0-21.2, 21.8) according to International Classification of Disease for Oncology (ICD-O-3) (Fritz et al., 2000). The colon subsite was further divided into cecum (C18.0), appendix (C18.1), ascending colon (C18.2), hepatic flexure of colon (C18.3), transverse colon (C18.4), splenic flexure of colon (C18.5),descending colon (C18.6), sigmoid colon (C18.7), overlapping lesion of colon (C18.8) and colon, not otherwise specified (C18.9).The anus and anal canal subsite included anus, not otherwise specified (C21.0), anal canal (C21.1), cloacogenic zone (C21.2) and overlapping lesion of rectum, anus and anal canal (C21.8). CRC was morphologically categorized into the following groups: adenocarcinoma, mucin & mucin producing, carcinoma, lymphoma and other morphology type.

Statistical Analysis

Incidence rates were age-adjusted using the direct method and 95% confidence intervals were estimated using the method described by keyfitz(Keyfitz, 1966). Measuring disparities in rates of cancer helps to better understanding of excess burden in specific subpopulation. For this aim, we chose rate ratio (RR) and rate difference (RD). The RR is a relative measure and is calculated as the ratio of two ASRs. The RD is an absolute measure and is defined as the difference between two ASRs. Cancer cases with unknown sex or age were excluded from all analyses. Data were analyzed using SPSS.V.13 and Open Source Epidemiologic Statistics for Public Health software (OpenEpi v.2.3.1). All tests were two sided, with statistical significance attributes to $P<0.05$.

Results

The analysis included all 19, 617 CRC patients who were registered during 2005-2009. The male to female sex ratio was 1.3:1. The overall mean age at diagnosis was 58.9 ± 15.4 years. 56% of patients were male and more than a quarter of them were less than 50 years of age. There was a significant difference in the age at diagnosis between the genders (male 59.6 ± 15.7 years vs. female 58.1 ± 15.1 years, $P<0.0001$).

The adenocarcinoma was the most common morphology type and the majority of tumors were detected in the colon. There was no significant difference in the age at diagnosis between anatomic subsite groups ($P>0.05$). The overall ASR in the four years period was 38.0 per 100,000 and was higher for men compared women (Table

Table 1. Age Standardized Rate by Sex, Age, Anatomic Subsite and Morphology

Characteristics	N (%)	ASR (CI 95%)
Overall	19,617 (100)	38.00 (37.47-38.53)
Sex:		
Male	10,991 (56.0)	39.96 (39.19-40.72)
Female	8,626 (44.0)	36.16 (35.39-36.93)
Age:		
<40	2,152(11.0)	2.75 (02.63-02.87)
40-50	3,027(15.4)	5.51 (05.30-05.72)
50-60	4,309(22.0)	10.22 (09.92-10.52)
>60	9,676(49.3)	19.51 (19.12-19.90)
Unknown	453(02.3)	-
Anatomic subsite:		
Colon	12,153 (62.0)	23.55 (23.13-23.97)
Rectosigmoid junction	2,755 (14.0)	5.37 (05.17-05.57)
Rectum	4,143 (21.1)	7.97 (07.73-08.21)
Anus & anal canal	566 (02.9)	1.10 (01.01-01.19)
Morphology:		
Adenocarcinoma	16,318 (83.2)	31.85 (31.36- 32.34)
Mucin & mucin-producing	2,049 (10.4)	3.80 (03.63-03.97)
Carcinoma	574 (02.9)	25.34 (23.25-27.43)
Lymphoma	195 (01.0)	0.35 (00.30-00.40)
Other morphology type	481 (02.5)	0.88 (00.80-00.96)

Table 2. Age Standardized Rate, Rate Ratio and Rate Difference According to Sex

Age	Men		Women		Men: Women (CI 95%)	
	N (%)	ASR (CI 95%)	N (%)	ASR (CI 95%)	Rate ratio	Rate difference
<40	1,178 (10.7)	2.91 (02.74-03.08)	974 (11.3)	2.58 (02.42-02.74)	1.13	0.33
40-50	1,625 (14.8)	5.77 (05.49-06.05)	1,402 (16.3)	5.23 (04.96-05.50)	1.10	0.54
50-60	2,216 (20.2)	11.26 (10.77-11.75)	2,093 (24.3)	9.32 (08.92-09.72)	1.21	1.94
>60	5,695 (51.8)	20.02 (19.50-20.74)	3,981 (46.2)	19.03 (18.44-19.62)	1.05	0.99
Unknown	277 (02.5)	-	176 (02.0)	-	-	-
Overall	10,991 (56.0)	39.96 (39.21-40.71)	8,626 (44.0)	36.16 (35.40-36.92)	1.10	3.80

1). Also ASR was estimated 8.26 (CI95%: 8.04-8.48) for individuals aged <50 years.

As seen in Table 2, incidence rate of CRC increased with age and highest rates were observed in the oldest age groups. The most difference in rates by sex was among individual aged 50-60 years and RR was greater in this age group.

Discussion

Findings of current study presented the useful information on CRC in subgroups of population. This information can provide a better picture of the disease in subgroups. Results showed that a relatively high incidence of CRC in Iran. About 25% of patients were age below 50 years and men had higher incidence rate than women. CRC tumors tended to occur more frequently in the colon than the other site.

In this study, the overall ASR in the four years period was estimated 38.0 per 100000and 39.96 and 36.16 per 100000 in male and female respectively, that is considered as relatively high rate compared to other Asian countries. The 5-years ASR was reported 5.8 and 5.3 per 100000 in male and female in Thailand(Suwanrungruang et al., 2006). Chong et al. (Rim et al., 2009) reported that the 5-years ASR (2001-2005) in Brunei Darussalam was 16.87 per 100000. Another study in the United States showed that the ASR was 51.5 per 100000 in the 5 years period (Rim et al., 2009).

Similar to other studies (Jiang et al., 2009; Rim et al., 2009; Rozen et al., 2012), the sex ratio of CRC in men was higher than women. In this study more than a quarter of CRC patients were less than 50 years of age that indicated that a younger age distribution compared to Western reports. In a study conducted by Rim et al. (Rim et al., 2009) only 8% of patients had less than 50 years of age. Another study in china has reported a similar age distribution (Jiang et al., 2009).The age distribution of CRC in Iran may be explained as follow: Iran has a young population and about 80% of its people are less than 50 years of age. On the other hand, etiology of CRC in Iran may be different with other countries and genetic factors maybe play an important role in the development of CRC in young people (Azadeh et al., 2008). Another study that conducted among Asian CRC patients living in California showed that more than of 20% of cases were below 50 years of age (Giddings et al., 2012). This issue wills reinforce the genetic nature of CRC in Asian population. For this reason, individuals with at least one relative affected by CRC at ages below 50 years can be considered as priority group for screening of familial CRC. Similar to other study (Rim et al., 2009, Tas & Keskin, 2011), according to findings of current study, ASR increased with increasing age, especially after age 50 years, therefore, about other people who are not at risk of familial CRC, onset of screening at age 50 would be appropriate.

In contrast with other studies (De Kok et al., 2008; Chong et al., 2009; Rim et al., 2009), gender disparity was not considerable in this study that could be due to similarity of etiologic factors in both sex. Although high risk behaviors such as smoking, alcohol consumption and drug abuse is more common in men but Iranian women are exposed with a major risk factor for CRC such as inactivity. On the other hand, the nature of disease in our country may be genetically than environmental and can affect on both sexes equally.

We observed that in 60% of cases, tumor was located at colon and in the other cases in the rectum. In other studies, this ratio is reported 70 to 30(Ponz et al., 2007; Chong et al., 2009; Rim et al., 2009). Pattern of distribution of tumor depends on etiologic factors (Azadeh et al., 2008; Safaee et al., 2010).Determination of related risk factors is suggested due to the higher incidence rate of rectal cancer in Iran.

This study is the first study in Iran that has calculated the 4 years incidence rate of CRC using National Cancer Registry data. In the interpretation of findings of this study, some limitations should be kept in mind. First, our analyses are based on data on CRC incidence by age, sex, anatomic subsite and morphologic type. Additional factors those are helpful in determination of screening strategies, such as stage of disease, were not available. Second, we used a retrospective method and the data was limited to what had been captured by the registries. Also we didn't access to details of the information such as anatomic subsite of tumor, for this reason we couldn't use a better categorization of anatomic subsite for comparison of distribution of tumor in colon and rectum (such as right colon vs. left colon or rectum). On the other hand, there was not information about type of CRC (familial or sporadic) for determination of disparities and use of its results for formulating of CRC screening.

In conclusion, results of present study indicated that incidence of colorectal cancer is relatively high in Iran. Incidence of CRC in people under 50 years and in rectum were reported higher than other countries that related etiologic factors should be investigate in further studies. According to the increasing of ASR after age 50 years, it seems that onset of screening at age 50 would be appropriate. If CRC screening is to be considered, all the discussed characteristics and differences would need to be taken into account. Further studies are suggested for evaluation of effectiveness of screening in 50 years or younger people.

References

Azadeh S, Moghimi-Dehkordi B, Fatem S R, et al (2008). Colorectal cancer in Iran: an epidemiological study. *Asian Pac J Cancer Prev*, **9**, 123-6.

Boyle P, Leon M E (2002). Epidemiology of colorectal cancer. *Br Med Bull*, **64**, 1-25.

Chong VH, Abdullah MS, Telisinghe PU, et al (2009). Colorectal cancer: incidence and trend in Brunei Darussalam. *Singapore Med J*, **50**, 1085-9.

De Kok I M, Wong C S, Chia K S, et al (2008). Gender differences in the trend of colorectal cancer incidence in Singapore, 1968-2002. *Int J Colorectal Dis*, **23**, 461-7.

Faivre J, Bouvier A M, Bonithon-Kopp C (2002). Epidemiology and screening of colorectal cancer. *Best Pract Res Clin Gastroenterol*, **16**, 187-99.

Fatemi S R, Shivarani S, Malek F N, et al (2010). Colonoscopy screening results in at risk Iranian population. *Asian Pac J Cancer Prev*, **11**, 1801-4.

Fritz A, Percy C, Jack A, et al 2000. International Classification of Diseases for Oncology, Genova: World Health Organization.

Giddings B H, Kwong S L, Parikh-Patel A, et al (2012). Going against the tide: increasing incidence of colorectal cancer among Koreans, Filipinos, and South Asians in California, 1988-2007. *Cancer Causes Control*, **23**, 691-702.

Haggar F A, Boushey R P (2009). Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clin Colon Rectal Surg*, **22**, 191-7.

Islamic Repulic of Iran. Ministry of Health and Medical Education. Center for Disease Control & Prevention. Noncommunicable Deputy. Cancer Office (2008-2009). Iranian Annual of National Cancer Registration Report.

Jackson-Thompson J, Ahmed F, German R R, et al (2006). Descriptive epidemiology of colorectal cancer in the United States, 1998-2001. *Cancer*, **107**, 1103-11.

Jiang S X, Wang X S, Geng C H, et al (2009). Altering trend of clinical characteristics of colorectal cancer: a report of 3,607 cases. *Ai Zheng*, **28**, 54-6.

Keyfitz N (1966). Sampling Variance of Standardized Mortality Rates. *Human Biology*, **38**, 309-17.

Moghimi-Dehkordi B, Safaee A, Zali M R (2008). Prognostic factors in 1,138 Iranian colorectal cancer patients. *Int J Colorectal Dis*, **23**, 683-8.

Pahlavan P S, Kanthan, R (2006). The epidemiology and clinical findings of colorectal cancer in Iran. *J Gastrointestin Liver Dis*, **15**, 15-9.

Ponz De Leon M, Rossi G, Di Gregorio C, et al (2007). Epidemiology of colorectal cancer: the 21-year experience of a specialised registry. *Intern Emerg Med*, **2**, 269-79.

Rim S H, Seeff L, Ahmed F, et al (2009). Colorectal cancer incidence in the United States, 1999-2004 : an updated analysis of data from the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results Program. *Cancer*, **115**, 1967-76.

Rozen P, Liphshitz I, Barchana M (2012). Changing Epidemiology of Colorectal Cancer Makes Screening Sigmoidoscopy Less Useful for Identifying Carriers of Colorectal Neoplasms. Dig Dis Sci.

Safaee A, Moghimi Dehkordi B, Fatemi S R, et al (2010). Epidemiological Differences between Colon Cancer and Rectum Cancer. *Iran J Cancer Prev*, **3**, 185-92.

Suwanrungruang K, Wiangnon S, Sriamporn S, et al (2006). Trends in incidences of stomach and colorectal cancer in Khon Kaen, Thailand 1985-2004. *Asian Pac J Cancer Prev*, **7**, 623-6.

Tas F, Keskin S (2011). Age-specific incidence ratios of colorectal cancer (CRC) in Turkey: CRC in older people is increasing. *Arch Gerontol Geriatr*. ??, ??

Yee Y K, Tan V P, Chan P, et al (2009). Epidemiology of colorectal cancer in Asia. *J Gastroenterol Hepatol*, **24**, 1810-6.