RESEARCH ARTICLE

Prevalence of Colorectal Polyps in a Group of Subjects at Average-risk of Colorectal Cancer Undergoing Colonoscopic Screening in Tehran, Iran between 2008 and 2013

Masoudreza Sohrabi[1], Farhad Zamani[1]*, Hossien Ajdarkosh[1], Naser Rakhshani[1], Mitra Ameli[1], Mehdi Mohamadnejad[1,2], Ali Kabir[1], Gholamreza Hemmasi[1], Mahmoudreza Khonsari[1], Nima Motamed[1]

Abstract

Background: Colorectal cancer (CRC) is one of the prime causes of mortality around the globe, with a significantly rising incidence in the Middle East region in recent decades. Since detection of CRC in the early stages is an important issue, and also since to date there are no comprehensive epidemiologic studies depicting the Middle East region with special attention to the average risk group, further investigation is of significant necessity in this regard. Aim: Our aim was to investigate the prevalence of preneoplastic and neoplastic lesions of the colon in an average risk population. Materials and Methods: A total of 1,208 eligible asymptomatic, average- risk adults older than 40 years of age, referred to Firuzgar Hospotal in the years 2008-2012, were enrolled. They underwent colonoscopy screening and all polypoid lesions were removed and examined by an expert gastrointestinal pathologist. The lesions were classified by size, location, numbers and pathologic findings. Size of lesions was measured objectively by endoscopists. Results: The mean age of participants was 56.5 ± 9.59 and 51.6% were male. The overall polyp detection rate was 199/1208 (16.5 %), 26 subjects having non-neoplastic polyps, including hyperplastic lesions, and 173/1208 (14.3%) having neoplastic polyps, of which 26 (2.15%) were advanced neoplasms .The prevalence of colorectal neoplasia was more common among the 50-59 age group. Advanced adenoma was more frequent among the 60-69 age group. The majority of adenomas were detected in the distal colon, but a quarter of advanced adenomas were found in the proximal colon; advance age and male gender was associated with the presence of adenoma. Conclusions: It seems that CRC screening among average-risk population might be recommended in countries such as Iran. However, sigmioidoscopy alone would miss many colorectal adenomas. Furthermore, the 50-59 age group could be considered as an appropriate target population for this purpose in Iran.

Keywords: Screening - colonoscopy - polyp - CRC

Asian Pac J Cancer Prev, **15 (22)**, 9773-9779

Introduction

Colorectal cancer (CRC) is one of the most common causes of mortality worldwide, particularly in western countries (Siegel et al., 2012; Ahnen et al., 2014; Somi et al., 2014). CRC is considered the third cause of cancer-related death in the world (Gupta et al., 2011; Siegel et al., 2012; Baghestani et al., 2014). Following breast cancer, it is the second most common cancer among women and is also the third most common cancer among men (Ansari et al., 2006; Ferlay et al., 2010; Siegel et al., 2012). Previous studies have illustrated variation in CRC incidence rates across countries. Generally, the western population is considered to have the highest incidence of CRC, but during the recent decades the incidence of CRC in developing countries has risen significantly. Although its incidence in the Middle East is not conclusive, it is estimated to be around 0.7-0.8% (Ansari et al., 2006; Ferlay et al., 2010; Ng, 2013).

Cancer is a major health problem and is the third most common cause of death in Iran (Kolahdoozan et al., 2010; Talaiezadeh et al., 2013). The most common cancers in Iran are gastric, esophagus and colorectal in men, and breast, esophagus, stomach and colorectal in women. It has also been reported that the incidence of colorectal cancer in Iran has increased during the last 25 years (Sadjadi et al., 2005; Azadeh et al., 2008; Abdifard et al., 2013; Roya and Abbas 2013). Reports also suggest that in our region CRC is more prevalent in the younger age compared to western countries, this could be attributed

*[1]Gastrointestinal & Liver Disease Research Center, Firoozgar Hospital, Iran University of Medical Sciences, [2]Digestive Disease Research Institute, Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran *For correspondence: zamani.f@iums.ac.ir, zamani.farhad@gmail.com*

to the predominantly young population and changing diet habits in Iran. (Ansari et al., 2006; Moghimi-Dehkordi et al., 2008; 2009; Ahnen et al., 2014).

The prevention and detection of colorectal cancer in an early stage has become an important issue in the health sector. The progression from adenoma to carcinoma is a slow phenomenon, and early detection and removal of the polyps with cancer cells could be considered as a preventive measure. Researchers have revealed that the five –year survival rate of patients with colorectal cancer would be 90%, 68% and 10% ; if the lesion is still localized, regionally spreading or has metastasized respectively (Jemal et al., 2010; Siegel et al., 2012; Winawer, 2012). Some studies reported a decline in the rate of colorectal cancer by the use of various screening modalities. According to them the mean mortality related to colorectal cancer was reduced by 10-22% after 12-18 years of following the screening program (Hewitson et al., 2008; Jemal et al., 2010; Siegel et al., 2012).

Statistically, colorectal cancer manifests after the sixth decade of life and the initiation of screening is advised to begin at least ten years earlier (Levin et al., 2008). The beginning of screening for colorectal lesions for the average-risk population is recommended at age 50 by many gastrointestinal professionals societies (Ness et al., 2000; Thoma et al., 2011). Studies regarding the effectiveness of CRC screening program support the benefit of screening programs as a means of decreasing morbidity and mortality of CRC (Winawer et al., 1993; Levin et al., 2008; Rex et al., 2009; Morois et al., 2014). According to Neugut et al. and Liberman et al; colonoscopy is a more efficient method of CRC detection compared to fecal occult blood, double contrast enema and sigmoidoscopy (Lieberman et al., 2000; Rex et al., 2009).

As of the last few decades, CRC incidence is on the rise in the eastern parts of the globe. Although, screening programs for CRC are widely used in western countries (Benson et al., 2008; Ng and Wong 2013; Benson et al., 2014), there currently does not exist recognized cancer screening programs in the Middle Eastern or: such as Iran. After a thorough study of the literature, it was noted that there have not been research efforts with regards to CRC screening among the average risk population in Iran. Therefore our study aimed to investigate the prevalence of neoplastic and preneoplastic lesions of the colon in the average risk population, and to propose an appropriate age group who would benefit from the screening program.

Materials and Methods

Patients

This is a cross-sectional study for CRC screening on "asymptomatic", average- risk adults between years 2008 and 2013. It includes both men and women over 40 years of age. This study was conducted in the endoscopy ward of Firoozgar general referral hospital, situated in Tehran where more than four thousand colonoscopies are annually performed and receives patients from across the country.

We offered total colonoscopy screening for subjects who came to various other clinics of our hospital, but had no symptoms of the lower gastrointestinal tract. All of them were interviewed and examined by two expert gastroenterologists. The eligible subjects were persons who didn't have the following: history of previous total colonoscopy, history of colorectal polyp or cancers, colorectal adenoma or cancer in first degree family, rectal bleeding, iron deficiency anemia, change of bowel habit recently, involuntary weight loss during last six months, abdominal pain, positive fecal occult blood test (FOBT), inflammatory bowel disease(IBD) and any contraindication for colonoscopy e.g. severe co-morbidity diseases.

Colonoscopy

The preparation was self-administration of Polyethylene glycol (PEG) 24 hours before colonoscopy along with diet restriction. Total colonoscopies were performed by two experienced gastroenterologists. Each of them had more than ten years experience in referral centers. The Fujinon colonoscopy 2200 was used for this purpose. The scope advanced to the ileoscecal orifice. Successful endoscopy was defined as cecal intubation which is confirmed by photography. Bowel preparation was determined by colonoscopists as good, fair or poor. Individuals with poor preparation were invited for a second colonoscopy. Those with a good or fair bowel preparation were included in the final analysis. All lesions such as polyp or polypoid lesion were removed or biopsies obtained and sent to the pathology center of the hospital for histopathologic evaluation. Size of the lesion was measured objectively by endoscopists. The specimens were studied by one expert gastrointestinal pathologist.

Data collection

A questionnaire, including demographic and clinical data, was completed for each patient and the results of the colonoscopy and pathology examinations were also recorded. The colorectal adenomas were classified by size, location, numbers and pathologic findings. If more than one lesion was detected in one subject, the finding was classified by the more advanced one. Size of the lesion was measured objectively by an open forceps that measured approximately 1 cm. The Distal colon was defined as the rectum, sigmoid and descending colon. We considered lesions >1cm in diameter, with a pathology of: high grade dysplasia, villous adenoma, and malignant transformation as an advanced pathologic finding. Hyperplastic or inflammatory polyps were considered as non –neoplastic polyps and any type of adenoma or adenocarcinoma was defined as a neoplastic lesion.

Statistical analysis

The results were analyzed by statististical package for the social sciences (SPSS) for windows (version 20.0 Chicago, IL, USA). Variables were analyzed by chi-square, one way ANOVA, student's t-test and fisher exact test as appropriate. Descriptive analysis was done for the prevalence lesions, sex and age. Forward LR logistic regression was used for evaluation of potential risk factors associated with adenoma. The P-value <0.05 was considered significance.

Table 1. Demographic data of Participants in Relation with Colonoscopic Finding

Age groups	Men, age					Women, age				
	40-49 N (%)	50-59 N (%)	60-69 N (%)	>70 N (%)	Total	40-49 N (%)	50-59 N (%)	60-69 No(%)	>70 N (%)	Total
No neoplasia (including non-neoplastic lesion)	136 (26.8)	151 (29.7)	162 (31.4)	59 (11.6)	508	158 (30)	187 (35.5)	128 (24.3)	54 (10.2)	527
Non advanced Adenoma	17 (17.9)	34 (35.8)	32 (33.7)	12 (12.6)	95	18 (34.6)	21 (40.4)	9 (17.3)	4 (17.7)	52
Advanced Adenoma	3 (15)	9 (45)	7 (35)	1 (5)	20	1 (16.7)	3 (50)	1 (16.7)	1 (16.7)	6
Total	156 (25.05)	194 (31.13)	201 (32.26)	72 (11.55)	623	177 (30.25)	211 (36.07)	138 (23.6)	59 (10.08	585

Ethics

The study was approved by the ethics committee of Firoozgar hospital; in accordance to the declaration of Helsinki. The colonoscopy procedure was explained to all the participants and a written informed consent was obtained.

Results

From 3150 patients, a total of 1208 eligible participants were enrolled in this study. There was no preference in age or gender of patients that the colonoscopist chose to conduct the procedure. Intravenous sedation with pethidin and midazolam were applied for all participants. The colonoscopy reached the cecum in 98% subjects no significant complications occurred in any of them. The average withdrawal time was 15minutes. Male to female ratio was 1.06. The mean age of participants was 56.45±9.59 years. Table 1 illustrates the demographic distribution of participants associated with colonoscopic findings.

Polypoid lesions were detected in 199/1208 (16.5%) of participants. Peduncolated polyps were seen in 171/199 (89.0%) of cases and 26/1208 (2.1%) of cases had non-neoplastic polyps. In addition, majority of the polypoid lesions were seen in the distal colon as rectom, sigmoid and descending colon with 67(33.7%), 45(22.6%) and 35(17.6%) respectively.In addition, 20/199 (10.0%) of subjects had multiple polyps. Neoplastic polyps (adenoma) were seen in 173/1208 (14.3%) subjects in which 26/1208 (2.15%) of them had advanced neoplastic lesions and only 2/1208 (0.16%) were malignant.

All analyses were done on adenomas lesions .The most common histopathologic finding was tubular adenoma, followed by tubule villous adenoma and dysplastic adenoma (Table 2). Our results also depict that a majority of advanced adenoma belongs to the 50-59 age group with a higher frequency among men (Table 1). Majority the adenoma was detected in the distal colon in 132/173(76.3%) subjects, neoplastic lesions were found in 41/173 (23.6%) subjects in the proximal part. The common locations of appearance of colorectal adenoma were: rectum 59(34.1%), sigmoid 37(21.3%) and descending colon 29(16.8%), respectively. Furthermore, 8/26 (30.7%) of the advanced adenomas were located in the proximal colon(Table 3).

The greater percentage of the proximal colon's adenomas was detected in the 50-59 year old group with 18(5.1%) subjects, followed by the 60-69 year old group with 13(3.8%) subjects. Furthermore, we did not observe any association between location of polyps and advanced colorectal adenoma. In multivariate analysis

Table 2. Histopathological Features of Sll Colorectal Lesions over 40 Years Dge Group (n=1208).

Finding	N (%)
No neoplasia (normal colonoscopy)	1009(83.5)
Total polyp	199(16.5)
Neoplastic polyp	173(14.3)
Non- neoplastic polyp	26(1.15)
Histologic classification	
Tubular	
Size<10mm	134(11.1)
Size >10 mm	5(0.41)
Tubulovillous	
Size<10mm	15(1.24)
Size >10 mm	0(0)
villous	
Size<10mm	4(0.33)
Size >10 mm	
Adenoma with high grade dysplasia	8(0.70)
Serrated Adenoma	5(0.41)
Colorectal malignancy	2(0.16)

Table 3. Colorectal Neoplasia Prevalence by Colon Location

		Distal only N (%)	Proximal only n (%)	Distal and proximal n (%)
Sex	Woman (n=585)	39 (6.6)	15 (2.6)	4 (0.7)
	Men (n=623)	86 (13.8)	26 (4.2)	3 (0.5)
Age (years)	40-49(n=333)	30 (9.0)	9 (2.7)	0
	50-59 (n=405)	46 (11.3)	17 (4.1)	4 (1.0)
	60-69 (n=339)	36 (10.6)	12 (3.5)	1 (0.3)
	≥70 (n=131)	13 (9.9)	3 (2.3)	3 (2.3)
Total (n=1208)		125 (10.33)	41 (3.39)	7 (0.57)
Trend (P value)		0.38	0.306	

Table 4. Adjusted ORs for Colorectal Adenoma at Screening Colonoscopy

		Men OR(95%CI)	Women OR(95%CI)	Total OR(95%CI)
Sex	Woman	-	-	1
	Men	-	-	1.82(1.33-2.49)
Age	40-49	1	1	1
	50-59	1.67(0.98-2.87)	1.04(0.59-1.85)	1.35(0.91-1.99)
	60-69	1.38(0.80-2.39)	0.52(0.24-1.54)	1.04(0.68-1.59)
	≥70	1.15(0.55-2.44)	0.56(0.20-1.54)	0.90(0.50-1.61)

Table 5. Adjusted ORs for Colorectal Adenoma by Colon Location

		Men OR (95% Cl)	Women OR (95% Cl)	Total OR (95% Cl)
Sex	Woman	-	-	1
	Men	-	-	0.69(0.34-1.38)
Any Proximal colon				
Age (years)	40-49	1	1	1
	50-59	0.28 (0.06-1.32)	0.53(0.06-4.2)	0.37(0.1-1.2)
	60-69	0.4 (0.09-1.70)	0.96(0.13-6.95)	0.57(0.18-1.8)
	≥70	1.61 (0.37-6.90)	0.56(0.06-5.2)	1.19(0.35-3.9)
Trend P value		0.01	0.80	0.08
Any Distal Colon				
Sex	Woman	-	-	1
	Men	-	-	0.83(0.4-1.74)
Any Proximal colon				
Age (years)	40-49	1	1	1
	50-59	0.15(0.02-0.87)	1.42(0.12-16)	0.37(0.1-1.36)
	60-69	0.34 (0.07-1.48)	1.75(0.16-18.61)	0.56(0.17-1.98)
	≥70	1.61 (0.37-6.90)	0.88(0.06-12.8)	1.40(0.4-4.89)
Trend P value		0.05	0.88	0.05

the pathological findings had no significant correlation with gender, age, location and number of lesions (Table 4 and 5).

Discussion

The incidence of CRC is rising in some eastern countries as a result of the changing environmental factors. In the present study we evaluated the yield of colonoscopy screening in a group of asymptomatic average-risk population from an area that was considered a low risk area for CRC. This study shows that colonoscopy screening is a valuable modality in the average risk population, as we found non-advanced adenoma, advanced adenoma and CRC in 14.3%, 2.1% and 0.16% of patients, respectively.

In comparison with other studies, our results are lower than previous reports from developed countries among the asymptomatic average-risk subjects (Lieberman et al., 2000; Choe et al., 2007; Rundle et al., 2008; Siegel et al., 2012; Ng and Wong 2013; Yang et al., 2014). Heitman et al reported in their meta-analysis that the prevalence of non-advanced, advanced adenoma and cancer in North America were 17.7%, 5.7% and 0.3%, respectively (Heitman et al., 2009). Researchers from Asian-pacific developed countries have also reported a significant increase of CRC over the last decades. It seems that these countries actually have the same incidence as western countries; this could be due to the "westernization" of lifestyles in these countries (Choe et al., 2007; Chung et al., 2010; Aswakul et al., 2012; Ng and Wong 2013; Yang et al., 2014). This discrepancy between our findings and theirs might be related to lifestyle, diet, younger population and also genetic differences. In addition, in this study we enrolled asymptomatic subjects without a family history of CRC; although, majority of previous studies involved subjects with a positive family history of colorectal neoplasia.

Nevertheless, there is not enough data about screening and prevalence of colorectal premalignant lesions in the Middle East region. As Middle East countries including Iran are considered low risk areas for CRC. (Jemal et al., 2010; Siegel et al., 2012; Talaiezadeh et al., 2013; Somi, et al., 2014), the prevalence of premalignant lesions are supposed to be lower in this region than industrial countries; but, during the last decades there was a rise in the trend of industrialization in this region. (Jemal et al., 2010; Safaee et al., 2012) that could influence the incidence of colorectal premalignant and malignant lesions.

Moreover, according to the recent studies conducted in Iran, the prevalence of total colorectal adenoma and CRC in symptomatic patients were 11.7% and 3.6%, respectively (Bafandeh et al., 2008; Abdifard et al., 2013). Aanother study has indicated that the prevalence of CRC is more common in younger Iranians compared to other reports around the world (Pahlavan and Kanthan 2006; Bafandeh et al., 2008). With regards to the fact that previous studies conducted in Iran involved symptomatic subjects and in contrast , our study was conducted on a greater sample size of asymptomatic subjects; our findings are of compelling importance in that it shows an increasing trend in the occurrence of colorectal neoplasia in our population.

It is expected that in an older age the prevalence of colorectal neoplasia would increase (Regula et al., 2006; Choe et al., 2007; Boursi et al., 2009; Corley et al., 2013). In our study, majority of the adenoma and advanced adenomas were found in subjects 50-59 years old followed by the 60-69 year old age group. Our findings have a discrepancy when compared to reports from western countries (Mehran et al., 2003; Heitman et al., 2009; Rex et al., 2009). Moreover, our findings shows that a noticeable number of colorectal neoplasia (11.7%) has been detected among the younger participants (40-49 years old). Although this result is lower than Thoma, Rundel and Chung's studies (Rundle et al., 2008; Chung et al., 2010; Thoma et al., 2011); when considering other factors such as the young population and westernization of the younger generation's lifestyle, it is suspected that we would be faced with a population holding a higher risk of colorectal adenoma in the future.

In addition, the prevalence of CRC in our study was

2/1208 (0.16%); where both of these patients were males and in the 60-69 age group. The prevalence of CRC in developed countries has been reported between 0.4 and 0.7%. These figures are not comparable with our results (Imperiale et al., 2000; Lieberman et al., 2000; Strul et al., 2006; Boursi et al., 2009; Yang et al., 2014). Genetics and environmental factors could be considered as attributing factors in the discrepancy of this contrast between the countries. Within the country, It is assumed that the noticeable difference in the diet of younger and the older population could affect this process (Table 3 and 4). As a result; it could be suggested that the 50-59 year age group be considered as a target population for colorectal screening.

Determining the prevalence of colorectal neoplasms in various anatomical sites of the colon can be an important factor to select the favorable modality of screening. In the present study, the common locations that colorectal adenoma manifests were rectum, sigmoid and descending colon, respectively. However, a remarkable portion (54%) of adenomas was detected beyond the rectosigmoid and was not detected by sigmoidoscopy alone. Chung also reported that two-thirds of the overall adenomas were detected above the sigmoid colon(Chung, Kim et al., 2010). Moreover, about 30% of advanced adenomas in our study were detected in the proximal colon which in turn advocates the performance of colonoscopy in the asymptomatic average-risk population as a preferable screening method. In similarity to previous reports, the presence of proximal adenoma were not associated with distal colon adenomas. Meanwhile, location of adenomas was not related to the lesion being an advanced adenoma (Table 7).

Moreover, in the present study proximal adenoma occurred mainly in ages greater than 50 years; although the presence of proximal adenoma was considerable among younger participants as well. It is also reported that advancing age is a risk factor for the development of advanced adenoma in the proximal colon and as a result, sigmoidoscopy alone is not an appropriate modality in the detection of proximal lesions and consequently neither in mortality reduction. Therefore, our result suggests that colonoscopy might be a preferred procedure for detecting colorectal neoplasia in those greater than 50 years of age. It seems that more documented evidence is required to advise the use of total colonoscopy instead of flexible sigmoidoscopy as a screening tool for younger people.

With consideration to the assumption that gender plays a role in prevalence of CRC a certain degree of influence could emerge with regards to which gender should be given more priority. Our study also showed that the prevalence of either neoplasia (overall) or advanced adenoma was more prevalent among men in different ages; but they were not significant (Table 5), which is comparable with previous reports (Lieberman et al., 2000; Bafandeh et al., 2005; Boursi et al., 2009; Ferlay et al., 2010; Ferlitsch et al., 2011; Thoma et al., 2011). Furthermore, adenoma in the proximal colon was detected more among males, although it was not significant. We could not present a clear explanation about this finding. However, we could consider the hormonal difference and also the greater exposure to potential environmental risk factors in men as predisposing factors. Some studies have also mentioned that increasing age in male gender could increase the risk of developing colorectal neoplasia. Therefore, some researchers have suggested considering gender as a factor for the time of initiation of colorectal screening. However, current guidelines do not recommend considering gender as a criteria for the initiation of screening (Choe et al., 2007; Corley et al., 2013). We could not indicate the appropriate age for the initiation of colorectal screening in men and women, separately.

Size of colorectal neoplasia has been another issue in our study. Some reports considered the size of a polyp as an indicator for advanced polyps. Although estimation of the size of polyps during endoscopy could be inaccurate, many advanced adenomas in our study had a diameter of less than one centimeter and also all lesions that were located in the proximal colon had diameters less than one centimeter. Our results are comparable with other reports, and in addition emphasizes that small polyps also have the potential risk for progression towards malignancy (Strul et al., 2006; Rondagh et al., 2012).

This study has some limitations; as mentioned before the number of participants in the age groups were not equal, the total number of participants were limited and all subjects had been selected from one referral center. We have also not assessed risk factors such as diet or medication history that might influence formation of colorectal adenoma. Further, we excluded subjects with lower gastrointestinal symptoms that would have caused selection bias.

In conclusion, although the prevalence of colorectal adenoma is lower than previous reports; there is an indication that its prevalence would increase in the future. In addition, most neoplastic lesions were located above the sigmoid colon in a way that they cannot be detected by sigmoidoscopy alone. Thus, colonoscopy could be considered as the preferred modality for colorectal cancer screening. Moreover, most cases with adenoma were detected in subjects aged over 50 years; therefore this study provides evidence that can suggest colonoscopy as a screening tool which should be considered for those over 50 years old in both genders in Iran.

Acknowledgements

The authors would like to thank, Afsane Rahbari, Shakira Ghafor, Ali Gholami and all staffs in GILDRC for their cooperation in this project.

References

Abdifard E, Ghaderi S, Hosseini S, Heidari M (2013). Incidence trends of colorectal cancer in the West of Iran during 2000-2005. *Asian Pac J Cancer Prev*, **14**, 1807-11.

Ahnen DJ, Wade SW, Jones WF, et al (2014). The increasing incidence of young-onset colorectal cancer: A call to action. *Mayo Clin Proc*, **89**, 216-24

Ansari R, Mahdavinia M, Sadjadi A, et al (2006). Incidence and age distribution of colorectal cancer in Iran: results of a population-based cancer registry. *Cancer Lett*, **240**, 143-7.

Aswakul P, Prachayakul V, Lohsiriwat V, Bunyaarunnate T,

Kachintorn U (2012). Screening colonoscopy from a large single center of Thailand - something needs to be changed? *Asian Pac J Cancer Prev*, **13**, 1361-4.

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

Bafandeh Y, Daghestani D, Esmaili H (2005). Demographic and anatomical survey of colorectal polyps in an Iranian population. *Asian Pac J Cancer Prev*, **6**, 537-40.

Bafandeh Y, Khoshbaten M, Eftekhar Sadat AT, Farhang S (2008). Clinical predictors of colorectal polyps and carcinoma in a low prevalence region: results of a colonoscopy based study. *World J Gastroenterol*, **14**, 1534-8.

Baghestani AR, Daneshvar T, Pourhoseingholi MA, Asadzade H (2014). Survival of colorectal cancer patients in the presence of competing-risk. *Asian Pac J Cancer Prev*, **15**, 6253-5.

Benson AB, Venook AP, Bekaii-Saab T, et al (2014). Colon cancer, version 3.2014. *J Natl Compr Canc Netw*, **12**, 1028-59.

Benson VS, Patnick J, Davies AK, et al (2008). Colorectal cancer screening: a comparison of 35 initiatives in 17 countries. *Int J Cancer*, **122**, 1357-67.

Boursi B, Halak A, Umansky M, et al (2009). Colonoscopic screening of an average-risk population for colorectal neoplasia. *Endoscopy*, **41**, 516-21.

Choe JW1, Chang HS, Yang SK, et al (2007). Screening colonoscopy in asymptomatic average-risk Koreans: analysis in relation to age and sex. *J Gastroenterol Hepatol*, **22**, 1003-8.

Chung SJ, Kim YS, Yang SY, et al (2010). Prevalence and risk of colorectal adenoma in asymptomatic Koreans aged 40-49 years undergoing screening colonoscopy. *J Gastroenterol Hepatol*, **25**, 519-25.

Corley DA, Jensen CD, Marks AR, et al (2013). Variation of adenoma prevalence by age, sex, race, and colon location in a large population: implications for screening and quality programs. *Clin Gastroenterol Hepatol*, **11**, 172-180.

Ferlay J, Shin HR, Bray F, et al (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*, **127**, 2893-917.

Ferlitsch M, Reinhart K, Pramhas S, et al (2011). Sex-specific prevalence of adenomas, advanced adenomas, and colorectal cancer in individuals undergoing screening colonoscopy. *JAMA*, **306**, 1352-8.

Gupta AK, Samadder J, Elliott E, Sethi S, Schoenfeld P (2011). Prevalence of any size adenomas and advanced adenomas in 40- to 49-year-old individuals undergoing screening colonoscopy because of a family history of colorectal carcinoma in a first-degree relative. *Gastrointest Endosc*, **74**, 110-8.

Heitman SJ, Ronksley PE, Hilsden RJ, et al (2009). Prevalence of adenomas and colorectal cancer in average risk individuals: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol*, **7**, 1272-8.

Hewitson P, Glasziou P, Watson E, Towler B, Irwig L (2008). Cochrane systematic review of colorectal cancer screening using the fecal occult blood test (hemoccult): an update. *Am J Gastroenterol*, **103**, 1541-9.

Imperiale TF, Wagner DR, Lin CY, et al (2000). Risk of advanced proximal neoplasms in asymptomatic adults according to the distal colorectal findings. *N Engl J Med*, **343**, 169-174.

Jemal A, Siegel R, Xu J, Ward E (2010). Cancer statistics, 2010. *CA Cancer J Clin*, **60**, 277-300.

Kolahdoozan S, Sadjadi A, Radmard AR, Khademi H (2010). Five common cancers in Iran. *Arch Iran Med*, **13**,143-6.

Levin B, Lieberman DA, McFarland B, et al (2008). Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American cancer society, the US multi-society task force on colorectal cancer, and the American college of radiology. *Gastroenterology*, **134**, 1570-95.

Lieberman DA, Weiss DG, Bond JH, et al (2000). Use of colonoscopy to screen asymptomatic adults for colorectal cancer. veterans affairs cooperative study group, **380**. *N Engl J Med*, **343**, 162-8.

Mehran A, Jaffe P, Efron J, Vernava A, Liberman A (2003). Screening colonoscopy in the asymptomatic 50- to 59-year-old population. *Surg Endosc*, **17**, 1974-7.

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

Moghimi-Dehkordi B, Safaee A, Zali MR (2009). Comparison of colorectal and gastric cancer: survival and prognostic factors. *Saudi J Gastroenterol*, **15**, 18-23.

Morois S, Cottet V, Racine A, et al (2014). Colonoscopy reduced distal colorectal cancer risk and excess cancer risk associated with family history. *Cancer Causes Control*. [Epub ahead of print]

Ness RM, Holmes AM, Klein R, Dittus R (2000). Cost-utility of one-time colonoscopic screening for colorectal cancer at various ages. *Am J Gastroenterol*, **95**, 1800-11.

Ng SC,Wong SH (2013). Colorectal cancer screening in Asia. *Br Med Bull*, **105**, 29-42.

Pahlavan PS, Kanthan R (2006). The epidemiology and clinical findings of colorectal cancer in Iran. *J Gastrointestin Liver Dis*, **15**, 15-19.

Regula J, Rupinski M, Kraszewska E, et al (2006). Colonoscopy in colorectal-cancer screening for detection of advanced neoplasia. *N Engl J Med*, **355**, 1863-72.

Rex DK, Johnson DA, Anderson JC, et al (2009). American College of Gastroenterology guidelines for colorectal cancer screening 2009. *Am J Gastroenterol*, **104**, 739-50.

Rondagh EJ, Bouwens MW, Riedl RG, et al (2012). Endoscopic appearance of proximal colorectal neoplasms and potential implications for colonoscopy in cancer prevention. *Gastrointest Endosc*, **75**, 1218-25.

Roya N, Abbas B (2013). Colorectal cancer trends in Kerman province, the largest province in Iran, with forecasting until 2016. *Asian Pac J Cancer Prev*, **14**, 791-3.

Rundle AG1, Lebwohl B, Vogel R, Levine S, Neugut AI (2008). Colonoscopic screening in average-risk individuals ages 40 to 49 vs 50 to 59 years. *Gastroenterology*, **134**, 1311-5.

Sadjadi A, Nouraie M, Mohagheghi MA, et al (2005). Cancer occurrence in Iran in 2002, an international perspective. *Asian Pac J Cancer Prev*, **6**, 359-63.

Safaee A, Fatemi SR, Ashtari S, et al (2012). Four years incidence rate of colorectal cancer in Iran: a survey of national cancer registry data - implications for screening. *Asian Pac J Cancer Prev*, **13**, 2695-8.

Siegel R, Naishadham D, Jemal A (2012). Cancer statistics, 2012. *CA Cancer J Clin*, 62,10-29.

Somi MH, Golzari M, Farhang S, Naghashi S, Abdollahi L (2014). Gastrointestinal cancer incidence in East Azerbaijan, Iran: update on 5 year incidence and trends. *Asian Pac J Cancer Prev*, **15**, 3945-9.

Strul H1, Kariv R, Leshno M, et al (2006). The prevalence rate and anatomic location of colorectal adenoma and cancer detected by colonoscopy in average-risk individuals aged 40-80 years. *Am J Gastroenterol*, **101**, 255-62.

Talaiezadeh A1, Tabesh H, Sattari A, Ebrahimi S (2013). Cancer incidence in southwest of iran: first report from Khuzestan population-based cancer registry, 2002-2009. *Asian Pac J Cancer Prev*, **14**, 7517-22.

Thoma MN1, Castro F, Golawala M, Chen R (2011). Detection of

colorectal neoplasia by colonoscopy in average-risk patients age 40-49 versus 50-59 years. *Dig Dis Sci*, **56**, 1503-8.

Winawer S J (2012). Colonoscopy: Colorectal cancer screening is a 'package'. *Nat Rev Gastroenterol Hepatol*, **9**, 130-1.

Winawer SJ1, Zauber AG, Ho MN,et al (1993). Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N Engl J Med*, **329**, 1977-81.

Yang MH, Rampal S, Sung J, et al (2014). The prevalence of colorectal adenomas in asymptomatic Korean men and women. *Cancer Epidemiol Biomarkers Prev*, 499-507