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Environmental Risk Factors Associated with Sporadic Colorectal Cancer in Isfahan, Iran

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Abstract

Background: Records from the cancer registry system of Iran indicate that colorectal cancer is the third most common cancer in Iranian men and fourth most common among Iranian women. In this study we have investigated the environmental factors associated with colorectal cancer in Isfahan, Iran.

Methods: In this case-control study, we randomly selected 187 patients with colorectal cancer who had positive results by colonoscopy and pathology (case group) and 250 persons who had negative colonoscopy results (control group) from the Colonoscopy Unit of Al Zahra Hospital and Colorectal Cancer Center of Seyed Al Shohada Hospital from 2014 to mid-2015. This study aimed to find the risk factors for sporadic colorectal cancer; therefore, we excluded patients with positive family history. Participants completed a self-administered questionnaire that asked about sex, age, body mass index, smoking status, job-related physical activity, and nonsteroidal anti-inflammatory drug consumption.

Results: This study enrolled 187 colorectal cancer patients (98 males and 89 females) and 250 individuals without colorectal cancer (107 males and 143 females). Multiple analysis demonstrated a significant association of age (odds ratio: 1.04; 95% confidence interval: 1.02, 1.06) and body mass index (odds ratio: 1.09; 95% confidence interval: 1.03, 1.15) with colorectal cancer risk. Men had an almost two-fold risk compared with women (odds ratio: 1.85; 95% confidence interval: 1.14, 2.99). Subjects who did not use nonsteroidal anti-inflammatory drugs had an almost three-fold risk compared with nonsteroidal anti-inflammatory drug consumers (odds ratio: 0.34; 95% confidence interval: 0.19, 0.62). Analysis for job-related physical activity, also indicated an association between the no/low active group with colorectal cancer (odds ratio no activity: 36.09; 95% confidence interval: 10.94, 119 and odds ratio low activity: 2.96; 95% confidence interval: 1.43, 6.13).

Conclusion: Knowledge of the risk factors involved in colorectal cancer incidence makes it possible to identify people at risk and begin risk reduction strategies as well as screening programs.

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Introduction

In developed regions, the annual incidence of colorectal cancer (CRC) has increased to 37.7 per 100,000 persons for men and 24.3 per 100,000 persons for women.[1,2] Although the incidence of CRC is higher in developed countries, its incidence is increasing rapidly in Asia, in general, and particularly in Iran.[3-6] Cancer is the third most common mortality factor in Iran after cardiovascular diseases and accidents; on the other hand, CRC is the third most common cancer in Iran.[3,7-9] It is well-known that CRC is a complex disease, influenced by both genetic and environmental factors.[10,11] Risk factors for CRC can be divided into non-modifiable and modifiable categories. Examples of non-modifiable risk factors include age, gender, family history of CRC or personal history of chronic inflammatory bowel disease. The prevalence of CRC is higher in men and in those with chronic inflammatory bowel disease. Body mass index (BMI) and smoking are recognized as modifiable risk factors for CRC progression. Several studies report an association between high physical activity and regular nonsteroidal anti-inflammatory drug (NSAID) consumption with lower CRC risk.[5,12-14] Knowledge of risk factors for CRC could inform risk reduction strategies for asymptomatic individuals and persons younger than 50 years. Therefore, some researchers suggest that identifying persons exposed to such risk factors might be beneficial. Screening strategies such as colonoscopies and fecal occult blood test (FBOT) before the age of 50 might benefit those with elevated risk for CRC.[15-18] The incidence of CRC changes with populations and time.[6,19] According to population lifestyle, risk factors are also different. Therefore, population-specific epidemiological studies provide new insights in the etiology of CRC and help to develop long-term plans for diagnosis and treatment.[20,21] As Iran is the second-largest nation in the Middle East with different life styles, determining the risk factors in this country would be beneficial. In order to evaluate risk factors for CRC in the Iranian population, we have analyzed the association of sex, age, BMI, cigarette smoking, NSAIDs consumption, and physical activity with CRC in Isfahan Province. This province, as a metropolis, can be a good representative for the entire country.

Materials and Methods

In this case-control study, we randomly selected 187 patients with CRC (case group) who had positive colonoscopy and pathology results and 250 persons who had negative colonoscopy results (control group) from the Colonoscopy Unit of Al Zahra Hospital and Colorectal Cancer Center of Seyed Al Shohada Hospital from 2014 to mid-2015.

The Medical Ethics Committee of Isfahan University of Medical Sciences approved this study. All subjects provided written consent for their participation in the experimental procedures. This study aimed to find the risk factors for sporadic CRC; therefore, we excluded patients with a positive family history. Both groups completed a self-administered questionnaire that asked about sex, age, smoking status, job-related physical activity, and regular NSAIDs consumption. Weight and height were measured by Registered Nurses in the Colonoscopy Unit. We calculated the BMI as weight (kg) divided by height (m^2).

Organization of information

We categorized the data into 4 groups according to physical activity. The questionnaire for physical activity focused on the type of work with 4 options in the questionnaire that described physical activity, as follows: no activity (unemployed or retired); low activity [sedentary or standing work (e.g., clerical work, taxi driving)]; moderate activity [work that involved walking and standing (e.g., delivery by walking, marketing, teachers, nurses)]; and high activity [labor work (e.g., construction work, agricultural work)]. Any person who smoked at least 10 cigarettes per day for >5 years or in the past year was labeled as a smoker. We considered NSAID consumers to be any person who used aspirin or non-aspirin NSAIDs occasionally or daily for >5 years.

Table 1. Demographics and lifestyle characteristics in case and control groups.

Characteristics	Case	Control	*P*-value
Sex			
Female	89 (47.6%)	143 (57.2%)	0.046*
Male	98 (52.4%)	107 (42.8)	
Age (years)	57.41±12.13	51.68 ±14.50	<0.001*
BMI (kg/m^2)	26.80±4.15	25.34±3.74	<0.001*
Smoking			
Yes	37 (19.8%)	30 (12%)	0.025*
No	150 (80.2%)	220 (88%)	
Physical activity			
No activity	39 (20.9%)	5 (2.0%)	
Low activity	86 (46.0%)	123 (49.2%)	<0.001*
Moderate activity	49 (26.2%)	75 (30.0%)	
High activity	13 (7.0%)	47 (18.8%)	
NSAIDs consumption			
Yes	24 (12.8%)	64 (25.6%)	0.001*
No	163 (87.2%)	186 (74.4%)	

*: *P*-value <0.05; BMI: Body mass index; NSAIDs: Nonsteroidal anti-inflammatory drugs

Statistical analysis

Initially, we tested the univariate association between every independent factor. Results are expressed as means±standard deviation with significance as $P<0.05$. Next, we conducted multivariable analysis to evaluate the association of different variables with CRC. Adjusted estimates of associations between risk factors and CRC were calculated using odds ratios (ORs) with 95% confidence interval (CI). The significance level was $P<0.05$. All statistical analyses were performed using SPSS22 (SPSS, Chicago, IL, USA).

Results

The study population consisted of 187 CRC patients (98 males and 89 females) and 250 individuals without CRC (107 males and 143 females).The mean age of the subjects was 57.41 years in the case group and 51.68 years in the control group. Smokers constituted less than 20% of total participants. Table 1 lists demographics and lifestyle characteristics of the participants.

Logistic regressions analysis showed significant association between age (OR: 1.04; 95% CI: 1.02, 1.06) and BMI (OR: 1.09; 95% CI: 1.03, 1.15) with CRC risk. Men had an approximately two-fold risk compared with women (OR: 1.85; 95% CI 1.14, 2.99). Subjects who did not use NSAIDs had an almost three-fold risk compared with NSAIDs consumers (OR: 0.34; 95% CI: 0.19, 0.62). Analysis for job-related physical activity also indicated an association between the no/low active groups with CRC (OR no activity: 36.09; 95% CI: 10.94, 119 and OR low activity: 2.96; 95% CI: 1.43, 6.13). In this study, there was no association found between smoking and CRC incidence. Table 2 lists the results from multiple logistic regression analysis.

Discussion

With respect to the importance of population-specific epidemiological data in defining etiology and prevention strategy of CRC; here, we have analyzed the association among gender, age, smoking status, job-related physical activity, BMI, and NSAIDs consumption regarding CRC. In this study, CRC had a higher prevalence in males compared with females. Accordingly, other studies mentioned that the CRC incidence rate is higher in men. The reasons are not completely understood but likely reflect complex interactions between gender-related differences in exposure to hormones and risk factors.[22] It has been estimated that 20% of cancer cases are due to excess weight gain, however this percentage is proposed to be less than the actual number. Several mechanisms link obesity/adiposity to high cancer risk and

Table 2. Logistic regression analysis to examine the association of different variables with colorectal cancer (CRC).

Characteristics	Beta	SE	*P*-value	OR (95% CI)
Sex	0.61	0.24	0.01	1.85 (1.14, 2.99)
Age (years)	0.04	0.009	<0.001	1.04 (1.02, 1.06)
BMI (kg/m^2)	0.08	0.02	0.003	1.09 (1.03, 1.15)
Smoking	0.17	0.33	0.59	1.19 (0.62, 2.83)
Physical activity				
No activity	3.58	0.60	<0.001	36.09 (10.94,119)
Low activity	1.08	0.37	0.004	2.95 (1.43, 6.12)
Moderate activity	0.85	0.38	0.02	2.53 (1.10, 5.03)
High activity				
NSAIDs consumption	-1.07	0.30	<0.001	0.34 (0.19, 0.62)

*: *P* value <0.05; OR: Odds ratio; CI: Confidence interval; BMI: Body mass index; NSAIDs: Nonsteroidal anti-inflammatory drugs

mortality, such as obesity-related insulin resistance, hyperglycemia, glucose intolerance, hyperinsulinemia, and inflammation.[23,24] Obesity is considered a prognostic factor for the development of CRC. The BMI is the main component used to calculate and assess obesity and overweight. Various studies have suggested that obesity and overweight increase CRC risk regardless of physical activity.[25-27] The results obtained in this study confirmed this association.

One of the most consistently reported correlations between CRC risk and its prevention is the protective effect of physical activity. Epidemiologic studies have found that high levels of physical activity decrease the risk of CRC.[28,29] We observed a significant association between high levels of physical activity and reduced risk of CRC. Several studies reported a close correlation between regular NSAIDs consumption and a decreased risk for developing CRC. Epidemiologic studies suggested a 40% to 50% reduction in mortality due to CRC in individuals that consumed NSAIDs.[30-32] In the present study, we observed a similar situation for subjects with long-term NSAID consumption. NSAID consumers had a reduced risk for CRC. The American Cancer Society does not currently recommend the consumption of these drugs for cancer prevention because of the potential side effects of gastrointestinal bleeding from aspirin and other traditional NSAIDs or heart attacks from selective COX-2 inhibitors.[33] The current study result has shown a positive, not significant association between smoking and CRC incidence. Several studies have reported that cigarette smoking is significantly associated with an increase in CRC risk.[34,35] The difference may be related to the small sample size.

In conclusion, it can be said that by knowing the risk factors for CRC development makes it possible to identify people at risk who could benefit from preventive therapeutic interventions and apply risk reduction strategies as well as screening programs. More studies should be done to evaluate the role of different risk factors involved in the development of CRC, especially those related with social and cultural behaviors with respect to different areas.

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Conflict of Interest

Non declared.

References

1. Ferlay J, Shin H-R, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008, Cancer incidence and mortality worldwide: IARC CancerBase No. 10. Lyon, France: International Agency for Research on Cancer. 2010;2010:29.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer.* 2010;127(12):2893-917. doi: 10.1002/ijc.25516.

3. Hosseini SV, Izadpanah A, Yarmohammadi H. Epidemiological changes in colorectal cancer in Shiraz, Iran: 1980-2000. *ANZ J Surg*. 2004;74(7):547-9.
4. Malekzadeh R, Bishehsari F, Mahdavinia M, Ansari R. Epidemiology and molecular genetics of colorectal cancer in iran: a review. *Arch Iran Med.* 2009;12(2):161-9.
5. Poomphakwaen K, Promthet S, Suwanrungruang K, Kamsa-ard S, Wiangnon S. Risk factors for colorectal cancer in Thailand. *Asian Pac J Cancer Prev.* 2015;16(14):6105-9.
6. Yee YK, Tan VP, Chan P, Hung IF, Pang R, Wong BC. Epidemiology of colorectal cancer in Asia. *J gastroenterol hepatol*. 2009;24(12):1810-6. doi: 10.1111/j.1440-1746.2009.06138.x.
7. Mehrabani D, Tabei S, Heydari S, Shamsina S, Shokrpour N, Amini M, et al. Cancer occurrence in Fars Province, Southern Iran. *Iran Red Crescent Med J.* 2008;2008(4):314-22.
8. Sadjadi A, Malekzadeh R, Derakhshan MH, Sepehr A, Nouraie M, Sotoudeh M, et al. Cancer occurrence in Ardabil: results of a population-based cancer registry from Iran. *Int J Cancer.* 2003;107(1):113-8.
9. Aleksandrova K, Pischon T, Jenab M, Bueno-de-Mesquita HB, Fedirko V, Norat T, et al. Combined impact of healthy lifestyle factors on colorectal cancer: a large European cohort study. *BMC Med.* 2014;12:168. doi: 10.1186/s12916-014-0168-4.
10. Sanchez NF, Stierman B, Saab S, Mahajan D, Yeung H, Francois F. Physical activity reduces risk for colon polyps in a multiethnic colorectal cancer screening population. *BMC Res Notes.* 2012;5:312. doi: 10.1186/1756-0500-5-312.
11. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. *Cell.* 1990;61(5):759-67.
12. Becker N. Epidemiology of colorectal cancer. [Article in German] *Radiologe.* 2003;43(2):98-104.
13. Durko L, Malecka-Panas E. Lifestyle modifications and colorectal cancer. *Curr Colorectal Cancer Rep.* 2014;10:45-54.
14. Pohl C, Hombach A, Kruis W. Chronic inflammatory bowel disease and cancer. *Hepatogastroenterology.* 2000;47(31):57-70.
15. Lieberman DA, Prindiville S, Weiss DG, Willett W; VA Cooperative Study Group 380. Risk factors for advanced colonic neoplasia and hyperplastic polyps in asymptomatic individuals. *JAMA*. 2003;290(22):2959-67.
16. Hong SN, Kim JH, Choe WH, Han HS, Sung IK, Park HS, et al. Prevalence and risk of colorectal neoplasms in asymptomatic, average-risk screenees 40 to 49 years of age. *Gastrointest Endosc.* 2010;72(3):480-9. doi: 10.1016/j.gie.2010.06.022.
17. Chung SJ, Kim YS, Yang SY, Song JH, Park MJ, Kim JS, et al. Prevalence and risk of colorectal adenoma in asymptomatic Koreans aged 40-49 years undergoing screening colonoscopy. *J Gastroenterol Hepatol.* 2010;25(3):519-25. doi: 10.1111/j.1440-1746.2009.06147.x.
18. Winawer S, Fletcher R, Rex D, Bond J, Burt R, Ferrucci J, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale-Update based on new evidence. *Gastroenterology*. 2003;124(2):544-60.
19. Haggar FA, Boushey RP. Colorectal cancer epidemiology: incidence, mortality, survival, and risk factors. *Clin Colon Rectal Surg*. 2009;22(4):191-7. doi: 10.1055/s-0029-1242458.
20. Aykan NF, Yalçın S, Turhal NS, Özdoğan M, Demir G, Özkan M, et al. Epidemiology of colorectal cancer in Turkey: A cross-sectional disease registry study (A Turkish Oncology Group trial). *Turk J Gastroenterol.* 2015;26(2):145-53. doi: 10.5152/tjg.2015.5685.
21. O'Connell JB, Maggard MA, Liu JH, Etzioni DA, Livingston EH, Ko CY. Rates of colon and rectal cancers are increasing in young adults. *Am Surg*. 2003;69(10):866-72.
22. Murphy G, Devesa SS, Cross AJ, Inskip PD, McGlynn KA, Cook MB. Sex disparities in colorectal cancer incidence by anatomic subsite, race and age. *Int J Cancer.* 2011;128(7):1668-75. doi: 10.1002/ijc.25481.
23. Booth A, Magnuson A, Fouts J, Foster M. Adipose tissue, obesity and adipokines: role in cancer promotion. *Horm Mol Biol Clin Investig.* 2015;21(1):57-74. doi: 10.1515/hmbci-2014-0037.
24. Donohoe CL, Doyle SL, Reynolds JV. Visceral adiposity, insulin resistance and cancer risk. *Diabetol Metab Syndr.* 2011;3:12. doi: 10.1186/1758-5996-3-12.
25. Ashktorab H, Paydar M, Yazdi S, Namin HH, Sanderson A, Begum R, et al. BMI and the risk of colorectal adenoma in African-Americans. *Obesity (Silver Spring).* 2014;22(5):1387-91. doi: 10.1002/oby.20702.
26. Zapatier J, Avalos D, Tandon K, Souqiyyeh A, Hernandez M, Rai S, et al. Can adjusting BMI for age and sex provide for a better predictor of colonic neoplasia? *Eur J Gastroenterol Hepatol.* 2015;27(8):974-80. doi: 10.1097/ MEG. 0000000000000391.
27. Larsson SC, Wolk A. Obesity and colon and rectal cancer risk: a meta-analysis of prospective studies. *Am J Clin Nutr*. 2007;86(3):556-65.
28. Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer.* 2009;100(4):611-6. doi: 10.1038/sj.bjc.6604917.
29. Samad AK, Taylor RS, Marshall T, Chapman MA. A meta-analysis of the association of physical activity with reduced risk of colorectal cancer. *Colorectal Dis.* 2005;7(3):204-13.
30. Saha D, Roman C, Beauchamp RD. New strategies for colorectal cancer prevention and treatment. *World J Surg.* 2002;26(7):762-6.