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Original Article

The Association between Dietary Quality Indices and Colorectal Cancer Risk: A Case-Control Study

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ABSTRACT

Background: Dietary habits have been suggested to play a role in incidence of colorectal cancer (CRC). The current study aimed to evaluate the relationship between dietary patterns (Healthy Eating Index-2015 (HEI-2015) and Dietary Quality Index-International (DQI-I)) and CRC risk among Iranian population.

Methods: This case-control study was performed in the CRC Surgery Department of Imam Khomeini Hospital enrolling simultaneously 71 participants with CRC as cases and 142 subjects without neoplastic and acute diseases from the same hospital as controls. Participants' food intake was assessed by a food frequency questionnaire (FFQ). Also, the scores of each of the dietary patterns (HEI-2015 and DQI-I) were classified into tertiles and analyzed.

Results: In the crude model, the odds of developing CRC in the third tertile was significantly lower than those in the first tertile of both HEI-2015 (Odds ratio (OR)=0.41; 95% confidence interval (CI)=0.20-0.83) and DQI-I (OR=0.48; 95%CI=0.23-0.98). In the adjusted model, the odds of developing CRC was significantly lower in the last tertile of HEI-2015 (OR=0.37; 95%CI=0.17-0.80) and second (OR=0.45; 95%CI=0.20-0.99) and last tertile of DQI-I (OR=0.30; 95%CI=0.12-0.74) in comparison to the first tertile.

Conclusion: A higher score of HEI-2015 and DQI-I was found to be significantly associated with a lower CRC risk. Further prospective studies in diverse populations are recommended to validate these findings.

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Introduction

Despite the progress in control and prevention of infectious diseases, the morbidity and mortality of chronic diseases such as cancers have increased in recent decades. Cancer is a global prevalent human affliction that no nationality, race, or social classes are free from it (1). Different cancers vary in their incidence among various populations worldwide (2). In Asian Pacific area, cancers of the stomach, lung, liver, colon or rectum, esophagus, breast, cervix, and leukemia were reported as prevalent ones (3); while among them, colorectal cancer (CRC) is globally one of the most prevalent cancers (4). According to the annual report of Iran's National Cancer Registry Organization, CRC ranks the third most common malignancy among Iranian women and the fifth most common in men, respectively (5). Several modifiable risk factors, including dietary habits, lifestyle, physical inactivity, and obesity have been implicated in CRC incidence. An increased consumption of animal products such as red meat, processed meat, and saturated fat was demonstrated to be associated with a higher risk of CRC; while conversely, higher consumption of vegetables and fruits could decrease CRC risk (6). Therefore, dietary constituents can offer greater benefits in reducing the risk of CRC based on their complex interactions and bioavailability (7, 8).

Iran, like many Middle-Eastern countries has undergone a transition from traditional diets to Western diets to be high in fats and sugars (9). A case-control study identified an association between the Iranian dietary pattern (IDP) characterized by refined grains, fried chicken, processed and red meat, black tea, and carbonated beverages and an increased risk of CRC (10). Also, another study among the Iranian population found that adhering to a healthy dietary pattern, including vegetables, fruits, nuts, legumes, fish, eggs and poultry, olive, and low-fat dairy products, was positively associated with a reduced risk of CRC. Conversely, a Western dietary pattern, comprising red and processed meat, full-fat dairy products, refined grains, sweets, and dessert, was negatively associated with CRC risk (6).

Several general dietary measures have been developed recently, including Diet Quality Index (DQI) and the Healthy Eating Index (HEI) (11). DQIs provide a hypothesis-oriented method to assess the role of overall dietary patterns, rather than individual food assessment, in various health outcomes (11). The DQI-International (DQI-I) is a composite measure of diet quality designed to evaluate dietary health within a country for regulatory purposes and across countries for comparison (12). Similarly, the HEI is a tool used to assess changes in diet quality over time and to evaluate the diets of populations (11). The HEI-2015 and DQI-I utilized in our study were not specifically developed based on Iranian dietary guidelines, and their implementation has been demonstrated to effectively assess the quality of Iranian diets and to evaluate the association between these indices and various health outcomes as described before (13, 14).

To our knowledge, no study has yet investigated the association between HEI-2015, the last version of HEI, and DQI-I with CRC risk among Iranian population. However, a prior research has indicated promising results demonstrating that higher scores on the HEI-2005 were linked to a reduced risk of CRC (15). Similarly, another study found that individuals, both women and men, with the highest HEI-2005 scores exhibited a 20-30% lower risk of CRC (16). Furthermore, a research has illustrated that high diet quality indices, as assessed by HEI-2010 and alternative HEI-2010, were inversely associated with CRC risk in men (17). Therefore, the present study seeked to address this gap by investigation the relationship between HEI-2015 and DQI-I scores and CRC risk among the Iranian population.

Materials and Methods

This study was conducted in the CRC Surgery Department of Imam Khomeini Hospital from September 2018 to January 2020 and was approved from the Medical Research and Ethics Committee of Shiraz University of Medical Science, Shiraz, Iran (IR.SUMS.SCHEANUT.REC.1401.011). The case group consisted of individuals aged 40-75 years who had been newly diagnosed with CRC based on pathological assessment ≤6 months before the interview. The individuals had no prior cancer diagnosis in other organs or a history of adenomatous polyposis. The control group was randomly selected from the same hospital and comprised subjects hospitalized for non-neoplastic and acute diseases during the same period. Initially, there were 89 patients in the case group and 178 in the control group. After screening, 24 patients declined to participate, and 30 were excluded due to total energy intake outside of the mean±3 standard deviations (SDs); finally, 142 controls and 71 cases were included. The participants' food intake was assessed using a 168-item semi-quantitative food frequency questionnaire (FFQ); while the reliability and validity of which were previously evaluated (18). The amount of consumed food was quantified in grams and to calculate the mean energy and nutrient intake, Nutritionist IV (version 7.0; N-Squared Computing, Salem, OR, USA) was employed.

Diet quality was evaluated using the HEI-2015, which compared dietary intake to the key recommendations of the 2015-2020 Dietary Guidelines for Americans. The HEI-2015 scores (19) were based on 13 components, comprising 9 adequacy and 4 moderation components, with a range of 0-100. The adequacy components included greens and beans, total fruits, whole fruits, total vegetables, whole grains, total protein foods, sea foods, dairy, and fatty acids. Scores for greens and beans, total and whole fruits, total vegetables, total protein and sea foods ranged from 0 to 5, while scores for whole grains, dairy and fatty acids ranged from 0 to 10, with the lowest intake receiving a score 0 and the highest intake received a score of 5 or 10. The moderation components, which include sugar, sodium, saturated fats, and refined grains, ranged from 0 to 10, with the lowest intake received a score of 10 and the highest intake received a score of 0.

DQI-I was utilized to investigate the quality of diets, comprising four parts. The first part evaluated food variety with two components including the overall variety of different food types (such as fish, meat, pulse and milk products, eggs, vegetables, fruits, and grains) and the within-group variety of protein foods (such as meat, pulse and milk products, fish, and eggs) and this part was scored from 0 to 20 points. The second part assessed adequacy for protein, grains, fruits, vegetables, fiber, iron, calcium, and vitamin C, with a score ranged from 0 to 40 points. The third part evaluated moderation, incorporating total and saturated fats, cholesterol, sodium, and empty-calorie foods, with a score range of 0 to 30. The fourth part measured overall balance, which considered macronutrient and fatty acid ratios, with a score range of 0 to 10. The total score of DQI-I ranged from 0 to 100, with higher scores indicating higher diet quality, and lower scores denoting to a lower diet quality (11, 12).

A trained nutritionist conducted measurements

Table 1: Basic characteristics of case and control groups.

Variable	Case (n=71)	Control (n=142)	*P* value
Age (year)[1]	58.2±10.4	57.7±10.4	0.746
Income ($)[2]	393.0 (253.0)	402.0 (302.0)	0.206
Physical activity (MET-h/day)[1]	36.8±3.6	36.7±4.8	0.932
HEI-2015 score[2]	62.8±7.9	66.1±7.4	0.003
DQI-I score[2]	77.6 (9.0)	79.6 (7.1)	0.016
BMI (kg/m^2)[1]	27.6±4.2	26.6±4.2	0.362
Smoking[3]			0.164
Never	57 (80.2)	101 (70.1)	
Former	8 (11.3)	15 (10.6)	
Current	6 (8.5)	26 (18.3)	
Method of vegetable consumption[3]			0.083
Raw/Fresh	29 (40.8)	78 (54.9)	
Boiled	8 (11.3)	18 (12.7)	
Fried, Fried/Freeze	34 (47.9)	46 (32.4)	
History of CRC[3]			0.017
Yes	7 (9.9)	3 (2.1)	
No	64 (90.1)	139 (97.9)	
Ibuprofen[3]			0.059
Yes	5 (7.0)	22 (15.5)	
No	66 (93.0)	120 (84.5)	
Aspirin[3]			0.016
Yes	1 (1.4)	14 (9.9)	
No	70 (98.6)	128 (90.1)	
Acetaminophen[3]			0.004
Yes	4 (5.6)	28 (19.7)	
No	67 (94.4)	114 (80.3)	
Mineral supplement[3]			0.015
Yes	8 (11.3)	35 (24.6)	
No	63 (88.7)	107 (75.4)	

HEI: Healthy eating index; DQI-I: Dietary quality index-international; BMI: Body mass index; CRC: Colorectal cancer; MET: Metabolic equivalent of task. Values were presented as mean±SD or median (IQR) for continuous and as percentage for categorical variables. [1]Independent samples T-test was utilized for normally distributed continuous variables. [2]Mann-Whitney U test was employed for non-normally distributed continuous variables. [3]chi-square test was used for categorical variables.

of weight, height, and other anthropometric indices. Additional information, including physical activity levels, family history of CRC, social and demographic characteristics, cooking methods, and medications usage, was obtained through questionnaires. Physical activity was determined using the International Physical Activity Questionnaire (IPAQ) (20). For the case group, physical activity levels from the previous year before CRC diagnosis were considered, while for the control group, physical activity levels from the previous year before the interview were taken into account.

For statistical analysis, SPSS software (Version 26.0, Chicago, IL, USA) was employed. The Kolmogorov-Smirnov test was utilized to assess the normality of the data. The chi-square test was employed for evaluating categorical variables; while for independent samples, T-test was used for analyzing normal continuous variables, and the Mann-Whitney U test for abnormal continuous variables. Crude and two adjusted model logistic regression analysis were conducted to evaluate the association between HEI-2015 and DQI-I and CRC risk. The adjusted models controlled smoking, history of CRC, energy intake, physical activity, administration of ibuprofen, aspirin, acetaminophen, and mineral supplements. A *p* value less than 0.05 was considered statistically significant.

Results

Table 1 presents the basic characteristics of the case and control groups. Significant differences were observed between the case and control groups for fiber intake, HEI-2015 score, DQI-I score, history of CRC, and the use of aspirin, acetaminophen, and mineral supplement. Table 2 represents the comparison of consumption for nutrient and food items between the case and control groups revealing that protein and fiber intake were significantly higher in the control group (p=0.048 and p<0.001, respectively), whereas fat intake was significantly higher in the case group (p<0.001). Additionally, intake of fruits (p=0.042), vegetables (p=0.002), and dairy products (p=0.032) was significantly higher in the control group, while consumption of refined grains (p=0.012) and sugar-sweetened beverages (p=0.006) was significantly lower in the control group compared with with the case group. Furthermore, as depicted in Table 3, in the crude model, the odds of developing CRC in the last tertile was significantly lower in comparison to the first tertile for both HEI-2015 (odds ratio (OR)=0.41; 95% confidence interval (95%CI)=0.20-0.83) and DQI-I (OR=0.48; 95%CI=0.23-0.98). After adjusting for confounders (adjusted model), the results remained significant (p for trend <0.05).

Discussion

In the present study, we examined the association between HEI-2015 and DQI-I scores and the risk of CRC. Our findings revealed a significant negative association between HEI-2015, DQI-I score and CRC risk. The DQI-I and HEI-2015 are priority indices that provide quantitative measures of overall intake relative to dietary guidelines and have been associated with the risk of chronic diseases (21). The DQI-I was demonstrated to measure four aspects of diet quality, including

Table 2: The consumption of nutrients and food items between the case and control groups.

Variable	Case (n=71)	Control (n=142)	*P* value
Energy (kcal/day)[1]	2262.3±450.1	2255.2±341.2	0.908
Protein (g/day)[1]	79.10±17.21	83.82±14.29	0.048
Fat (g/day)[1]	65.85±8.08	60.52±8.39	□**0.001**
Carbohydrate (g/day)[1]	347.51±89.65	354.80±71.80	0.522
Fiber (g/day)[1]	18.9±2.3	20.4±3.1	□**0.001**
Whole grains (g/day)[2]	46.53 (74.39)	57.40 (88.12)	0.288
Refined grains (g/day)[2]	344.30 (239.74)	291.12 (194.07)	0.012
Fruits (g/day)[2]	219.88 (147.74)	242.49 (218.75)	0.042
Vegetables (g/day)[2]	245.23 (168.94)	314.87 (190.37)	0.002
Nuts and legumes (g/day)[2]	38.31 (31.17)	38.42 (31.24)	0.742
Sugar sweetened beverages (g/day)[2]	39.13 (78.25)	21.41 (34.48)	0.006
Meats and processed meats (g/day)[2]	50.25 (29.82)	51.42 (35.51)	0.405
Dairy (g/day)[2]	258.60 (266.32)	305.63 (278.58)	0.032
Fishes (g/day)[2]	7.11 (6.98)	8.42 (9.69)	0.264
Vegetable oils (g/day)[2]	10.29 (8.67)	10.07 (7.77)	0.459
Animal fats (g/day)[2]	5.03 (11.67)	4.16 (8.49)	0.129

Values were presented as mean±SD or median (IQR) for continuous and as percentage for categorical variables. [1]Independent samples T-test was utilized for normally distributed continuous variables. [2]Mann-Whitney U test was employed for non-normally distributed continuous variables. Significant values are shown in bold.

Table 3: Crude and multivariable-adjusted odds ratios and 95%CIs across tertile of HEI and DQI-I.

Variable	Case/Control	Crude model	Adjusted model
HEI-2015			
T_1 (≤61)	30/42	Ref.	Ref.
T_2 (62-68)	24/42	0.80 (0.40-1.58)	0.61 (0.29-1.32)
T_3 (≥69)	17/58	0.41 (0.20-0.83)	0.37 (0.17-0.80)
P trend		0.015	0.010
DQI-I			
T_1 (≤76.6)	30/39	Ref.	Ref.
T_2 (76.7-81.3)	22/52	0.55 (0.27-1.09)	0.45 (0.20-0.99)
T_3 (≥81.4)	19/51	0.48 (0.23-0.98)	0.30 (0.12-0.74)
P trend		0.043	0.010

HEI: Healthy eating index; DQI-I: Dietary quality index-international. The adjusted model controlled for variables of smoking, history of CRC, energy intake, physical activity, and ibuprofen, aspirin and acetaminophen uses, and mineral supplement intake. The results were presented as odds ratios with 95% confidence intervals and were obtained from logistic regression analysis.

variety, adequacy, moderation, and balance in order to identify insufficient and weak diet-related factors (22). Also, the HEI evaluates three significant diet aspects (adequacy, moderation, and variety) based on Food Guide Pyramid and dietary guidelines (22). The components of HEI-2015 are the same as HEI-2010, except that added sugars and saturated fats are replaced by empty calories, resulting in 13 components. Additionally, in HEI-2015, there is a change in the allocation of legumes. Former versions of the HEI accounted for legumes in either the two protein food or the two vegetable components, whereas HEI-2015 counts legumes in all four components. To assess dietary effects on CRC, focusing on the whole diet is more logical than individual foods, since they are not consumed alone. Previous knowledge of a 'healthy diet' was used to create approaches like HEI and DQI-I (19).

In agreement with our study, numerous researchers reported that HEI could be associated with a lower risk of CRC. A population-based case-control study showed a significant association between higher HEI-2005 scores and lower CRC risk in both genders (15). Additionally, a cohort study on postmenopausal women over 12 years of follow-up demonstrated that higher adherence to HEI-2010 had a significant inverse association with CRC risk (23). Jarvandi *et al.* who assessed the role of diet in the association between diabetes and CRC, reported a significant synergistic role of poor HEI-2005 scores for the effect of diabetes on CRC risk (24). In another study conducted in Iran, researchers found a significant inverse association between higher HEI-2010 scores and the incidence of CRC and colorectal adenomas (25). Moreover, Park *et al.* showed a higher adherence to HEI-2005 was associated with a lower risk of CRC (26). Further, a cohort study by Reedy *et al.* exhibited that a healthy eating pattern characterized by intake of fruit, vegetables, and foods with lower fat and lower consumption of meats and potatoes was associated with a decreased CRC risk in men; while among women, a higher HEI-2005 score was associated with a lower risk of CRC, and higher meat and potato consumption increased the risk of CRC (16). The Dietary Guidelines for Americans have evolved over time based on scientific evidences, and the updated version of the HEI was designed to keep up with this evolution (19). Therefore, in the present study, we used the latest version of HEI to investigate its relationship with CRC.

Several potential mechanisms have been proposed to explain the protective effects of HEI on CRC risk. As our results demonstrated, higher HEI-2015 scores were associated with increased consumption of whole grains, fruits, vegetables, nuts, legumes, dairy products, and fish; while all of which were considered healthy dietary patterns and were associated with lower CRC risk (27). Liu *et al.*'s study found that following a healthy plant-based diet was associated with a reduced risk of CRC; while following an unhealthy plant-based diet was associated with an increased risk of CRC (28). Healthy diets encompass many beneficial nutrients, such as fiber, calcium, and vitamin D, which could help prevent CRC (29). Furthermore, an inverse relationship between certain micronutrients such as vitamin A, vitamin K, B_5, and phosphorus and the risk of CRC has been reported (30). Moreover, food groups like fruits and vegetables containing polyphenols, carotenoids, and vitamins C and E play an antioxidant role in decreasing inflammation biomarkers, improving endothelial dysfunction, and protecting against deoxyribonucleic acid (DNA) oxidative damage, ultimately preventing the onset and progression of cancer (31-34). In addition, fruits contain phytochemical compounds like resveratrol, saponins, and quercetin, which inhibit the growth of CRC cells by suppressing the activation pathway of nuclear factor-κB (NF-kB) (35). Additionally, high fat and protein intake, which lead to the production of polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs), can contribute to CRC development (36). Increased tumor formation through the secretion of secondary bile acids and damaging the integrity of the colon epithelium are other adverse effects of consuming red meats high in fats (37). Moreover, it has been found that HEI could be associated with the composition and diversity of gut microbiota, which may serve as a mechanism that promoting colorectal carcinogenesis and CRC development (38).

As previously mentioned, the present study revealed a significant negative relationship between DQI-I and the risk of CRC. To the best of our knowledge, no studies have investigated the association between DQI-I and CRC risk. However, a study by Fung *et al.* found that the DQI- Revised (DQI-R) was not associated with postmenopausal breast cancer risk (39). Conversely, a case-control study found that DQI-I had a significant inverse association with the risk of nasopharyngeal carcinoma (40). Given the limited and conflicting nature of these studies, further studies are needed to elucidate the relationship between DQI-I and cancer risk. Despite the strengths of the present study, such as use of a valid FFQ by trained nutritionists, which facilitated accurate estimation of exposure, our study has some limitations that should be considered. Firstly, although we employed a priori design to assess diet patterns, the case-control design of this study precludes the determination of a causal relationship between HEI-2015 and CRC risk. Secondly, recall bias is another inherent limitation associated with the use of FFQ in our research, and like other dietary studies, measurement error is unavoidable.

Conclusion

Our study suggests that adherence to HEI-2015 and DQI-I, characterized by a higher intake of whole grains, fruits, vegetables, dairy, and white meats, along with a lower intake of refined grains, sweetened sugar beverages, and processed meats that may have a protective effect on CRC. However, further studies with prospective designs can warrant confirming these findings in other populations.

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Authors' Contribution

ETN, SMJ, SE, MR and ZS: Contributed to writing the first draft. MN and BR: Contributed to all data and statistical analysis, and interpretation of data. MN and ZS: Contributed to the research concept, supervised the work and revised the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

None declared.

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