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Inflammatory diet and risk for colorectal cancer: A population-based case–control study in Newfoundland, Canada

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ABSTRACT

Objective: Chronic inflammation is implicated in causing cancer. Diet plays an important role in regulating chronic inflammation by altering circulating levels of inflammatory biomarkers. Effect of single food or nutrient on cancer often is inconclusive; perhaps due to dietary interactions and multicolinearity. The aim of this study was to determine prediagnostic inflammatory potential of overall diet in relation to risk for colorectal cancer (CRC).

Methods: In all, 547 patients with CRC from Newfoundland Familial Colorectal Cancer Registry and 685 controls from the general population were identified. Data on sociodemographic, medical history, lifestyle, and a 169-item food frequency questionnaire were collected retrospectively from both groups. Energy-adjusted Dietary Inflammatory Index (DII) score was calculated and used as both categorical and continuous variables for analysis. Odds ratio was estimated using multivariable logistic regression after adjusting potential confounders. A linear test for trend was performed using the median value in each quartile.

Results: Overall energy-adjusted mean DII score was −0.81 (range −5.19 to 6.93). Cases (−0.73 ± 1.5) had slightly higher DII scores than controls (−0.89 ± 1.6; $P = 0.04$). After adjusting the potential confounders, a statistically significant association was found between DII score and CRC risk. Using DII as a continuous variable (odds ratio $[OR]_{continuous}$ 1.10, 95% confidence interval [CI] 1.01–1.20) and categorical variable ($OR_{quartile\ 1\ versus\ 4}$ 1.65, 95% CI 1.13–2.42; $P_{trend} = 0.02$).

Conclusion: Our findings indicate that proinflammatory diets are associated with an increased risk for CRC in the Newfoundland population.

Introduction

Colorectal cancer (CRC) is one of the leading causes of cancer-related deaths worldwide. It is the third most common cancer in men and second in women [1]. CRC varies widely with higher incidence rates in developed nations and lower rates in Asian, African, and many Latin American countries [2]. CRC has become one of the major health problems in Canada, with an estimated 26 100 new cases and 9308 deaths in 2016 [3]. According to the Canadian Cancer Society, Newfoundland and Labrador (NL), the

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most eastern province, has the highest age-standardized incidence rate of CRC in Canada, at 96 per 100 000 compared with the national average of 67 per 100 000 [3]. The high rates of the disease in NL can be explained, in part by a high prevalence of families with a predisposition to hereditary colon cancer [4]. However, environmental factors that are an important component to CRC risk play a vital role in both the risk for and progression of the disease [5–9].

Genetic predisposition [4], age [10], and sex [11] are nonmodifiable risk factors; whereas physical inactivity, overweight/obesity, poor diet, excess alcohol consumption, and smoking are modifiable factors associated with risk for CRC [12,13]. Dietary behavior is considered to be one of the important determinants for cancer [14]. Diet plays an important role in the regulation of chronic inflammation [15] by altering levels of circulating inflammatory biomarkers [16]. Inflammatory microenvironment involves production of cytokines and chemokines leading to tumor initiation, growth, and invasion [17] by activating signaling pathways favoring carcinogenesis [18] and is particularly notable in CRC and other epithelial cancers [19].

Refined and processed foods, a typical Western dietary pattern including high-calorie drinks, soda, canned foods with heavy syrups, cheese, sugary and refined cereals, refined and processed meats, and so on, have higher inflammatory potential [20], whereas a prudent diet pattern with higher intake of fruits and vegetables are antiinflammatory in nature [21]. Despite food, and nutrients including supplements that have been studied independently in relation to the risk for the disease and survival of patients with CRC, little is known about the net inflammatory potential of overall diet on risk for the disease and survival of patients with it, as diet involves complex interactions of nutrients [22,23]. Because foods and nutrients act together [24–27], any assessment of a single food or nutrient is likely to be confounded [28,29]. The Dietary Inflammatory Index (DII) assesses the overall dietary inflammatory potential of the diet based on the food–nutrient response to the six inflammatory biomarkers (interleukin [IL]-1 β, IL-4, IL-6, IL-10, tumor necrosis factor [TNF]-α, and C-reactive proteins [CRPs]) [30]. The higher the DII score, the greater the potential for inflammation. The DII has been validated and used in different studies to assess the effect of dietary inflammation on the risk for and survival of chronic diseases and cancers [31,32].

Compared with other parts of Canada, NL has largely maintained its traditional diet, a Western-style with high proportion of red meat and less vegetables and fruits [33]. Although several studies have suggested the possible connection between food or nutrients and risk for CRC [33–35] in this population, the overall effect of diet has not been assessed. This study aimed to determine the prediagnostic inflammatory potential of an individual's diet and its association with the risk for CRC in the NL population.

Material and methods

Study population

This study used data from the previous population-based case–control study from NL [33]. CRC cases were recruited using the Newfoundland Familial Colorectal Cancer Registry (NFCCR), which was modeled on the Ontario Familial Colorectal Cancer Registry. Histopathologically confirmed cases 20 to 74 y of age between 1999 and 2003 were included. Incident CRC diagnosis was identified using codes from the International Classification of Diseases ninth revision. Controls were selected from the NL population through random-digit dialing using telephone numbers provided by Bell Aliant (a local telephone company in NL). Controls were age matched with cases by 5-y strata. Both cases and controls were residents of NL at time of diagnosis or interview. We included 1232 participants (547 cases and 685 controls) in the study. Detailed description for the selection of cases and controls is described elsewhere [33]. Informed consent was obtained from all research participants, and the study was carried out with the approval of the Health Research Ethics Authority, Memorial University of Newfoundland, in accordance with the Declaration of Helsinki.

Exposure variables

Information including personal history, lifestyle, and dietary characteristics was collected using a personal history questionnaire and a food frequency questionnaire (FFQ), which were developed as part of the larger study and were collected retrospectively 1 y before diagnosis or interview. Briefly, the personal history questionnaire consisted of 74 questions including history of bowel screening, medical conditions, use of medications, diet, physical activity, intake of alcohol, tobacco use, sociodemographic and economic information, and reproductive factors for women. Similarly, dietary intake data were collected using a 169-item FFQ similar to the Ontario FFQ customized to include foods from NL. Nutrient content was calculated using the Canadian Nutrient File, 2005.

Dietary inflammatory index score was calculated as described elsewhere [30]. Briefly, an individual's intake of food or nutrients was linked to a global database with mean and standard deviation (SD) consumption of ≤45 food–nutrient parameters. For each participant and each food parameter, a *z* score was derived. These scores were converted to a centered percentile score to reduce the effective skewness and multiplied by the respective food parameter effect derived from the literature review and scoring of 1943 articles. All food parameter–specific DII scores were summed to determine an individual's DII score. The DII score was adjusted for the energy (from macronutrients and alcohol) using the residual method for both men and women separately [36]. Ninety-five percentile data for energy were used for the analysis to remove the extreme values from both extremes of the distribution.

A higher DII score represents a greater inflammatory potential of diet. For the present study, 29 food parameters were available and used in computing the DII score: carbohydrates; proteins; total fat; alcohol; onion; tea; tea (herbal); pepper; β-carotene; vitamins B_6, B_{12}, E, D, and C; caffeine; cholesterol; energy; fiber; folic acid; iron; monounsaturated fatty acids (MUFAs); polyunsaturated fatty acids (PUFAs); niacin; magnesium; riboflavin; saturated fatty acids; selenium; thiamine; and zinc. Calculated DII scores were analyzed categorically and as continuous variables. Quartiles were based on DII scores in controls, and the respective quartiles are quartile I (<−2.036), quartile II (−2.036 to <−0.88), quartile III (−0.88 to <0.358), and quartile IV (≥0.3582).

Adjustment variables

Potential confounding factors include age, sex, body mass index (BMI; classified as <25, 25–29.99, and ≥30 kg/m^2), physical activity measured (metabolic equivalent h/wk [METs/wk classified as <10, 10–49.99, and ≥50]), medical history including cholesterol level, triacylglycerols (TGs), family history of CRC, polyps, diabetes, history of colon screening, cigarette smoking (classified as: yes and no, with yes meaning smokes one cigarette daily for ≥3 mo), and alcohol consumption (classified as standard drink/wk; not at all, <15 standard drink/wk, and ≥15 standard drink/wk), regular use of medications including nonsteroidal antiinflammatory drugs (NSAIDs), and reported hormone replacement therapy (HRT, women only).

Theory/calculation

Statistical analyses were performed using SAS statistical software (version 9.4 SAS Institute, Cary, NC, USA). The characteristics of cases and controls were compared by *t* test and analysis of variance for continuous variables, and χ^2 test for categorical variables.

Baseline characteristics were examined across the quartiles of DII. Odds ratio (OR) and 95% confidence interval (CI) were estimated using multivariable logistic regression model adjusting for age in the crude model and age of diagnosis, sex, smoking, history of screening, diabetes, high cholesterol, polyps, and physical activity in the final model. The basis for assessing the role of potential confounding factors included:

1. Existing evidence;
2. Biological plausibility;
3. Whether the regression coefficient of the primary dependent variable changed by ≥10% after addition of the potentially confounding variable; or
4. Whether the covariate entered the model at $P < 0.10$.

A stepwise selection procedure was used to identify potential confounding factors.

OR for continuous variables were calculated using DII score as a continuous variable. A linear test for trend was performed using the median value in each quartile. All tests of statistical inference employed a two-sided α level of 0.05.