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Fruit and Vegetable Consumption and the Risk of Proximal Colon, Distal Colon, and Rectal Cancers in a Case-Control Study in Western Australia

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ABSTRACT

Background Fruits and vegetables (F/V) have been examined extensively in nutrition research in relation to colorectal cancer (CRC). However, their protective effect is subject to debate, possibly because of different effects on different subsites of the large bowel.

Objective To determine whether any association between F/V consumption and risk of CRC differed by subsite of the bowel (proximal colon, distal colon, and rectum).

Design The Western Australian Bowel Health Study is a population-based, case-control study conducted between June 2005 and August 2007. Complete food frequency questionnaire data were analysed from 834 CRC cases and 939 controls. Logistic regression analysis was used to estimate the effects of quartiles of F/V intake on risk of CRC at different subsites. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for CRC overall and for the three separate subsites.

Results Risk of proximal colon cancer and rectal cancer was not associated with intakes of total F/V, total vegetable, or total fruit. Brassica vegetable intake was inversely related with proximal colon cancer (Q4 vs Q1 OR 0.62; 95% CI 0.41 to 0.93). For distal colon cancer, significant negative trends were seen for total F/V, and total vegetable intake. Distal colon cancer risk was significantly decreased for intake of dark yellow vegetables (Q4 vs Q1 OR 0.61; 95% CI 0.41 to 0.92) and apples (Q4 vs Q1 OR 0.51; 95% CI 0.34 to 0.77). An increased risk for CRC was found to be associated with intake of fruit juice (Q4 vs Q1 OR 1.74; 95% CI 1.24 to 2.45).

Conclusions Our results suggest that different F/V may confer different risks for cancer of the proximal colon, distal colon, or rectum. Future studies might consider taking into account the location of the tumor when examining the relation between F/V consumption and risk of CRC.

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Colorectal cancer (CRC) was the second most common cancer type in men and women in Australia in 2007, with an age-standardized rate of 63 out of 100,000 population (1). It is more common in men than in women (ratio of 1.4) and is rare before age 40 years, with age-specific rates increasing steeply after age 60 years. Mortality from CRC is much lower than incidence (age-standardized rate 18 out of 100,000 population).

Along with low physical activity, increased body mass index, and excess alcohol intake, another modifiable environmental risk factor for CRC may be a poor diet (2-5). Fruits and vegetables (F/V) have been examined extensively as potential risk factors for CRC. A review by a panel on behalf of the World Cancer Research Fund (6) concluded that, for CRC, there was reasonable evidence only for a protective effect of garlic intake. Although there were many studies of fruits and non-starchy vegetables, the results were inconsistent and the panel concluded

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there was limited evidence of a protective effect of these two groupings. Another meta-analysis showed that the reduced risk associated with vegetables was stronger in case-control compared to cohort studies, although no significant difference in the results between study type was shown for fruit intake (7).

Previous studies on CRC have often failed to distinguish between the different sites of origin of cancers in the large bowel, even though it is now well established that tumors in the proximal colon develop along different pathways to those of the distal colon and rectum (8,9) and that risk of cancer varies by subsite within the colorectum (8,10). There are a few studies that have looked specifically at CRC site, and these suggest that there may be a protective effect of high vegetable consumption on the risk of distal colon and rectal cancer but not proximal colon cancer (11-14). Results from studies of fruit consumption are more contradictory with high fruit intake being associated with increase (15) and decrease (7,14) in rectal cancer but no association with colon cancer.

The ongoing controversy regarding the association between F/V intake and risk of CRC may in part be due to the lack of accurate information on tumor subsite. A case-control design was used to investigate whether F/V intake was associated with the risk of CRC, and if any risk differed by the site of CRC origin in the proximal colon, distal colon, or rectum.

PARTICIPANTS AND METHODS

Study Design

The Western Australian Bowel Health Study is a case-control study designed to identify environmental and genetic risk factors for CRC that are specific to the anatomic site of origin in the large bowel, either a proximal, distal, or rectal origin of cancer (16). Proximal or right-sided colon cancers were defined as originating in the cecum, ascending colon, hepatic flexure, or transverse colon. Distal or left-sided colon cancers arose in the splenic flexure, descending colon, and sigmoid colon. Rectal cancers arose in the rectum or recto-sigmoid junction. Information on tumor site for each case was obtained from the pathology report stored at the Western Australian Cancer Registry. Almost all CRC histopathology reports in Western Australia are presented as synoptic reports in a standardized format that includes information on the site of origin of the tumor. Participants were recruited in Western Australia between June 1, 2005, and August 31, 2007. All procedures in the study protocol were approved by the Human Research Ethics Committee at the University of Western Australia and the Confidentiality of Health Information Committee, Western Australia Department of Health. Written informed consent was obtained from all participants.

Participants

Cases were eligible if they were histologically confirmed first incident cases of CRC (International Classification of Diseases version 10 [ICD-10] C18-C20) diagnosed during the study period and reported to the Western Australian Cancer Registry, resident in Western Australia, and aged between 40 and 79 years. There were 1,770 CRC cases notified to the Cancer Registry, of which 51 were ineligible for inclusion for the following reasons: living outside Western Australia (n=13), not adenocarcinoma or doubtful diagnosis (n=52), did not speak English (n=8), not well enough to participate (n=5), hereditary nonpolyposis colorectal cancer (n=2), incorrect address or age (n=8), clinician declined permission (n=33), or died within 3 months of diagnosis (n=105). Of the remaining 1,544 patients who were invited to participate, 1,009 consented and 918 (59.5%) returned the questionnaires.

Controls were randomly selected from the Western Australian electoral roll, excluding those with previous reported CRC. All Australian adults are obliged to register for the electoral roll. Controls were frequency matched for age and sex to cases based on the approximate distribution of CRC in Western Australia for 2002. A total of 2,247 controls were selected; of these, 49 were ineligible for participation for the following reasons: previous diagnosis of CRC (n=4), incorrect age (n=4), ill health (n=5), did not speak English (n=2), or incorrect address (n=34). Of the remaining 2,198 eligible controls, 1,021 participated (46.5%).

Data Collection

Data were collected via a self-completed postal questionnaire and a food frequency questionnaire (FFQ). Participants were asked in the postal questionnaire whether they had ever been told they had diabetes or high blood sugar, what type they had, and whether they were having daily insulin injections. From these data, participants were categorized as having insulin-dependent or noninsulin-dependent diabetes or high blood sugar only. Body mass index (BMI) at age 20 years was calculated from reported height and weight at age 20 years and was categorized according to World Health Organization guidelines (17). Although information on weight at several ages was available, the variable BMI at age 20 years was chosen because the strongest relationship was found for BMI at this age in this study. Other data collected included smoking status at the time of the survey (never smoked, exsmoker, or current smoker) and physical activity levels between the ages of 19 and 34 years (categorized as above and below 150 minutes/week).

To adjust for socioeconomic status, participants were assigned a socieconomic index for areas score based on a subject's address at the time of diagnosis or enrollment in the study. The socieconomic index for areas score is produced by the Australian Bureau of Statistics and measures and ranks areas according to socioeconomic conditions (18).

Dietary intake was assessed using a 74-item FFQ developed by the Cancer Council Victoria. The questionnaire included three questions on alcohol intake and further listed 74 foods, which were divided into food groups on the questionnaire. The fruit food group consisted of 13 food items and the vegetable food group included 25 food items. Each food had 10 frequency response options, ranging from "never" to "three or more times per day." A validation study against current weighed food records found reasonable correlations for all nutrients except retinol (19). This FFQ was specially modified to assess diet 10 years earlier and was found to be as reliable as other FFQs designed to measure recent dietary intake when