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BRIEF ARTICLE

Dietary polyphenols and colorectal cancer risk: The Fukuoka colorectal cancer study

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Abstract

AIM: To investigate the associations between dietary intake of polyphenols and colorectal cancer.

METHODS: The study subjects were derived from the Fukuoka colorectal cancer study, a community-based case-control study. The study subjects were 816 cases of colorectal cancer and 815 community-based controls. The consumption of 148 food items was assessed by a computer-assisted interview. We used the consumption of 97 food items to estimate dietary intakes of total, tea and coffee polyphenols. The Phenol-Explorer database was used for 92 food items. Of the 5 foods which were not listed in the Phenol-Explorer Database, polyphenol contents of 3 foods (sweet potatoes, satoimo and daikon) were based on a Japanese study and 2 foods (soybeans and fried potatoes) were estimated by ORAC-based polyphenol contents in the United States Department of Agriculture Database. Odds ratios (OR) and 95%CI of colorectal cancer risk according to quintile categories of intake were obtained by using logistic regression models with adjustment for age, sex, residential area, parental history of colorectal cancer, smoking, alcohol consumption, body mass index 10 years before, type of job, leisure-time physical activity and dietary intakes of calcium and n-3 polyunsaturated fatty acids.

RESULTS: There was no measurable difference in total or tea polyphenol intake between cases and controls, but intake of coffee polyphenols was lower in cases than in controls. The multivariate-adjusted OR of colorectal cancer according to quintile categories of coffee polyphenols (from the first to top quintile) were 1.00 (referent), 0.81 (95%CI: 0.60-1.10), 0.65 (95%CI: 0.47-0.89), 0.65 (95%CI: 0.46-0.89) and 0.82 (95%CI: 0.60-1.10), respectively (P_{trend} = 0.07). Similar, but less pronounced, decreases in the OR were also noted for the third and fourth quintiles of total polyphenol intake. Tea polyphenols and non-coffee polyphenols showed no association with colorectal cancer risk. The site-specific analysis, based on 463 colon cancer cases and 340 rectal cancer cases, showed an inverse association between coffee polyphenols and colon cancer. The multivariate-adjusted OR of colon cancer for the first to top quintiles of coffee polyphenols were 1.00 (referent), 0.92 (95%CI: 0.64-1.31), 0.75 (95%CI: 0.52-1.08), 0.69 (95%CI: 0.47-1.01), and 0.68 (95%CI: 0.46-1.00), respectively (P_{trend} = 0.02). Distal colon cancer showed a more evident inverse association with coffee polyphenols than proximal colon cancer. The association between coffee polyphenols and rectal cancer risk was *U*-shaped, with significant decreases in the OR at the second to fourth quintile categories. There was also a tendency that the OR of colon and rectal cancer decreased in the intermediate categories of total polyphenols. The decrease in the OR in the intermediate categories of total polyphenols was most pronounced for distal colon cancer. Intake of tea polyphenols was not associated with either colon or rectal cancer. The associations of coffee consumption with colorectal, colon and rectal cancers were almost the same as observed for coffee polyphenols. The trend of the association between coffee consumption and colorectal cancer was statistically significant.

CONCLUSION: The present findings suggest a decreased risk of colorectal cancer associated with coffee consumption.

Key words: Colorectal cancer; Colon cancer; Rectal cancer; Polyphenols; Coffee; Tea

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INTRODUCTION

Colorectal cancer is one of the most common cancers in the world and the second most common cause of cancer death in developed countries[1]. In Japan, the incidence rate of colorectal cancer, especially of colon cancer, has increased dramatically until the 1990s[2]. Lifestyle factors such as physical inactivity, obesity and alcohol use are known to confer increased risk of colorectal cancer. Of dietary factors, high intake of red meat has been related to increased risk of colorectal cancer, and fiber-containing plant foods and calcium have been considered to be protective[3].

Polyphenols are the most abundant antioxidants in foods and have drawn much interest as potentially anticarcinogenic compounds. The flavonoids have been identified as potential cancer-preventive components of fruits and vegetables[4]. Catechins and tea polyphenols inhibit tumorigenesis at initiation, promotion, and progression stages in animal experiments[5]. Coffee is the major source of polyphenol intake in populations in which coffee is commonly consumed[6], and phenolic compounds in coffee such as chlorogenic acids also have anticarcinogenic effects in animal models[7]. Epidemiological studies have suggested that polyphenol-rich foods such as fruits and vegetables[3,8] and beverages such as tea[9-13] and coffee[14,15] may be protective against colorectal cancer. Experimental studies on colorectal cancer cell lines also support a protective role of polyphenols in carcinogenesis by exerting antioxidant and anti-proliferative effects and by inducing cell cycle arrest[16]. In the study reported here, we addressed the association of dietary intake of polyphenols with colorectal cancer risk using data from a community-based case-control study in Japan[17].

MATERIALS AND METHODS

The present data were derived from the Fukuoka colorectal cancer study, a community-based case-control study in Fukuoka, Japan. The research protocol was approved by the ethics committee of Kyushu University and collaborating hospitals. Details of the design and conduct of the study have been described elsewhere[17].

Study subjects

Cases were histologically confirmed incident cases of colorectal adenocarcinomas who were admitted for surgical treatment to one of the collaborating hospitals in Fukuoka City and three adjacent areas during the period from September 2000 to December 2003. Of 1053 eligible cases, a total of 840 cases (80%) participated in the interview; the eligible cases were aged between 20-74 years at the time of diagnosis; lived in the study area; had no prior history of partial or total removal of the colon, familial adenomatous polyposis or inflammatory bowel disease; and were mentally competent to give informed consent and to complete the interview. Research staff visited each hospital regularly, determined the eligibility of cases by referring to admission logs and medical records, and interviewed him/her if written informed consent was obtained.

Eligibility criteria for controls were the same as described for the cases except that they had no history of colorectal cancer. A total of 1500 control candidates were randomly selected by a two-stage random sampling on the basis of a resident registry with the frequency by sex and 10-year age class matched to expected sex- and age-specific frequencies of cases. Recruitment was initiated by a letter of invitation, which was followed by phone calls if available. After exclusion of 113 who were found to be ineligible and 5 who were diagnosed with colorectal cancer after the interview, 833 (60%) participated in the interview.

In the analysis, we excluded those who were in the top 1% or bottom 1% of total energy intake within each stratum of sex and age class (< 55, 55-64, and ≥ 65 years of age). A total of 816 cases and 815 controls remained.

Lifestyle questionnaire

Cases and controls were interviewed in person regarding smoking, alcohol use, physical activity and other factors using a uniform questionnaire. The index date was taken as the date of onset of symptoms or the screening leading to the diagnosis of colorectal cancer for cases and the date of interview for controls. Anthropometric questions inquired about height (cm) and body weight (kg) at the time of interview and 10 years earlier. Body mass index (kg/m^2) 10 years earlier was used in the analysis because the current body mass index was unrelated to the risk[18]. For 4 cases and 11 controls, body weight 10 years before was not ascertained, and the current body weight was used for substitution. The amount of alcohol was expressed using the conventional Japanese unit; one go (180 mL) of sake, one large bottle (633 mL) of beer and half a go (90 mL) of shochu were each expressed as one unit; and one drink (30 mL) of whisky or brandy and one glass (100 mL) of wine were each converted to half a unit. Regarding smoking, ever smokers reported years of smoking and the numbers of cigarettes per day for each decade of life, and we calculated the cumulative exposure to cigarette smoking until the beginning of the previous decade of age. Types of job and non-job physical activities 5 years before were ascertained. The amount of non-occupational physical activity was expressed as a sum of metabolic equivalents (MET) multiplied by the hours of weekly participation in each activity, *i.e.*, MET-hours per week. History of parental colorectal cancer also was obtained.

Dietary assessment

Consumption frequencies and portion sizes of 148 food and beverage items were ascertained by a computer-assisted interview. Details of the dietary interview have been described elsewhere[19]. Participants were asked to report their usual consumption during the past 12 mo. Intakes of nutrients were calculated based on the food composition tables in Japan[20]. To estimate dietary intake of polyphenols, we used 97 food items, including cereals, soybeans, vegetables, fruits, beverages and condiments.

Table 1 Characteristics of colorectal cancer cases and controls

Variables	Cases (n = 816)	Controls (n = 815)
Male	60%	62%
Age (yr), mean ± SD	60.5 ± 9.1	58.9 ± 10.7
Dietary intake, median (IQR)[1]		
Total polyphenols (mg/d)	1025 (698-1487)	1047 (736-1431)
Tea polyphenols (mg/d)[2]	432 (226-576)	397 (215-509)
Coffee polyphenols (mg/d)[3]	187 (0.2-619)	260 (39-643)

[1]Polyphenols and food intakes were energy-adjusted to 2000 kcal/d; [2]Included green tea, black tea and oolong tea; [3]Included coffee infusion, instant coffee and coffee drinks. IQR: Interquartile range.

Polyphenols for 92 food items were derived from the Phenol-Explorer Database, which is a compilation of polyphenol contents of 452 daily foods and beverages based on 638 published analytical studies[21]. As for the remaining 5 foods which were not listed in the Phenol-Explorer Database, polyphenol contents of 3 foods (sweet potatoes, satoimo and daikon) were based on a Japanese study[22], and 2 foods (soybeans and fried potatoes) were estimated by ORAC-based polyphenol contents in the United States Department of Agriculture Database[23].

Statistical analysis

Dietary intakes of the nutrients and polyphenols were transformed to a natural log-scale and were adjusted to a total energy intake of 2000 kcal/d by the regression residual method[24]. Subjects were divided into quintile categories according to intakes of polyphenols among controls. Logistic regression analysis was used to estimate odds ratios (OR) and 95%CI of colorectal cancer for each category with the lowest quintile category as the referent group. We also calculated the OR according to coffee consumption in terms of the number of cups per week or day, with an assumption that one cup corresponded to 150 g of coffee infusion.

Confounding variables under consideration were age, sex, residential area (Fukuoka City or others), parental history of colorectal cancer, smoking (0, 1-399, 400-799 or > 800 cigarettes/year), alcohol consumption (0, 0.1-0.9, 1.0-1.9 or ≥ 2 units per day), body mass index 10 years before (< 22.5, 22.5-24.9, 25.0-27.4 or ≥ 27.5 kg/m^2), type of job (sedentary or non-sedentary), leisure-time physical activity (0, 1-5.9 or ≥ 6 MET-h/wk) and dietary intakes of calcium and n-3 polyunsaturated fatty acids (PUFA). Calcium and n-3 PUFA intakes were related to decreased risk of colorectal cancer in the study population[25-29]. Trends of the associations were assessed with ordinal scores assigned to quintile categories of intake. Statistical significance was declared with the two-sided $P < 0.05$. Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC, United States).

RESULTS

Demographic and lifestyle characteristics of colorectal

Table 2 Association of dietary polyphenol intakes with colorectal cancer risk

Nutrient (unit)	Quintile of intake					P_{trend}
	Q1 (low)	Q2	Q3	Q4	Q5 (high)	
Total polyphenols						
Median (mg/d)	534	812	1047	1335	2104	
Cases/controls	190/163	170/163	142/163	138/163	176/163	
OR (95%CI)[1]	1 (reference)	0.85 (0.62, 1.16)	0.72 (0.52, 0.98)	0.74 (0.54, 1.02)	0.95 (0.70, 1.31)	0.52
OR (95%CI)[2]	1 (reference)	0.85 (0.62, 1.16)	0.72 (0.52, 1.00)	0.74 (0.54, 1.03)	0.97 (0.70, 1.33)	0.59
Tea polyphenols						
Median (mg/d)	65	224	397	475	853	
Cases/controls	128/163	151/163	184/163	157/163	196/163	
OR (95%CI)[1]	1 (reference)	1.14 (0.82, 1.58)	1.37 (0.99, 1.89)	1.13 (0.81, 1.58)	1.37 (0.99, 1.90)	0.09
OR (95%CI)[2]	1 (reference)	1.13 (0.81, 1.57)	1.36 (0.98, 1.88)	1.16 (0.83, 1.62)	1.38 (0.99, 1.92)	0.08
Coffee polyphenols						
Median (mg/d)	0	82	260	541	1287	
Cases/controls	220/163	167/163	133/163	129/163	167/163	
OR (95%CI)[1]	1 (reference)	0.80 (0.59, 1.08)	0.65 (0.48, 0.90)	0.64 (0.46, 0.87)	0.83 (0.60, 1.13)	0.09
OR (95%CI)[2]	1 (reference)	0.81 (0.60, 1.10)	0.65 (0.47, 0.89)	0.65 (0.46, 0.89)	0.82 (0.60, 1.12)	0.07
Polyphenols other than coffee						
Median (mg/d)	280	466	631	790	1104	
Cases/controls	131/163	158/163	181/163	166/163	180/163	
OR (95%CI)[1]	1 (reference)	1.17 (0.85, 1.63)	1.29 (0.93, 1.79)	1.13 (0.81, 1.58)	1.23 (0.88, 1.72)	0.35
OR (95%CI)[2]	1 (reference)	1.19 (0.86, 1.66)	1.31 (0.94, 1.82)	1.20 (0.85, 1.69)	1.31 (0.93, 1.84)	0.19

[1]Adjusted for age, sex, residence area, parental history of colorectal cancer, smoking, alcohol drinking, body mass index 10 years before, type of job and leisure-time physical activity; [2]Further adjusted for calcium and n-3 polyunsaturated fatty acids. OR: Odds ratio.

cancer cases and controls were previously described[25-29]. The two groups did not differ much with respect to sex, age, residence area and most other factors. Body mass index was greater and a history of parental colorectal cancer was slightly more frequent in the cases than in the controls. There was no measurable difference in total or tea polyphenol intake between cases and controls, but intake of coffee polyphenols was lower in cases than in controls (Table 1). In the whole sample, intake of total polyphenols derived from tea and coffee was 38% and 34%, respectively.

The associations of intakes of total, tea and coffee polyphenols with colorectal cancer are shown in Table 2. Statistically significant decreases in the OR were observed in those with high intake of coffee polyphenols (the third and fourth quintile categories) compared with the lowest quintile, but the OR for the top quintile did not decrease further, showing an upward tendency. Similar, but less pronounced, decreases in the OR were also noted for the third and fourth quintiles of total polyphenol intake. Tea polyphenols and non-coffee polyphenols showed no clear association with colorectal cancer risk regardless of adjustment for the dietary factors.

Multivariate-adjusted ORs in the subsite-specific analysis are summarized in Table 3. Cases of colon and rectal cancers numbered 463 and 340, respectively. There were 188 cases who had proximal colon cancer only and 272 cases with distal colon cancer alone. The OR of colon cancer decreased with increasing intakes of coffee polyphenols; although the individual OR for the third to fifth quintiles were not significantly different from unity, a decreasing trend was statistically significant. Distal colon cancer showed a more evident inverse association with coffee polyphenols than proximal colon cancer. The association between coffee polyphenols and rectal cancer was *U*-shaped, with significant decreases in the OR at the second to fourth quintile categories. Again, there was a tendency for the OR of colon and rectal cancer to decrease in the intermediate categories of total polyphenols. The decrease in the OR in the intermediate categories of total polyphenols was most pronounced for distal colon cancer. Intake of tea polyphenols was not associated with either colon or rectal cancer.

Additionally, we analyzed the associations of coffee consumption with colorectal cancers (Table 4). The associations of coffee consumption with colorectal, colon, and rectal cancers were almost the same as observed for coffee polyphenols. Nonetheless, the trend of the association between coffee consumption and colorectal cancer was statistically significant. The trend of an inverse association with coffee was also statistically significant for distal colon cancer. The OR of proximal colon cancer tended to decrease with increasing consumption of coffee, but the trend failed to reach statistical significance.

DISCUSSION

The present study showed protective associations of coffee polyphenols and coffee consumption with the risk of colorectal cancer, especially of colon cancer. Non-coffee polyphenols showed no measurable association with the overall or site-specific risk of colorectal cancer. Thus, a modestly decreased risk of colorectal cancer associated with total polyphenol intake was probably ascribed to coffee polyphenols.

The association between coffee consumption and colorectal cancer has been examined in many studies in different populations. A meta-analysis of 12 cohort stud-

Table 3 Multivariate-adjusted odds ratio (95%CI) of colon and rectal cancers according to polyphenols intake

Nutrient	Quintile of intake					P_{trend}
	Q1 (low)	Q2	Q3	Q4	Q5 (high)	
Total polyphenols						
Colon						
Cases/controls	111/163	110/163	76/163	80/163	86/163	
OR (95%CI)[1]	1 (reference)	0.90 (0.63, 1.29)	0.66 (0.45, 0.96)	0.73 (0.50, 1.07)	0.81 (0.55, 1.18)	0.13
Proximal colon						
Cases/controls	40/163	45/163	34/163	38/163	31/163	
OR (95%CI)[1]	1 (reference)	0.91 (0.55, 1.52)	0.78 (0.46, 1.33)	0.91 (0.53, 1.54)	0.79 (0.45, 1.38)	0.44
Distal colon						
Cases/controls	70/163	64/163	42/163	42/163	54/163	
OR (95%CI)[1]	1 (reference)	0.86 (0.56, 1.31)	0.57 (0.36, 0.91)	0.61 (0.38, 0.98)	0.79 (0.50, 1.23)	0.11
Rectum						
Cases/controls	77/163	60/163	62/163	56/163	85/163	
OR (95%CI)[1]	1 (reference)	0.73 (0.48, 1.10)	0.73 (0.48, 1.11)	0.70 (0.46, 1.07)	1.08 (0.72, 1.62)	0.74
Tea polyphenols						
Colon						
Cases/controls	64/163	92/163	103/163	98/163	106/163	
OR (95%CI)[1]	1 (reference)	1.37 (0.91, 2.05)	1.50 (1.00, 2.23)	1.34 (0.89, 2.03)	1.42 (0.95, 2.14)	0.18
Proximal colon						
Cases/controls	21/163	33/163	44/163	41/163	49/163	
OR (95%CI)[1]	1 (reference)	1.38 (0.75, 2.54)	1.77 (0.98, 3.19)	1.42 (0.77, 2.61)	1.82 (1.01, 3.30)	0.08
Distal colon						
Cases/controls	43/163	58/163	58/163	56/163	57/163	
OR (95%CI)[1]	1 (reference)	1.36 (0.85, 2.19)	1.32 (0.82, 2.12)	1.26 (0.77, 2.06)	1.18 (0.72, 1.92)	0.74
Rectum						
Cases/controls	62/163	57/163	80/163	56/163	85/163	
OR (95%CI)[1]	1 (reference)	0.89 (0.57, 1.36)	1.25 (0.83, 1.88)	0.91 (0.59, 1.42)	1.27 (0.84, 1.93)	0.25
Coffee polyphenols						
Colon						
Cases/controls	128/163	103/163	82/163	75/163	75/163	
OR (95%CI)[1]	1 (reference)	0.92 (0.64, 1.31)	0.75 (0.52, 1.08)	0.69 (0.47, 1.01)	0.68 (0.46, 1.00)	0.02
Proximal colon						
Cases/controls	52/163	41/163	34/163	32/163	29/163	
OR (95%CI)[1]	1 (reference)	0.89 (0.55, 1.44)	0.75 (0.45, 1.25)	0.76 (0.45, 1.27)	0.70 (0.41, 1.20)	0.15
Distal colon						
Cases/controls	76/163	61/163	47/163	42/163	46/163	
OR (95%CI)[1]	1 (reference)	0.89 (0.58, 1.35)	0.72 (0.46, 1.12)	0.62 (0.39, 0.98)	0.66 (0.42, 1.04)	0.02
Rectum						
Cases/controls	90/163	62/163	48/163	53/163	87/163	
OR (95%CI)[1]	1 (reference)	0.65 (0.44, 0.98)	0.50 (0.33, 0.77)	0.55 (0.36, 0.84)	0.93 (0.63, 1.37)	0.51

[1]Adjusted for age, sex, residence area, parental history of colorectal cancer, smoking, alcohol drinking, body mass index 10 years before, type of job, leisure-time physical activity, calcium and n-3 polyunsaturated fatty acid. OR: Odds ratio.

ies found a relative risk (RR) of 0.91 (95%CI: 0.81-1.02) of colorectal cancer for the highest versus lowest coffee consumption[15]. A slightly pronounced decrease in the RR of colorectal cancer for the highest versus lowest consumption was noted in a combined analysis of 3 Japanese cohort studies (RR = 0.83, 95%CI: 0.62-1.10)[15]. On the other hand, a decrease in the risk of colorectal cancer associated with coffee use was more pronounced in a meta-analysis of 24 case-control studies[14]. The pooled OR for the highest versus non/low consumption was 0.70 (95%CI: 0.60-0.81) for colorectal cancer, 0.75 (95%CI: 0.60-0.81) for colon cancer and 0.87 (95%CI: 0.75-1.00) for rectal cancer[14]. A weaker association in the cohort studies is probably ascribed to a different time of exposure under consideration[14]. Coffee consumption in the recent past was assessed in most case-control studies. In the cohort studies, a follow-up shorter than 10 years was more likely to result in an inverse association between coffee consumption and colorectal cancer risk than a longer follow-up[15]. In a recent large cohort study[30], coffee consumption was associated with a decreased risk of proximal colon cancer, but not of distal colon cancer. The present study showed no such site-specific association with coffee.

Coffee polyphenolic compounds include chlorogenic, caffeic, ferulic and cumaric acids, and diterpenes (cafestol and kahweol) have been shown to possess anticarcinogenic properties[7]. Possible mechanisms by which coffee polyphenols are protective against colorectal cancer include reduction in bile acid secretion[31], reduction in the synthesis of bile by down-regulation of the expression of bile acid homeostatic genes[32] and increase in colonic motility[33].

The present study did not provide any evidence for a decreased risk of colorectal cancer associated with dietary intake of tea polyphenols. Tea polyphenols have been

Table 4 Association of frequency of coffee consumption with colorectal cancer risk

	Frequency of coffee consumption					P_{trend}
	< 1 cup/wk	1-3 cups/wk	4-6 cups/wk	1-3 cups/d	⩾ 4 cups/d	
Colorectal						
Cases/controls	245/181	93/83	66/78	265/317	147/156	
OR (95%CI)[1]	1 (reference)	0.88 (0.61, 1.26)	0.66 (0.45, 0.99)	0.65 (0.50, 0.85)	0.82 (0.59, 1.13)	0.01
Colon						
Cases/controls	145/181	62/83	40/78	141/317	75/156	
OR (95%CI)[1]	1 (reference)	1.04 (0.69, 1.57)	0.75 (0.47, 1.18)	0.64 (0.47, 0.87)	0.78 (0.53, 1.14)	0.01
Proximal colon						
Cases/controls	60/181	22/83	19/78	62/317	25/156	
OR (95%CI)[1]	1 (reference)	0.84 (0.47, 1.50)	0.88 (0.48, 1.62)	0.69 (0.45, 1.06)	0.69 (0.39, 1.21)	0.08
Distal colon						
Cases/controls	84/181	40/83	21/78	78/317	49/156	
OR (95%CI)[1]	1 (reference)	1.16 (0.72, 1.89)	0.65 (0.37, 1.15)	0.58 (0.40, 0.85)	0.82 (0.52, 1.29)	0.02
Rectum						
Cases/controls	98/181	29/83	26/78	118/317	69/156	
OR (95%CI)[1]	1 (reference)	0.63 (0.38, 1.04)	0.55 (0.32, 0.93)	0.63 (0.45, 0. 88)	0.82 (0.54, 1.23)	0.10

[1]Adjusted for age, sex, residence area, parental history of colorectal cancer, smoking, alcohol drinking, body mass index 10 years before, type of job, leisure-time physical activity, calcium and n-3 polyunsaturated fatty acid. OR: Odds ratio.

shown to have anti-cancer properties in numerous *in vitro* and *in vivo* studies[34,35], but epidemiologic findings are inconsistent as regards tea and colorectal cancer risk. In China, regular green tea consumption was associated with a reduced risk of colorectal cancer in male non-smokers, but not in male smokers[9] and in women[10]. On the other hand, in cohort studies of Chinese in Singapore[11] and Japan[13], green tea consumption was unrelated to colorectal cancer risk in men and women combined. A pooled analysis of 13 cohort studies in Western countries showed an increased risk associated with tea consumption; the RR for a consumption of > 900 g in liquid/d) versus no consumption was 1.28 (95%CI: 1.02-1.61) in men and women combined[12]. A combined analysis of two Japanese prospective studies found no association between green tea consumption and colorectal cancer risk[13].

We examined the associations with polyphenol and coffee for proximal and distal colon cancer separately, because these two cancers have distinct molecular mechanisms in carcinogenesis[36]. It was recently suggested that molecular changes in colorectal cancer were continuous, rather than dichotomous, from rectum to ascending colon[37]. The number of colorectal cancer cases was not large enough to perform a detailed subsite analysis in the present study. It should be noted that the difference in the molecular changes among the detailed subsites of proximal colon was less marked as compared with the difference between proximal and distal colon cancer.

In addition to a large sample size and the use of community controls, the detailed dietary assessment was a notable strength in the present study. The dietary interview was conducted as an in-person interview with typical dishes and serving sizes shown on a computer display. The present study had some weaknesses to be mentioned. The retrospective assessment of diet is a problem inherent to case-control studies. Dietary intakes in the past year may not have captured a habitual consumption relevant to the development of colorectal cancer. Additionally, the participation rate was lower in the controls (60%) than in the cases (80%), and this may have caused a selection bias.

In conclusion, a case-control study in Japan showed protective associations of coffee polyphenols and coffee consumption with the risk of colorectal cancer, especially of colon cancer.

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COMMENTS

Background

Polyphenols are the most abundant antioxidants in foods and have drawn much interest as potentially anticarcinogenic compounds. Epidemiological studies have suggested that polyphenol-rich foods and beverages may be protective against colorectal cancer.

Research frontiers

The Phenol-Explorer Database has enabled researchers to study the association between polyphenol intake and cancer risk. Evidence from meta-analyses

indicates that coffee may be protective against colorectal cancer.

Innovations and breakthroughs

This was the first Japanese epidemiological study reporting that coffee polyphenol intake was associated with a decreased risk of colorectal cancer, particularly of colon cancer.

Applications

Understanding the role for coffee polyphenols in colorectal carcinogenesis may advance a future strategy in the prevention of colorectal cancer.

Terminology

The flavonoids are plant antioxidative compounds and possess anticaricinogeneic properties. Tea catechins are a class of flavonoids, and are shown to inhibit tumorigenesis in animal experiments. Coffee is the major source of polyphenol intake such as chlorogenic and caffeic acids.

Peer review

The present study is a very timely and well performed study that investigates the associations between intake of dietary polyphenols and colorectal cancer. The authors have done a tremendous job of designing and executing the project, and the data analysis and interpretations are very logical. I think these data are very important and provide another dimension and validity to the growing awareness of diet and its link to colorectal cancer.

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