Null Results in Brief

No Association between Fat and Fatty Acids Intake and Risk of Colorectal Cancer[1]

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Introduction

The results of *in vitro* and *in vivo* studies, along with those of animal studies, suggest that some types of polyunsaturated fatty acids, such as ω-3 fatty acids, EPA,[3] and DHA, present in fish oil, may be inversely associated with colorectal cancer risk (1, 2). On the contrary, ω-6 fatty acid, specifically linoleic acid, may be positively associated with risk (3). We examined total fat, fat types, and specific fatty acids in relation to colorectal cancer risk in a population-based prospective cohort of Swedish women.

Materials and Methods

The design of our study has been described in detail elsewhere (4). In brief, from 1987 to 1990 a population-based mammography-screening program was introduced in two counties in central Sweden. The study cohort comprised 61,463 women who had returned questionnaires and were cancer-free at the start of follow-up. Participants were asked how often over the past 6 months they had consumed 67 commonly eaten food items. The validity estimate for total fat consumption was measured as a Pearson correlation coefficient between the food questionnaire and food records ($r = 0.5$). The validity of saturated fat was $r = 0.4$, monounsaturated fat $r = 0.5$, and polyunsaturated fat $r = 0.4$. The validity of polyunsaturated fat relative to adipose tissue composition was $r = 0.05$.

Cases of invasive colon and rectum cancers were identified through matching of the cohort with the computerized Regional Cancer Registers through December 31, 1998, documented to be 98% complete. Dates of deaths and emigration in the cohort were ascertained through matching with the Swedish Death Register and the Swedish Population Register. Cox proportional hazards models were used to estimate hazard RRs with 95% CIs. As a basis for the trend tests, median values of each category of categorized variables were placed together in the model.

Results

Intake of total, saturated, monounsaturated, and polyunsaturated fats were not associated with colorectal cancer at any subsite, including proximal and distal colon. The ratio of saturated fat: polyunsaturated fat was not associated with risk (RR for the highest compared with the lowest quartile was 1.08; 95% CI, 0.80–1.47). The ratio of ω-3:ω-6 fatty acids was not associated with risk (RR for the highest compared with the lowest quartile was 0.99; 95% CI, 0.74–1.31) with no dose-risk trend. The ratio of DHA + EPA:linoleic acid showed a similar lack of association. We observed no associations for any of the specific polyunsaturated fatty acids (Table 1), including linoleic acid (18:2; ω-6), α-linolenic acid (18:3; ω-3), EPA (ω-3), DHA (ω-3), or sum of ω-6 fatty acids or ω-3 fatty acids. Linoleic acid and also sum of ω-6 fatty acids, where linoleic acid is predominant, showed some suggestion of a positive association with rectal cancer risk, but trends were not statistically significant. With 460 cases of colorectal cancer, given a 5% significance level and a proportion $P = 0.25$ of exposed subjects, the power to detect a RR of 1.5 is over 85%. Excluding cases that occurred during the first 3 years of follow-up did not alter our results.

We could not adjust our RR estimates for the potentially confounding effect of exercise, because this information was not collected at baseline. Energy intake, a rough indicator of physical activity, was not associated with colorectal cancer in our data, and our results were not altered by adjustment for the effects of energy intake or body mass index. Our data were further limited by the likelihood of some degree of measurement error of the dietary fat exposures. Such nondifferential misclassification would tend to attenuate RR estimates; therefore, we cannot rule out the possibility of weak associations that were not observed in our data.

In conclusion, we found no clear association between any of the studied dietary fats or fatty acids and colorectal cancer risk. These null findings are consistent with previous studies (5) of major fat types, the majority of which show weak or null associations. Our results are also consistent with the few previous studies (5) of specific fatty acids that show neither strong nor consistent associations in relation to colon or rectal cancer risk. True associations, if they exist, are likely to be weak.

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[3] The abbreviations used are: EPA, eicosapentaenoic acid, DHA, docosahexaenoic acid; RR, rate ratio; CI, confidence interval.

Table 1 Multivariate-adjusted[a] RRs for fat intake in relation to colorectal cancer risk

	Medians	Colorectal $n = 460$ RR (95% CI)	Colon $n = 291$[b,c] RR (95% CI)	Rectal $n = 159$ RR (95% CI)
Linoleic acid				
Lowest	3.7	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Second quartile	4.9	0.97 (0.72–1.29)	0.74 (0.52–1.05)	1.59 (0.95–2.65)
Third quartile	6.0	1.09 (0.82–1.45)	0.77 (0.54–1.11)	2.02 (1.21–3.35)
Highest	7.4	1.06 (0.78–1.45)	0.88 (0.61–1.30)	1.53 (0.87–2.69)
P for trend		0.53	0.67	0.12
α-Linolenic acid				
Lowest	0.45	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Second quartile	0.50	0.96 (0.73–1.27)	0.96 (0.68–1.35)	0.95 (0.60–1.52)
Third quartile	0.54	0.96 (0.72–1.28)	0.96 (0.67–1.37)	0.92 (0.56–1.49)
Highest	0.70	0.99 (0.75–1.32)	0.90 (0.63–1.28)	1.11 (0.70–1.78)
P for trend		0.99	0.57	0.65
EPA				
Lowest	0.03	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Second quartile	0.05	0.88 (0.68–1.15)	0.76 (0.54–1.06)	1.17 (0.75–1.83)
Third quartile	0.07	0.96 (0.73–1.26)	0.81 (0.58–1.15)	1.29 (0.80–2.06)
Highest	0.09	0.96 (0.72–1.28)	0.85 (0.60–1.21)	1.25 (0.75–2.06)
P for trend		0.91	0.46	0.35
DHA				
Lowest	0.08	1.0 (Referent)	1.0 (Referent)	1.0 (Referent)
Second quartile	0.11	0.88 (0.67–1.15)	0.84 (0.60–1.17)	1.03 (0.66–1.61)
Third quartile	0.13	0.87 (0.66–1.15)	0.74 (0.51–1.06)	1.16 (0.73–1.84)
Highest	0.18	0.90 (0.67–1.20)	0.88 (0.61–1.26)	1.03 (0.62–1.71)
P for trend		0.49	0.41	0.79

[a] Multivariate models included age, body mass index, education level, energy intake, intakes of red meat and alcohol, energy, dietary fiber, calcium, vitamin C, folic acid, and vitamin D. Saturated fat, monounsaturated fat, and polyunsaturated fat were included in the same model.
[b] Seventy-two cases of colon cancer were of unspecified location.
[c] Ten colorectal cancers were diagnosed in both the colon and rectum.

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