Colon Cancer, Physical Activity, and Occupational Exposures

A Case–Control Study

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A case–control study on colon cancer was conducted encompassing 329 cases and 658 controls. Occupations and various exposures were assessed by questionnaires. A decreased risk was found in persons with physically active occupations. This effect was most pronounced in colon descendens and sigmoideum with an odds ratio (OR) of 0.49 whereas no reduced risk was found for right-sided colon cancer. Regarding specific jobs, reduced ORs were found for agricultural, forestry, and saw mill workers and increased OR for railway employees. High-grade exposure to asbestos or to organic solvents gave a two-fold increased risk. Regarding exposure to trichloroethylene in general, a slightly increased risk was found whereas such exposure among dry cleaners gave a seven-fold increase of the risk.

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COLON CANCER was the third most common cancer among Swedish males in 1984 representing 7.3% of all cancer cases. In females colon cancer was the second most common malignant disease with 8.1% of all cases. The incidence increased slowly between 1965 and 1984 with an annual change of 0.6% in males and 0.5% in females. The age standardized annual incidence rate per 100.000 was 32.9 among males and 26.9 among females in 1984. It is known since before that the incidence is lower in the northern part of the country. The population underlying this case–control study lives in the catchment area of Umeå University Hospital corresponding to the three most northern counties of Sweden where the age adjusted annual incidence rate per 100.000 was 27.1 among males and 25.4 among females in 1984.

The etiology of colon cancer is not well understood. Correlation studies of the incidence and mortality rates of colon cancer and food habits indicate that dietary factors may play an etiologic role. Investigations of migrants support that concept. Dietary fat increases the secretion of bile acids and neutral steroids which may act as promoters. Another mechanism might involve carcinogens formed by bacterial degradation.[1,2] High consumption of meat may increase the risk through the formation of carcinogenic amino acid degradation products in the large bowel or carcinogens produced by frying or boiling the meat.[3,4] Mutagenic substances such as fecapentaenes and ketosteroids have been identified in extracts of the feces of approximately one third of individuals on Western diet.[5,6] Fibers, indoles, beta-carotene, vitamin C, selenium, and calcium in the diet have been discussed as possibly preventive factors for colon cancer.[7]

Although colorectal cancer has not generally been considered an occupational disease, heavy asbestos exposure has been suggested to increase the risk.[8] An increased risk for colorectal cancer has been reported in metal workers, but also among workers in yarn or textile industries and leather goods manufacture.[9]

An association between physical activity and colon cancer was suggested by Jones and Godding.[10] This relationship was also discussed in a study on colon cancer by Hardell,[11] where it was noted that use of motor saws was twice as common among the controls than among the cases indicating a possible preventive effect of physical activity. In a more recently published study, men with sedentary jobs were found to have a colon cancer risk of 1.6 times that of men with jobs requiring a high level of activity.[12] The complementary preventive effect of physical activity was strongest in the descending colon. No correlation was seen between job activity and risk for rectal cancer. In another study,[13] the overall relative risk (RR) of colon cancer in sedentary occupations was estimated

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to 1.3 with the highest risk for the transverse colon (RR = 1.6).

This report presents the results of analyses relating to occupational factors only. The effects of diet, drugs, *etc.*, will be presented in another report, but these factors have been considered to some extent from the point of view of confounding, however.

Materials and Methods

Cases

The cases of the study consisted of all persons aged 30 to 75 years with large bowel cancer adenocarcinoma (ICD-8 code 153.01–153.89) who had been diagnosed between 1980 and 1983 as reported to the Swedish Cancer Registry, and who were residents of the admission region of the Department of Oncology in Umeå. Only persons who were alive at the time of the data collection for the study (1984–1986) were included. In total 402 cases (206 women, 196 men) were originally identified according to the criteria described, but 58 cases died and were therefore excluded. One case had been used as a control in a previous case–control study and was excluded for ethical reasons, *i.e.*, for avoiding another contact. Of the remaining 344 cases another eight were excluded due to inadequate histopathologic data and one case turned out to have a rectal adenocarcinoma having been miscoded and was therefore also excluded. Six additional cases were unable to participate for medical reasons such as older age and dementia. Eventually, the study therefore included 329 cases; 165 men and 164 women.

Controls

For each case two persons from the same county, of the same sex and closest in age were drawn as controls from the National Population Register. Thirty-five controls were unable to answer the questionnaire due to medical reasons. For these as well as for 24 controls who recently died who were still in the population register, the next closest control in age was used instead, so that the number of the controls was twice that of the cases or 658.

Assessment of Exposure

An 18-page questionnaire was mailed to all included cases and controls. In the first part of the questionnaire occupational histories until retirement were mapped. Details on specific occupations and exposures were also collected. Questions on food and drinking habits were included in the second part of the questionnaire, as well as previous diseases and drug intake. If necessary, data were supplemented over the phone, *i.e.*, when the questions were not completely answered or apparently misunderstood.

TABLE 1. Anatomical Localizations of the 312 Cases of Colon Cancer (ICD 8)

Localization	ICD 8	No. (%)
Appendix	153.01	9 (2.9)
Cecum	153.02	77 (24.7)
Ascendens/ileocecum	153.03	37 (11.9)
Transversum/flexura	153.11	57 (18.3)
Descendens	153.21	25 (8.0)
Sigmoideum	153.31	105 (33.6)
Multiple	153.87	2 (0.6)

Jobs were scored for physical activity, III for high level of activity, I for sedentary jobs, and II for the intermediate group. Housewives were included in category II and pretime retired persons in category I. Employment years in the three categories were assessed for cases and controls (Table 2).

In a further analysis the number of the employment years in each category for each individual were multiplied by a score taken as 1, 2, and 3 so as to obtain an exposure index reflecting the duration and intensity of physical activity. Then, in the calculations of odds ratios (OR) the individuals were grouped according to their indices into the categories 0 to 66, 67 to 132, and 133 to 198, labelled A, B, and C, respectively (Table 3).

Occupational exposures to asbestos, impregnating agents, and organic solvents were independently classified as high grade or low grade by three persons well experienced in occupation health: two physicians and one hygienist.

Statistical Methods

The statistical analyses of the data were based on Mantel-Haenszel methods.[14] The confidence intervals were obtained with the approximative procedure as described by Miettinen.[15] Years of employment were also compared between cases and controls in terms of a formal OR (Table 2) not to be confused with the traditional epidemiologic OR concept based on numbers of cases and controls with and without exposure and as used elsewhere in this report.

Results

Of the 329 finally included cases, 17 (5.2%) refused to participate leaving 156 male and 156 female cases in the study. Of the 658 controls included, 35 (5.3%) were lost for the same reason, whereas 306 male and 317 female controls answered the questionnaire. The mean age of cases as well as controls was 63 years. The anatomical localizations are presented in Table 1.

TABLE 2. Employment Years and Their Odds Ratios in the Three Categories of Physical Activity

	III			II			I		
	M	F	Total	M	F	Total	M	F	Total
Cases	8670	1671	10341	6197	4599	10796	1134	6511	7645
Controls	19848	4480	24328	11613	8842	20455	2118	11869	13987
OR	0.82	0.68	0.78	1.00	0.95	0.97	(1.0)	(1.0)	(1.0)
χ^2	27.3	141.4	186.2	0.01	4.9	3.6	—	—	—

M: males; F: females; OR: odds ratios.

III: physically active jobs; I: sedentary jobs; II: intermediate group; category I taken as the reference.

The distribution of employment years in the three categories of physical activity are presented in Table 2. A significantly decreased odds ratio in physically active jobs (category III) was found both for males and females, *i.e.*, an OR of 0.82 and 0.68 with a chi-square value of 27.3 and 141.4, respectively.

However, by using the score index categories for the total material of cases and controls, only a relatively weak preventive effect was found for job-related physical activity. Considering the anatomical localizations of the cancers (Table 3) a right-sided to left-sided decrease of the risk was noted among physically active persons with an OR for cancer in colon descendens and sigmoideum of 0.49 with a 95% confidence interval (CI_{95}) of 0.25 to 0.93. A corresponding but weaker effect was also seen in the intermediate group of physical activity (OR = 0.73, CI_{95} = 0.48–1.2).

Some further analyses considered occupation and colon cancer. Since ulcerative colitis is a well-defined risk factor for colon cancer and an aggregation of such cases might be suspected to occur in some occupations, the ten cases and two controls who had reported that disease in the questionnaire were excluded in the further analyses. The material was then stratified for sex, age, and score index categories for physical activity. Table 4 presents OR for various occupations. An increased OR was seen for railway employees, in men 2.4, (CI_{95} = 1.1–5.1) and in women 2.3, (CI_{95} = 0.4–11.6). For male painters a risk of 3.0 was obtained (CI_{95} = 0.9–9.2). No clearly elevated and/or consistent risks were found for other occupations (Table 4). For agricultural, forestry, and saw mill workers there were reduced OR in men, *i.e.*, 0.7 (CI_{95} = 0.4–1.0),

TABLE 3. Odds ratios and Confidence Intervals for Different Localizations of Colon Cancer by Categories of Physical Activity in the Whole Material

	OR (CI_{95})		
	A	B	C
153.01, 02, 03	(1.0)	0.92 (0.58–1.5)	1.22 (0.63–2.4)
153.11	(1.0)	0.82 (0.45–1.5)	0.66 (0.28–1.6)
153.21, 31	(1.0)	0.73 (0.48–1.2)	0.49 (0.25–0.93)

A: sedentary jobs; C: physical active jobs; B: intermediate group; 153.01: appendix; 153.02: cecum; 153.03: ascendens; 153.11: flexura, transversum; 153.21: descendens; 153.31: sigmoideum; OR: odds ratios; CI_{95}: 95% confidence intervals.

TABLE 4. Number of Exposed Male and Female Cases and Controls in Various Occupations When Exceeding Five*

		Exposed		
Occupation	M/F	Case/Control	MHOR	CI_{95}
Cabinet maker	M	4/10	0.8	0.3–2.6
Chemical worker†	M	8/23	0.7	0.3–1.5
	F	11/12	2.0	0.9–4.7
Cleaner	F	29/50	1.2	0.7–2.1
Construction worker	M	26/64	0.8	0.5–1.3
Dress maker	F	5/15	0.6	0.2–1.8
Dry cleaner	F	5/5	2.0	0.5–7.1
Farmer	M	50/131	0.7	0.4–1.0
	F	47/112	0.8	0.5–1.2
Gardener	M	6/9	1.3	0.5–3.5
	F	7/7	2.5	0.8–7.9
Ladies' hairdresser	F	3/5	1.1	0.3–4.6
Lumberer	M	64/160	0.7	0.4–1.0
Mechanic	M	6/16	0.8	0.3–2.0
Metal worker	M	10/23	0.9	0.4–1.9
Miner	M	6/17	0.7	0.3–1.9
Motor car driver	M	29/47	1.2	0.7–2.1
Motor mechanic	M	11/17	1.3	0.6–2.8
Needle worker	F	6/4	3.0	0.9–10.6
Nurse	F	3/6	1.0	0.5–2.1
Painter	M	7/5	3.0	0.9–9.2
Paper mill worker	M	2/6	0.5	0.1–2.8
Pulp worker	M	10/26	0.7	0.3–1.6
Railway worker	M	16/14	2.4	1.1–5.1
	F	3/3	2.3	0.4–11.6
Road worker	M	18/48	0.7	0.4–1.3
Saw mill worker	M	19/68	0.5	0.3–0.9

* Mantel-Haenszel odds ratios (MHOR) and 95% confidence intervals (CI_{95}) for colon cancer by stratification on age and physical activity are given for each sex.

† Unspecified.

0.7 (CI_{95} = 0.4–1.0), and 0.5 (CI_{95} = 0.3–0.9), respectively. For women there was a decreased OR for farmers (0.8, CI_{95} = 0.5–1.2).

Risk ratios with regard to specific exposures are listed in Table 5. No increased risk was found for exposure to pesticides such as phenoxy acetic acids, dichloro-diphenyl-trichloroethane (DDT), or impregnating agents. High-grade exposure to organic solvents gave an OR of 2.1 (CI_{95} = 0.8–5.8). Also for high-grade exposure to asbestos a somewhat increased OR was found (2.1, CI_{95} = 0.8–5.8). The OR for exposure to man-made fibers, that is glasswool and rockwool, were less than unity. A slightly increased risk was found for exposure to trichloroethylene in general, whereas such exposure among dry cleaners gave an OR of 7.4 (CI_{95} = 1.1–47.0).

TABLE 5. Odds Ratios and 95% Confidence Intervals for Exposure to Various Agents*

Agents	OR	CI_{95}
Asbestos		
High grade	2.1	0.8–5.8
Low grade	1.2	0.6–2.4
Asphalt†	1.7	0.3–11.7
Glasswool†	0.6	0.3–1.1
Hexachlorophene	0.6	0.1–2.0
Impregnating agents		
High grade	0.9	0.2–3.5
Low grade	0.7	0.3–1.3
Organic solvents		
High grade	2.1	0.8–5.8
Low grade	1.3	0.8–2.0
Thinners	1.2	0.6–2.4
Trichloroethylene	1.5	0.4–5.7
Trichloroethylene among dry cleaners	7.4	1.1–47.0
White spirit	1.1	0.5–2.3
Pesticides	1.6	0.8–3.0
DDT	1.3	0.8–2.1
Phenoxyacetic acids	1.3	0.7–2.4
Rockwool†	0.7	0.4–1.3
Smoker (including exsmokers)	1.0	0.7–1.3
Snuff	1.5	0.9–2.5

OR: odds ratios; CI_{95}: 95% confidence intervals; DDT: dichloro-diphenyl-trichloroethane.

* Cases and controls were stratified for age, sex, and scoring index of physical activity.

† Only men.

Discussion

This investigation showed a decreased risk for colon cancer in jobs classified as physically active. There was a right-sided to left-sided trend with the highest prevention for cancer in the descending colon and sigmoideum. This is in agreement with some of the previous findings. After stratification for physical activity, farming, forest work, and saw mill work were still associated with a reduced risk for colon cancer in men, thereby indicating the possibility of other preventive factors in these individuals. On the other hand, physically active jobs with high-grade exposure to agents like organic solvents or asbestos might not show a reduced risk because of some effect of such agents. It has been postulated by Burkitt *et al.*[16] that increased bowel activity is preventive for colon cancer. This may be the reason for the decreased risk in persons with physically active jobs, but there could also be other preventive factors associated with physical activity that exerts the preventive effect.

A significantly increased risk for colon cancer was found among persons employed by the Swedish railways. This is a somewhat surprising finding for which there is no particular explanation and it should be noted that the elevated risk for this employment category persists also after stratification for degree of physical activity. In view of the current interest for electromagnetic fields as a risk factor for cancer, it may be mentioned that the Swedish railroads are electrified to a great extent, presumably causing considerable exposure to low frequency electromagnetic fields for many of the employees.

Exposure to organic solvents has previously not been described as a risk factor for colon cancer. An especially high risk was found in this study among dry cleaners exposed to trichloroethyelene. Although this finding was surprising, this substance is known to be mutagenic.[17] There is also a suggestion of pneumocystosis of the colon as possibly relating to trichloroethylene exposure, which to some extent could suggest the colon to be a potential target organ for effects of this chlorinated ethylene.[18] Further studies are required before any definitive conclusions can be made.

Exposure to asbestos has in some, but not all, investigations been associated with an increased risk for colorectal cancer.[8] In this study a somewhat increased risk was seen for persons with high-grade exposure although with a confidence interval including unity.

Since colon cancer is more common in higher age groups the controls were originally drawn as similar to the cases with regard to age. This allowed for an equal number of employment years within various occupations for cases and controls and age was taken care of by stratification in the analyses. Furthermore, only alive subjects were included in order to avoid information bias due to second hand information from relatives. This is of special importance regarding food habits, previous diseases, and drug intake as also assessed in the study and as not found to correlate with particular occupations and exposure to such a degree as likely to explain the observations made with regard to the deviating risk patterns in relation to various jobs or exposures. The relationship of colon cancer, eating habits, previous diseases, and the use of various drugs will be discussed in forthcoming publications.

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