

RESEARCH COMMUNICATION

Constipation and Colorectal Cancer Risk: The Fukuoka Colorectal Cancer Study

Naotaka Tashiro^{1*}, Sanjeev Budhathoki¹, Keizo Ohnaka², Kengo Toyomura¹, Suminori Kono¹, Takashi Ueki³, Masao Tanaka³, Yoshihiro Kakeji⁴, Yoshihiko Maehara⁴, Takeshi Okamura⁵, Koji Ikejiri⁶, Kitaroh Futami⁷, Takafumi Maekawa⁷, Yohichi Yasunami⁸, Kenji Takenaka⁹, Hitoshi Ichimiya¹⁰, Reiji Terasaka¹¹

Abstract

Constipation has been suspected to be linked to colorectal cancer risk, but epidemiological evidence is inconclusive. We described the prevalence of constipation and related lifestyle factors in a community and examined the relation of constipation and other bowel habits to colorectal cancer risk. The prevalence study was based on 833 community controls in the Fukuoka Colorectal Cancer Study, and 212 cases of Dukes' stage A were used in a study on bowel habits and colorectal cancer risk. Bowel habits were assessed by in-person interview. Odds ratio (OR) and 95% confidence interval (CI) of colorectal cancer were estimated with adjustment for dietary and nondietary factors. Constipation was reported by 10.3% of men and 27.7% of women. Individuals with less frequent bowel movements had a lower intake of total energy and were physically less active. The multivariate-adjusted OR (95% CI) of colorectal cancer were 1.51 (1.02-2.25) for self-reported constipation, 1.60 (1.05-2.44) for functional constipation, and 1.24 (0.81-1.90) for infrequent bowel movements (<1 stool/day). Self-reported constipation was fairly common in Japanese adults. Constipation was associated with a moderately increased risk of colorectal cancer.

Keywords: Bowel habits - constipation - colorectal cancer - Japanese

Asian Pacific J Cancer Prev, 12, 2025-2030

Introduction

Constipation is a fairly common symptom among patients in routine clinical practice and also in free-living populations. Chronic constipation is perceived by approximately 10-30% of adults in Western countries (Higgins et al., 2004; Peppas et al., 2008). A Japanese study reported that the prevalence of self-perceived constipation was 14% among men and 36% among women in a rural middle-aged and elderly population (Nakaji et al., 2004), while another study in Korea showed that 10% among men and 23% among women felt constipation (Jun et al., 2006).

Constipation has long been suspected to be linked to colorectal cancer risk, but epidemiological evidence is limited and inconclusive. Previous studies have been based on self-reported constipation, frequency of bowel movements, or use of laxatives. Several case-control

studies have reported an increased risk of colorectal cancer associated with constipation (Wynder et al., 1967; Haenszel et al., 1973) or infrequent bowel movement (Vobecky et al., 1983; Roberts et al., 2003), whereas others have not shown an association with constipation (Higginson, 1966; Wynder et al., 1969; Jain et al., 1980; Nakamura et al., 1984). One case-control study showed an increased risk of colorectal cancer associated with constipation, but not with infrequent bowel movement (Kune et al., 1988). A meta-analysis of 9 case-control studies reported an odds ratio (OR) of 1.48 (95% confidence interval [CI] 1.32-1.66) for constipation or infrequent bowel movement (Sonnenberg and Müller, 1993). Use of laxatives has also been a matter of interest, because it is more objective than self-reported constipation. Laxative use was positively associated with colorectal cancer, the OR being 1.46 (95% CI 1.33-1.61) in a meta-analysis of 11 case-control studies (Sonnenberg and Müller, 1993). At least 6 prospective

Departments of ¹Preventive Medicine, ²Geriatric Medicine, ³Surgery and Oncology, ⁴Surgery and Science, Graduate School of Medical Sciences, Kyushu University, ⁵Department of Gastroenterological Surgery, National Kyushu Cancer Center, ⁶Division of Surgery, National Kyushu Medical Center, ⁷Department of Surgery, Fukuoka University Chikushi Hospital, ⁸Department of Regenerative Medicine and Transplantation, Faculty of Medicine, Fukuoka University, ⁹Division of Surgery, Fukuoka City Hospital, ¹⁰Division of Surgery, Hamanomachi General Hospital, ¹¹Division of Surgery, Fukuoka Red Cross Hospital, Fukuoka, Japan *For correspondence: ntashiro@phealth.med.kyushu-u.ac.jp

studies have addressed the association of bowel movement or laxative use with colorectal cancer risk (Watanabe et al., 2004; Kojima et al., 2004; Simons et al., 2010; Otani et al., 2006; Park et al., 2009; Dukas et al., 2000). A non-significant increase in the risk of colorectal cancer was observed among men and women combined with less than a bowel movement per day compared to those who had daily or more bowel movement in one study (Watanabe et al., 2004), and very infrequent bowel movement (every 6 days or less) was associated with a more than 2-fold increase in the risk of colorectal cancer in women but not in men in another study (Kojima et al., 2004). On the contrary, frequent bowel movement was associated with an increased risk of colorectal cancer in a recent prospective study (Simons et al., 2010). In that study, constipation was related to a decreased risk (Simons et al., 2010). One of these studies showed a marked increase in the risk associated with use of laxatives (Watanabe et al., 2004). Neither bowel movement nor laxative use was measurably associated with colorectal cancer risk in three prospective studies in Japan (Otani et al., 2006), Europe (Park et al., 2009), and USA (Dukas et al., 2000). None of these previous prospective studies, except for one (Simons et al., 2010), examined the relationship between self-reported constipation and colorectal cancer risk.

In the study reported here, we examined the relation of constipation and bowel movement to colorectal cancer risk in a community-based case-control study in Japan (Kono et al., 2004). We also described the prevalence of constipation in the community and lifestyle factors related to constipation

Materials and Methods

The Fukuoka Colorectal Cancer Study is a community-based case-control study to investigate etiological factors of colorectal cancer among residents in Fukuoka City and three adjacent areas. The study has been approved by the ethics committee of Kyushu University and collaborating hospitals. Details of the methods have been described elsewhere (Kono et al., 2004).

Study subjects

Cases comprised a consecutive series of patients with histologically confirmed incident colorectal adenocarcinomas who were admitted to one of the eight participating hospitals for the first surgical treatment. Eligible cases were aged 20–74 years at time of diagnosis, lived in the study area, had no prior history of partial or total removal of the colorectum, familial adenomatous polyposis or inflammatory bowel disease, and were mentally competent to give informed consent and to complete the interview. During the period from September 2000 to December 2003, 840 (80%) of 1,053 eligible cases participated in the interview. The number of cases according to the Dukes' classification was as follows: stage A 215, stage B 226, stage C 281, stage D 116, and unrecorded 2. In the analysis on the relation between bowel habits and colorectal cancer risk, we used only cases with Dukes' stage A.

Controls were randomly selected in the study area by

frequency-matching with respect to gender and 10-year age class. Eligible criteria were the same as described for the cases except that controls had no history of colorectal cancer. A total of 1,500 persons living in 15 geographical areas were selected as control candidates by two-stage random sampling, and were invited to participate in the study by mail. There were 113 persons who were found to be ineligible, and 5 persons were diagnosed as having colorectal cancer after the interview survey. After exclusion of these 118 persons, 833 (60%) of the 1,382 eligible candidates participated in the study.

We described bowel habits in the 833 community-based control subjects. The association between bowel habits and colorectal cancer risk was examined in the 212 cases of Dukes' stage A and 791 controls aged 40 years or older. When dietary factors were assessed, we excluded subjects who were in the top or bottom 1% of energy intake within each stratum of sex and age categories (<55, 55–64 and ≥65 years).

Bowel habits and lifestyle features

Research nurses interviewed cases and controls in person regarding bowel habits as well as lifestyle factors, using a uniform questionnaire. The index dates were the date of onset of symptom or screening for cases and the time of interview for controls. Bowel habits in the past year were ascertained by closed-ended questions with respect to 10 items: self-reported constipation, frequency of bowel movements, consistency of stool, abdominal bloating, feeling of incomplete evacuation, time required for defecation, regularity of bowel movements, use of laxatives, and 2 items about incontinence of feces (Table 1). Eight options were prepared for the question on the frequency of bowel movements, and 5 pre-coded answers were given to the question on the time for defecation. Regularity of the bowel habit and feeling of incomplete evacuation were answered dichotomously. Three to four options were prepared for the remaining 7 questions. Answers to most of the questions, except for regularity of bowel movements and feeling of incomplete evacuation with two precoded answers, were collapsed into 2 or 3 categories in the analysis.

Approximately one year after the survey, 29

Table 1. Questions on Bowel Habits and Reproducibility of Each Response*

Question	Options	κ †
1. How often have you felt constipation?	4	0.68
2. How often have you had a bowel movement?	8	0.68
3. What has the consistency of your stool been?	4	0.42
4. How often have you had abdominal distension?	3	0.61
5. Have you had a feeling of incomplete evacuation?	2	0.49
6. How long has it taken to pass a bowel movement?	5	0.61
7. Have your bowel movements been regular?	2	0.58
8. How often have you used laxatives?	4	0.67
9. How often have you had fecal incontinence?	3	--‡
10. How often have you had your underwear stained with feces?	3	0.65

*Agreement between the first and the second survey with a one-year interval among 29 subjects was assessed; κ , eighted kappa; †Used Fleiss-Cohen weights. Unweighted kappa statistics were used for questions with two options; ‡All of the subjects were in a single cell of cross tabulation

control subjects were re-interviewed by using the same questionnaire. Reproducibility was assessed by kappa statistics ranged 0.42 to 0.68 (see Table 1). Fecal incontinence was not included in the present analysis because those who reported fecal incontinence were very few. With reference to Rome Criteria III (Longstreth et al., 2006), those who reported 2 or more of the following 5 symptoms were classified as having functional constipation: less than one bowel movement per 3 days, hard stools, feeling of incomplete evacuation, taking more than 5 minutes to have a bowel movement, and use of laxatives more than once per week.

Details of the methods on lifestyle factors have been described elsewhere (Kono et al., 2004). Smoking habit was categorized into lifelong non-smoker, former smoker, and current smoker. Alcohol consumption 5 years prior to the index date was ascertained. Individuals reported height (cm), current body weight (kg), and body weight (kg) 10 years earlier. Current body mass index (kg/m^2) and body mass index (kg/m^2) 10 years earlier were obtained. Questions on physical activities elicited type of job, activities in commuting and housework and leisure-time activities 5 years before. As described in detail previously (Isomura et al., 2006), leisure-time physical activity (including activities in commuting and housework) was expressed as a sum of metabolic equivalents (MET) multiplied by hours of weekly participation in each activity, i.e., MET-hours per week. Parental colorectal cancer was also elicited.

Dietary assessment

The method of dietary assessment was described previously (Uchida et al., 2007). Consumption frequencies and portion sizes of 148 food/beverage items over one year prior to the index date were ascertained by a computer-assisted interview. Typical dishes for each item were shown on the display window of the personal computer. Individuals were asked to report their usual consumption over one year prior to the index date. Intakes of nutrients and alcohol were calculated based on the food composition tables in Japan (Science and Technology Agency, Japan: Standard Tables of Food Composition, 2000). Estimated intakes of nutrients and foods generally showed a fairly high validity in comparison with those based on the 28-day diet record over one year (Uchida et al., 2007). Pearson correlation coefficients of log-transformed values of total energy intake, energy-adjusted dietary fiber, and alcohol between the first interview (and the second interview in parentheses) and diet record were as follows: total energy intake 0.56 (0.34), energy-adjusted dietary fiber 0.48 (0.44), and alcohol 0.65 (0.58).

Statistical analysis

Between-group comparisons of proportions were assessed by χ^2 -test. Age-adjusted means and proportions were used in examining the characteristics of the controls according to the frequency of bowel movements; age-adjusted means were obtained by analysis of covariance using a continuous variable for age, and age-adjusted proportions were calculated by the direct method of standardization with men and women each in 3 age classes

(<55, 55–64 and ≥ 65 years) as standard population. Trend was assessed by Mantel-Haenszel method for proportions and linear regression analysis for means. Current alcohol intake and current BMI were used in the analysis on lifestyle factors in relation to constipation and bowel movement.

Logistic regression analysis was used to estimate OR and 95% CI of colorectal cancer for each bowel habit category. Statistical adjustment was made for sex, age (year), residential area (Fukuoka City or others), parental history of colorectal cancer, past and current smoking status, alcohol drinking 5 years before (0, 0.1–0.9, 1.0–1.9 or ≥ 2 units per day), body mass index 10 years earlier (<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, 0.1–15.9 or ≥ 16 MET-hours per week) and natural logarithm of total calorie intake. Body weight 10 years before was not ascertained for 2 cases and 10 controls, and was replaced with the current body weight. Statistical significance was declared if two-sided p was <0.05. Statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary: NC, USA).

Results

Table 2 summarizes bowel habits in the control subjects by sex. Constipation was reported by 10.3% of men and 27.7% of women. Individuals with less than one bowel movement per day were more frequent among women compared with men. Laxative use and irregular bowel movement were almost three-fold more frequent in women than in men. Hard stools and abdominal distension were also more common in women. On the other hand, defecation time was shorter in women than in men, and there was no difference in the feeling of incomplete evacuation between men and women.

Table 3 shows characteristics of bowel habits according to self-reported constipation by sex. In both

Table 2. Bowel Habits in the Controls by Sex

Bowel habits	Men	Women	P*
Self-reported constipation (–)	461 (89.7)	230 (72.3)	<0.01
(+)	53 (10.3)	88 (27.7)	
Frequency >1 stool/day	86 (16.8)	38 (12.0)	<0.01
1 stool/day	369 (71.9)	198 (62.5)	
<1 stool/day	58 (11.3)	81 (25.6)	
Consistency of stool Hard	37 (7.2)	39 (12.4)	<0.01
Normal	371 (72.5)	248 (79.0)	
Loose	104 (20.3)	27 (8.6)	
Abdominal distention Never	361 (70.4)	204 (64.2)	0.06
Ever	152 (29.6)	114 (35.8)	
Incomplete evacuation (–)	408 (81.0)	245 (79.0)	0.50
(+)	96 (19.0)	65 (21.0)	
Defecation time (min) 1-2	147 (28.6)	148 (46.5)	<0.01
3-5	262 (51.0)	137 (43.1)	
≥ 6	105 (20.4)	33 (10.4)	
Regularity Regular	463 (90.1)	227 (71.4)	<0.01
Irregular	51 (9.9)	91 (28.6)	
Laxative use† (–)	491 (95.5)	278 (87.4)	<0.01
(+)	23 (4.5)	40 (12.6)	

Number (%), total numbers differ due to missing values; *P value was calculated by χ^2 -test; † (+), once per week or more frequent use

Table 3. Bowel Habit Characteristics According to Self-reported Constipation by Sex*

Bowel habits	Men		Women	
	(-)	(+)	(-)	(+)
Number	461	53	230	88
<1 stool/day	29 (6.3)	29 (54.7)	29 (12.7)	52 (59.1)
Hard stool	16 (3.5)	21 (40.4)	12 (5.3)	27 (30.7)
Abdominal dist	120 (26.1)	32 (60.4)	57 (24.8)	57 (64.8)
Incomplete evac	76 (16.8)	20 (39.2)	27 (12.1)	38 (44.2)
Long defecation	83 (18.0)	22 (41.5)	15 (6.5)	18 (20.5)
Irreg movement	22 (4.8)	29 (54.7)	31 (13.5)	60 (68.2)
Laxative use	11 (2.4)	12 (22.6)	9 (3.9)	31 (35.2)

*All $p < 0.01$ between (-) and (+) based on χ^2 -test.

Table 4. Lifestyle Characteristics According to Bowel Movements

Characteristics*	Bowel movement (per day)			P for trend†
	>1	1	<1	
Men				
Number	86	369	58	
Age, mean±SD	60±9	59±10	60±12	0.62
Parental CRC (%)	8.3	5.4	1.4	0.10
Current smoking (%)	37.3	48.7	49.8	0.06
Alcohol ≥20 g/day (%)	45.8	52.9	34.6	0.34
Sedentary job (%)	62.7	63.0	56.6	0.55
High physical act (%)‡	40.8	32.7	26.3	0.07
Height, mean±SD (cm)	164±6	166±6	166±7	0.04
BMI, mean±SD (kg/m ²)	24±3	23±2	23±3	0.10
Dietary intake, geometric mean				
Total energy (kcal/day)	2377	2311	2151	0.02
Carbohydrate (g/day)§	267	264	272	0.60
Protein (g/day)§	70.7	69.7	67.7	0.09
Fat (g/day)§	52.0	51.5	54.1	0.38
Fiber (g/day)§	12.7	12.4	13.4	0.36
Women				
Number	38	198	81	
Age, mean±SD	63±8	59±11	56±13	0.001
Parental CRC (%)	2.1	6.2	5.3	0.86
Current smoking (%)	22.7	16.3	11.0	0.26
Alcohol ≥20 g/day (%)	6.2	5.6	2.6	0.53
Sedentary job (%)	76.9	83.7	82.2	0.56
High physical act (%)‡	43.7	39.6	34.5	0.33
Height, mean±SD (cm)	153±5	153±6	154±5	0.65
BMI, mean±SD (kg/m ²)	23±3	23±4	22±3	0.36
Dietary intake, geometric mean				
Total energy (kcal/day)	2087	1972	1846	0.01
Carbohydrate (g/day)§	271	266	272	0.63
Protein (g/day)§	79.8	76.9	75.3	0.03
Fat (g/day)§	59.9	61.0	60.5	0.91
Fiber (g/day)§	16.5	15.6	15.2	0.09

*Proportions were age-standardized by the direct method, and means were age-adjusted by analysis of covariance; †Mantel-Haenszel method for proportions and linear regression analysis for means; ‡Those who have ≥16 MET-hours/week; §Energy-adjusted per 2000 kcal/day

men and women, those reporting constipation were more likely to have infrequent bowel movements, hard stools, abdominal distention, feeling of incomplete evacuation, long time for defecation (≥6 min), and irregular bowel movements. Functional constipation was defined for 41% of those who reported constipation (58/141), and for 6% of subjects who did not perceive constipation (44/691). The concordance between self-reported constipation and functional constipation was moderate, kappa statistics being 0.39.

Table 5. Bowel Habits and Colorectal Cancer Risk*

Habits	Cases	Controls	OR†(95% CI)	OR‡(95% CI)
Self-reported constipation				
(-)	166	660	1.00 (reference)	1.00 (reference)
(+)	46	130	1.43 (0.97-2.10)	1.51 (1.02-2.25)
Functional constipation§				
(-)	172	694	1.00 (reference)	1.00 (reference)
(+)	40	97	1.66 (1.11-2.50)	1.60 (1.05-2.44)
Stool frequency				
>1/day	42	123	1.41 (0.94-2.10)	1.35 (0.89-2.05)
1/day	131	537	1.00 (reference)	1.00 (reference)
<1/day	39	128	1.25 (0.83-1.90)	1.24 (0.81-1.90)
Stool consistency				
Hard	28	72	1.71 (1.06-2.77)	1.72 (1.04-2.82)
Normal	129	590	1.00 (reference)	1.00 (reference)
Loose	54	122	2.10 (1.44-3.08)	2.02 (1.36-3.00)

*Total numbers differed due to missing values; †Adjusted for sex, age, and resident area; ‡Adjusted for sex, age, resident area, cigarette smoking, alcohol consumption, body mass index 10 years earlier, type of job, leisure-time physical activity, parental colorectal cancer, total calorie intake; §Functional constipation was defined if two or more of the following five symptoms were reported; less than one bowel movement/3days, having hard stools, feeling of incomplete evacuation, taking more than 5 minutes to have a bowel movement, and laxative use more than once per week

Lifestyle characteristics according to bowel movement frequency are shown in Table 4. Individuals with less frequent bowel movements had lower intake of total energy intake in both men and women. Physical activity tended to be lower in both men and women with less than daily bowel movements. Men with less frequent bowel movement were taller, and such women consumed less protein. Smokers were more frequent in men with infrequent bowel movements and in women with frequent bowel movements. Fiber intake tended to be lower in women with infrequent bowel movements.

Table 5 shows adjusted OR of colorectal cancer risk according to bowel habits. In the multivariate model, both self-reported constipation and functional constipation were statistically significantly related to a moderately increased risk of colorectal cancer. Loose or hard stool was also associated with an increased risk of colorectal cancer.

Discussion

The present study showed that self-reported constipation was fairly common in Japanese adults, the prevalence being 10% in men and 28% in women. It was also found that individuals with a lower intake of total energy had fewer frequencies of bowel movement. While bowel movement was unrelated to colorectal cancer risk, self-reported constipation, functional constipation, and loose or hard stool were associated with a moderately increased risk of colorectal cancer.

The prevalence rates of self-reported constipation observed here were comparable to the rates reported in Japan (Nakaji et al., 2004) and Korea (Jun et al., 2006). In these studies, 10-14% of men and 23-36% of women reported constipation. Infrequent bowel movements (less than once per day) was reported among 11% of men and 26% of women in the present study. These figures are also

in agreement with those reported elsewhere in Japan, i.e., 8-12% in men and 23-32% in women (Watanabe et al., 2004; Kojima et al., 2004; Otani et al., 2006).

Functional constipation defined on the basis of specific items of bowel habits was found to be less concordant with self-perceived constipation in the present study. The definition of functional constipation used in the present study did not necessarily accord with the Rome Criteria III (Longstreth et al., 2006), but a large discordance between self-reported and functional constipation has been observed in different populations. For instance, only 14% of women who reported constipation were diagnosed with functional constipation according to the Rome Criteria III in a study of outpatients (Digesu et al., 2010).

A positive association between total energy intake and bowel movements in this study corroborated previous community-based studies (Otani et al., 2006; Dukas et al., 2000). The present study also added a supportive evidence for a protective association between physical activity and bowel movement (Müller-Lissner et al., 2005). There was no evident association between dietary fiber and bowel movement. Although wheat bran increases stool weight and shortens oroanal transit time (Müller-Lissner, 1988), dietary fiber intake does not seem to differ between individuals reporting constipation and those not (Müller-Lissner et al., 2005).

While fewer bowel movements (<3 per week) was related to an increased risk of colorectal cancer in some case-control studies (Vobecky et al., 1983; Roberts et al., 2003), no such association has been observed in prospective studies in Western countries (Park et al., 2009; Dukas et al., 2000) as well as in Japan (Otani et al., 2006). The present study did not provide evidence that fewer bowel movements were related to an increased risk of colorectal cancer. On the other hand, the present study suggested an increased risk of colorectal cancer associated with self-reported constipation and functional constipation. It is notable that both self-reported and functional constipation were associated with colorectal cancer risk to almost the same extent. Having loose or hard stool was associated with an increased risk of colorectal cancer in the present study. Self-reported diarrheal stool was associated with a 11-fold increase in the risk of rectal cancer, not of colon cancer, only in women in a Japanese prospective study, in which the usual state of stool was classified into hard, normal, soft, diarrheal, and diarrhea alternated with constipation (Otani et al., 2006). In the EPIC-Norfolk study in which stool consistency was classified into hard, soft, and loose stool, loose stool was associated with 3-fold increased risk of colorectal cancer in men and women combined (Park et al., 2009). Hard stool was not associated with the risk of colorectal cancer in either of these two studies (Otani et al., 2006; Park et al., 2009). The present findings on loose stool are consistent with the previous observations, and loose stool may be a reflection of bowel inflammation, and thereby being associated with an increased risk of colorectal cancer. We have no proper explanation to the present finding on hard stools.

A strength of the study was that bowel habits were evaluated in a random sample in the community,

although the participation rate did not exceed 60%. Another advantage was that multi-facets of bowel habits were evaluated in relation to self-reported constipation. However, the retrospective assessment of bowel habits in relation to colorectal cancer risk was a limitation.

In conclusion, using data from a community-based case-control study in Japan, the present study reported the prevalence of self-reported constipation as well as of functional constipation in the general population. Both self-reported and functional constipation were related to an increased risk of colorectal cancer

Acknowledgements

This study was supported by a Grant-in-Aid for Scientific Research on Innovative Areas (No. 221S0001) from the Ministry of Education, Culture, Sports, Science and Technology, Japan. The authors acknowledge support from Emeritus Professors Keizo Sugimachi, Seiyo Ikeda, Sumitaka Arima, and Takayuki Shirakusa and from Drs. Motonori Saku, Yoichi Ikeda, Soichiro Maekawa, Kazuo Tanoue, Kinjiro Sumiyoshi, and Shoichiro Saito in conducting the survey of cases. The following physicians kindly supervised the survey of controls at their clinics: Drs. Hideaki Baba, Tomonori Endo, Hiroshi Hara, Yoichiro Hirokata, Motohisa Ikeda, Masayoshi Ishibashi, Fumiaki Itoh, Yasuhiro Iwanaga, Hideki Kaku, Shoshi Kaku, Minoru Kanazawa, Akira Kobayashi, Ryunosuke Kumashiro, Shinichi Matsumoto, Soukei Mioka, Umeji Miyakoda, Osamu Nakagaki, Nobuyoshi Nogawa (deceased), Nobuyuki Ogami, Toyoaki Okabayashi, Hironao Okabe, Nishiki Saku, Masafumi Tanaka, Masahiro Ueda, Bunichi Ushio, and Koheisho Yasunaga.

References

- Digesu GA, Panayi D, Kundi N, et al (2010). Validity of the Rome III Criteria in assessing constipation in women. *Int Urogynecol J Pelvic Floor Dysfunct*, **21**, 1185-93.
- Dukas L, Willett WC, Colditz GA, et al (2000). Prospective study of bowel movement, laxative use, and risk of colorectal cancer among women. *Am J Epidemiol*, **151**, 958-64.
- Haenszel W, Berg JW, Segi M, Kurihara M, Locke FB (1973). Large-bowel cancer in Hawaiian Japanese. *J Natl Cancer Inst*, **51**, 1765-79.
- Higgins PD, Johanson JF (2004). Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol*, **99**, 750-9.
- Higginson J (1966). Etiological factors in gastrointestinal cancer in man. *J Natl Cancer Inst*, **37**, 527-45.
- Isomura K, Kono S, Moore MA, et al (2006). Physical activity and colorectal cancer: The Fukuoka Colorectal Cancer Study. *Cancer Sci*, **97**, 1099-1104.
- Jain M, Cook GM, Davis FG, et al (1980). A case-control study of diet and colo-rectal cancer. *Int J Cancer*, **26**, 757-68.
- Jun DW, Park HY, Lee OY, et al (2006). A population-based study on bowel habits in a Korean community: prevalence of functional constipation and self-reported constipation. *Dig Dis Sci*, **51**, 1471-7.
- Kojima M, Wakai K, Tokudome S, et al (2004). Bowel movement frequency and risk of colorectal cancer in a large cohort study of Japanese men and women. *Br J Cancer*, **90**, 1397-1401.

- Kono S, Toyomura K, Yin G, Nagano J, Mizoue T (2004). A case-control study of colorectal cancer in relation to lifestyle factors and genetic polymorphisms: design and conduct of the Fukuoka colorectal cancer study. *Asian Pac J Cancer Prev*, **5**, 393-400.
- Kune GA, Kune S, Field B, Watson LF (1988). The role of chronic constipation, diarrhea, and laxative use in the etiology of large-bowel cancer. *Dis Colon Rectum*, **31**, 507-12.
- Longstreth GF, Thompson WG, Chey WD, et al (2006). Functional bowel disorders. *Gastroenterology*, **130**, 1480-91.
- Müller-Lissner SA (1988). Effect of wheat bran on weight of stool and gastrointestinal transit time: a meta analysis. *Br Med J*, **296**, 615-7.
- Müller-Lissner SA, Kamm MA, Scarpignato C, Wald A (2005). Myths and misconceptions about chronic constipation. *Am J Gastroenterol*, **100**, 232-42.
- Nakaji S, Matsuzaka M, Umeda T, et al (2004). A population-based study on defecatory conditions in Japanese subjects: methods for self-evaluation. *Tohoku J Exp Med*, **203**, 97-104.
- Nakamura GJ, Schneiderman LJ, Klauber MR (1984). Colorectal cancer and bowel habits. *Cancer*, **54**, 1475-7.
- Otani T, Iwasaki M, Inoue M, Sasazuki S, Tsugane S (2006). Bowel movement, state of stool, and subsequent risk for colorectal cancer: The Japan Public Health Center-Based Prospective Study. *Ann Epidemiol*, **16**, 888-94.
- Park JY, Mitrou PN, Luben R, Khaw KT, Bingham SA (2009). Is bowel habit linked to colorectal cancer? – Results from the EPIC-Norfolk study. *Eur J Cancer*, **45**, 139-45.
- Peppas G, Alexiou VG, Mourtzoukou E, Falagas ME (2008). Epidemiology of constipation in Europe and Oceania: a systematic review. *BMC Gastroenterol*, **8**, 5.
- Roberts MC, Millikan RC, Galanko JA, Martin C, Sandler RS (2003). Constipation, laxative use, and colon cancer in a North Carolina population. *Am J Gastroenterol*, **98**, 857-64.
- Science and Technology Agency, Japan (2000): *Standard Tables of Food Composition in Japan, Fifth Revised Edition*. Tokyo: Ministry of Finance Printing Bureau.
- Simons CC, Schouten LJ, Weijenberg MP, Goldbohm RA, van den Brandt PA (2010). Bowel movement and constipation frequencies and the risk of colorectal cancer among men in the Netherlands Cohort Study on Diet and Cancer. *Am J Epidemiol*, **172**, 1404-14.
- Sonnenberg A, Müller AD (1993). Constipation and cathartics as risk factors of colorectal cancer: a meta-analysis. *Pharmacology*, **47**, 224-33.
- Uchida K, Kimura Y, Shirota T, Kono S (2007). Validity and reproducibility of the PC-assisted dietary interview used in the Fukuoka Colorectal Cancer Study. *Asian Pac J Cancer Prev*, **8**, 583-90.
- Vobecky J, Caro J, Devroede G (1983). A case-control study of risk factors for large bowel carcinoma. *Cancer*, **51**, 1958-63.
- Watanabe T, Nakaya N, Kurashima K, et al (2004). Constipation, laxative use and risk of colorectal cancer: The Miyagi Cohort Study. *Eur J Cancer*, **40**, 2109-15.
- Wynder EL, Shigematsu T (1967). Environmental factors of cancer of the colon and rectum. *Cancer*, **20**, 1520-61.
- Wynder EL, Kajitani T, Ishikawa S, Dodo H, Takano A (1969). Environmental factors of cancer of the colon and rectum. *Cancer*, **23**, 1210-20.