

Colorectal Polypectomy and Risk of Colorectal Cancer by Subsite: The Fukuoka Colorectal Cancer Study

Daigo Yoshida¹, Suminori Kono¹, Malcolm A. Moore¹, Kengo Toyomura¹, Jun Nagano¹, Tetsuya Mizoue¹, Ryuichi Mibu², Masao Tanaka², Yoshihiro Kakeji³, Yoshihiko Maehara³, Takeshi Okamura⁴, Koji Ikejiri⁵, Kitaroh Futami⁶, Yohichi Yasunami⁷, Takafumi Maekawa⁸, Kenji Takenaka⁹, Hitoshi Ichimiya¹⁰ and Nobutoshi Imaizumi¹¹

Departments of ¹Preventive Medicine, ²Surgery and Oncology, and ³Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, ⁴Department of Gastroenterological Surgery, National Kyushu Cancer Center, Fukuoka, ⁵Division of Surgery, National Kyushu Medical Center, Fukuoka, ⁶Department of Surgery, Fukuoka University Chikushi Hospital, Chikushino, Fukuoka, ⁷The First and ⁸Second Departments of Surgery, Fukuoka University School of Medicine, Fukuoka, ⁹Division of Surgery, Fukuoka City Hospital, Fukuoka, ¹⁰Division of Surgery, Hamanomachi General Hospital, Fukuoka and ¹¹Division of Surgery, Fukuoka Red Cross Hospital, Fukuoka, Japan

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Background: Colorectal adenomas are well-established precursor lesions for colorectal cancer and removal of polyps is deemed to reduce the risk of colorectal cancer. However, benefit of colorectal polypectomy in routine practice is still uncertain. We therefore investigated subsite-specific risks of colorectal cancer in relation to history of colorectal polypectomy in a case-control study.

Methods: Both case patients and control subjects were residents aged 20–74 years in Fukuoka City and three adjacent areas. The case group comprised 840 patients undergoing surgery for a first diagnosis of colorectal cancer, while the control subjects were 833 residents who were selected in the community by two-stage random sampling. Past history of selected diseases, surgery and lifestyle factors were ascertained by in-person interview. Statistical adjustment was made for sex, 5-year age class, residence, smoking, alcohol drinking, physical activity, body mass index and parental history of colorectal cancer.

Results: Overall, 74 case patients (9%) and 85 control subjects (10%) reported a prior history of colorectal polyps, and 50 cases (6%) and 64 controls (8%) had a history of colorectal polypectomy. The adjusted odds ratio associated with colorectal polypectomy was 0.71 (95% confidence interval [CI] 0.48–1.06) for the overall risk of colorectal cancer. The corresponding values for cancer of the proximal colon, distal colon, and rectum were 1.68 (95% CI 0.98–2.88), 0.71 (95% CI 0.41–1.26) and 0.24 (95% CI 0.11–0.52), respectively.

Conclusions: The findings indicate that colorectal polypectomy in current practice confers a decreased risk of rectal cancer and possibly of distal colon cancer.

Key words: colorectal cancer – colorectal polypectomy – case-control study – Japanese

INTRODUCTION

Colorectal cancer is one of the most common cancers in the world, accounting for nearly 10% of all incident cases of cancer (1). In Japan, mortality from colorectal cancer, especially from colon cancer, has increased markedly during

For reprints and all correspondence: Daigo Yoshida, Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidashi, Higashi-ku, Fukuoka 812-8582, Japan.
E-mail: dyoshida@phealth.med.kyushu-u.ac.jp

the past 50 years (2), and Japan is currently among the countries with the highest incidence rates of colorectal cancer worldwide (3). Because colorectal adenomas are well-established precursor lesions for colorectal cancer, it is recommended to remove polyps when detected, search the colon for additional polyps, and arrange for long-term surveillance of the subjects (4).

Adenomas, particularly of large size and with any villous component and dysplasia, are often accompanied by cancerous lesions (5–7). Progression of polyps to cancer has been documented in an early follow-up study of patients with unresected lesions (8), although clearly many do not develop to cancer (9). The adenoma–carcinoma sequence is also supported by progressive accumulation of genetic alterations involved in colorectal carcinogenesis (10). Furthermore, patients undergoing colorectal polypectomy have been found to exhibit a lower incidence of colorectal cancer than the general population in different countries (11–13). It is, however, uncertain to what extent colorectal polypectomy confers reduction in the risk of colorectal cancer in Japan. Only a small prospective study suggested a lower risk of colorectal cancer among patients undergoing polypectomy as compared with those with their polyps unresected (14). In the present study we therefore examined the relation between a history of colorectal polypectomy and subsequent risk of colorectal cancer in the Fukuoka Colorectal Cancer Study (15).

SUBJECTS AND METHODS

The Fukuoka Colorectal Cancer Study is a case-control study of incident cases of colorectal cancer at eight large hospitals in the study area (Fukuoka City and three adjacent areas) and community controls. The study protocol was approved by the ethical committee of the Faculty of Medical Sciences, Kyushu University. Details of the methods have been described elsewhere (15). Methodological issues relevant to the present study are briefly described below.

SUBJECTS

Cases comprised a consecutive series of patients with histologically confirmed incident cases of colorectal adenocarcinoma, who were admitted to two university hospitals or six affiliated hospitals for surgical treatment during the period from September 2000 to December 2003. Eligibility criteria included the following characteristics: age of 20–74 years at the time diagnosis, residence in the study area, no prior history of partial or total removal of the colorectum, familial adenomatous polyposis or inflammatory bowel disease, mental competence to give informed consent and to complete the interview. Research nurses visited each hospital weekly and determined eligibility of cases by referring to admission logs and medical records. Of 1053 eligible cases, 840 (80%) participated in the survey. Numbers of the interviewed cases according to the locations of colorectal cancer were as follows: proximal colon 191, distal colon 279,

rectum 354 and multiple sites 16. Cecum, ascending colon and transverse colon were combined as proximal colon, and distal colon included descending and sigmoid colon.

Eligibility criteria for controls were the same as described for cases except for the two items, i.e. having no diagnosis of colorectal cancer and age of 20–74 years at the time of selection. A total of 1500 persons were selected as control candidates by two-stage random sampling, by frequency matching to the expected distribution of incident cases with respect to sex and 10-year age class. The first step was a random selection of 15 small areas out of 178 in total and approximately 100 persons were randomly selected in each small area. At most four additional letters of invitation were mailed to control candidates. A total of 833 persons participated in the survey. Reasons for exclusion and non-participation were death ($n = 7$), migration from the study area ($n = 22$), undelivered mail ($n = 44$), mental incompetence ($n = 19$), history of partial or total removal of the colorectum ($n = 21$), diagnosis of colorectal cancer after the survey ($n = 5$), no response ($n = 158$), and refusal ($n = 391$). After exclusion of the first six categories of outcomes ($n = 118$), the net participation rate was calculated as 60% (833/1382). Interviews were conducted at community halls, collaborative clinics, or other places.

INTERVIEW

Research nurses interviewed cases and controls in person regarding physical activity, smoking, alcohol use, parental history of colorectal cancer, past history of selected diseases, and bowel habit by using a uniform questionnaire. Most of the questions were closed-ended, and some of the quantitative questions were open-ended. Prior histories of physician's diagnosis and surgery included colorectal polyp and colorectal polypectomy among others.

STATISTICAL ANALYSIS

The association of a history of colorectal polyp and polypectomy with the risk of colorectal cancer was examined by use of multiple logistic regression analysis. Statistical adjustment was made for gender, 5-year age class, resident area (Fukuoka City or suburban area), alcohol drinking, cigarette smoking, occupational physical activity, leisure-time physical activity, body mass index and parental history of colorectal cancer. Cigarette smoking was categorized into 0, 1–399, 400–799, and 800+ cigarette-years, which were calculated by multiplying the average number of cigarettes smoked per day by years of smoking. Alcohol use was categorized into 0, 0.1–0.9, 1.0–1.9 and 2.0+ units per day on the basis of the average amount of alcohol per day 5 years before; one unit corresponded roughly to one large bottle of beer (633 ml) or one go of sake (180 ml). Occupational physical activity was classified with sedentary and non-sedentary jobs. Leisure-time physical activity was evaluated in terms of a metabolic equivalent (MET)-hour score; the MET

(intensity of physical activity) of an individual type of physical activity was multiplied by hours spent for the activity. Body mass index was calculated by using body weight 10 years before and body mass index were categorized by using quartiles in the distribution in the controls. Adjusted odds ratio (OR) and 95% confidence interval (CI) were obtained from the logistic regression coefficient and its standard error for an indicator variable representing a specific category of the covariate. Statistical significance was declared if 95% CI did not include unity. All statistical analyses were done using the SAS version 8.2 (SAS Institute Inc., Cary, NC).

RESULTS

Males numbered 501 (60%) in the cases and 515 (62%) in the controls. Mean age of the cases was 61 years (range 27–74), and that of the controls was 59 years (range 22–75). Residents in Fukuoka City accounted for 61% of the cases and 65% of the controls. There were 74 cases and 86 controls who reported a history of physician's diagnosis of colorectal polyps, and 50 cases and 64 controls had a history of colorectal polypectomy (Table 1). The years of these two events (diagnosis and polypectomy) were identical with 49 cases and 59 controls each, and the diagnosis of polyp preceded 1–9 years prior to polypectomy in the remaining of cases and controls. The overall risk of colorectal cancer was moderately lowered in individuals with a history of colorectal polypectomy; adjusted odds ratios associated with colorectal polypectomy was 0.71 (95% CI 0.48–1.06).

Table 2 shows results from the analysis by location. Cases with multiple-site cancers were excluded. A statistically significant decrease in the risk associated with a history of colorectal polypectomy was observed for rectal cancer. A less marked, statistically non-significant decrease in the risk of distal colon cancer was also seen among those with an episode of colorectal polypectomy. The risk of proximal

colon cancer was slightly increased among those with a history of colorectal polypectomy. Adjusted odds ratios associated with colorectal polypectomy for cancer of the proximal colon, distal colon and rectum were 1.68 (95% CI 0.98–2.88), 0.71 (95% CI 0.41–1.26) and 0.24 (95% CI 0.11–0.52), respectively.

Although the majority of the subjects reporting a history of colorectal polyp had a history of colorectal polypectomy, we stratified the subjects with a history of colorectal polyp by the presence of polypectomy (Table 3). Adjusted ORs for those having a history of colorectal polyp but not of colorectal polypectomy did not measurably differ from unity. However, the risks of colorectal cancer and subsite-specific cancers among those reporting colorectal polypectomy were almost the same as described above.

Medians of the duration after colorectal polypectomy among the 50 cases and 64 controls with a history of colorectal polypectomy were each 4.0 years (range 0–15). We examined the association of colorectal polypectomy with overall and subsite-specific risks of colorectal cancer according to the length in time (<5 and 5+ years) after colorectal polypectomy. In individuals with colorectal polypectomy within 5 years before, adjusted ORs of colorectal, proximal colon, distal colon and rectal cancers were 0.59 (95% CI 0.35–0.99), 1.13 (95% CI 0.53–2.38), 0.72 (95% CI 0.36–1.48) and 0.24 (95% CI 0.09–0.62), respectively. The corresponding values for those having undergone polypectomy 5 or more years before were 0.89 (95% CI 0.50–1.59), 2.53 (95% CI 1.22–5.22), 0.67 (95% CI 0.27–1.63) and 0.25 (95% CI 0.07–0.84), respectively.

DISCUSSION

The present study showed that a history of colorectal polypectomy was associated with a substantial decrease in the risk of rectal cancer, and there was also a suggestive, protective association between colorectal polypectomy and distal colon cancer. The present findings indicate that colorectal polypectomy in the current practice is protective against cancer at the distal segment of the colorectum, but not in the proximal colon in Japan.

Because we did not ascertain details regarding the method of colorectal examination by which polyps were diagnosed and the location of polyps removed in the present study, it is difficult to explain why the decreased risk associated with colorectal polypectomy was only limited to rectal and distal colon cancers. Detection of the majority of colorectal polyps was probably on the basis of the fecal occult blood (FOB) screening and it could be speculated that the FOB screening may have resulted in a greater detection of polyps at the distal segment. However, it was shown that the FOB screening was as effective for cancers proximal to the sigmoid colon as for distal cancers (16,17). It was also observed that the FOB screening was associated with reduced mortality from colon and rectal cancers equally (18,19). Polyps of the

Table 1. Risk of colorectal cancer in relation to a history of colorectal polyp development and polypectomy

Past history	No. (%) of cases	No. (%) of controls	Crude OR (95% CI)	Adjusted OR (95% CI)*
Colorectal polyp				
None	766 (91.2)	747 (89.8)	1.00 (referent)	1.00 (referent)
Present	74 (8.8)	86 (10.2)	0.84 (0.61–1.16)	0.77 (0.55–1.08)
Colorectal polypectomy				
None	790 (94.0)	769 (92.3)	1.00 (referent)	1.00 (referent)
Present	50 (6.0)	64 (7.7)	0.76 (0.52–1.12)	0.71 (0.48–1.06)

OR, odds ratio; CI, confidence interval.

*Adjusted for sex, 5-year age class, residence, cigarette smoking, alcohol drinking, occupational physical activity, leisure-time physical activity, body mass index, and parental history of colorectal cancer.

Table 2. Risks of proximal colon, distal colon, and rectal cancers in relation to a history of colorectal polyp development and polypectomy

Past history	Proximal colon		Distal colon		Rectum	
	No.	OR (95% CI)*	No.	OR (95% CI)*	No.	OR (95% CI)*
Colorectal polyp						
None	164	1.00 (referent)	256	1.00 (referent)	332	1.00 (referent)
Present	27	1.39 (0.85–2.27)	23	0.67 (0.40–1.10)	22	0.53 (0.32–0.87)
Colorectal polypectomy						
None	168	1.00 (referent)	261	1.00 (referent)	346	1.00 (referent)
Present	23	1.68 (0.98–2.88)	18	0.71 (0.41–1.26)	8	0.24 (0.11–0.52)

*OR, odds ratio; CI, confidence interval; Adjusted for sex, 5-year age class, residence, cigarette smoking, alcohol drinking, occupational physical activity, leisure-time physical activity, body mass index, and parental history of colorectal cancer.

rectum and distal colon may have been more effectively diagnosed and removed than proximal colon polyps in the present study population. Two case-control studies in the USA (20,21) investigated the association between screening sigmoidoscopy and the risk of colorectal cancer and reported that decreased risk associated with sigmoidoscopy was observed almost exclusively for cancer of the rectum and sigmoid colon. In another case-control study in the USA, however, decreased risks of both colon and rectal cancers were observed for any endoscopic procedures (22). Screening endoscopy with no distinction between sigmoidoscopy and colonoscopy was also associated with a marked

decrease in the overall risk of colorectal cancer in a case-control study in Germany (23).

The risk of distal colon and rectal cancer was decreased in individuals with a history of colorectal polypectomy almost equally in the recent (<5 years) and distant (5+ years) past, but the risk of proximal colon cancer was rather elevated among those having undergone colorectal polypectomy 5+ years earlier. The latter finding may have been ascribed to chance, but needs consideration with respect to effectiveness of the current practice of colorectal endoscopy in Japan. Polyps detected at the distal segment generally warrant total colonoscopy in search for lesions in proximal sites of the colon (4). It is well documented that the presence of distal colorectal polyps, especially adenomas, is predictive of proximal colon neoplasms (24–27). It is thus possible that a portion of proximal colon polyps were undetected or excised incompletely. In fact, patients with colorectal adenomas or polyps removed during the period when sigmoidoscopy rather than colonoscopy was common, experienced a higher risk of colon or colorectal cancer compared with the general population (28,29).

In the present study, there was no measurable increase or decrease in the risk of overall or subsite-specific colorectal cancer in individuals with a history of colorectal polyps but not of colorectal polypectomy. However, because numbers of such persons were small in cases and controls, the findings need to be interpreted with caution. It is well known that individuals bearing colorectal polyps or adenomas have increased risk of colorectal cancer. For instance, patients with polyps who had not undergone polypectomy had an eight-fold increased risk of subsequent colorectal cancer as compared with general population in Osaka, Japan (14).

The fairly large size of the study, use of community controls and a high participation rate in the case group were strengths of the present study. There were several weaknesses to be discussed, however. In the present study, the participation rate was not as high in the controls as attained in the cases. It is generally difficult to attain a high participation rate for community controls. In the recruitment of controls in

Table 3. Risks of colorectal cancer by subsite according to the combination of histories of colorectal polyp development and polypectomy

	Polyp (–)	Polyp (+)	
		Polypectomy (–)	Polypectomy (+)
All cases			
No.	766	24	50
OR (95% CI)*	1.00	0.94 (0.52–1.70)	0.71 (0.48–1.06)
Proximal colon cancer			
No.	164	4	23
OR (95% CI)*	1.00	0.72 (0.24–2.17)	1.67 (0.97–2.85)
Distal colon cancer			
No.	256	5	18
OR (95% CI)*	1.00	0.56 (0.21–1.52)	0.70 (0.40–1.24)
Rectal cancer			
No.	332	14	8
OR (95% CI)*	1.00	1.37 (0.68–2.76)	0.25 (0.11–0.53)

*OR, odds ratio; CI, confidence interval; Adjusted for sex, 5-year age class, residence, cigarette smoking, alcohol drinking, occupational physical activity, leisure-time physical activity, body mass index and parental history of colorectal cancer.

the present study, the invitation was repeated four times at most. Although a higher participation rate is of course desirable, the participation rate of 60% is considered to be acceptable (30). History of colorectal polyps and polypectomy was based on self-reporting. Individuals categorized as having no history of colorectal polyps may have had such lesions undiagnosed. The prevalence of reported colorectal polyps is influenced by previous participation in the screening for colorectal cancer and also by screening method. However, we did not elicit previous participation in the screening for colorectal cancer. It is another concern how representative the control subjects were with respect to the history of colorectal polyps and polypectomy. If individuals with a history of colorectal polypectomy had been more likely to participate in the study, the observed decrease in the risk associated with prior history of colorectal polypectomy would have been overestimated. Furthermore, case and control subjects may have recalled their past medical history differentially. However, it is unlikely that the cases recalled a prior history of colorectal polypectomy differentially according to different sites of colorectal cancer. Thus the present findings can not be totally ascribed to the so-recall bias.

In conclusion, in a large-scale case-control study of colorectal cancer, a prior history of colorectal polypectomy was associated with a substantial decrease in the risk of rectal cancer and possibly of distal colon cancer.

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Conflict of interest statement

None declared.

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