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Obesity and Adenomatous Polyps of the Sigmoid Colon

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The relation between obesity and adenomatous polyps of the sigmoid colon was investigated in male self-defense officials who received a retirement health examination at three hospitals of the Self-Defense Forces in Japan between January 1991 and December 1992. Body mass index (BMI) and waist-hip circumference ratio (WHR) were used as indices of obesity. A total of 228 adenoma cases and 1484 controls with normal sigmoidoscopy were identified in 2228 men: cases having small adenomas (<5 mm in diameter) and those with large adenomas (5 mm or greater) numbered 115 and 102, respectively. Smoking, alcohol use, physical activity, rank, and hospital were controlled for by multiple logistic regression analysis. BMI and WHR were classified into four levels using the 30th, 60th, and 90th percentiles of each distribution in the control as cut-off points. There was a significant two-fold elevation in the overall adenoma risk among men at the highest BMI level (≥26.95) compared with those at the lowest level (<22.48), but the risk did not linearly increase: a similar increase was also noted for large adenomas. While WHR was only weakly related to the overall adenoma risk, the risk of large adenomas progressively increased with increasing levels of WHR: odds ratio (OR) 2.9 (95% confidence interval (CI) 1.4–5.9) for the highest (≥0.958) versus lowest (<0.878) levels. BMI was not materially associated with adenoma risk after additional adjustment for WHR, but a positive association between WHR and large adenomas was independent of BMI: OR 3.4 (95%CI 1.5–7.6) for the highest versus lowest levels. These findings suggest that obesity is associated with an increased risk of colon adenomas, probably with adenoma growth.

Key words: Colon adenoma — Waist-hip ratio — Obesity — Case-control study — Body mass index

Epidemiologic findings on the relation between obesity and colon cancer are inconsistent. While several prospective studies found that obesity as measured by relative weight or body mass index (BMI=kg/m^2) was related to an increased risk of colon cancer in men,[1-5] other prospective studies failed to find such an association.[6,7] One of the latter studies even showed an inverse relation between obesity and colorectal cancer.[7] Most colon cancers are known to arise from adenomas, and their presence is associated with an increased risk of colorectal cancer.[8-10] The use of this precursor lesion as an endpoint preceding the occurrence of colon cancer has methodological virtues due to the reduction in the time period between exposure and outcome. Only a few studies have examined the relation between obesity and colorectal adenomas. A case-control study in the United States reported that BMI was positively associated with adenoma risk in women and weakly so in men.[11] Another case-control study in Germany reported that the risk of adenoma with high potential of malignancy was increased with high levels of BMI in a male population.[12] Yet, in other studies, BMI was not associated with colorectal adenomas in either men[13,14] or women.[14]

The use of BMI or relative weight may be inadequate in evaluating adiposity, especially in men.[15] Furthermore, weight related to height does not provide information on the anatomic distribution of fat. Central obesity as usually measured by waist-hip circumference ratio (WHR) has been related to various metabolic and hormonal abnormalities, independently of and more strongly than BMI.[16-18] To our knowledge, none of the previous studies of colorectal cancer or adenomas has addressed the relationship with central obesity or body fat distribution. We examined the relation of WHR as well as of BMI to adenomas of the sigmoid colon in middle-aged Japanese men.

MATERIALS AND METHODS

This is a cross-sectional study of male self-defense officials who received a retirement health examination at

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the Self-Defense Forces Hospitals in Fukuoka and Kumamoto between January 1991 and December 1992, and in Sapporo from April to December 1992. The health examination and data collection have been described elsewhere.[19-21] The health examination is part of a nationwide program for those retiring from the Self-Defense Forces, and the three hospitals cover most areas in Kyushu and Hokkaido.

The health examination was done during a five-day admission, and included flexible sigmoidoscopic or colonoscopic examination of the rectum and sigmoid colon as a routine procedure. More proximal sites were also studied at Fukuoka Hospital if the subjects tolerated the procedure and at Sapporo Hospital if they had a positive fecal occult blood test or prior history of large bowel disease. Colonoscopy with intubation of less than 60 cm and not reaching the sigmoid-descending junction was regarded as unsatisfactory unless pathological lesions were found. Histological diagnosis of biopsied or polypectomized specimens was referred to the pathology department at the Sapporo Hospital, the pathology department of a university hospital at the Fukuoka Hospital, and the laboratory center of the Kumamoto City Medical Association at the Kumamoto Hospital.

In the series of 2228 men (490 in Sappro, 1197 in Fukuoka, and 541 in Kumamoto), a total of 2124 underwent colonoscopy or sigmoidoscopy. Among them, 246 men were found to have at least one adenoma at a distance of 11–60 cm from the anus, which is defined as the sigmoid colon here, and 1543 men had normal colonoscopy. Excluding men with known colorectal polyps, prior history of colorectal polypectomy, colectomy, or malignant neoplasms and those with newly diagnosed malignant neoplasms, 228 cases of sigmoid colon adenomas and 1484 controls remained in the present study. Numbers of cases and controls by hospital are summarized in Table I, together with numbers of cases by adenoma size; the size was not recorded for 11 cases of adenoma. In this analysis, adenoma which was 5 mm or greater in diameter was defined as a large adenoma.

Waist and hip circumferences were measured in the horizontal plane at the level of the umbilicus and at the largest circumference around the buttocks, respectively. Height (in centimeters) and body weight (in kilograms) were recorded.

A self-administered questionnaire was distributed on the first day of admission and collected on the second day with a supplemental interview. The questionnaire inquired about smoking and drinking habits, physical activity, and other lifestyle characteristics. Questions on physical activity ascertained weekly frequency of exercise with precoded answers, usual type of exercise, average amount of time spent per occasion, and also time spent for exercise inducing shortness of breath. Since physical activity is well known to increase serum high-density lipoprotein (HDL) cholesterol level, it was used to choose an appropriate variable of physical activity. Weekly frequency was more strongly correlated with HDL cholesterol level (Spearman $r=0.13$) than the amount of time spent for either total exercise ($r=0.12$) or that inducing shortness of breath ($r=0.09$). Thus, weekly frequency of exercise was used as an index of physical activity. Questions on smoking and drinking habits distinguished between former and never smokers and between former and never drinkers as described previously.[20] Alcohol intake in current drinkers was calculated from reported consumption frequencies and quantities of five different alcoholic beverages.[19]

Multiple logistic regression analysis was used to control for smoking, alcohol use, physical activity, rank, and hospital. Ages of the study subjects were distributed in a limited range from 49 to 55 years, and about 90% were those aged 51 or 52 years. Thus age was not taken into consideration in the present analysis. Levels of BMI and WHR were divided into four categories with cut-off points at the 30th, 60th, and 90th percentiles in the control group. Smoking habit was classified into four categories of 0, 1–399, 400–799, or ≥ 800 cigarette-years (the number of cigarettes smoked per day multiplied by years of smoking); alcohol use into five categories of never, past, and current drinkers consuming <30, 30–59, or ≥ 60 ml of alcohol per day; weekly frequency of exercise

Table I. Numbers of Controls and Cases of Sigmoid Colon Adenomas by Hospital

Hospital	Control	Adenoma case		
		All	Small[a]	Large[b]
Sapporo	316	58	27	29
Fukuoka	753	127	72	47
Kumamoto	415	43	16	26
Total	1484	228	115	102

a) Largest adenoma less than 5 mm in diameter.
b) Largest adenoma 5 mm or greater in diameter.

Table II. Means (Standard Error) of Body Mass Index (BMI) and Waist-Hip Ratio (WHR) in the Controls by Hospital

Hospital	BMI (kg/m^2)	WHR
Sapporo	23.95 (0.14)	0.890 (0.003)
Fukuoka	23.45 (0.09)	0.903 (0.002)
Kumamoto	25.16 (0.11)	0.906 (0.002)
ANOVA[a]	$P<0.0001$	$P<0.0001$

a) One-way analysis of variance.

Table III. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Adenomatous Polyps of the Sigmoid Colon According to Body Mass Index (BMI) and Waist-Hip Ratio (WHR)[a]

Category	No. of controls	All adenomas			Large adenomas		
		No.	Crude OR	Adjusted OR (95% CI)	No.	Crude OR	Adjusted OR (95% CI)
BMI (kg/m^2)							
<22.48	440	61	1.0	1.0 (Referent)	25	1.0	1.0 (Referent)
22.48–24.30	444	76	1.2	1.3 (0.9–1.9)	37	1.5	1.5 (0.9–2.6)
24.31–26.94	451	58	0.9	1.0 (0.7–1.5)	23	0.9	0.9 (0.5–1.7)
≥26.95	149	33	1.6	1.9 (1.2–3.0)	17	2.0	2.1 (1.1–4.1)
WHR							
<0.878	429	54	1.0	1.0 (Referent)	18	1.0	1.0 (Referent)
0.878–0.911	445	61	1.1	1.2 (0.8–1.8)	28	1.5	1.5 (0.8–2.9)
0.912–0.957	453	84	1.5	1.6 (1.1–2.3)	38	2.0	2.1 (1.1–3.8)
≥0.958	157	29	1.5	1.5 (0.9–2.5)	18	2.7	2.9 (1.4–5.9)

a) Based on logistic regression analysis controlling for smoking, alcohol use, physical activity, rank and hospital.

into four categories of 0, 1–3, or 4–5 days per week, and almost daily: and the rank in the Self-Defense Forces into three classes. Indicator terms for levels of factors were always used in logistic models. Odds ratios were the antilogarithms of regression coefficients of the corresponding indicator terms, and their 95% confidence intervals were calculated by using standard errors of the regression coefficients. Possible interaction with hospital was evaluated by log-likelihood ratio tests.[22] All statistical computations were performed by using the Statistical Analysis System (SAS).[23]

RESULTS

Because both BMI and WHR varied substantially with hospitals (Table II), we first examined whether the relation between BMI or WHR and adenoma risk was differential according to hospital, but there was no measurable interaction with hospital regarding either BMI or WHR in separate analyses of all, large, and small adenomas (data not shown).

Table III shows adenoma risk according to BMI and WHR. With adjustment for smoking, alcohol use, physical activity, rank, and hospital, a significant increase in adenoma risk was noted among men at the top 10% of BMI, and the risk of large adenoma also showed a similar increase among them. WHR tended to be positively associated with the overall risk of adenomas, and the risk of large adenoma was progressively increased with increasing levels of WHR.

Although BMI and WHR were highly correlated with each other (correlation coefficient=0.55 in the control group), it was of particular interest to know whether BMI and WHR were independently associated with adenoma, especially with large adenoma. After adjustment for WHR, the increased risk of either all or large adenomas at the highest category of BMI was substantially reduced toward unity (Table IV). On the other hand, the association with WHR did not change after adjustment for BMI. A positive relation between WHR and large adenomas was slightly more pronounced.

Table IV. Adjusted Odds Ratios and 95% Confidence Intervals for Adenomatous Polyps of the Sigmoid Colon According to Body Mass Index (BMI) and Waist-Hip Ratio (WHR) after Mutual Adjustment[a]

Category	All adenomas	Large adenomas
BMI (kg/m^2)		
<22.48	1.0 (Referent)	1.0 (Referent)
22.48–24.30	1.2 (0.8–1.7)	1.2 (0.7–2.1)
24.31–26.94	0.8 (0.5–1.3)	0.6 (0.3–1.2)
≥26.95	1.5 (0.8–2.5)	1.2 (0.5–2.5)
WHR		
<0.878	1.0 (Referent)	1.0 (Referent)
0.878–0.911	1.2 (0.8–1.8)	1.6 (0.9–3.2)
0.912–0.957	1.6 (1.0–2.4)	2.3 (1.2–4.6)
≥0.958	1.5 (0.8–2.6)	3.4 (1.5–7.6)

a) Based on logistic regression analysis controlling for smoking, alcohol use, physical activity, rank, hospital, and either BMI or WHR.

Because physical activity is one of the major determinants of an individual's obesity level,[24] it is important to examine the relation between physical activity and adenoma risk. Weekly frequency of exercise was not materially associated with either the overall risk of adenomas or the risk of large adenomas, although odds ratio of large adenomas was below unity among men participating in exercise almost daily (Table V). These results were essentially the same as those without adjustment for WHR.

Table V. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Adenomatous Polyps of the Sigmoid Colon According to Weekly Frequency of Exercise[a)]

Frequency per week	No. of controls	All adenomas			Large adenomas		
		No.	Crude OR	Adjusted OR (95% CI)	No.	Crude OR	Adjusted OR (95% CI)
0	419	66	1.0	1.0 (Referent)	30	1.0	1.0 (Referent)
1–3	633	90	0.9	1.0 (0.7–1.4)	47	1.0	1.2 (0.8–2.0)
4–5	251	44	1.1	1.3 (0.9–2.1)	19	1.1	1.5 (0.8–2.9)
Daily	181	28	1.0	1.2 (0.8–2.0)	6	0.5	0.7 (0.3–1.7)

a) Based on logistic regression analysis controlling for smoking, alcohol use, rank, hospital and waist-hip ratio.

DISCUSSION

This study had several methodological advantages. The retirement health examination program covered almost all men retiring from the Self-Defense Forces, and most of them underwent colonoscopy unselectively. Selection bias was thus negligible. Furthermore, subjects were homogenous with respect to age and occupational background. A weakness of this study is the lack of consistency in examining the colon proximal to the sigmoid. The control group at the Kumamoto Hospital may have included more men with adenomas of the proximal colon than those at the other two hospitals because only sigmoidoscopy was done at the Kumamoto Hospital. But the effect of this misclassification would not cause a spurious association. It also should be mentioned that detection rate of adenomas seemed to differ between hospitals as indicated by the ratios of adenoma cases to controls: Kumamoto 0.10, Fukuoka 0.17, and Sapporo 0.18. However, large adenomas of the sigmoid colon were detected almost equally in the three hospitals; the ratios of large adenomas to controls in Kumamoto, Fukuoka, and Sapporo were 0.06, 0.06, and 0.09, respectively. Therefore, at least the findings on large adenomas are unlikely to be ascribed to the different degree of scrutiny in colonoscopy between hospitals.

Our data first demonstrated that WHR was associated with an increased risk of colon adenomas, especially large adenomas. BMI was not associated with adenoma risk independently of WHR. BMI and WHR are collinear to each other, and it may be difficult to draw a conclusion as to which is important for adenoma risk. WHR may simply be a better index of obesity than BMI in our study population. Discrepancies in previous studies of colon cancer[1-7)] and colon adenomas[11-14)] in relation to obesity may be explained partly by inadequacy of BMI or relative weight as a measure of obesity.

We have no explanation as to the mechanism underlying the observed association between obesity and colon adenomas. Obesity may be a surrogate marker for increased fat or caloric intake, which is considered as a risk factor for colon cancer and adenomas.[13, 25)] Low physical activity is another possible explanation, although our data failed to show an association between physical inactivity and adenoma risk. Apart from the underlying mechanisms, our findings suggest that obesity may be linked with the growth of colon adenomas, thereby also increasing the risk of colon cancer.

Many,[5, 26-29)] but not all,[6, 30, 31)] studies have found an inverse association between physical activity and colon cancer. A few epidemiologic studies have reported inconsistent results on physical activity and colon adenomas.[13, 32)]

Our previous study of male self-defense officials showed that physical activity, as expressed by the amount of time spent doing strenuous activities during leisure time, was inversely related to the risk of adenomas of the sigmoid colon.[33)] The lack of association between physical activity and adenoma risk in the present study may not necessarily contradict our previous findings since the way of ascertaining physical activity was different between the two studies. In the earlier study, participations in a wide variety of physical activities were ascertained, and the time spent for strenuous activity was used as an index of physical activity. The weekly frequency of exercise may be too crude to detect an association between physical activity and adenoma risk. Further studies are needed on physical activity and colon adenomas.

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