Original Article

Association Between Rectosigmoid Adenomas and Cardiovascular Risk Factors: A Hospital-based, Cross-sectional Study

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Abstract

Introduction: Little was known about the association between colorectal adenomas and cardiovascular risk factors in Taiwan. The aim of this study was to assess the association between rectosigmoid adenomas and related factors. Materials and Methods: This was a hospital-based, cross-sectional study. We analysed subjects receiving self-referred health examinations at 1 medical centre in Taiwan between 2001 and 2004. In total, 4413 subjects were enrolled in this study. There were 2444 men (55.4%) and 1969 women (44.6%). The mean age was 49.3 ±12.3 years (range, 20 to 87). All subjects underwent a 60-cm flexible sigmoidoscopic examination and laboratory survey. Adjusted odds ratio (OR) and 95% confidence interval (CI) were expressed using a multivariate logistic regression analysis. Results: In the final model, increasing age (OR, 1.05; 95% CI, 1.03-1.06), hypertriglyceridemia (OR, 1.49; 95% CI, 1.07-2.07), and alcohol consumption (OR, 2.11; 95% CI, 1.47-3.04) were the risk factors for rectosigmoid adenomas in men. Increasing age was the only risk factor for rectosigmoid adenomas in women (OR, 1.03; 95% CI, 1.01-1.06). Conclusion: Age, hypertriglyceridemia and alcohol consumption are associated with rectosigmoid adenomas in men, and only age is significantly associated with rectosigmoid adenomas in women.

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Key words: Alcohol, Cardiovascular, Hypertriglyceridemia

Introduction

Cancer is the leading cause of death in Taiwan in 2005.[1] However, colorectal cancer is the third leading cause of death from cancer and accounts for approximately 4111 deaths in Taiwan in 2005.[1] Due to a westernisation of lifestyle, its incidence is increasing annually.[2] Colorectal adenomas are currently believed to be pre-cancerous lesions for most colorectal cancers.[3-5] The hypothesis of colorectal adenoma-carcinoma sequence is now widely accepted.[3-5] Although the exact cause of colorectal cancer remains controversial, numerous epidemiological studies have demonstrated that family history, dietary factors, alcohol consumption and cigarette smoking are common risk factors for colorectal cancer.[6-9] Recently, several studies have identified that insulin resistance and/or hyperinsulinemia may contribute to the development of colorectal cancer.[10-12]

On the other hand, insulin resistance and/or hyperinsulinemia seem to be the key determinant to the development of metabolic syndrome.[13-15] An alternative hypothesis that links colorectal cancer and metabolic syndrome has been presented.[10-12,16-18] Nevertheless, the components of metabolic syndrome also markedly increase the risk for cardiovascular disease.[19-21] In Taiwan, cerebrovascular disease, cardiovascular disease, diabetes mellitus and hypertension were the second, third, fourth and tenth leading causes of death in 2005.[1]

Since the majority of colorectal cancers arise from pre-existing adenomas,[3-5] it is of greater concern to determine the risk factors for colorectal adenomas in the early stages of colorectal neoplasm. To date, only a few epidemiological studies have published the related reports of colorectal adenomas in Taiwan.[22-24] For the above reasons, we conducted a hospital-based, cross-sectional study to address the following objectives: (i) what was the relationship between rectosigmoid adenomas and cardiovascular risk factors and (ii) what were the risk factors for rectosigmoid adenomas?

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Materials and Methods

Study Population

This was a hospital-based, cross-sectional study. We analysed the medical records of all subjects undergoing self-referred health examination at 1 medical centre located at Taichung city in Taiwan between 2001 and 2004. The institutional review board of this medical centre approved this retrospective research. Subjects with previous malignant diseases were excluded from the research. All subjects underwent a 60-cm flexible sigmoidoscopic examination and laboratory survey. A total of 4413 subjects were included for analysis.

Data Collection

Subjects who never smoked were classified as non-smokers. Long-duration heavy smokers who quit smoking 1 month before the health examination were also classified as non-smokers. Subjects who currently smoked were classified as smokers. Subjects who never drank alcohol were classified as non-drinkers. Subjects who reported drinking alcohol often were classified as habitual drinkers. Blood pressure was measured by a mercury sphygmomanometer while the subject was in a sitting position. Weight and height were measured. Body mass index (BMI) was measured as follows: weight (kg) ÷ height $(m)^2$. Waist circumference (WC) was measured as the minimum circumference with the tape positioned between the xyphoid process and the umbilicus at the end of a normal expiration.[25] Venous blood samples were obtained in the morning after a 12-hour overnight fast. A number of biochemical markers, such as total cholesterol (TC), triglyceride (TG), low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol and fasting glucose were measured by a

Table 1. The Basic Characteristics of the Study Population (Univariate Analysis)

Variable (mean ± SD)	Men (n = 2444) (%)	Women (n = 1969) (%)	*P* value
Age (y)	48.9 ± 11.9	49.8 ± 12.7	0.01
Body mass index (kg/m^2)	24.5 ± 3.3	23.5 ± 3.7	<0.001
Waist circumference (cm)	87.6 ± 8.7	80.3 ± 9.9	
Systolic pressure (mmHg)	124.8 ± 16.0	118.0 ± 19.7	<0.001
Diastolic pressure (mmHg)	79.9 ± 10.3	74.6 ± 10.9	<0.001
Fasting glucose (mg/dL)	5.7 ± 1.9	5.5 ± 1.5	<0.001
Total cholesterol (mg/dL)	5.25 ± 1.01	5.19 ± 1.02	0.04
Triglyceride (mg/dL)	1.5 ± 1.6	1.1 ± 0.8	<0.001
LDL (mg/dL)	3.4 ± 0.9	3.2 ± 0.9	<0.001
HDL (mg/dL)	1.11 ± 0.28	1.35 ± 0.34	<0.001
Ratio of TC/HDL	4.9 ± 1.4	4.0 ± 1.1	<0.001
Smoke use			<0.001
Non-smoker	1435 (58.7)	1846 (93.8)	
Smoker	1009 (41.3)	123 (6.2)	
Alcohol use			<0.001
Non-drinker	2017 (82.5)	1908 (96.9)	
Habitual drinker	427 (17.5)	61 (3.1)	
Sigmoidoscopic examination			<0.001
Normal	1997 (81.7)	1762 (89.5)	
Adenoma	154 (6.3)	71 (3.6)	
Mixed adenoma and hyperplastic polyp	23 (0.9)	6 (0.3)	
Adenocarcinoma	4 (0.2)	1 (0.1)	
Hyperplastic polyp	147 (6.0)	67 (3.4)	
Inflammatory polyp or other lesion	19 (0.8)	12 (0.6)	
Polyp without polypectomy or biopsy	99 (4.1)	50 (2.5)	

P value of the *t*-test or the chi-square test

biochemical autoanalyser (Hitachi 736-15, Tokyo, Japan) at the Department of Clinical Laboratory of this medical centre.

Diagnostic Criteria

BMI ≥27(kg/m^2) was defined as generalised obesity.[26] Central obesity was defined as WC ≥90 cm for men and ≥80 cm for women.[27] Hypercholesterolemia was defined as fasting total cholesterol level ≥5.2 mmol/L.[28] Hypertriglyceridemia was defined as fasting triglyceride level ≥1.7 mmol/L.[21] High level of LDL was defined as fasting LDL ≥3.4 mmol/L.[28] Low level of HDL was defined as fasting HDL <1.03 mmol/L for men and <1.3 mmol/L for women, respectively.[21] The ratio of TC/HDL >5 was defined as abnormal.[29] Diabetes mellitus was defined as fasting glucose level ≥6.9 mmol/L or subjects with anti-diabetic drug treatment.[30] Subjects were considered to have hypertension if the average of both arm readings exceeded 140 mmHg systolically and/or 90 mmHg diastolically or subjects with antihypertensive drug treatment.[31]

Statistical Analysis

We used a SPSS package (Taiwan Version 10.0, Sinter Information Corp, Taipei, Taiwan). The *t*-test and the chi-square test were used for statistical analysis. Relative risks were estimated by adjusted odds ratio (OR) and 95% confidence interval (CI) using a multivariate logistic regression analysis. A *P* value less than 0.05 was considered statistically significant.

Results

Characteristics of the Study Population

There were 2444 men (55.4%) and 1969 women (44.6%). The mean age was 49.3 ±12.3 years (range, 20 to 87). In Table 1, there were statistically significant differences in the mean values of age, BMI, WC, systolic blood pressure, diastolic blood pressure, fasting glucose, TC, TG, LDL, HDL and ratio of TC/HDL between men and women by the *t*-test. There were also statistically significant differences in the proportions of smoking and alcohol consumption between men and women by the chi-square test.

Among 4413 subjects undergoing rectosigmoidoscopy, 3759 subjects (85.2%) had normal findings, and the remaining 654 subjects (14.8%) had at least 1 rectosigmoid polyp. Among 654 subjects with polyps, 505 subjects underwent a polypectomy or biopsy. The histological findings consisted of 254 (50.3%) adenomas (including 29 subjects with adenomas and hyperplastic polyps), 6 (1.2%) adenocarcinomas, 214 (42.4%) hyperplastic polyps and 31 (6.1%) inflammatory polyps or other lesions. Finally, 3759 subjects with normal finding and 254 subjects with adenomas were included for further analysis. There were 149 subjects with polyps found on examination but no polypectomy or biopsy was taken.

Comparison of Cardiovascular Risk Factors Between People With and Without Adenomas by Univariate Analysis

Using the chi-square test, the significantly related factors for adenomas in men were age (P <0.001), hypertension (P = 0.003), hypertriglyceridemia (P = 0.013) and alcohol use (P <0.001). In women, the significantly related factors for adenomas were increasing age (P <0.001), central obesity (P = 0.003), hypertension (P <0.001), diabetes mellitus (P <0.001), hypercholesterolemia (P = 0.001), hypertriglyceridemia (P = 0.001) and a high level of LDL (P = 0.006) (Table 2).

Risk Factors for Rectosigmoid Adenomas by Multivariate Logistic Regression

Only the significantly related factors identified in univariate analysis were further analysed. In the final model, multivariate logistic regression analysis showed that the related risk factors for adenomas in men were increasing age (OR 1.05, 95% CI 1.03-1.06, P <0.001), hypertriglyceridemia (OR 1.49, 95% CI 1.07-2.07, P <0.05) and alcohol consumption (OR 2.11, 95% CI 1.47-3.04, P <0.001). The only related risk factor for adenomas in women was increasing age (OR 1.03, 95% CI 1.01-1.06, P <0.01) (Table 3).

Discussion

There were 149 subjects with polyps found on examination but no biopsy was taken. As commented by gastroenterologists, these polyps were usually too small and so it was not necessary to perform biopsies. However, more frequent colonoscopic surveillance was suggested. As we did not enroll these subjects, there should not be any confounding effect on the analysis.

Epidemiological studies regarding the association between colorectal adenomas and the related factors have shown conflicting results. In addition, relatively few studies were analysed separately according to sex. In our study, hypertriglyceridemia was one of the risk factors for rectosigmoid adenomas in men. The mean value of triglyceride was higher in patients with colorectal adenomas in some studies.[23,32,33] In Fujimori et al,[34] a significantly lower value of triglyceride was found in daily drinkers with adenoma than in those without. So far, no consistent data exist on the association between triglyceride and the risk for colorectal adenomas. We still suggest that men with hypertriglyceridemia should be evaluated for the likelihood of colorectal adenomas.

In our study, alcohol consumption was one of the risk factors for rectosigmoid adenomas in men. To date,

Table 2. Comparison of Cardiovascular Risk Factors between People With and Without Adenomas in Both Gender by Chi-square Test

	Men (n = 2175)			Women (n = 1839)		
Variable	**Normal**	**Adenoma**	***P* value**	**Normal**	**Adenoma**	***P* value**
Age (y) (Mean ± SD)	48.0 ± 11.7	54.4 ± 11.7	<0.001	49.2 ± 12.7	57.6 ± 11.7	<0.001
Generalised obesity (%)			0.912			0.076
No	1609 (91.9)	143 (8.1)		1503 (96.2)	60 (3.8)	
Yes	388 (91.7)	35 (8.3)		259 (93.8)	17 (6.2)	
Central obesity (%)			0.791			0.003
No	1205 (92.0)	106 (8.1)		920 (97.1)	27 (2.9)	
Yes	792 (91.7)	72 (8.3)		842 (94.4)	50 (5.6)	
Hypertension (%)			0.003			<0.001
No	1449 (92.9)	110 (7.1)		1390 (97.0)	43 (3.0)	
Yes	548 (89.1)	68 (11.0)		372 (91.6)	34 (8.4)	
Diabetes mellitus (%)			0.600			<0.001
No	1756 (91.7)	159 (8.3)		1623 (96.3)	62 (3.7)	
Yes	241 (92.7)	19 (7.3)		139 (90.3)	15 (9.7)	
Hypercholesterolemia (%)			0.282			0.001
No	1032 (92.5)	84 (7.5)		942 (97.3)	26 (2.7)	
Yes	965 (91.2)	94 (8.9)		820 (94.1)	51 (5.9)	
Hypertriglyceridemia (%)			0.013			0.002
No	1439 (92.8)	113 (7.3)		1545 (96.4)	58 (3.6)	
Yes	558 (89.6)	65 (10.4)		217 (91.9)	19 (8.1)	
High level of LDL (%)			0.274			0.006
No	1067 (92.5)	88 (7.6)		1097 (96.8)	36 (3.2)	
Yes	930 (91.2)	90 (8.8)		665 (94.2)	41 (5.8)	
Low level of HDL (%)			0.063			0.858
No	1104 (92.9)	85 (7.1)		897 (95.7)	40 (4.3)	
Yes	893 (90.7)	92 (9.3)		865 (95.9)	37 (4.1)	
TC/HDL>5 (%)			0.079			0.157
No	1107 (92.8)	86 (7.2)		1440 (96.1)	58 (3.9)	
Yes	890 (90.7)	91 (9.3)		322 (94.4)	19 (5.6)	
Smoke use (%)			0.153			0.709
Non-smoker	1204 (92.5)	97 (7.5)		1652 (95.8)	73 (4.2)	
Smoker	793 (90.8)	81 (9.2)		110 (96.5)	4 (3.5)	
Alcohol use (%)			<0.001			0.795
Non-drinker	1676 (92.9)	130 (7.1)		1707 (95.8)	75 (4.2)	
Habitual drinker	321 (87.0)	48 (13.0)		55 (96.5)	2 (3.5)	

the published data on the association between alcohol consumption and the risk for colorectal adenomas remains inconclusive. Alcohol consumption was a significantly related factor for colorectal adenomas in some studies.[8,32,35] In Boutron et al,[36] in which the data were analysed separately according to sex, alcohol consumption was a related factor for colorectal adenomas in men. Boutron et al also made a hypothesis that alcohol acted as an early promoter of colorectal carcinogenesis but played no role in malignant changes.[36] However, in Nagata et al,[37] alcohol consumption was not a related factor for colorectal adenomas in men. Despite wide variations about the role of alcohol

Table 3. Odds Ratio of Risk Factors For Adenomas in Both Gender By Multivariate Logistic Regression

Variable	Men		Women	
	OR	95% CI	OR	95% CI
Age (increasing one year)	1.05	1.03-1.06***	1.03	1.01-1.06**
Hypertension	1.16	0.83-1.62	1.58	0.93-2.70
Hypertriglyceridemia	1.49	1.07-2.07*	1.38	0.77-2.49
Alcohol consumption	2.11	1.47-3.04***		
Central obesity			1.11	0.66-1.88
Diabetes mellitus			1.50	0.79-2.85
Hypercholesterolaemia			1.44	0.72-2.88
High level of LDL			1.18	0.61-2.26

*P <0.05, **P<0.01, ***P <0.001

consumption, we also propose a special emphasis that men with alcohol consumption should be assessed for the possibility of colorectal adenomas.

In our study, increasing age was one of the risk factors for colorectal adenomas in both sexes, which was consistent with other studies.[22,32,38] We think that after long-term exposure to the environmental related factors, it may cause the increased likelihood of formation of colorectal adenomas. Therefore, the older the person, the higher the risk for colorectal adenomas. As colorectal adenomas are at risk of progression to carcinoma, early detection of colorectal adenomas in people with advancing age is of special importance. As expected, once the age and sex distribution are taken into account in the multivariate analysis, the magnitude of the association with most factors appears to be attenuated. In fact, many factors lost significance in our study. That was why no other related factor for colorectal adenomas was detected in women in our study.

Limitation

This study has several limitations. First, because of a bias of sampling population, a hospital-based study could not be extrapolated to the general population. Second, only sigmoidoscopy, not colonoscopy, was performed. Thus, the preval ence of colorectal adenomas could be underestimated. Third, because we did not classify users of lipid-lowering drugs with normal blood lipid levels, the prevalence of hyperlipidemia could be underestimated. Fourth, because we did not quantify the amounts of smoking and alcohol, operational definitions of smoking and alcohol consumption could not be specified. Fifth, blood insulin level and/or insulin-like growth factor levels were not analysed, so we could not further make the hypothesised link between colorectal adenomas and cardiovascular disease. Finally, because of the inherent nature of this cross-sectional study, it precludes any proper assessment of the causality of reported associations.

Conclusion

These data add to the evidence that increasing age, hypertriglyceridemia and alcohol consumption are the risk factors for rectosigmoid adenomas in men. Increasing age is the only risk factor for rectosigmoid adenomas in women.

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