Original Article

Related factors for Rectosigmoid Hyperplastic Polyps: A Hospital-Based Study

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ABSTRACT

Objectives: Little evidence is available about the related factors for colorectal hyperplastic polyps in Taiwan. The aim of this study was to explore the prevalence of rectosigmoid hyperplastic polyps and to determine the related factors.
Setting: Medical center in Taichung city, Taiwan
Design: Retrospective hospital-based, cross-sectional study.
Subjects: We analyzed the medical records of all subjects receiving periodic health examination at one medical center in Taichung city in Taiwan from 2001 to 2004. A total of 4413 subjects were enrolled in this study.
Intervention Main Outcome Measure: All subjects underwent a 60-cm flexible sigmoidoscopic examination and laboratory survey.
Main Outcome Measure: Prevalence of hyperplastic Polyps and related factors
Results: There were 2444 men (55.4%) and 1969 women (44.6%). The mean age was 49.3 years (standard deviation 12.3, range from 20 to 87). The overall prevalence of hyperplastic polyps was 5.5%, with higher prevalence in men than in women (6.9% Vs 3.7%, $p < 0.001$). After controlling for the other co-variates, multivariate logistic regression model showed that the related factors for hyperplastic polyps were increasing age (OR = 1.03, 95% CI = 1.02 - 1.05, $p < 0.001$), male gender (OR = 1.79, 95% CI = 1.31 - 2.46, $p < 0.001$), generalized obesity (OR = 1.59, 95% CI = 1.10 - 2.28, $p = 0.012$), and smoking (OR = 1.40, 95% CI = 1.02 - 1.93, $p = 0.038$).
Conclusions: These findings reveal that increasing age, male gender, generalized obesity and smoking are the related factors for rectosigmoid hyperplastic polyps.

KEY WORDS: hyperplastic polyp, obesity, rectosigmoid, smoking

INTRODUCTION

In 2006, cancer was the first leading cause of death in Taiwan[1]. However, colorectal cancer ranked as the third leading cause of cancer death for people in Taiwan and accounted for approximately 4284 deaths in 2006. Most colorectal cancers are currently thought to arise from pre-existing polyps conventionally called adenomas[2]. The hypothesis of colorectal adenoma-carcinoma sequence is now widely established[3-5].

On the other hand, another type of colorectal polyp known as hyperplastic polyp has a type of cellular proliferation different from that of an adenoma[6,7]. Unlike adenoma, It has been traditionally believed as a benign non-neoplastic lesion[2,8]. That is, hyperplastic polyps are generally thought to lack malignant potential. Therefore, patients with hyperplastic polyps are not at increased risk of colorectal cancer[2]. It is not necessary to perform surveillance colonoscopy in patients with hyperplastic polyps. Recently, several studies and case reports have identified that some hyperplastic polyps are not always harmless, and even have neoplastic evolution[2,8-11]. Now, there is marked evidence that hyperplastic polyps may play a role as the precursor of colorectal cancers with DNA methylation and deficient DNA mismatch repair[2]. As the literature shows, the risk factors for neoplastic evolution of hyperplastic polyps include multiplicity, large size, right-sided polyps, and found in association with a family history of carcinoma[8,10,12]. Although little is known about the etiology of the hyperplastic polyps, numerous epidemiological studies have demonstrated that several factors including serum insulin levels, dietary factors, alcohol consumption, cigarette smoking, use of aspirin and other non-steroidal anti-inflammatory drugs were related to colorectal hyperplastic polyps[9,13-18].

According to the above reviews, colorectal hyperplastic polyps should be clinically thought of as a unique entity. Thus, it may not be correct to

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do nothing about hyperplastic polyps. Therefore, we hypothesize a link between the neoplastic evolution of hyperplastic polyps and the risk factors. That is, interplayed by the detrimental effect of the risk factors, patients with colorectal hyperplastic polyps may have a more complex neoplastic evolution under certain circumstances.

To the best of our knowledge, there is little prospective evidence of colorectal hyperplastic polyps in Taiwan. As it concerns public health, it will be necessary to identify the risk factors for hyperplastic polyps that are especially prone to initiate tumor genesis. If more epidemiological studies can be undertaken, effective screening of individuals at increased risk for neoplastic evolution of hyperplastic polyps can be advocated. Therefore, the purpose of this present study is to address the following objectives: (a) what is the prevalence of rectosigmoid hyperplastic polyps in Taiwan? and (b) what are the related factors for rectosigmoid hyperplastic polyps?

MATERIALS AND METHODS

Study population

This was a retrospective hospital-based, cross-sectional study. We analyzed the medical records of all subjects undergoing self-referred health examination at one medical center located at Taichung city in Taiwan from 2001 to 2004. The institutional review board of this medical center approved this study. Subjects with previous malignant diseases were excluded from the study. 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 currently smoked were classified as smokers. The others were defined as non-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 calculated as follows: weight (kg) ÷ height $(m)^2$. Waist circumference (WC) was measured as the minimum circumference with the tape positioned between xyphoid process and the umbilicus at the end of a normal expiration[19]. Venous blood samples were obtained in the morning after a 12-hour overnight fasting. A number of biochemical markers, such as total cholesterol, triglyceride, low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), fasting glucose and uric acid were measured by a biochemical autoanalyser (Hitachi 736-15, Tokyo, Japan) at the Department of Clinical Laboratory of this medical center. Hepatitis B surface antigen was detected by ELISA test (Enzygnost, Dade Behring Marburg GmbH, Marburg, Germany). Antibody to hepatitis C virus was detected by EIA test (Abbott HCV EIA, third generation, Abbott Laboratories, Abbott Park, IL).

Diagnostic criteria

Generalized obesity was defined as BMI ≥ 27(kg/m^2)[20-22]. Abdominal obesity was defined as WC ≥ 90 cm for men and ≥ 80 cm for women, respectively with adoption of the Asian criteria[20-22]. Hypercholesterolemia was defined as fasting total cholesterol level ≥ 5.2 mmol/l[23]. Hypertriglyceridemia was defined as fasting triglyceride level ≥ 1.7 mmol/l[24]. High level of LDL was defined as fasting LDL ≥ 3.4 mmol/l[24]. Low level of HDL was defined as fasting HDL < 1.03 mmol/l for men and < 1.3 mmol/l for women, respectively[24]. Diabetes mellitus was defined as fasting plasma glucose level ≥ 6.9 mmol/l or people on drug treatment of elevated glucose[25]. Subjects were considered to have hypertension if the average of both arm readings exceeded 140 mmHg systolic and / or 90 mmHg diastolic or people on antihypertensive drug treatment[26]. Hyperuricemia was defined as serum uric acid level ≥ 420 μmol/l for men and ≥ 390 μmol/l for women, respectively[27]. Metabolic syndrome was defined as involving three or more of the following conditions proposed by American Heart Association / National Heart, Lung, and Blood Institute in 2005[24]. High blood pressure was defined as blood pressure ≥ 130/85 mmHg or people on antihypertensive drug treatment. Hyperglycemia was defined as fasting plasma glucose level ≥ 5.6 mmol/l or people on drug treatment of elevated glucose. Hypertriglyceridemia was defined as fasting triglyceride level ≥ 1.7 mmol/l. Low level of HDL was defined as fasting HDL < 1.03 mmol/l for men and < 1.3 mmol/l for women, respectively. Abdominal obesity was defined as WC ≥ 90 cm for men or ≥ 80 cm for women, with adoption of the Asian criteria for abdominal obesity.

Statistical analysis

We used a SPSS package (Taiwan Version 10.0, Sinter Information Corp, Taipei, Taiwan). The t test was performed for continuous variables and the chi-squared test was performed for qualitative variables. The relative risks were estimated by adjusted odds ratio (OR) and 95% confidence interval (CI) using a multivariate logistic regression model. A p-value of 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 (age range from 20 to 87). Among 4413 subjects undergoing 60-cm flexible sigmoidoscopy, 3759 subjects (85.2%)

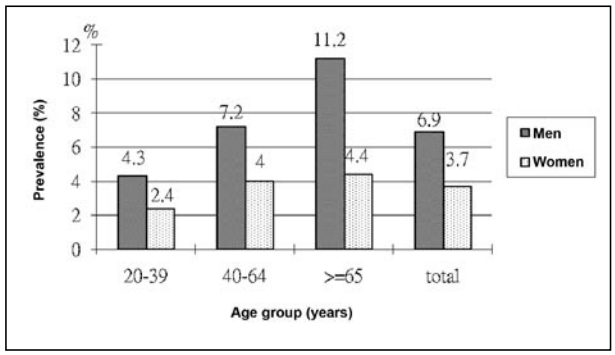

Fig. 1: Prevalence of hyperplastic polyps in both genders and three age groups (prevalence higher in men than in women, $p < 0.001$)

had normal finding, and the remaining 654 subjects (14.8%) had at least one rectosigmoid polyp. Among 654 subjects with polyps, 505 subjects underwent a polypectomy or biopsy. The histological findings revealed that 225 subjects had adenomas only, 214 subjects had hyperplastic polyps only, 29 subjects with mixed adenomas and hyperplastic polyps, six subjects with adenocarcinomas, and 31 subjects with inflammatory polyps or other lesions. There were 149 subjects with polyps found on examination but no polypectomy or biopsy was taken (Table 1). We compared the clinical and the demographic features between people with isolated hyperplastic polyps only and those with mixed adenomas and hyperplastic polyps. There were no related factors that distinguished the two groups. Finally, 243 subjects with hyperplastic polyps (including 214 subjects with hyperplastic polyps only, and 29 subjects with mixed adenomas and hyperplastic polyps) and 3759 normal subjects were included for further analysis.

Fig. 1, shows the prevalence of hyperplastic polyps in both gender and three age groups. The overall prevalence of hyperplastic polyps was 5.5% (243 / 4413). The prevalence was significantly higher in men than in women (6.9% Vs 3.7%, $p < 0.001$). Men also had higher prevalence than women did among the same age groups ($p = 0.016$, $p < 0.001$ and $p = 0.011$, respectively). The prevalence also increased with age in men and in women ($p < 0.001$ and $p < 0.001$, respectively).

Comparison of related factors between subjects with normal findings and with hyperplastic polyps was done using univariate analysis

Table 1: Basic characteristics of the study population

Variables	Men n (%)	Women n (%)	Total n (%)
Age (years) (mean±SD)	48.9 ± 11.9	49.8 ± 12.7	49.3 ± 12.3
Age group (years)			
20 - 39	539 (22.1)	418 (21.2)	957 (21.6)
40 - 64	1636 (66.9)	1279 (65.0)	2915 (66.1)
≥ 65	269 (11.0)	272 (13.8)	541 (12.3)
Histological findings			
Normal	1997 (81.7)	1762 (89.5)	3759 (85.2)
Adenoma	154 (6.3)	71 (3.6)	225 (5.1)
Hyperplastic polyp	147 (6.0)	67 (3.4)	214 (4.8)
Mixed adenoma and hyperplastic polyp	23 (0.9)	6 (0.3)	29 (0.7)
Adenocarcinoma	5 (0.2)	1 (0.1)	6 (0.1)
Inflammatory polyp or other lesion	19 (0.8)	12 (0.6)	31 (0.7)
Polyp without polypectomy or biopsy	99 (4.1)	50 (2.5)	149 (3.4)

Table 2: Related factors for hyperplastic polyps by univariate analysis

Variables	Normal n = 3759 (%)	Hyperplastic polyps n = 243 (%)	p-value
Age (years) (mean ± SD)	48.6 ±12.2	53.2 ± 11.3	< 0.001
Gender			
Men	1997 (53.1)	170 (70.0)	< 0.001
Women	1762 (46.9)	73 (30.0)	
Generalized obesity			
No	3112(82.8)	177(72.8)	< 0.001
Yes	647(17.2)	66(27.2)	
Abdominal obesity			
No	2125(56.5)	118(48.6)	0.015
Yes	1634(43.5)	125(51.4)	
Diabetes mellitus			
No	3379 (89.9)	204 (84.0)	0.003
Yes	380 (10.1)	39 (16.0)	
Hypertension			
No	2839 (75.5)	152 (62.6)	< 0.001
Yes	920 (24.5)	91 (37.4)	
Hypercholesterolemia			
No	1974 (52.5)	123 (50.6)	0.566
Yes	1785 (47.5)	120 (49.4)	
Hypertriglyceridemia			
No	2984 (79.4)	180 (74.1)	0.049
Yes	775 (20.6)	63 (25.9)	
High level of LDL			
No	2164 (57.6)	133 (54.7)	0.386
Yes	1595 (42.4)	110 (45.3)	
Low level of HDL			
No	2001 (53.2)	113 (46.5)	0.042
Yes	1758 (46.8)	130 (53.5)	
Metabolic syndrome			
No	2583 (68.7)	136 (56.0)	< 0.001
Yes	1176 (31.3)	107 (44.0)	
Hyperuricemia			
No	2638 (70.2)	176 (72.4)	0.457
Yes	1121 (29.8)	67 (27.6)	
HBsAg positive			
No	3208 (85.3)	198 (81.5)	0.101
Yes	551 (14.7)	45 (18.5)	
HCV-Ab positive			
No	3591 (95.5)	228 (93.8)	0.218
Yes	168 (4.5)	15 (6.2)	
Smoke use			
Non-Smoker	2856 (76.0)	160 (65.8)	< 0.001
Smoker	903 (24.0)	83 (34.2)	
Alcohol use			
Non-drinker	3383 (90.0)	203 (83.5)	0.001
habitual drinker	376 (10.0)	40 (16.5)	

Using the chi-square test, subjects with hyperplastic polyps were compared with those with normal findings. The statistically related factors for hyperplastic polyps were gender ($p < 0.001$), generalized obesity ($p < 0.001$), abdominal obesity ($p = 0.015$), diabetes mellitus ($p = 0.003$), hypertension ($p < 0.001$), hypertriglyceridemia ($p = 0.049$), low level of HDL ($p = 0.042$), metabolic syndrome ($p < 0.001$), smoking ($p < 0.001$), and alcohol consumption ($p = 0.001$). There was also statistical difference in the mean age by the t test ($p < 0.001$) (Table 2).

Related factors for hyperplastic polyps by multivariate logistic regression

Only the statistically related factors identified in univariate analysis were further analyzed. After controlling for the other co-variates, multivariate logistic regression model exhibited that the related factors for hyperplastic polyps were increasing age (OR = 1.03, 95% CI = 1.02 - 1.05, $p < 0.001$), male gender (OR = 1.79, 95% CI = 1.31 - 2.46, $p < 0.001$), generalized obesity (OR = 1.59, 95% CI = 1.10 - 2.28, $p = 0.012$), and smoking (OR= 1.40, 95% CI = 1.02 - 1.93, $p = 0.038$) (Table 3).

Table 3: Odds ratio of related factors for hyperplastic polyps

Variables	OR	95% CI
Age (every one year)	1.03	1.02 -1.05**
Gender (men Vs women)	1.79	1.31 -2.46**
Generalized obesity (yes Vs no)	1.59	1.10 - 2.28*
Abdominal obesity (yes Vs no)	0.92	0.64 - 1.32
Diabetes mellitus (yes Vs no)	1.05	0.71 - 1.55
Hypertension (yes Vs no)	1.23	0.90 - 1.69
Hypertriglyceridemia (yes Vs no)	0.89	0.63 - 1.26
Low level of HDL (yes Vs no)	1.20	0.89 - 1.62
Metabolic syndrome (yes Vs no)	1.10	0.71 - 1.68
Smoke use (yes Vs no)	1.40	1.02 - 1.93*
Alcohol use (yes Vs no)	1.43	0.97 - 2.11

*$p < 0.05$, ** $p < 0.001$, OR = odds ratio, CI = confidence intervals

DISCUSSION

To date, there is little evidence about the information of colorectal hyperplastic polyps in Taiwan. That is why we performed this study. In autopsy studies, the prevalence of colorectal hyperplastic polyps is 4.9 - 13%[28,29]. The prevalence is 5.5% in our study. The prevalence might be underestimated because there were 149 subjects with polyps found on examination where no biopsy was taken. As commented by the gastroenterologists at this medical center, these polyps were usually too small and so it was not necessary to perform a biopsy. However, more frequent colonoscopic surveillance was suggested. We did not enroll these subjects, so as to avoid the effect of confounding factors on the analysis. However, as suggested by the literature[30,31], all polyps should be removed or biopsied to determine their type during sigmoidoscopy or colonoscopy because the high prevalence of adenomas among small polyps is noted.

A retrospective case-control study in Japan and a necropsy study in New Zealand[18,32], showed that age is a related factor for hyperplastic polyps. In Vatn's study[33], the prevalence of hyperplastic polyps increases with age in men, but not in women. In our study, the prevalence increases with age in both genders. Multivariate logistic regression model also showed that increasing age is one of the related factors for hyperplastic polyps. We think that after a long duration of exposure to numerous environmental factors and potential genetic factors, the likelihood of hyperplastic polyp formation increases. That is, the older the people, the higher the risk for hyperplastic polyps.

After controlling for the other co-variates, our study showed that BMI ≥ 27 is also related to hyperplastic polyps. To the best of our knowledge, only two studies have revealed that body mass index is positively associated with hyperplastic polyps[14,32]. Prior studies have disclosed that increased BMI is associated with the risk for colorectal adenomas and cancers[33-35]. The above results strongly support the hypothesis that generalized obesity is a risk factor for colorectal hyperplastic polyps, adenomas, and cancers. As suggested by Yamaji[34], body weight reduction can be used to decrease this risk.

In our study, smoking is one of the related factors for hyperplastic polyps, and this finding is compatible with previous studies[9,13-18]. Prior studies have disclosed that cigarette smoking is associated with increased risk for colorectal adenomas and cancers[15,36,37]. These findings strongly support the concept that the adverse effect of smoking may play an important role in the formation of colorectal hyperplastic polyps, adenomas and cancers. As suggested by Shrubsole[15], quitting smoking may substantially reduce this risk.

In Kim study[38], metabolic syndrome was an important risk factor for colorectal adenoma. In our study, although metabolic syndrome was related to hyperplastic polyps in the chi-square test, we could not find this result in the multivariate logistic regression model. Similarly, several other factors were not informative. We also could not find an association between abdominal obesity, diabetes mellitus, hypertriglyceridemia or alcohol consumption and hyperplastic polyps. In contrast, these factors were found to be related to colorectal adenomas and cancers in prior studies[39-42]. Thus, we think that colorectal hyperplastic polyps, adenomas and cancers do not completely share common risk factors.

Growing evidence of neoplastic evolution of hyperplastic polyps is elicited by morphological and molecular studies. Recent new morphological data have recognized the model of hyperplastic polyp-

serrated adenoma-adenocarcinoma pathway[43,44], that is apparently different from the classic adenoma-to-carcinoma sequence[3,4,5].

Recent strong molecular evidence has also shown that extensive DNA methylation, deficient DNA mismatch repair, and microsatellite instability may characterize hyperplastic polyps in the pathogenesis of neoplastic evolution[2,45]. Under the molecular level, the progression through sequential steps of the pathway is driven. At first, neoplastic changes may begin in a hyperplastic polyp, then progressing to atypical hyperplastic polyp (known as sessile serrated adenoma), further to dysplastic serrated adenoma, and ultimately to serrated carcinoma[46,47]. In the interest of public health, early detection of morphological and molecular changes of hyperplastic polyps which are more likely to have the potential of neoplastic evolution is needed. Thus, colorectal cancer can be prevented.

LIMITATION

There are several limitations in this study. The first, using flexible sigmoidoscopy rather than a full colonoscopy precluded identification of hyperplastic, adenomatous polyps, and serrated adenomas in the right colon, which are also more likely to be detected in the right colon. The prevalence of hyperplastic polyps may be underestimated. The second, although the literature now recognizes that some previously termed hyperplastic polyps do carry malignant potential, we cannot recheck the pathologic slides to determine whether any of the hyperplastic polyps removed during the examination had histologic features of serrated adenomas. The third, because this study was retrospective (review of medical records), history of first-degree relatives with colorectal neoplasia and polyps, dietary factors, use of aspirin and other non-steroidal anti-inflammatory drugs, could not be included in details due to incomplete documentation. The fourth, there is a bias of sampling population. Since the study participants were all from one hospital in Taiwan, there is limited generalizability of the results. The fifth, because of inherent limitations to a cross-sectional design, a causal-effect relationship between an exposure of interest and an outcome cannot be established. The sixth, because no pathology reports were available in 149 subjects with polyps, they could not be categorized and had to be excluded. Finally, only 243 subjects with hyperplastic polyps (including 214 subjects with hyperplastic polyps only, and 29 subjects with mixed adenomas and hyperplastic polyps) and 3759 normal subjects were included for further analysis.

CONCLUSION

Based on these preliminary data, we find that increasing age, male gender, generalized obesity and smoking are risk factors for rectosigmoid hyperplastic polyps in Taiwan. Whereas the clinical significance of hyperplastic polyps remains inconclusive and a consensus for regular colonoscopic surveillance is not available, lifestyle modification including smoking cessation and body weight reduction can still be suggested by clinicians to reduce the risk of hyperplastic polyps. Further detailed studies are needed to confirm these conclusions.

Conflict of interest: The authors report no conflicts of interest.

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