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Usefulness of an Original Metabolic Syndrome Score in Large Intestinal Cancer Screening

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Background and Aims： Recently, it was reported that metabolic syndrome (MS) is related to the large intestinal neoplasm. Therefore, we studied the relationship between MS and the colonic neoplasm using our original scoring system, *i.e.,* the Gastrointestinal Metabolic Syndrome Score (GIMS). **Patients and Methods：** The participants were medical examinees who underwent total colonoscopy (CS) from January to December 2006. Regarding body mass index, blood pressure, triglyceride, high density lipoprotein cholesterol and fasting blood sugar results in each case, we referred to the criteria of MS and scored them from 0-2 (0：normal range, 1：aberration minor, 2：aberration). We added up the values to calculate the GIMS. We defined neoplastic lesions as adenoma or adenocarcinoma. When we found a neoplastic lesion in CS, we examined the case using the GIMS. **Results：** The average of GIMS in the neoplastic cases was significantly higher than that of the non-neoplastic cases ($p < 0.05$). Considering the higher rate in the efficiency and in the therapeutic patients, we decided that the positive standard was two or more scores in GIMS. **Conclusions：** GIMS is easily calculated and can be used to support diagnosis of large intestinal neoplasm in the future. (Kitakanto Med J 2008；58：183～187)

Key Words： metabolic syndrome, large intestinal neoplasm, screening

Introduction

Recently, the relationship between metabolic syndrome (MS) and large intestinal neoplasms has been reported. In Japan, specific health examinations will start in April 2008. The examinations will be performed to check whether the disease is specifically MS. Thus, we defined an original scoring method (Gastrointestinal Metabolic Syndrome Score；GIMS) which correlates MS and large intestinal neoplastic lesions.

Herein, we report on the relationship between MS and large intestinal neoplasms in cases subjected to colonoscopy in health examinations.

Patients and Methods

The participants were patients who underwent a health examination in this university-affiliated institution from January to December 2006 and presented no digestive symptoms. Fecal occult blood tests (FOB) and total colonoscopy (CS) was performed in all cases. One hundred (93 male, 7 female) cases in the FOB-negative group and 72 (46 male, 26 female) cases in the FOB-positive group were examined in our study (Table 1). We defined carcinoma and adenoma as neoplastic lesions；however hyperplastic polyp and anal polyp were defined as non-neoplastic lesions. Furthermore, the neoplastic cases were defined to point out the neoplastic lesions in the colonoscopic examination and non-neoplastic cases were defined as non-neoplastic lesions. The endoscopic view was diagnosed by pit pattern examination[1] or biopsy specimen. We distinguished the therapeutic cases and non-therapeutic cases according to whether any therapy was performed or not.

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Table 1. Details of patients in this study

	FOB			
	Positive		Negative	
	Male	Female	Male	Female
Number	46	26	93	7
Mean age (Range)	54.9 (36-79)	56.4 (38-73)	56.9 (44-80)	56.6 (50-61)

FOB : fecal occult blood test

Among the test values at the time of health examination, a score from 0 to 2 corresponding to three phases was assigned to each category including body mass index (BMI), blood pressure (BP), triglyceride (TG), high density lipoprotein cholesterol (HDL-C), fasting blood sugar (FBS). The reference values of our institutional tests included in GIMS are defined in Table 2. The GIMS was calculated as follows : the test value of each item (BMI, BP, TG, HDL-C, FBS) was assigned 0, 1, or 2 points in three phases as shown in Table 2 and the total score for the five items was determined. In cases in which the disease was being treated presently, we added one point to each score. FOB tests based in the two days method were performed using the kit OC-Hemodia® Auto III (Eiken Chemical Co., Ltd., Tokyo, Japan) assuming the principle of latex agglutination reaction. FOB values less than 100 ng/ml were considered normal. In this study, we examined the negative cases which were defined as those with values within a negative range on both days. The study was performed based on our ethical rules and the Helsinki Declaration of 2000.[2]

Statistical analysis was performed using the Mann-Whitney U-test and χ^2 test. Values of $p<0.05$ were considered significant.

Results

Comparison of scores among each examination item by presence of neoplasms

The Mann-Whitney U-test did not indicate any statistical significant difference in the average score of examination of each item between the neoplastic cases and non-neoplastic cases. Considering these results, we added up the five items (BMI, BP, TG, HDL-C and FBS) included in the definition of conventional diagnostic criteria of MS (NECP-ATP III) to calculate the scores in this study. In cases in which the disease was currently being treated at present, we added one point to each score.

Relations between GIMS and presence of neoplasm (Table 3)

The positive rates of neoplastic lesions were significantly higher in cases with a score of more than 1 and cases with a score of more than 2 in GIMS-positive criterion using the χ^2 test. In the FOB-negative group, the presence of neoplasms was significantly

Table 3. Relations between GIMS and presence of neoplasms

GIMS	FOB			
	Positive		Negative	
	neo(+)	neo(−)	neo(+)	neo(−)
0	7	18	4	23
1	10	10	16	15
2	7	5	12	8
>3	7	8	14	8

FOB : fecal occult blood test, neo : neoplasm

Table 2. GIMS calculation method

Item	Value	Score
BMI	<25.0	0
	≧25.0, <30.0	1
	≧30.0	2
BP (mmHg)	Sys <130 and Dia <85	0
	Sys ≧130, <160 and/or Dia ≧85, <100	1
	Sys ≧160 and/or Dia ≧100	2
Triglyceride (mg/dL)	<150	0
	≧150, <200	1
	≧200	2
HDL-C (mg/dL)	≧40.0	0
	≧35.0, <40.0	1
	<35.0	2
FBS (mg/dL)	<110	0
	≧110, <126	1
	≧126	2

GIMS is calculated by adding up each score of five items.
BMI : body mass index, BP : blood pressure,
Sys : systolic blood pressure, Dia : diastolic blood pressure,
HDL-C : high density lipoprotein cholesterol, FBS : fasting blood sugar

Table 4. Examination of positive criterion of GIMS

	FOB positive group (%)		FOB negative group (%)	
	More than 1	More than 2	More than 1	More than 2
Sensitivity	77.4	45.2	91.3	54.3
Specificity	43.9	68.3	31.5	70.4
False-positive rate	56.1	31.7	68.5	29.6
False-negative rate	22.6	54.8	8.7	45.7
Prevalence	43.1	43.1	46.0	46.0
Test-positive rate	65.3	37.5	79.0	41.0
Efficiency	58.3	58.3	59.0	63.0

Table 5. Rate of therapeutic cases (in FOB-positive group)

GIMS	Therapy (number)		Rate of therapeutic cases (%)
	+	−	
0	4	21	16.0
1	5	15	25.0
2	4*	7	36.4
>3	5**	11	31.3
Total	18	54	25.0

4* : 2 carcinomas involved in 4 cases
5** : 1 carcinoma involved in 5 cases

Table 6. Rate of therapeutic cases (in FOB-negative group)

GIMS	Therapy (number)		Rate of therapeutic cases (%)
	+	−	
0	1	26	3.7
1	2	30	6.3
2	3	17	15.0
>3	4	17	19.0
Total	10	90	10.0

higher in cases with a GIMS score of 2 or more than in other cases using the χ^2 test.

Examination of sensibility, specificity and efficacy (Table 4)

Sensibility, specificity, false-positive rate, false-negative coefficient, and efficacy were calculated from each result and we tried to examine positive basis of GIMS. The efficacy of more than 2 criterion was 63.0% and higher than that of more than 1 criterion.In addition, the specificity and positive rates for more than 2 criterion were superior to those for more than 1 criterion.

Examination of GIMS and the cases which required therapy (Table 5, Table 6)

Ten patients in the FOB-negative group were judged in need of treatment and received additional therapy. As for the results of GIMS, 1 case was GIMS 0, 2 cases were GIMS 1, 3 cases were GIMS 2 and 4 cases were GIMS 3. Endoscopic therapy (endoscopic mucosal resection (EMR) in 4 cases, polypectomy in 6) was performed and the pathologic diagnosis was tubular adenoma in all cases. In the FOB-positive group, 18 cases underwent therapy (an operation in 1 case, EMR in 13, polypectomy in 4). Three cases among these were diagnosed with cancer (early cancer in 2, advanced cancer in 1). In cases with more than 2 GIMS criterion, the ratio of additional required therapy tended to be higher than in cases with less than 1 GIMS criterion ($p=0.10$).

Discussion

According to the trends of health in Japan in 2005, large bowel cancer was the leading cause of death due to carcinoma among women and fourth among men. It is thought that large bowel cancer is influenced by environmental factors such as dietary habits and has increased due to the recent Westernization of eating habits. According to conventional reports, the intake of vegetables, fruit, and dietary fiber was thought to be a prophylactic factor. However, there are some negative reports on this theory and these reports are now under investigation[3−5] on the contrary, recent epidemiologic studies have revealed that physical activity may be considered a prophylactic factor in the carcinogenesis of large bowel cancer.[5−7] Furthermore, obesity was determined to be a convincing risk factor in a World Health Organization (WHO) report in 2003.

It is thought that insulin resistance contributes significantly to large bowel carcinogenesis associated with obesity and physical activity.[8,9] It has been reported that large bowel cancer and colorectal adenomas are related to MS, but there are still few reports.[10−14]

On the other hand, large bowel cancer tends to be misdiagnosed due to so-called FOB false-negative cases in detection of large intestinal neoplasmas, and when we perform follow-up the FOB is negative. Therefore, we developed an original metabolic syndrome scoring system from constituent factors of MS and tried to examine the connection between large bowel neoplas-

mas and MS for non-symptomatic, particularly FOB-negative patients. The items in the GIMS calculation are set it in accordance with the criteria of MS. The patients' smoking histories were examined but no significant difference was shown between the neoplastic cases and non-neoplastic cases.So we added up five items (BMI, BP, TG, HDL-C and FBS) included in the definition of conventional diagnostic criteria of MS (NECP-ATP Ⅲ) to calculate the scores in this study. It has been reported that MS patients in foreign countries and Japan have a high risk for the incidence of large bowel neoplasmas due to insulin resistance. In this study, we were not able to review the presence of insulin resistance, but we performed blood glucose endurance tests in individual treatment medical examinations. However, no significant difference in blood glucose levels was shown among groups with a presence of large intestinal neoplasmas by the blood glucose endurance tests. In addition, regarding the other items, we could not point out the intervention of specific items because there were no significant differences between neoplastic cases and non-neoplastic cases. Therefore, as various factors can leave examination,[15] future examination will be required.

Furthermore, we examined whether the positive basis of GIMS was a score of more than 1 or more than 2. Considering the higher rate of the therapeutic cases and efficacy, we determined the positive basis of GIMS to more than 2. When we set it as more than 3, the sensibility and efficacy were low, and the false-negative rate was high. Thus, we determined the positive basis of GIMS to be more than 2 levels.

The false-negative rate in the two-day FOB method was reported to be 25.0% by Fujita[16] and 36.4% by Nakama.[17] Among the patients in this study, 46 out of 100 cases (46.0%) were regarded as false-negative cases. Among these 46 patients, 25 were GIMS-positive cases and 21 were GIMS-negative cases. Therefore, by taking account of GIMS, we can reduce the rate of false-negative cases to 21/100 (21.0%). However, there were no cases of cancer in the FOB-negative group in this study, and thus we did not sufficiently review the usefulness in cancer cases. In light of this, we should evaluate the FOB-negative cases without digestive symptoms through further investigation in local medical exams and outpatient tests.

In addition, 10 patients who underwent endoscopic treatment as part of the second round of this medical examination had neoplastic lesions larger than 5mm. The lesions were often presented in the oral site (11/15, 73.3%) of large intestine and the forms were often presented in II a type (10/15, 66.7%). These findings are supported by the fact that FOB-negative cases often have so-called flat or collapsed- type tumors present in the oral side of the colon. When we performed the CS, we decided to investigate the so-called flat or collapsed-type tumors in FOB-negative and GIMS-positive patients more carefully. The GIMS measurement items which we have set in this study are generally used in medical examinations and can be calculated easily.

Since 2007, abdominal circumference as well as BMI has been determined in medical examinations. However, the use of abdominal circumference as a standard is now under discussion. Thus, we used BMI in this study. In the future, as we examine GIMS, we may be able to find a more relevant measurement. This is likely to be an important issue in future medical examinations.

There are some problems with using GIMS in medical examinations, but it is easily calculated from the data as described above. We have herein reported on the utility of GIMS in supplementing diagnosis of FOB-false negative cases.

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