SPANDIDOS PUBLICATIONS

MOLECULAR AND CLINICAL ONCOLOGY 2: 124-128, 2014

Predicting the occurrence of cancer-associated colorectal polyp using a metabolic risk score

NUENGRUETAI ORANNAPALAI[1], WORAPAT ATTAWETTAYANON[1], SAMORNMAS KANNGERN[2,3], TEERANUT BOONPIPATTANAPONG[1,3] and SURASAK SANGKHATHAT[1,3]

[1]Department of Surgery; [2]Anatomical Pathology Unit, Department of Pathology; [3]Tumor Biology Research Unit, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla 90110, Thailand

Received July 26, 2013; Accepted October 14, 2013

DOI: 10.3892/mco.2013.204

Abstract. This study was conducted with the aim of developing a metabolic risk score to help identify patients who are likely to have a cancer-associated polyp (CAP) on colonoscopy, based on a metabolic syndrome-related clinical profile. The clinical history and anthropometric and metabolic profiles of patients who came for a screening colonoscopy at our institute between June, 2010 and December, 2012 were prospectively collected. The data were analyzed for their association with the occurrence of CAP. Subsequently, six parameters were selected in order to construct a metabolic risk score that correlated with the presence of CAP. A total of 286 subjects (132 males and 154 females), with an age range of 19-85 years, were included in this study. The colonoscopy detected polyps in 56 cases (19.6%). Anthropometric parameters that were significantly associated with CAP included a body mass index (BMI) of >23.4 kg/m^2 and a waist circumference of >32 inches in females. Laboratory profiles that were significantly associated with CAP were fasting blood sugar (FBS) >110 mg%, hemoglobin A1C (HbA1C) >7%, aspartate transaminase (SGOT) >40 IU/l, alanine transaminase (SGPT) >50 IU/l and uric acid >7 mg%. When a metabolic risk score was constructed, it was observed that moderate (2-3) and high risk (4-6) was significantly associated with CAP [odds ratio (OR)=4.9, 95% confidence interval (CI): 2.0-12.0 and OR=13.7, 95% CI: 4.4-43.0, respectively]. The association between the risk score and CAP was stronger in the subgroup of patients aged <65 years, in whom the moderate and high metabolic risk groups exhibited ORs of 5.6 (95% CI: 1.8-17.9) and 39.0 (95% CI: 8.2-186.6), respectively. In conclusion, this study demonstrated that it is possible to use a metabolic profile to construct a reliable scoring method to identify patients at higher risk of having CAP who should be fast-tracked for a colonoscopy.

Correspondence to: Dr Surasak Sangkhathat, Department of Surgery, Faculty of Medicine, Prince of Songkla University, 15 Karnchanavanich Road, Hat Yai, Songkhla 90110, Thailand
E-mail: surasak.sa@psu.ac.th

Key words: metabolic risk score, colonic adenoma

Introduction

Metabolic syndrome is a global health problem of increasing prevalence in Western, as well as Asian, countries (1,2). In addition to its known association with cardiovascular diseases (3), recent evidence has suggested an association between the metabolic syndrome and various types of cancer, including colorectal cancer (CRC) (4,5).

Accumulating evidence suggested that visceral obesity, insulin resistance and systemic inflammation may be implicated in the pathophysiological link between metabolic syndrome and CRC development (6). Cytokines produced by adipose tissue may promote inflammation and lead to subsequent adenomatous changes in the colonic epithelium (7). Various studies demonstrated an association between individual components of the metabolic syndrome and colorectal adenoma, a pre-cancerous lesion of CRC (8,9). In this study, we evaluated the association between clinical profiles associated with the metabolic syndrome and the occurrence of colorectal adenoma in Thai patients. Furthermore, a metabolic risk scoring system was constructed, based on clinical and laboratory items that exhibited a significant association with this disease.

Patients and methods

Patient history. Patients aged >15 years who underwent a colonoscopy at the NKC Institute of Gastroenterology and Hepatology, Songklanagarind Hospital, between June, 2010 and December, 2012, were enrolled in this study. Cases with known colonic pathology, either colonic polyp or CRC, were excluded. Medical history regarding a previous diagnosis of hypertension, dyslipidemia, diabetes mellitus or cancer in a family member was obtained through a structured interview. Lifestyle history included tobacco smoking, alcohol consumption, vegetable consumption and exercise. Anthropometric measurements were performed on the date of the endoscopy. Blood pressure was measured twice with a 10-min interval, using a manual sphygmomanometer.

Laboratory profiles. Laboratory profiles, including fasting blood sugar (FBS), hemoglobin A1C (HbA1C), triglyceride, low- and high-density lipoprotein, aspartate

Table I. Association between metabolic syndrome-related laboratory parameters and CAP.

Parameters	Cases (n=286)	CAP		P-value
		Absent (%)	Present (%)	
Total	286	230 (80.4)	56 (19.6)	
Age (years)				<0.01
<65	241	203 (84.2)	38 (15.8)	
>65	45	27 (60.0)	18 (40.0)	
Gender				0.21
Male	132	102 (77.3)	30 (22.7)	
Female	154	128 (83.1)	26 (16.9)	
History of hypertension				<0.01
No	226	194 (85.8)	32 (14.2)	
Yes	60	36 (60.0)	24 (40.0)	
History of dyslipidemia				<0.01
No	255	213 (83.5)	42 (16.5)	
Yes	31	17 (54.8)	14 (45.1)	
History of DM				<0.01
No	265	218 (82.3)	47 (17.7)	
Yes	21	12 (57.1)	9 (42.9)	
Hypertension				0.02
No	231	192 (83.1)	39 (16.9)	
Yes	55	38 (69.1)	17 (30.9)	
BMI (kg/m^2)				0.02
≤23.4	148	127 (85.8)	21 (14.2)	
>23.4	138	103 (74.6)	35 (25.4)	
Waist circumference (in.)				
Male				0.82
≤35	116	90 (77.6)	26 (22.4)	
>35	16	12 (75.0)	4 (25.0)	
Female				0.02
≤32	122	106 (86.9)	16 (13.1)	
>32	32	22 (68.6)	10 (31.3)	
Hip circumference (in.)				
Male				0.56
≤37	102	80 (78.4)	22 (21.6)	
>37	30	22 (73.3)	8 (26.7)	
Female				0.07
≤37	111	96 (86.5)	15 (13.5)	
>37	43	32 (74.4)	11 (25.6)	

CAP, cancer-associated polyp; DM, diabetes mellitus; BMI, body mass index; in., inches.

transaminase (SGOT), alanine transaminase (SGPT) and uric acid levels were recorded on the morning of the endoscopy. All colonoscopies were performed by or under the close supervision of a colorectal surgeon. The endoscopist was blinded to the metabolic history and laboratory results. Once a polyp was detected, a biopsy sample was collected for histopathological examination. A polyp was characterized as a cancer-associated polyp (CAP) when it was found to be an adenomatous polyp including elements of tubular, villous, tubulovillous or serrated adenoma. Other types of polyp or carcinoma were excluded from the association analysis.

Statistical analysis. Continuous data are presented as the means unless stated otherwise. Non-continuous data are presented as numbers with percentage values. The possible associations between demographic or metabolic parameters and CAP were analyzed using the Chi-square test and univariate logistic regression analysis. P<0.05 was considered to indicate a statistically significant difference.

Table II. Association between metabolic syndrome-related laboratory parameters and CAP.

Parameter	Cases (n=286)	CAP		P-value
		Absent (%)	Present (%)	
FBS (mg%)				<0.01
≤110	263	218 (82.9)	45 (17.1)	
>110	23	12 (52.2)	11 (47.8)	
HbA1C (%)				<0.01
≤7.0	274	224 (81.8)	50 (18.3)	
>7.0	12	6 (50.0)	6 (50.0)	
HDL (mg%)				0.44
≤34.9	19	14 (73.7)	5 (26.3)	
>34.9	267	216 (80.9)	51 (19.1)	
LDL (mg%)				0.241
≤160	164	128 (78.0)	36 (22.0)	
>160	122	102 (83.6)	20 (16.4)	
TG (mg%)				0.973
≤200	255	205 (80.4)	50 (19.6)	
>200	31	25 (80.7)	6 (19.3)	
SGOT (IU/l)				<0.01
≤40	262	216 (82.4)	46 (17.6)	
>40	24	14 (58.3)	10 (41.7)	
SGPT (IU/l)				<0.01
≤50	268	200 (82.6)	68 (17.9)	
>50	18	10 (55.6)	8 (44.4)	
Uric acid (mg%)				<0.01
≤7	213	180 (84.5)	33 (15.5)	
>7	73	50 (68.5)	23 (31.5)	

CAP, cancer-associated polyp; FBS, fasting blood sugar; HbA1C, hemoglobin A1C; HDL, high-density lipoprotein; LDL, low-density lipoprotein; TG, triglyceride; SGOT, aspartate transaminase; SGPT, alanine transaminase.

Results

Demographic data. A total of 289 subjects underwent a colonoscopy at our institute during the study period. Three cases of CRC were excluded, leaving a total of 286 subjects (132 males and 154 females) for association analysis. The mean age of the patients was 52 years, with 45 cases (16%) aged >65 years. The mean body mass index (BMI) of the patients was 23.4 kg/m^2 (range, 13.3-50 kg/m^2). The reasons for undergoing a colonoscopy included hematochezia (101 cases, 35%), abdominal pain (50 cases, 18%), changes in bowel habits (45 cases, 16%), asymptomatic (49 cases, 17%), constipation (31 cases, 10%) and other (10 cases, 3%). The overall polyp detection rate was 25% (72 out of the 286 cases). CAP was detected in 56 cases (19.6%). The incidence of CAP was not found to be associated with any symptoms that would lead the physician to recommend a colonoscopy (Table I).

Univariate and multivariate analysis of the association between metabolic profiles and CAP. On univariate analysis, a clinical history of chronic disease, including hypertension, diabetes mellitus and dyslipidemia was significantly associated with the occurrence of CAP (Table I). The anthropometric parameters that exhibited an association with CAP were high blood pressure and BMI >23.4 kg/m^2. In females, a high waist and hip circumference (>32 and >37 inches, respectively) were also significantly associated with CAP. None of the lifestyle history items were found to be associated with CAP.

The laboratory profiles that were associated with CAP included FBS, HbA1C, hepatic transaminases and uric acid levels (Table II). Notably, lipid profiles did not exhibit a significant correlation with the occurrence of polyps. The parameters that were found to be association with CAP are summarized along with their odds ratios (ORs) in Table III.

On multivariate analysis, three factors were found to be independently associated with CAP: age >60 years (OR=3.9, 95% CI: 2.0-7.4), FBS >110 mg% (OR=2.9; 95% CI: 1.1-7.4) and uric acid >7 mg% (OR=2.0; 95% CI: 1.0-3.9).

Construction and validation of metabolic scoring system. Six metabolic items were selected to construct a metabolic scoring system that may accurately predict the occurrence of CAP in patients scheduled for a colonoscopy, irrespective of their age and presenting symptoms. This metabolic risk

Table III. Parameters significantly associated with CAP.

Parameters	OR	95% CI
Age >65 years	3.30	1.67-6.50
History of hypertension	4.04	2.14-7.65
History of DM	3.48	1.39-8.73
History of dyslipidemia	4.18	1.91-9.12
BMI >23.4 kg/m^2	2.06	1.13-3.75
Hypertension[a]	2.20	1.13-4.29
FBS >110 mg%	4.44	1.84-10.69
HbA1C >7%	4.48	1.39-14.47
SGOT >40 IU/l	3.35	1.40-8.02
SGPT >50 IU/l	3.67	1.38-9.78
Uric acid >7 mg%	2.51	1.35-4.65

[a]Systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg. CAP, cancer-associated polyp; DM, diabetes mellitus; OR, odds ratio; CI, confidence interval; BMI, body mass index; FBS, fasting blood sugar; HbA1C, hemoglobin A1C; SGOT, aspartate transaminase; SGPT, alanine transaminase.

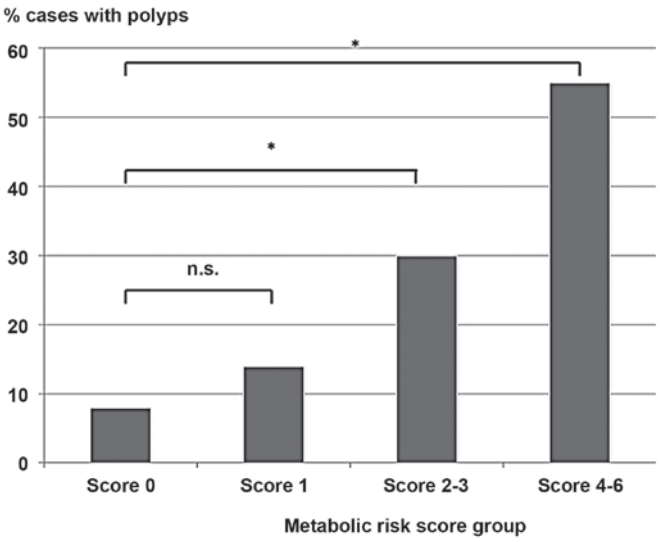

Figure 1. Frequency of polyp detection and progressive stratification of the metabolic risk score. *Statistically significant difference; n.s., not significant.

Table IV. Metabolic risk score constructed by clinical history, anthropometric measurements and laboratory profiles.

Clinical history	Anthropometric and laboratory parameters	Points
Obesity	BMI >23.4 kg/m^2	1
Hypertension	History of hypertension, or SBP >140 mmHg, or DBP >90 mmHg	1
DM	History of DM, or FBS >110 mg%, or HbA1C >7%	1
Dyslipidemia	History of dyslipidemia	1
Transaminitis	SGOT >40 IU/l; SGPT >50 IU/l	1
Hyperuricemia	Serum uric acid >7 mg%	1
Total	-	6

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; DM, diabetes mellitus; FBS, fasting blood sugar; HbA1C, hemoglobin A1C; SGOT, aspartate transaminase; SGPT, alanine transaminase.

Table V. Odds ratios of metabolic risk score, compared between all patients and the subgroup of patients aged <65 years.

	Metabolic risk score			
Patient subgroup	0	1	2-3	4-6
All patients	Reference	1.8 (0.7-4.9)	4.9 (2.0-12.0)	13.7 (4.4-43.0)
Subgroup <65 years	Reference	2.3 (0.7-8.1)	5.6 (1.8-17.9)	39.0 (8.2-186.6)

scoring system is presented in Table IV. When the score was validated with the cases, it was observed that moderate (2-3) and high scores (4-6) were significantly associated with CAP at ORs of 4.9 (95% CI: 2.0-12.0) and 13.7 (95% CI: 4.4-42.9), respectively (Table V, Fig. 1). Taking into consideration the age of the patients as an interacting factor, the subgroup analysis demonstrated that the metabolic score was associated with CAP only in the subgroup aged <65 years, but not in that aged ≥65 years. In the <65-year subgroup, the OR for moderate and high metabolic scores was increased to 5.6 (95% CI: 1.8-17.9) and 39.0 (95% CI: 8.2-186.6), respectively (Table V).

Discussion

The detection and removal of an adenomatous polyps has been proven to be an effective screening tool that reduces

CRC-related mortality (10,11). However, the standard protocol recommends that screening is initiated after the age of 50 years. Previous studies have suggested that there is a certain degree of correlation between metabolic syndrome and colorectal adenoma, a precancerous lesion of CRC (12-14), our study aimed to develop a risk determinant for younger patients who may benefit from screening on the basis of their metabolic profiles and associated clinical history.

The general adenoma detection rate of 20% for both sexes, 23% in males and 17% in females, is in line with standard quality indicators in colonoscopic practice (15). Our data confirmed a certain degree of correlation between individual clinical parameters associated with metabolic syndrome and colorectal adenoma and demonstrated that the association was stronger in the subgroup of patients aged <65 years. This finding may be explained by the fact that age exerts a significant effect on the incidence of CRC. When the factor of age was subtracted, the association between other parameters and the disease became more apparent.

We investigated fundamental clinical parameters, such as history of chronic diseases, with the hypothesis that, under certain circumstances, these parameters may be more revealing compared to laboratory tests. One example from our study that confirmed this hypothesis was the case of dyslipidemia, for which the medical history, but not the lipid profiles, indicated an association with CAP in our patients. The metabolic risk score was then constructed to cover all the aspects of the metabolic syndrome, by using less objective data, such as medical history, and more objective items, including anthropometric measurements and laboratory profiles. Our positive findings indicated that further validation of our approach in another set of subjects is required.

Unlike other cohorts (14,15), we did not identify a significant association between serum lipid profiles and CAP detection. This may be attributed to the relatively smaller size of our study compared to earlier studies. Furthermore, a number of our patients were receiving medication for dyslipidemia. Under such circumstances, it may be more useful to investigate other markers of visceral obesity that are not interfered with by treatment, such as serum adipokines.

In conclusion, our study confirmed a correlation between individual parameters in the metabolic syndrome and the occurrence of colorectal adenoma in Thai subjects. Furthermore, this study constructed a metabolic risk scoring system that may help identify patients at risk of having CAP.

Acknowledgements

The authors would like to thank the staff at the NKC Institute of Gastroenterology and Hepatology for their contribution in conducting this study.

References

1. Zimmet P, Magliano D, Matsuzawa Y, Alberti G and Shaw J: The metabolic syndrome: a global public health problem and a new definition. J Atheroscler Thromb 12: 295-300, 2005.
2. Chen M, He M, Min X, *et al*: Different physical activity subtypes and risk of metabolic syndrome in middle-aged and older Chinese people. PLoS One 8: e53258, 2013.
3. Eckel RH, Grundy SM and Zimmet PZ: The metabolic syndrome. Lancet 365: 1415-1428, 2005.
4. Esposito K, Chiodini P, Colao A, Lenzi A and Giugliano D: Metabolic syndrome and risk of cancer: a systematic review and meta-analysis. Diabetes Care 35: 2402-2411, 2012.
5. Aleksandrova K, Nimptsch K and Pischon T: Influence of obesity and related metabolic alterations on colorectal cancer risk. Curr Nutr Rep 2: 1-9, 2013.
6. Pais R, Silaghi H, Silaghi AC, Rusu ML and Dumitrascu DL: Metabolic syndrome and risk of subsequent colorectal cancer. World J Gastroenterol 15: 5141-5148, 2009.
7. Guffey CR, Fan D, Singh UP and Murphy EA: Linking obesity to colorectal cancer: recent insights into plausible biological mechanisms. Curr Opin Clin Nutr Metab Care 16: 595-600, 2013.
8. Wang YY, Lin SY, Lai WA, Liu PH and Sheu WH: Association between adenomas of rectosigmoid colon and metabolic syndrome features in a Chinese population. J Gastroenterol Hepatol 20: 1410-1415, 2005.
9. Liao KF, Lai HC, Lai SW, Cheng KC and Lin CH: Association between rectosigmoid adenomas and cardiovascular risk factors: a hospital-based, cross-sectional study. Ann Acad Med Singapore 38: 630-636, 2009.
10. Winawer SJ, Zauber AG, Ho MN, *et al*: Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. N Engl J Med 329: 1977-1981, 1993.
11. Walsh JM and Terdiman JP: Colorectal cancer screening: scientific review. JAMA 289: 1288-1296, 2003.
12. Yang MH, Rampal S, Sung J, *et al*: The association of serum lipids with colorectal adenomas. Am J Gastroenterol 108: 833-841, 2013.
13. Ulaganathan V, Kandiah M, Zalilah MS, *et al*: Colorectal cancer and its association with the metabolic syndrome: a Malaysian multi-centric case-control study. Asian Pac J Cancer Prev 13: 3873-3877, 2012.
14. Kim BC, Shin A, Hong CW, *et al*: Association of colorectal adenoma with components of metabolic syndrome. Cancer Causes Control 23: 727-735, 2012.
15. Rex DK, Petrini JL, Baron TH, *et al*: Quality indicators for colonoscopy. Am J Gastroenterol 101: 873-885, 2006.