Original Articles/นิพนธ์ต้นฉบับ

Development of Scoring System for Screening Colorectal Cancer: an Alternative Access to Health Care Services

Napaphat Poprom[1,2], Chumpon Wilasrusmee[1], Chakrapan Euanorasetr[1], Weerapat Suwanthanma[1], Sirima Mongkolsomlit[2]

[1] *Department of Surgery, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*

[2] *Faculty of Public Health, Thammasat University, Pathumthani, Thailand*

Abstract

We aimed to develop a screening scoring scheme for colorectal cancer (CRC). The baseline and clinical information from the patients at the outpatient unit of Surgery Department, Faculty of Medicine Ramathibodi Hospital was used to develop a screening model. A binary logistic regression model was used to identify the independent risk variables and the beta-coefficients and a simple point scoring system was developed. The risk variables scoring system was based on 8 risk parameters: gender, family history of CRC in the first-degree relatives, exercise, bleeding per rectum, abdominal pain, weight loss, low density lipoprotein level and high density lipoprotein. The total score ranged from 0 to 11.5. The likelihood of colorectal cancer in people with low risk (scores < 3) was 1.77, moderate risk (scores 3.0-4.5) was 3.00, almost high risk (scores 4.5-5.5) was 5.91 and high risk patients (scores > 5.5) was 6.50. The receiver operating characteristic (ROC) curve of the study was 0.85 (95% CI 0.81-0.90). Our screening scoring system is simple and easy to use especially in primary care units. However, this study is the primary phase of developing of screening scoring system for colorectal cancer.

Keywords: colorectal cancer, scoring system, colorectal cancer screening

Corresponding author: Sirima Mongkolsomlit
Faculty of Public Health, Thammasat University, Pathumtani 12121, Thailand.
Email address: tu.sirima@gmail.com, sirima@fph.tu.ac.th

Introduction

Colorectal cancer (CRC) is one of the most important cancers in the world. The annual incidence of CRC was more than 1,200,000 cases worldwide, especially the western countries such as Canada and USA, and the sufferers who died from CRC are approximately 608,700 cases per year[1]. In Asia, especially in the developed countries such as Singapore, Japan, and South Korea, the incidence rate of colorectal cancer per 100,000 men is 41.6, 41.7 and 46.9 respectively[2]. The mortality rate of CRC in Asia increases because of several risk factors[3-6]. The incidence of CRC in Thailand between 1988 and 2000 increases[7-9]. Three provinces in Thailand that show the highest incidence of CRC are Bangkok, Lampang and Chiang Mai[10].

The CRC has long asymptomatic period of 3 to 5 years[11]. Early diagnosis is important for treatment planning and cure, while the physicians would suggest surgery in 95% and those who receive early diagnosis and surgery have 95% chance of cure[12-15]. Physicians suggest people aged over 50 years old should be screened for CRC while several screening methods such as digital rectal examination, fecal occult blood, flexible sigmoidoscopy, colonoscopy, barium enema, and CT colonoscopy have been used[16]. However, these investigations are high cost and are not widely available. We therefore aimed to develop a screening scoring scheme for CRC.

Material and Methods

Study design

We conducted a case control study design. Data collection from the outpatient unit at the Department of Surgery, Ramathibodi Hospital, Thailand. The study was approved by the Ethical Review Committee for Research in Human Subjects of the Faculty of Medicine Ramathibodi Hospital, Mahidol University and Thammasat University.

Study population

Eligible subjects of the study were patients aged > 20 years old, without a history of pre-diagnosed CRC and immunodeficiency, underwent CT colonoscopy or colonoscopy between October 2014 and July 2015. We classified 100 subjects with CRC in an early stage (1 or 2) as the case group and 150 subjects who had negative findings for CRC by CT colonoscopy or colonoscopy were classified as a control group. The sample size was calculated based on ability of the scoring system according to the review of literature to determine risk factors of CRC. The authors expected 90% power to detect CRC with 95% confident interval based on the logistic regression[15].

Data collection

The medical history was retrieved from medical records. Clinical characteristics were age, gender, occupations, duration of working, BMI, family history, ulcerative colitis, Crohn's disease, diabetes, working posture, smoking, drinking, dietary, exercise, constipation, flatulence, diarrhea, bleeding, abdominal pain, and weight loss. Laboratory data included total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides, stool occult blood, and carcinoembryonic antigen (CEA).

Statistical analysis

Univariate analysis was used to identify the association between risk factors and CRC. Logistic regression was used to define associated factors with CRC after adjusting for covariates. Regression coefficients were transformed into item scores and added up to a total score. The scoring accuracy was present with area under the receiver operating characteristic

(ROC) curve. The *P*-value of < 0.05 was considered statistically significant.

Results

Among the 250 eligible subjects with an early stage of CRC, the factors which were significantly different between CRC and normal group were gender, family history of CRC in the first-degree relatives, positive stool occult blood, exercise, cholesterol level, and HDL level in female (Table 1).

The univariate analysis was performed for each independent variable and they were chosen to enter into the multivariate logistic regression model. The multivariate logistic regression analysis for identifying the risk factors for CRC showed 8 independent risk factors. These risk factors were sex, family history of CRC in first-degree relatives, exercise ≥ 30 minutes for 5 days per week, bleeding per rectum, weight loss, abdominal pain, LDL level, and HDL level (≥ 40 mg/dL in male, ≥ 50 mg/dL in women) (Table 2). The coefficient values were transformed by dividing with the lowest coefficient values in the model (0.78). The total scores ranged from 0 to 11.5 (Table 2).

When the total scores in the logistic model were applied, the screening scoring system explained 85.4% of the probability for the presence of CRC, which was demonstrated by the area under ROC curve (Fig 1).

The scores were separated into four levels; low risk group (scores < 3), moderate risk group (scores 3.0–4.5), almost high risk group (scores 4.5–5.5), and

Table 1 Baseline characteristic in colorectal cancer and non-colorectal cancer groups

Characteristics	Control (n=150)	Case (n=100)	*P*
Mean Age (year)	64.01 (11.22)	63.81 (10.28)	0.89
Male gender	57 (38.00)	57 (57.00)	< 0.01
Weight (kg)	61.82 (11.03)	63.95 (16.43)	0.26
Height (cm)	157.03 (7.67)	158.66 (16.29)	0.35
BMI (kg/m^2)	25.05 (4.10)	24.92 (6.15)	0.86
Family history of CRC in first-degree relatives	13 (8.67)	21 (21.00)	0.01
History of ulcerative colitis	38 (25.33)	22 (22.00)	0.55
History of Crohn's disease	30 (20.00)	23 (23.00)	0.57
Diabetes	29 (19.33)	22 (22.00)	0.61
Hypertension	63 (42.00)	45 (45.00)	0.64
Exercise (times/week)	3.40 (1.27)	4.57 (0.79)	0.03
Alcohol drinking (glasses/week)	18.38 (15.51)	26.40 (18.52)	0.06
Smoking (roll/week)	107.69 (63.03)	124.17 (69.62)	0.45
Cholesterol level (mg3IL)	185.84 (50.71)	199.49 (46.35)	0.03
LDL (mg/dL)	105.43 (39.32)	114.73 (45.60)	0.09
HDL (mg/dL)			
HDL in male	50.88 (13.44)	49.47 (15.09)	0.60
HDL in female	53.11 (13.30)	61.95 (21.78)	< 0.01
Triglyceride level (mg/dL)	114.82 (54.36)	118.63 (89.54)	0.70
Positive stool occult blood	49 (32.67)	70 (70.00)	< 0.01

Values are presented as number (%) or mean (SD)

Table 2 Risk factors associated with colorectal cancer in the multiple logistic regression analysis

Risk factors	Coefficient	95% CI of coefficient	*P*	Score point
Sex				
Male	1.12	0.44-1.79	< 0.01	1.5
Female	0			0
Family history of colorectal cancer in the first-degree relatives				
Yes	0.93	0.03-1.82	0.05	1
No	0			0
Exercise (30 minutes for 5 days/week)				
No	1.39	0.29-2.49	0.02	1.5
Yes	0			0
Bleeding per rectum				
Yes	1.73	1.05-2.42	0.05	2
No	0			0
Weight loss				
Yes	1.93	1.20-2.65	0.04	2
No	0			0
Abdominal pain				
Yes	0.78	0.03-1.53	< 0.01	1
No	0			0
LDL level (mg/dL)				
≥ 130	0.91	0.18-1.64	< 0.01	1
<130	0			0
HDL level				
Abnormal (≥ 40 mg/dL in male, ≥ 50 mg/dL in women)	1.21	0.26-2.16	0.05	1.5
Normal	0			0

high risk group (scores > 5.5) as shown in Table 3. The likelihood ratio (LR+) for CRC in the low risk group was 1.77 and high risk group was 6.50 times more likely for the presence of CRC (Table 3).

Discussion

The risk factors for screening CRC in these studies are relatively similar to the previous studies[15,16]. Eight risk factors are sex, family history of CRC in first-degree relatives, exercise, bleeding per rectum, weight loss, abdominal pain, LDL level and HDL level were included in the scoring system. A simple point scoring system was used for calculating the risk for CRC.

Performance of the CRC scoring system between two groups was significant (P <0.01). The highest score was found in the high risk group. The score was able to identify those who had a high or low risk

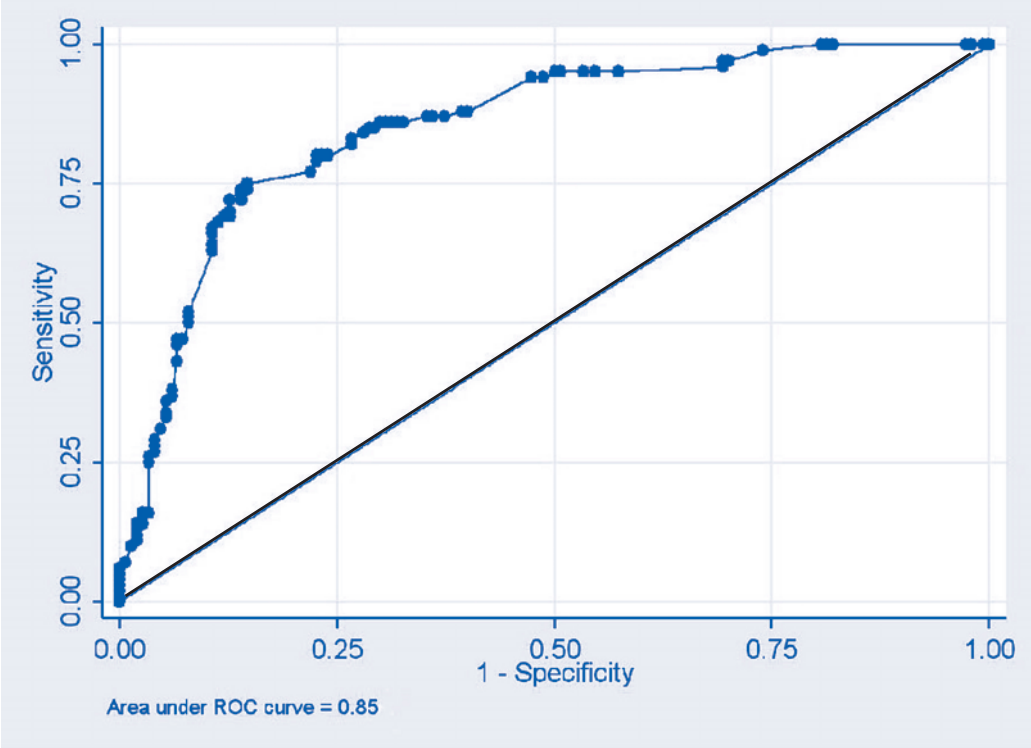

Figure 1 *Area under receiver operating characteristic (ROC) curves.*

Table 3 Distribution of score and likelihood ratio of colorectal cancer

Level of risk	Score	Control, n (%)	Case, n (%)	LR+	*P*
Low	< 3	70 (46.7)	5 (5.0)	1.77	< 0.01
Moderate	3.0 – 4.5	40 (26.7)	12 (12.0)	3.00	
Almost high	4.5-5.5	24 (16.0)	20 (20.0)	5.91	
High	> 5.5	16 (10.7)	63 (63.0)	6.50	

of CRC. The total scores were divided into four risk groups: low risk group (scores < 3), moderate risk group (scores 3.0–4.5), almost high risk group (scores 4.5–5.5), and high risk group (scores > 5.5). The scoring system could predict CRC with an area under ROC curve of 85.4%. This score is effective to identify CRC and can be simply used particularly in a primary health care setting. We suggested that people with risk scores less than 3, 3.0-4.5, and 4.5-5.5 should be followed for evaluation every 3 years, 1 year, and 6 months, respectively. The patients with high risk, score more than 5.5, should be undertaken for further investigations to exclude CRC.

Several limitations of this study were noted. Firstly, this study had a possibility of recalling bias because our study design was a case-control study. Secondly, this study would further need internal and external validation. Thirdly, the study had small sample size and short time periods of follow up. Finally, these scores were tested in the tertiary care center therefore the studied patients may not represent the general population.

Conclusion

From the study, our screening scoring system for CRC (low risk, moderate risk, almost high risk, and high risk), based on sex, family history of CRC, exercise, bleeding per rectum, abdominal pain, weight loss, LDL level, and HDL level, is a useful tool to determine the people who are at risk for CRC. It is simple and easy to use. This screening scoring system is helpful for the physicians to decide to perform more investigations such as colonoscopy and tissue biopsy, computed tomo-graphy, and magnetic resonance imaging. We proposed this scoring system is appropriate for the health care units, especially primary health care units. However, this study is the primary phase of developing screening scoring system for CRC and further studies to validate this scoring system are needed.

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Original Articles/นิพนธ์ต้นฉบับ

การพัฒนาระบบคะแนนช่วยคัดกรองโรคมะเร็งลำไส้ใหญ่: ทางเลือกในการเข้าถึงบริการสุขภาพ

ณปภัช โพธิ์พรหม[1,2], จุมพล วิลาศรัศมี[1], จักรพันธ์ เอื้อนรเศรษฐ์[1], วีรพัฒน์ สุวรรณธรรมา[1], สิริมา มงคลสัมฤทธิ์[2]

[1] ภาควิชาศัลยศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี มหาวิทยาลัยมหิดล
[2] คณะสาธารณสุขศาสตร์ มหาวิทยาลัยธรรมศาสตร์

บทคัดย่อ

การศึกษานี้มีวัตถุประสงค์เพื่อพัฒนาระบบคะแนนช่วยคัดกรองมะเร็งลำไส้ใหญ่ สำหรับเป็นทางเลือกหนึ่งในการเข้าถึงบริการสุขภาพ รูปแบบการศึกษา case-control study กลุ่มศึกษา (case) คือผู้ที่ได้รับการวินิจฉัยเป็นมะเร็งลำไส้ใหญ่ระยะที่1 หรือ 2 และกลุ่มควบคุม (control) คือผู้ที่ไม่เป็นมะเร็งลำไส้ใหญ่ เก็บข้อมูลที่ภาควิชาศัลยกรรม คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี วิเคราะห์ข้อมูลด้วยสถิติ Binary logistic regression เพื่อค้นหาตัวแปรที่มีผลต่อการเกิดมะเร็งลำไส้ใหญ่และพัฒนาเป็นระบบคะแนน ทำการทดสอบประสิทธิภาพของระบบคะแนนด้วย ROC curve

ผลการศึกษา พบปัจจัย 8 ชนิดที่เป็นความเสี่ยงต่อการเกิดโรคมะเร็งลำไส้ใหญ่ คือ เพศ ประวัติครอบครัวในการตรวจพบมะเร็งลำไส้ใหญ่ ประวัติการออกกำลังกาย อาการถ่ายเป็นเลือดเรื้อรัง อาการปวดท้องเรื้อรัง ภาวะน้ำหนักลด ไขมันชนิด LDL และไขมันชนิด HDL คะแนนของระบบคะแนนช่วยคัดกรองมีค่า 0-11.5 คะแนน แบ่งระดับความเสี่ยงออกเป็น 4 ระดับ คือ ความเสี่ยงต่ำมีคะแนนน้อยกว่า 3.0 ความเสี่ยงปานกลางมีคะแนนอยู่ระหว่าง 3.0-4.5 ความเสี่ยงสูงมีคะแนนอยู่ระหว่าง 4.5-5.5 และความเสี่ยงสูงมากมีคะแนนมากกว่า 5.5 ค่าประสิทธิภาพในการทำนายเท่ากับร้อยละ 85.42

สรุปผล ระบบคะแนนช่วยคัดกรองโรคมะเร็งลำไส้ใหญ่สามารถนำไปใช้ได้ง่ายโดยเฉพาะในระบบบริการสุขภาพขั้นพื้นฐาน เพื่อเป็นทางเลือกในการเข้าถึงบริการทางด้านสาธารณสุข

คำสำคัญ: มะเร็งลำไส้ใหญ่ ระบบคะแนน การคัดกรองโรคมะเร็งลำไส้ใหญ่

Corresponding author: สิริมา มงคลสัมฤทธิ์
คณะสาธารณสุขศาสตร์ มหาวิทยาลัยธรรมศาสตร์ ปทุมธานี 12121 ประเทศไทย
Email address: tu.sirima@gmail.com, sirima@fph.tu.ac.th