RMJ Ramathibodi Medical Journal

Rama Med J | Original Article

Visceral Fat Quantitated From CT Colonography Is Associated With the Presence of Colorectal Polyps

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Background: An adenomatous polyp is known as a precancerous lesion of colorectal cancer. Detection and removal of adenomatous polyps are essential for colon cancer prevention. Previous studies have found the association between obesity and adenomatous polyp using many parameters.

Objective: To determine the association between visceral fat visualized on computed tomography (CT) colonography (CTC) and colorectal polyps.

Methods: This retrospective case-control study consisted of 280 adult subjects who underwent colon cancer screening by CTC at Ramathibodi Hospital; 129 cases with CT detected colorectal polyps who underwent polypectomy within 6 months, and 151 control subjects who were negative for significant polyps on CTC. Visceral fat areas of all subjects were measured on CT at the umbilical level by a semiautomatic method. Statistical analysis was performed to ascertain associations with the presence of colorectal polyps.

Results: Of 280 adult subjects, there were classified into 4 groups; no polyps (n = 151), hyperplastic polyp (n = 23), low-risk adenomatous polyp (n = 75), and high-risk adenomatous polyp (n = 31). The mean visceral fat areas in 4 groups were 125.1 ± 55.7 cm^2, 140.2 ± 63.8 cm^2, 147.9 ± 74.2 cm^2, and 156.6 ± 63.7 cm^2, respectively. There were statistically significant differences in these means visceral fat between the no polyp group and both the low-risk and high-risk adenomatous polyp groups. In multivariate analyses, subjects who had visceral fat areas more than 168.60 cm^2 were more likely to have polyps than subjects whose visceral fat areas were less than 93.65 cm^2 ($P < .05$).

Conclusions: Visceral fat was positively associated with the presence of adenomatous colorectal polyps.

Keywords: Visceral fat, Colorectal polyp, Adenomatous polyp, Computed tomography

Rama Med J: doi:10.33165/rmj.2020.43.2.240071

Received: March 23, 2020 **Revised:** May 28, 2020 **Accepted:** June 8, 2020

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Introduction

Colorectal cancer is the third most common cancer and the fourth leading cause of cancer-related death worldwide.[1] According to European data from 2012, colorectal cancer represented 13.2% of all cancer cases in men and 12.7% in women, and caused 215,000 deaths; that was 11.6% and 13.0% of all cancer deaths in men and women, respectively.[2]

In Thailand, 2010 data from the hospital-based cancer registry of the National Cancer Institute (NCI), Thailand, showed that colorectal cancer accounted for 21.5% of all male cancers and 10.4% of all female cancers.[3] The etiology and risk factors of colorectal carcinoma include old age, history of adenomatous polyps, family history of colorectal cancer or adenomatous polyps, smoking, physical activity and obesity, history of inflammatory bowel disease, heavy alcohol consumption, and high-fat diets.[4] It is known that an adenomatous polyp is a precancerous lesion of colorectal cancer. Thus, detection and removal of adenomatous polyps are essential for colon cancer prevention and decreased colorectal cancer mortality.[5-8]

One of potential risk factors of colorectal cancer is obesity, which has been reported in many prior studies.[9-12] There are several methods to assess obesity including overall body fat, body mass index (BMI), and waist circumference. BMI is easy to obtain as a measure of the weight and height. Cross-sectional study in 2009 found an association between waist circumference and risk of colorectal adenoma, but BMI was not associated with risk of colorectal polyp.[9] It is known that visceral fat tissue releases numerous cytokines and adipokines, causing proinflammatory process and can lead to tumorgenesis in the local environment, whereas peripheral fat does not.[13, 14] However, the association between BMI, percentage of body fat, body fat distribution, and health risks were different across populations and ethnic groups. For instance, the proportion of Asian populations with a high risk of type 2 diabetes and cardiovascular disease is substantial at BMIs lower than the existing World Health Organization (WHO) cutoff point for overweight (greater than or equal to 25 kg/m^2).[15]

This study aimed to determine whether there is an association between visceral fat quantitated from computed tomography (CT) colonography (CTC) and the presence and type of colorectal polyps.

Methods

Ethics

This retrospective case-control study was approved by the institutional review board and ethics committee on human right related to research involving human subjects (No. MURA2015/503 on September 21, 2015), and individual informed consent was waived.

Study Design

The study retrospectively reviewed the radiological database of subjects who underwent CTC at Ramathibodi Hospital during the period of August 2014 to January 2015. The "cases" consisted of 129 adults with greater than or equal to 6 mm CT detected colorectal polyps who underwent polypectomy. The controls consisted of 151 subjects who were negative for significant colorectal polyp (none greater than or equal to 6 mm) on CTC. Potential subjects were excluded from the study if they had a known primary cancer, history of inflammatory bowel disease or history of familial adenomatous polyposis.

The data of the included subjects were retrieved and reviewed from electronic medical records, picture archiving and communication system (PACS), and pathologic reports. The weight and height of subjects were recorded at the day of CTC to calculate BMI.

CT Technique and Interpretation

Bowel Preparation

The bowel cleansing regimen for CTC included eating a soft, low residue diet for 2 days prior to the study. On the day before the exam, 3 doses (15 mL each) of hospital-made 30% w/v barium-based, fecal tagging agent were taken after breakfast, lunch, and dinner. Also, 3 doses of the laxative agent, sodium phosphate (Swiff, Berlin Pharmaceutical Industry Co, Ltd, Thailand), were taken orally at 5 PM, 7 PM, and 9 PM.

CT Colonography Scanning

All CT scans were performed by either the 64-slice CT scanner (SOMATOM Sensation 64; Siemens Medical System, Forchheim, Germany) or 320-slice CT scanner (Aquilion ONE; Toshiba Medical Systems Corp, Tokyo, Japan). Before colonic insufflation via a rectal tube with room air, 10 mL of hyoscine N-butylbromide (Government Pharmaceutical Organization [GPO], Thailand) was given intravenously to relax the colon and decrease peristalsis. The scans were taken during a single breath holds for both prone and supine positions. CT parameters included 120 kV, 100 - 50 mAs, 0.6 mm collimation with 1 mm reconstruction and 0.7 mm increment for the 64-slice CT scanner, and 120 kV, automated mAs with 0.5 mm collimation with 1 mm reconstruction and 0.5 mm increment for the 320-slice CT scanner.

All studies were interpreted by experienced radiologists who had attended CTC training and had been interpreting CTC for more than 5 years. CT images were assessed in both 2D and 3D by using Toshiba Vitrea Workstation or Siemens Syngo Workstation. Study results were reported using a CT Colonography Reporting and Data System (C-RADS).[9]

Optical Colonoscopy

Subjects with CT-detected polyps underwent optical colonoscopy with polypectomy or biopsy within 6 months after CTC by gastroenterologists. The polyp findings at optical colonoscopy and histopathology served as the reference standard for polyps in this study.

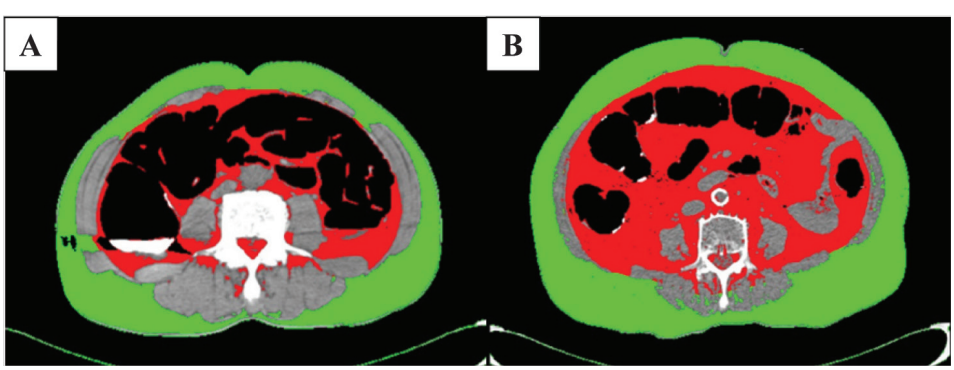
Visceral Fat Measurement

The quantification of visceral fat areas by using a semiautomatic method on a single cross-sectional image at an umbilical level has been validated in an earlier study, and visceral fat areas were positively correlated with total visceral fat volume measurements.[16]

Visceral fat areas of all subjects were measured by a single technologist with 20 years of CT experience. A single cross-sectional image at the umbilical level was selected. The area of fat including subcutaneous and visceral fat, as defined by attenuation between -50 and -150 Hounsfield units (HU), was automatically calculated and labeled with a yellow color. The abdominal cavity was outlined manually.

The visceral fat area was obtained by subtraction of the subcutaneous fat. The last image obtained from this method showed a visceral fat in a red color and a subcutaneous fat in green color. Finally, this red area was quantitated as the visceral fat area (cm^2). The last images of subjects with fat areas in the 1st and the 4th quartile obtained from this method were determined (Figure 1).

Figure 1. The Last Images Obtained From a Fat Quantification Method



Visceral fat area showed in red color and subcutaneous fat in green color. A, a subject with visceral fat in the 1st quartile. B, a subject with visceral fat in the 4th quartile.

Statistical Analysis

Data were analyzed using statistical software, STATA version 14.1 (StataCorp. Version 14. College Station, TX: StataCorp LP; 2015), and *P* values less than .05 were considered statistically significant. Continuous variables (such as age) were summarized as mean, while categorical variables were summarized as number and percentage.

The mean of visceral fat areas in each group of subjects was calculated. The *t* test was used to compare means of visceral fat areas of the control group and each polyp-positive group. The visceral fat data of all subjects were stratified into 4 quartiles. The odds ratios (ORs) for having polyp of each quartile were computed by dividing the odds of visceral fat quartile by the odds of the 1st quartile.

Multivariable logistic regression analysis for the presence of at least one colonic polyp was also performed. The independent variables were categorized visceral fat area, gender (male), obesity (BMI greater than or equal to 25 kg/m^2), old age (greater than 60 years), and family history (present) of colorectal cancer.

Results

A total of 280 subjects were included in the study and classified into 4 groups; no polyp (n = 151), hyperplastic polyp (n = 23), low-risk adenomatous polyp (tubular adenoma) (n = 75), and high-risk adenomatous polyp (tubulovillous adenoma, villous adenoma, and adenocarcinoma) (n = 31). If the subject had more than one polyp, he would be classified into a more advanced histopathology. There was no significant difference in the means of age among the studied groups. The characteristics of the 4 groups of subjects are summarized (Table 1).

The visceral fat areas of all subjects were divided into 4 equal quartiles. The cut points of visceral fat areas between quartiles from smallest to largest number were 93.65 cm^2, 126.81 cm^2, and 168.60 cm^2, respectively. Univariate and multivariate analyses were determined (Table 2).

The mean area of visceral fat of subjects with adenomatous colorectal polyps was significantly larger than that of subjects without polyps. Larger areas of visceral fat were associated with a greater risk of adenomatous polyps.

The OR of having polyp of the 4th quartile of visceral fat area versus the 1st quartile of the visceral fat area was 2.9, and the adjusted OR was 2.5 with statistical significance ($P < .05$). The OR of being male gender was 2.9, and the adjusted OR was 2.7 with statistical significance ($P < .05$).

Table 1. Characteristics of the Subjects Without Polyp, With Hyperplastic Polyp, Low-Risk Adenomatous Polyp, and High-Risk Adenomatous Polyp

Variable	No. (N = 280)				
	Controls (n = 151)	Cases With Polyp (n = 129)	Hyperplastic Polyp (n = 23)	Low-Risk Adenomatous Polyp (n = 75)	High-Risk Adenomatous Polyp (n = 31)
Gender (male/female)	44/107	70/59	11/12	39/36	20/11
Mean age, y	60.0	63.0	62.7	63.1	62.8
Age > 60 y	61	67	15	33	19
BMI ≥ 25 (kg/m^2)	48	66	10	39	17
Family history of colon cancer	8	6	2	4	0
Visceral fat area, mean (SD), cm^2	125.1 (55.7)	148.6 (69.7)	140.2 (63.8)	147.9 (74.2)	156.6 (63.7)

Abbreviations: BMI, body mass index; SD, standard deviation.

Table 2. Odds Ratios of Factors Assessed for Association With Colorectal Polyps in Univariate and Multivariate Analyses

Variable	Univariate Analysis			Multivariate Analysis		
	OR	95% CI	*P* Value	OR	95% CI	*P* Value
Male gender	2.9	1.80 - 4.70	< .001	2.7	1.61 - 4.47	< .001
Age > 60 years	1.6	1.00 - 2.60	.054	1.4	0.84 - 2.30	.192
Obesity (BMI ≥ 25 kg/m^2)	1.0	0.60 - 1.70	.887	0.9	0.55 - 1.57	.798
Family history of colorectal cancer	0.9	0.30 - 2.60	.805	1.0	0.16 - 0.59	.954
Visceral fat area						
1st quartile (< 93.65 cm^2)	1.0	-	-	1.0	-	-
2nd quartile (93.66 - 126.80 cm^2)	1.4	0.73 - 2.85	.298	1.6	0.77 - 3.12	.214
3rd quartile (126.81 - 168.60 cm^2)	1.7	0.87 - 3.38	.123	1.8	0.90 - 3.71	.094
4th quartile (> 168.60 cm^2)	2.9	1.45 - 5.72	.003	2.5	1.18 - 5.15	.017

Abbreviations: OR, odds ratio; CI, confident interval; BMI, body mass index.

Discussion

Many studies have investigated the relationship between obesity and adenomatous polyps, using many parameters. A cross-sectional study in South Korea,[9] showed that the mean waist circumference of subjects with adenoma was significantly larger than that of subjects without polyps, and obese subjects (BMI greater than or equal to 25 kg/m^2) had a significant higher risk of adenoma than normal BMI subjects (BMI less than 23 kg/m^2) (OR, 1.76; 95% CI, 1.0 - 3.1). However, there was no significant association between BMI and adenoma after adjusting for waist circumference. In a study in the USA of 126 adult men,[12] investigators found that males with BMI greater than or equal to 30 kg/m^2 were 6.5 times more likely to have greater than or equal to 3 polyps than males with BMI less than 25 kg/m^2. Moreover, males with BMI greater than or equal to 30 kg/m^2 were more likely to have a tubular adenoma compared to the likelihood that males with BMI less than 25 kg/m^2 would have a tubular adenoma (OR, 7.8; 95% CI, 2.0 - 30.8). Results were different in a study from Turkey, where the BMI and waist circumference of subjects with colorectal adenoma and colorectal cancer were lower than the BMI in control subjects. Interestingly, subjects with colorectal adenoma and carcinoma had visceral fat areas smaller than that in controls but this difference was not statistically significant. The authors postulated that the different results may be associated with weight loss in the cancer subjects by the time of imaging.[17] This present study showed that an increased BMI was not associated with the presence of the colorectal polyp. The different results from many studies may suggest that the BMI is not a good predictor for colorectal polyps, probably because of the association between BMI and body fat depends on many factors including age, gender, and ethnicity.[15]

This present study found that visceral fat areas larger than 168.6 cm^2 on CTC in subjects were associated with an increased risk of colorectal polyps, which are known to be a precursor of colorectal cancer. The odds ratio of having at least one polyp increased progressively from 1.4, 1.7 to 2.9, when going from the second to the highest quartiles of the visceral fat area, respectively. The odds ratio of presence of polyp in the highest visceral fat area quartile was 2.9 times compared to the lowest quartile and was 2.5 times after adjusting for other variables. The mean areas of visceral fat were significantly larger in both low-risk and high-risk adenomatous polyps than in that of the control group. This outcome supported results from the prior studies that patients with higher visceral fat measurements are at greater risk for the presence of colonic polyps.[10, 18, 19]

A study from Japan showed the significant association of visceral fat area in subjects with colorectal cancer, but not in subjects with adenomatous polyps.[18] Another study from the USA, reported that measurements of visceral fat

volume fraction on CTC, were correlated with an increased risk of adenomatous and hyperplastic polyps.[12]

In obesity, plasma adeponectin concentration is decreased, and low adeponectin level results in increased insulin resistance and has been thought to be associated with tissue inflammation and cancer development.[20-22]

In the present study, additional finding was that being male was associated with increased risk of having colorectal polyps, similar to results in a prior study.[23] Male gender significantly increased the risk of having colonic polyps, but there was no significant change in risk among the remaining variables assessed (old age, family history of colorectal cancer, and obesity). By performing multivariate analysis with adjustment of other factors, there was a persistent increased risk of colonic polyps in male gender along with a slight decrease in the strength of the relationship.

The result of this study suggested that having large areas of visceral fat may be a risk factor for colorectal cancer and may be considered for inclusion in screening guidelines. In obese subjects, a decrease in visceral fat would probably decrease the probability of developing colonic polyps and cancer. Visceral fat quantification may be added in the future to our routine CTC screening program and used to categorize obese patients into relatively higher and lower risk groups. Patients with a high probability of having colonic adenomas based on a high visceral fat value could be identified early and encouraged to change their lifestyles to decrease obesity.

There are many limitations of this study. Because of the retrospective nature of the study, some data were not recorded in the database. Many subjects were excluded due to no data of optical colonoscopy resulting in small number of the cases. It is possible those excluded subjects could bias the results of this study. Most subjects in the group without significant polyp on CTC did not have a subsequent optical colonoscopy. Thus, there was no confirmation that these subjects actually had no polyps (that they were true negatives in CTC). However, this is likely since CTC has been accepted as a screening test for colorectal cancer with 96.1% sensitivity as assessed by meta-analysis.[24] Additionally, in practice, the patient who is negative for polyps on CTC will not get an optical colonoscopy. However, previous data of CTC demonstrated the positive predictive value of 95.7%, the sensitivity for polyps greater than or equal to 6 mm were 87.3% and there was high to excellent interobserver agreement to detect polyps greater than or equal to 6 mm.[25] Another limitation has to mention is subjects did not get an optical colonoscopy on the same day of CTC which may affect the result. Last, this study did not have the associated clinical data such as diabetes, dyslipidemia, hypertension, and metabolic syndrome to analyze, which could be the confounding factors. This study suggested that further study is done prospectively and include assessment of more potential factors that may be associated with colorectal polyps.

Conclusions

The area of visceral fat in the group with polyps was significantly larger than that in the group without polyps. The visceral fat area appears to be correlated with increased risk of colonic polyps and remains a predictor even after adjustment for other factors. Subjects with either low-risk or high-risk adenomatous polyps have significantly more visceral fat than ones without any polyps.

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ไขมันในช่องท้องที่วัดได้จากการตรวจด้วยเอกซเรย์คอมพิวเตอร์ลำไส้ใหญ่มีความสัมพันธ์กับการพบติ่งเนื้อของลำไส้ใหญ่

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บทนำ: ติ่งเนื้อลำไส้ชนิด Adenoma เป็นรอยโรคก่อนเกิดมะเร็งลำไส้ใหญ่ การตรวจพบและตัดติ่งเนื้อชนิดนี้ออกเป็นการป้องกันการเกิดมะเร็งลำไส้ใหญ่ได้ มีข้อมูลพบว่าติ่งเนื้อชนิด Adenoma มีความสัมพันธ์กับโรคอ้วน

วัตถุประสงค์: เพื่อหาความสัมพันธ์ระหว่างปริมาณไขมันภายในช่องท้อง (Visceral fat area) ที่วัดได้จากเอกซเรย์คอมพิวเตอร์กับการพบติ่งเนื้อในลำไส้ใหญ่

วิธีการศึกษา: การศึกษาข้อมูลผู้ป่วยย้อนหลังแบบมีกลุ่มควบคุม โดยเก็บข้อมูลผู้ป่วยที่ได้ทำการตรวจคัดกรองมะเร็งลำไส้ใหญ่ด้วยเอกซเรย์คอมพิวเตอร์ จำนวน 280 คน โดยเป็นกลุ่มที่พบติ่งเนื้อจากการตรวจเอกซเรย์คอมพิวเตอร์และได้รับการตรวจและตัดติ่งเนื้อด้วยการส่องกล้องลำไส้ใหญ่ จำนวน 129 คน และกลุ่มควบคุมซึ่งไม่พบติ่งเนื้อจากการตรวจด้วยเอกซเรย์คอมพิวเตอร์ จำนวน 151 คน การวัดไขมันภายในช่องท้องทำโดยการวัดไขมันจากการตรวจเอกซเรย์คอมพิวเตอร์ที่ตำแหน่งระดับสะดือโดยเทคนิค Semiautomatic method จากนั้นทำการวิเคราะห์ทางสถิติเพื่อหาความสัมพันธ์กับการพบติ่งเนื้อของลำไส้ใหญ่

ผลการศึกษา: ผู้ป่วย จำนวน 280 คน แบ่งเป็น 4 กลุ่มคือ กลุ่มที่ไม่พบติ่งเนื้อ (151 คน) กลุ่มที่พบติ่งเนื้อชนิด Hyperplastic (23 คน) กลุ่มที่พบติ่งเนื้อชนิด Low-risk adenoma (75 คน) และกลุ่มที่พบติ่งเนื้อชนิด High-risk adenoma (31 คน) พบว่าปริมาณไขมันในช่องท้องมีค่าเฉลี่ยเท่ากับ 125.1 ± 55.7, 140.2 ± 63.8, 147.9 ± 74.2, และ 156.6 ± 63.7 ตารางเซนติเมตร ตามลำดับ โดยค่าเฉลี่ยของไขมันในช่องท้องระหว่างกลุ่มที่ไม่พบติ่งเนื้อ และกลุ่มที่พบติ่งเนื้อทั้งชนิด Low-risk adenoma และ High-risk adenoma มีความแตกต่างกันอย่างมีนัยสำคัญ และค่าเฉลี่ยของไขมันในช่องท้องระหว่างกลุ่มที่พบติ่งเนื้อชนิด Hyperplastic และกลุ่มที่ไม่พบติ่งเนื้อไม่มีความแตกต่างกันอย่างมีนัยสำคัญ จากการวิเคราะห์พหุตัวแปรพบว่า คนที่มีไขมันในช่องท้องมากกว่า 168.60 ตารางเซนติเมตร มีโอกาสพบติ่งเนื้อที่ลำไส้ใหญ่เมื่อเทียบกับคนที่มีไขมันในช่องท้องน้อยกว่า 93.65 ตารางเซนติเมตร ($P < .05$)

สรุป: ไขมันภายในช่องท้องสัมพันธ์กับการพบติ่งเนื้อในลำไส้ใหญ่

คำสำคัญ: ไขมันในช่องท้อง ติ่งเนื้อในลำไส้ใหญ่ ติ่งเนื้อชนิด Adenoma เอกซเรย์คอมพิวเตอร์

Rama Med J: doi:10.33165/rmj.2020.43.2.240071

Received: March 23, 2020 **Revised:** May 28, 2020 **Accepted:** June 8, 2020

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