Increased Risk of Advanced Colorectal Neoplasia Among Korean Men With Metabolic Abnormality and Obesity

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BACKGROUND & AIMS: **Obesity and metabolic abnormality are risk factors for colorectal cancer and adenoma. We evaluated the risk of advanced colorectal neoplasm (AN) according to metabolic status and obesity in Koreans.**

METHODS: **We performed a retrospective cross-sectional study of 70,428 individuals in Korea who underwent colonoscopy and whose metabolic state and body mass index were examined, from 2003 through 2012, at Kangbuk Samsung Hospital in Korea. We calculated odds ratios (ORs) for AN in people who were metabolically healthy but obese, people with metabolic abnormality who were not obese, and people with metabolic abnormality who were obese. The reference group was metabolically healthy nonobese peoples. AN was defined as adenoma ≥10 mm in diameter, adenoma with any component of villous histology, high-grade dysplasia, or invasive cancer.**

RESULTS: **No increased risk of AN was observed in the metabolically healthy but obese (OR, 0.99; 95% confidence interval [CI], 0.67–1.46; $P = .825$) and metabolic abnormality who were not obese groups (OR, 1.01; 95% CI, 0.85–1.21; $P = .765$). In contrast, risk of AN was increased in the metabolic abnormality who were obese group (OR, 1.33; 95% CI, 1.12–1.58; $P = .006$). In men, risk of AN showed a greater increase in the metabolic abnormality who were obese group (OR, 1.48; 95% CI, 1.20–1.83; $P = .001$). This association was not observed in women (OR, 1.21; 95% CI, 0.84–1.75; $P = .476$).**

CONCLUSIONS: **Men with 1 or more metabolic abnormality and obesity are at increased risk for AN.**

Keywords: BMI; Metabolic Abnormality; Diabetes; Advanced Colorectal Neoplasm Risk Factors.

Q4 Colorectal cancer (CRC) is the second most common cancer in men and the third most common cancer in women. The incidence and mortality of CRC are on the rise in Korea.[1] It is well documented that most CRC arises from colorectal adenoma (CRA).[2] Advanced CRA is a definite precancerous lesion and the development of CRC can be prevented through screening colonoscopy when advanced CRA is detected and removed.[3]

The identification of risk factors for CRA would be helpful for preventing CRC. Several studies have reported positive associations between metabolic abnormality (MetA) including insulin resistance, proatherogenic lipoprotein profile, and CRA.[4] Obesity and overweight, as determined by body mass index (BMI), are also important risk factors for CRC and CRA.[5]

Most patients with obesity have 1 or more MetAs. However, some are metabolically healthy. In addition, some people without obesity also have some form of MetA. Recently, the subgroup of people with obesity and obesity-related MetA has become of interest. Many studies have examined the associations between cardiovascular health and obesity and MetA.[6] A recent report found that people who are metabolically healthy but are obese (MHO) are not at increased risk of developing cardiovascular diseases compared with normal control subjects.[6] However, the association between CRC and these subgroups has not been clearly evaluated and few studies have examined risk of advanced colorectal neoplasm (AN). The aim of this study was to determine whether a relationship exists between development of AN and metabolic state and obesity among Korean people who underwent screening colonoscopy.

Abbreviations used in this paper: **AN, advanced colorectal neoplasm; AO, abdominal obesity; BMI, body mass index; CRA, colorectal adenoma; CRC, colorectal cancer; FOBT, fecal occult blood test; MANO, metabolically abnormal nonobese; MAO, metabolically abnormal obese; MetA, metabolic abnormality; MetS, metabolic syndrome; MHNO, metabolically healthy nonobese; MHO, metabolically healthy obese; OR, odds ratio.**

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Methods

Study Population

Participants who underwent a health examination between 2003 and 2012 at Kangbuk Samsung Hospital, College of Medicine, Sungkyunkwan University were enrolled. We excluded patients with (1) history of other cancers, (2) history of inflammatory bowel disease, (3) previous colonoscopy, (4) colon surgery, (5) incomplete colonoscopy, and (6) missing data. The inclusion and exclusion flow chart is described in Figure 1. This study was approved by the Institutional Review Board of Kangbuk Samsung Hospital.

Definitions

Except for abdominal obesity (AO), MetA was defined according to the modified National Cholesterol Education Program Adult Treatment Panel III criteria[7] as follows: (1) hypertriglycerides (triglycerides ≥150 mg/dL or specific treatment for this lipid abnormality), (2) high-density lipoprotein cholesterol abnormality (high-density lipoprotein-cholesterol <40 mg/dL for men and <50 mg/dL for women), (3) hypertension-related factor (elevated blood pressure ≥130/85 mm Hg or use of antihypertensive medications), and (4) diabetes mellitus–related factor (fasting plasma glucose ≥100 mg/dL or hemoglobin A_{1c} ≥6.5%, or use of diabetes medications). The National Cholesterol Education Program Adult Treatment Panel III has a waist circumference standard for AO; however, it is for people in Western countries. According to the Korean Society for the Study of Obesity, metabolic risk is increased in men with waist circumference ≥90 cm and in women with waist circumference ≥85 cm in Korea; therefore, we used these guidelines.[8] The Asia-Pacific criteria for obesity based on BMI guidelines were used to diagnose obesity (BMI ≥25 kg/m^2).[9] MetA was defined as any abnormality in the National Cholesterol Education Program Adult Treatment Panel III criteria except that AO or waist circumference criteria were from the Korean Society for the Study of Obesity. Metabolic syndrome (MetS) was defined as 3 or more abnormalities from those criteria.

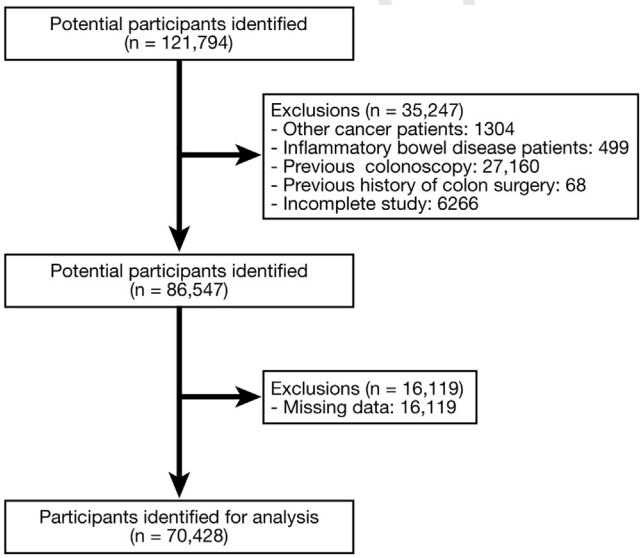

Figure 1. Flow diagram of participant enrollment.

Study participants were assigned to 4 groups based on BMI scores and MetA status as follows: (1) subjects with no MetA and who were not obese were categorized as metabolically healthy nonobese (MHNO), (2) subjects with no MetA and who were only obese were categorized as MHO, (3) subjects with 1 or more MetA and who were not obese were categorized as metabolically abnormal nonobese (MANO), and (4) subjects with 1 or more MetA and who were obese were categorized as metabolically abnormal obese (MAO). Participants were assigned to the 4 groups when data collection was complete.

Measurements

Data on medical history, medication use, and health-related behaviors were collected through a self-administered questionnaire under the supervision of a well-trained interviewer. Alcohol consumption and smoking were identified. Heavy drinker was defined as a subject who drinks more than 4 times per week. Family history of CRC was defined as CRC in 1 or more first-degree relatives at any age. Weekly frequency of moderate to vigorous physical activity was also assessed.

Physical measurements and serum biochemical parameters were measured by trained nurses. Blood pressure was measured using a standard mercury sphygmomanometer with participants seated after at least 10 minutes of rest. Blood samples were taken from the antecubital vein after at least 10 hours of fasting. The Laboratory Medicine Department at Kangbuk Samsung Hospital in Seoul, Korea, has been accredited by the Korean Society of Laboratory Medicine and the Korean Association of Quality Assurance for Clinical Laboratories.

Diagnosis of Colorectal Neoplasm

Colonoscopies were performed by experienced colonoscopists unaware of the present study. Bowel preparations were carried out using 4-L Colyte solution. Histologic assessment of all polyps was performed by experienced pathologists unaware of the clinical data. AN was defined as CRA ≥10 mm in diameter, CRA with any component of villous histology, high-grade dysplasia, or invasive cancer.[10]

Statistical Analyses

Continuous variables were expressed as means ± standard deviations and compared using analysis of variance. Categorical variables were expressed as