Prevalence and Risk Factors of Colorectal Neoplasms according to Coronary Artery Obstructive Disease

Ki Tae Suk, M.D., Hyun Soo Kim, M.D.1, Hyun Jun Min, M.D., Hong Jun Park, M.D.1, Hyo Keun Jeon, M.D.1, Moon Young Kim, M.D.1, Jae Woo Kim, M.D.1, Soon Koo Baik, M.D.1, Sang Ok Kwon, M.D.1

Department of Internal Medicine, Hallym University College of Medicine, Chuncheon, Yonsei University Wonju College of Medicine, Wonju, Korea

Background/Aims: Both colorectal neoplasm (CN) and coronary artery obstructive disease (CAOD) are prevalent and major leading causes of death in Korea. Although CN and CAOD share similar risk factors such as male gender, smoking, hyperlipidemia, diabetes mellitus, and obesity, few studies of both CN and CAOD have been reported. In this study, we evaluated clinical correlations between CN and CAOD. Methods: Between June 2003 and December 2007, 176 patients (Male: 101, average age: 62.1±9.7 yr) who underwent colonoscopy after or before coronary angiography were retrospectively enrolled. The colonoscopic findings (normal, adenoma, or cancer) of patients as well as clinical and laboratory data according to the extent of CAOD (normal, minimal CAOD, or CAOD) were compared. Results: CAOD negative, minimal CAOD, and CAOD patients totaled 36, 40, and 100, respectively. The presence of CN (adenoma and adenocarcinoma) in CAOD negative, minimal CAOD, and CAOD cases was 42%, 48%, and 63%, respectively, which was significantly different (P<0.05). In multivariate analysis, old age (≥ 60 yr; P=0.03, odds ratio 2.47) and the presence of CAOD (P=0.02, odds ratio 4.11) were associated with the presence of CN. Conclusions: The prevalence of CN increased in proportion to the severity of CAOD. Colorectal cancer screening by fecal occult blood tests or colonoscopy should be a priority in patients with CAOD, particularly the elderly. (Intest Res 2011;9:112-116)

Key Words: Colorectal Neoplasms; Colonoscopy; Coronary Artery Disease

INTRODUCTION

Colorectal cancer is the second most prevalent cancer worldwide and the fourth leading cause of cancer-related deaths in Korea.1 Colorectal neoplasms (CN), including adenomas and adenocarcinomas, are prevalent and rapidly increasing.2 Coronary artery obstructive disease (CAOD) is also among the industrialized world’s leading causes...
It has been demonstrated that CN and CAOD share similar risk factors such as lifestyle, high-fat and low-fiber diets, obesity, diabetes mellitus, and hypertension. Male gender has also been reported to be an important risk factor in both CN and CAOD. In addition, smoking was reported to be associated with CN and with atherosclerosis development in patient with CAOD. Recently, metabolic syndrome is being increasingly recognized as a significant health problem. However, there are only a few reports in the literature investigating the association between these two conditions. Correa et al. suggested an association between adenomatous polyps and atherosclerosis of the aorta. Other reports also found increased CN incidence in patients with CAOD. Korea is progressively adopting a westernized lifestyle and the incidence of CN and CAOD is approaching that of western countries. In the present study, we evaluated the prevalence and risk factors of CN according to the presence of CAOD.

**MATERIALS AND METHODS**

1. **Patients**

From June 2003 to December 2007, we retrospectively included a total of 238 patients (M:F=131:107, average age: 62.7±10.3 yr) who underwent colonoscopy before/after coronary angiography at Wonju Christian Hospital. We reviewed the medical charts and those with incomplete colonoscopy examinations were excluded from the final analysis. Patients were also excluded if the duration between colonoscopy and angiography was >2 years (8 patients), if colonoscopy was performed as the result of a warning sign such as bleeding, palpable mass, significant weight loss, bowel habit change, or jaundice (50 patients), and if there was a history of colorectal cancer (4 patients). Finally, 176 patients who underwent colonoscopy as part of a check-up (158 patients) or abdominal pain (18 patients) were enrolled in the analysis. The study was carried out in accordance with the Helsinki Declaration after the approval of the Institutional Review Board of the hospital.

The colonoscopic findings (normal, polyp, or cancer) of patients according to the presence of CAOD (normal, minimal CAOD, or CAOD) were evaluated. Clinical and laboratory data of each colonoscopic finding were compared. The studied variables were gender, age, past history, laboratory findings, presence of metabolic syndrome, presence of fatty liver on ultrasound, body mass index (BMI), and colonoscopic findings. CAOD was defined as the presence of at least 50% stenosis in at least one major coronary artery. Minimal CAOD was defined as <50% stenosis of the coronary artery. Metabolic syndrome was diagnosed if the patients met at least three of the following five criteria: 1) fasting glucose ≥110 mg/dL, 2) triglyceride ≥150 mg/dL, 3) high-density lipoproteins (female) <50 and (male) < 40 mg/dL, 4) the presence of hypertension, 5) a BMI >24. Fatty liver was diagnosed by abdominal ultrasound and defined by the number of criteria met (mild= 1, moderate= 2, and severe= 3) which included an increased liver parenchymal echo-pattern, poorly visualization of the vascular wall of the liver, and obliteration of the view of the diaphragmatic wall.

Colonoscopy and abdominal ultrasound were performed by gastroenterologists with >2 years of experience and the duration of the colonoscopy procedure was >5 min to minimize the chance of lesions being missed.

2. **Statistical analysis**

We used the t-test to compare the continuous variables. Data were expressed as means with SD. The relationship between CN and other parameters was assessed using the chi-square test, binary logistic regression analysis, and ANOVA. Data were analyzed with statistical software (SPSS, version 13.0, SPSS Inc., Chicago, IL, USA). A P value <0.05 was considered statistically significant in all tests.

**RESULTS**

1. **Baseline characteristics of patient and pathology**

The clinical characteristics of the patients are presented in Table 1. The mean age of the patients was 62.1 years (±9.7). According to BMI, 12 patients were designated as obese and 64 were considered overweight. Metabolic syndrome was diagnosed in 46 patients (26%). Through abdominal ultrasound, severe fatty liver was found in 3 patients, moderate fatty liver
in 20, mild fatty liver in 36, and normal liver in 66.

2. Characteristics according to the severity of CAOD

Upon analysis of characteristics according to the severity of CAOD, male gender, older age, presence of past history (diabetes mellitus or hypertension), and presence of metabolic syndrome positively correlated with the severity of CAOD ($P<0.01$). In the sub-analysis of the colonoscopic findings, the prevalence of adenoma was 28\% with normal coronary arteries, 23\% with minimal CAOD, and 38\% with CAOD. In addition, the prevalence of adenocarcinoma was 14\% with normal coronary arteries, 25\% with minimal CAOD, and 25\% with CAOD. Taken together, the overall prevalence of CN according to the severity of CAOD was 42\% in normal cases, 48\% with minimal CAOD, and 63\% with CAOD (Table 2).

3. Multivariate analysis of CN

In the multivariate analysis, age $>60$ years ($P=0.03$, odds ratio 2.47) and the presence of CAOD ($P=0.02$, odds ratio 4.11) were associated with the presence of CN (Table 3).

**DISCUSSION**

In the present study, the prevalence of CN increased with the severity of CAD (42\%, 48\%, and 63\%). This result was similar to that of a previous report.\(^\text{12}\) Some reports suggested an indirect positive relationship between CAOD and CN by comparing atherosclerosis, insulin resistance, fatty liver, and CN.\(^\text{13,14}\) Moreover, recent evidence suggests a strong coexistence of CN and CAOD.\(^\text{6,12}\) Based on these results, we postulated that the
association between the two conditions was due to exposure to common risk factors.

According to recent data, the prevalence of CN and advanced neoplasms in asymptomatic patients was 18.5% and 4.5%, respectively. These findings were comparable with those found in western populations, which suggests that the lifestyle has changed in Korea and that the prevalence of CN and CAOD could increase even more in the future.

In this study, many patients with CAOD (63%) had CN, especially older patients (>60 years old) with CAOD. This finding is notable. Other reports demonstrated that only 26-34% of CAOD patients had concomitant CN, which is higher than that found in the normal population.6,12 Despite selection bias, our results showed a higher prevalence of CN in patients with CAOD. Our result suggests that patients with CAOD, especially older patients, might be considered at high risk for colorectal cancer. Therefore, above all, those patients should be screened by stool occult test or colonoscopy.

Coronary angiography is not a routine procedure during health check-ups but a second modality for selected patients with heart problem. On the contrary, colonoscopy is currently a routinely used method for the diagnosis of CN. As such, in this retrospective study, there was no control group of patients who had undergone coronary angiography during health check-ups. As a result, although we excluded patients with warning signs, the prevalence of colorectal cancer was high (40 patients) in this study. Currently, it is becoming more routine to examine the heart using computed tomography coronary angiography. Therefore, it may be possible to evaluate the relation between the two diseases prospectively in the near future.

Male gender, age, past history of hypertension or diabetes mellitus, fasting glucose, presence of metabolic syndrome, and CN all positively correlated with CAOD severity. In contrast, alcohol intake, smoking, BMI, and fatty liver were not associated with CAOD. However, the positive relationship was not confirmed in multivariate analysis. Only age >60 years and the presence of CAOD were associated with the presence of CN in that analysis.

Inflammation is recognized as a main pathogenesis of both CAOD and CN.15-18 Inflammation may result from the underlying risk factors such as increased C-reactive protein and inflammatory cytokines. Aspirin and statins have been proven to be beneficial in both conditions via anti-inflammatory mechanisms.19-21 A previous report suggested that inflammatory biomarkers could help to diagnose disease progression.22 However, in the two investigated conditions, information on the effect of biomarkers on inflammation is limited. In the current study, we investigated only the co-existence of both CN and CAOD; therefore, future studies investigating both the mechanisms and causation are needed.

This retrospective study has certain limitations. Colonoscopy was not performed in all patients who underwent angiography and we excluded patients with a history of cancer, with at least one warning sign, and

| Variables                      | P-value | OR      | CI       |
|-------------------------------|---------|---------|----------|
| Gender (Male/Female*)         | NS      | 0.54    | 0.21–1.54|
| Past history No*              | NS      | 0.95    | 0.35–2.61|
| DM                            | NS      | 1.46    | 0.38–5.64|
| HTN                           | NS      | 1.90    | 0.52–6.93|
| DM + HTN                      | NS      | 0.49    | 0.17–1.41|
| Metabolic syndrome (Yes/No*)  | NS      | 1.14    | 0.52–2.50|
| Presence of fatty liver (Yes/No*) | NS  | 2.47    | 1.07–5.62|
| Age (>60 yr/ <60 yr*)         | 0.03    | 4.11    | 1.30–13.00|
| Presence of CAOD No*          | <0.01   | 1.14    | 0.52–2.50|
| Minimal CAOD                  | NS      | 0.95    | 0.29–3.12|
| CAOD                          | 0.02    | 4.11    | 1.30–13.00|

CN, colorectal neoplasms; OR, odds ratio; CI, confidence interval; HTN, hypertension; DM, diabetes mellitus; CAOD, coronary artery obstructive disease.

*Reference category.
with long durations between colonoscopy and angiography. Moreover, there was no control group of patients who underwent coronary angiography during health check-ups. This may result in selection bias towards underestimating the prevalence of CAOD. Despite the limitations of the current study, the results are intriguing. It would be ideal to perform an age- and sex-matched study in both CAOD-positive and CAOD-negative groups to study the association between the two diseases. Further large-scale prospective studies are required.

In conclusion, in this study we found that the prevalence of CN increased in proportion to the severity of CAOD. Colorectal cancer screening such as fecal occult blood test or colonoscopy should be a priority in patients with CAOD, especially older patients (>60 years).

요 약

목적: 대장 종양과 관상동맥폐색질환이 국내에서 모두 유행율이 높아 주된 사망의 원인이다. 나이, 혈연, 고지혈증, 당뇨, 그리고 비만과 같은 위험인자들은 관상동맥폐색질환을 유발하고 있지만, 관상동맥폐색질환이 따른 대장 종양의 유행율에 대한 보고는 거의 없다. 따라서, 저자들은 이 연구에서 대장 종양과 관상동맥폐색질환 간의 임상적 연관성을 조사하였다.

대상 및 방법: 2003년 5월부터 2007년 12월까지 대장내시경검사 전후에 관상동맥 조영술을 시행한 176명(남자: 101명, 평균나이: 62.1±9.7세)의 환자를 후향적으로 조사하였다. 관상동맥 폐색질환(정상, 경도의 관상동맥폐색질환, 또는 관상동맥폐색질환의 중등도에 따른 대장내시경 검사소견(정상, 선종, 또는 암)과 임상 및 혈액학 검사 자료를 비교분석하였다.

결과: 정상, 경도의 관상동맥 폐색질환, 그리고 관상동맥폐색질환 환자는 각각 36명, 40명, 그리고 100명이었다. 정상 관상동맥, 경도의 관상동맥폐색질환 환자 그리고 관상동맥폐색질환 환자에서 대장 종양(선종과 대장암)의 유행율은 각각 42%, 48%, 63%이었고 각 군별로 통계학적으로 차이를 보였다(P<0.05). 비만과 당뇨는 고혈압(60세, P=0.03, Odds ratio 2.47)과 관상동맥 폐색질환의 존재(P=0.02, Odds ratio 4.11)는 대장 신생물의 위험인자였다. 결과: 관상동맥폐색질환의 경중도에 비해 대장 종양의 유행율이 증가하였다. 따라서 관상동맥 폐색질환을 가진 환자 특히, 고혈압의 환자에서는 대장암의 선별을 위한 대변검사나 대장내시경검사가 우선적으로 시행되어야 한다.

색인어: 대장 종양, 대장내시경, 관상동맥질환

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