Effects of Metabolic Syndrome and Findings From Baseline Colonoscopies on Occurrence of Colorectal Neoplasms

Han-Mo Chiu,[*,‡] Yi-Chia Lee,[*,‡] Chia-Hung Tu,[*,‡] Li-Chun Chang,[§] Wen-Feng Hsu,[‖] Chu-Kuang Chou,[¶] Kun-Feng Tsai,[#] Jin-Tung Liang,[**] Chia-Tung Shun,[‡‡] and Ming-Shiang Wu[*,‡]

*Department of Internal Medicine, ‡Health Management Center, **Department of Surgery, ‡‡Department of Pathology, National Taiwan University Hospital, Taipei, Taiwan; §Department of Internal Medicine, National Taiwan University Hospital, Bei-Hu Branch, Taipei, Taiwan; ‖Department of Internal Medicine, National Taiwan University Hospital, Hsin-Chu Branch, Taipei, Taiwan; ¶Division of Gastroenterology and Hepatology, Chia-Yi Christian Hospital, Chia-Yi, Taiwan; #Department of Internal Medicine, National Taiwan University Hospital, Jin-Shan Branch, Taipei, Taiwan

BACKGROUND & AIMS: **Metabolic syndrome is associated with increased risk of colorectal neoplasm, but little is known about its effects on the occurrence of neoplasm after colonoscopy. We investigated the effects of metabolic syndrome on the risk of advanced neoplasm after colonoscopy.**

METHODS: **We performed a prospective study of 4483 subjects age 50 years and older who underwent screening and surveillance colonoscopies as part of an annual health check-up at National Taiwan University Hospital. Baseline demographic data and colonoscopic findings were recorded. Subjects with either advanced adenoma or 3 or more adenomas detected at baseline were classified as high risk; those with fewer than 3 nonadvanced adenomas were classified as low risk; and those without any neoplastic lesions were classified as normal. The cumulative risk of detecting an advanced neoplasm during surveillance colonoscopies (3 and 5 years later) was correlated with risk group and metabolic syndrome. Hazard ratios (HRs) were calculated for occurrence of neoplasm according to baseline colonoscopic findings and clinical risk factors, including metabolic syndrome.**

RESULTS: **Advanced neoplasms were detected during the surveillance colonoscopies in 1.3% of subjects in the normal group and in 2.4% of those in the low-risk group at 5 years, and in 8.5% of subjects in the high-risk group at 3 years. Subjects with metabolic syndrome had a significantly higher risk for subsequent advanced neoplasms ($P < .0001$). After stratification based on findings from baseline colonoscopies, the risk for neoplasm was significant in the normal ($P < .001$) and low-risk groups ($P = .04$), but not in the high-risk group ($P = .48$). In Cox regression analysis, metabolic syndrome had significant effects on the risk for advanced neoplasms in the normal (HR, 2.07; 95% confidence interval, 1.13–3.81) and low-risk groups (HR, 2.34; 95% confidence interval, 1.01–5.41), but not in the high-risk group.**

CONCLUSIONS: **Metabolic syndrome is a significant risk factor for occurrence of an advanced adenoma after a negative or low-risk finding from a baseline colonoscopy. Metabolic syndrome should be considered in risk stratification for surveillance intervals.**

Keywords: Colon Cancer; Diabetes; Obesity; Tumor; Metabolic Syndrome (MetS).

Colonoscopy with removal of adenomas is effective in reducing the incidence of and mortality from colorectal cancer (CRC).[1,2] Subjects with a colorectal neoplasm at initial colonoscopy are prone to develop subsequent recurrent neoplasms, thus periodic surveillance examinations are mandatory.[3] Accordingly, identification of predictors of recurrence of colon polyps is crucial to improving the efficacy of colonoscopy surveillance. Previous studies in this field have shown that in addition to patient characteristics such as older age and male sex, polyp characteristics at baseline colonoscopy including size, multiplicity, and advanced histology of neoplastic lesions were associated strongly with the risk of recurrence of adenoma or advanced adenoma.[4–6]

Abbreviations used in this paper: CI, confidence interval; CRC, colorectal cancer; HR, hazard ratio; MetS, metabolic syndrome.

1542-3565/$36.00
http://dx.doi.org/10.1016/j.cgh.2014.10.022

Current guidelines thus recommend an optimal surveillance interval based on baseline findings. Adherence to the recommended surveillance interval not only can reduce the risk of so-called *postcolonoscopy CRC*, but also can facilitate more appropriate use of colonoscopy.

Based on the findings of most recent colonoscopies, the current recommended surveillance interval is 3 years for patients with high-risk adenoma, 5 to 10 years for those with low-risk adenoma, and 10 years for those with no adenoma.[7] Increasing evidence, however, suggests that factors other than colonoscopic findings may influence the risk of colorectal neoplasm occurrence. This observation deserves further investigation.[8] Among these factors, patient-related factors such as smoking and metabolic disorders including obesity, dyslipidemia, and diabetes have been established as risk factors for colorectal neoplasm. The metabolic syndrome (MetS) is a complex metabolic disease characterized by the constellation of glucose intolerance, obesity, hypertension, and dyslipidemia. MetS has been assumed to be associated with the development of some cancers, particularly CRC.[9] This hypothesis is based mainly on similar risk factors found among cardiovascular diseases, diabetes, and CRC, and supported by epidemiologic studies.[9] Intriguingly, MetS and related disorders are associated not only with initial cancer risk, but also with cancer recurrence.[10–12] Regarding colorectal adenoma, Jacobs et al[13] showed that obesity increased the risk of adenoma recurrence after polypectomy, and Yamaji et al[8] showed that body weight reduction reduced the risk of adenoma recurrence; however, Laiyemo et al[14] found that weight loss or gain did not affect adenoma recurrence. Clusters of MetS components, including obesity, dyslipidemia, hypertension, and hyperglycemia, theoretically have a greater impact on adenoma recurrence than does a single risk factor. Previous studies, including ours, have shown that subjects with MetS had a higher risk of proximal and synchronous colorectal neoplasms than did those without these risk factors.[15] The impact of MetS on adenoma recurrence after colonoscopy, however, rarely is studied. Taken together, identification of both modifiable patient factors and colonoscopic findings related to adenoma recurrence after colonoscopy potentially may guide the risk stratification schema for optimization of surveillance.[3–5]

To test this hypothesis, we examined the associations among MetS, baseline endoscopic characteristics, and the risk of neoplasm occurrence in subsequent colonoscopy by analyzing a prospective collected cohort with comprehensive data collection and complete screening and follow-up colonoscopy.

Materials and Methods

Study Population

Subjects who underwent a colonoscopy as part of a thorough annual health check-up at the National Taiwan University Hospital comprised the screening and follow-up colonoscopy cohort. The details of this screening program have been described elsewhere, and this study was approved by the Institutional Review Board.[15] All participants were asked to complete a standard medical questionnaire before the health check-up. All participants were asked to describe the following: (1) smoking, alcohol consumption, and other health-related habits; (2) any family history of cancer, including CRC; (3) a personal history of CRC, adenomas, or a polypectomy; and (4) the use of medications, including insulin, oral hypoglycemic agents, antihypertensive medications, lipid-lowering agents, aspirin, or nonsteroidal anti-inflammatory drugs. The enrollment period was from December 2003 to July 2011. The eligibility criteria included the following: (1) subjects 50 years of age and older who had not undergone a CRC screening test at the first visit; (2) available baseline anthropometric measurements and laboratory data including fasting blood sugar, triglyceride, and cholesterol levels; and (3) documented baseline and follow-up colonoscopy. Only subjects who met the earlier-described criteria during the study period were enrolled for analysis.

Subjects with invasive cancer diagnosed at baseline colonoscopy were excluded from the analyses, and these patients were advised to follow the postoperative surveillance guidelines.

Colonoscopy

The colonoscopy procedure at the National Taiwan University Hospital has been described in detail previously.[15] The size and location of all detected neoplasms were recorded and stored in a central database. Any neoplastic lesion detected at any colonoscopy was resected endoscopically as indicated. Invasive cancers were managed surgically as indicated. We recommended surveillance intervals based on the current guidelines.[7]

Definition

Occurrence of a neoplasm. Histology of colorectal neoplasm was classified according to the World Health Organization classification.[16] An advanced neoplasm was defined as a lesion larger than 10 mm, or with a villous component or high-grade dysplasia, or invasive cancer.

The occurrence of a neoplasm includes both recurrent and incident neoplasms. Recurrent neoplasm was defined as at least 1 neoplasm detected at a surveillance colonoscopy in subjects who had any neoplasm resected at the baseline colonoscopy. Incident neoplasm was defined as at least 1 neoplasm detected at surveillance colonoscopy in subjects who had a negative baseline colonoscopy.

Metabolic syndrome. MetS was defined according to the modified National Cholesterol Education Program