Higher serum uric acid levels and advanced age are associated with an increased prevalence of colorectal polyps

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Abstract. The present study retrospectively analyzed the laboratory data of patients who had undergone a colonoscopy between April 2011 and March 2014, with the aim of assessing whether these variables could be used to predict the presence of colorectal polyps (CP). A total of 1,471 patients were enrolled (731 men, 68.5±10.8 years; 740 women, 66.7±10.8 years). One-way analysis of variance was performed to analyze the association between the presence of CP and a range of laboratory variables. Logistic regression analysis was performed to establish a regression equation to predict the presence of CP. Receiver-operator characteristic analysis was applied to investigate the performance of the regression equation. Patients with CP were older than those without CP (P<0.0001). Serum uric acid (UA) levels were higher in patients with CP, compared to those without CP (P=0.0007). To investigate the possibility that older age and higher UA levels could predict the presence of CP, logistic regression analysis was performed (P=0.0008). The regression equation was as follows: ln(p/1 - p) = 2.79015 - 0.01836 x age - 0.28542 x UA (mg/dl), where p indicates the presence of CP. Receiver-operator characteristic analysis showed the area under the curve to be 0.62092 and the threshold value of P was 0.4370. Sensitivity and specificity of the threshold value were 77.6 and 44.2%, respectively. Advanced age and higher serum UA levels were associated with the presence of CP. In conclusion, logistic regression analysis obtained a regression equation that predicted the presence of CP with a higher sensitivity, but poorer specificity, compared to fecal occult blood testing.

Introduction

Colorectal cancer is frequently encountered in clinical practice (1). Long-term surveillance indicates that the majority of colorectal cancers arise from colorectal polyps (CP) (2). Polypectomy reduces the risk of fatality from colorectal cancer (3,4). Screening using colonoscopy has also been shown to reduce the risk of colorectal cancer-related fatality (5,6). However, colonoscopy is not available to all populations or patients, as it requires a skilled operator and therefore is associated with a significant cost (7). As colonoscopy is a limited resource, screening methods are required to select patients to undergo the procedure.

Fecal occult blood testing is widely available and reduces mortality from colorectal cancer (8). Fecal occult blood testing is useful for the diagnosis of advanced colorectal cancer (9); however, such an advanced cancer would not be amenable to polypectomy and therefore fecal occult blood testing is not suitable for the detection of patients with CP (10).

It is recommended that laboratory tests are completed prior to subjecting a patient to a colonoscopy, as this practice is associated with reduced rates of complications and lower costs (11). A correlation between laboratory test results and the presence of CP, however, has not been reported.

The rate of CP detection is 37% for surveillance colonoscopy and 25% for screening (12). Kim et al (13), in an analysis of risk factors for CP, reported that CPs were identified in 47% of patients who underwent colonoscopy. The authors analyzed the association of CP with total cholesterol (T-Chol), triglycerides (TG), high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol levels. In a similar study, Huang et al (14) analyzed the association between CP and TG, HDL cholesterol, LDL cholesterol and glycated hemoglobin (HbA1c). These two studies concluded that the presence of CP is associated with metabolic risk factors. Therefore, it is expected that laboratory variables may be correlated with the presence of CP. The present study investigated whether laboratory variables are useful for predicting the presence of CP.

Materials and methods

Patients. Patient records for the period between April 2011 and March 2014 were analyzed retrospectively. A total of
1,520 patients underwent colonoscopy during this period. The majority of colorectal cancers arise from CP, which progress via the adenoma-carcinoma sequence (15). In rare cases, de novo colorectal cancers occur (16) and it can sometimes be hard to distinguish between the adenoma-carcinoma sequence and de novo carcinogenesis. Patients with colorectal cancer (n=49) were therefore excluded from the analysis, leaving 1,471 eligible patients; 731 men (mean age, 68.5±10.8 years) and 740 women (mean age, 66.7±10.8 years). The study was submitted to the institutional ethical committee at the National Hospital Organization, Shimoshizu Hospital (Yotsukaido, Chiba, Japan) and assigned as not a clinical trial, since it was performed as part of routine clinical practice. Patient anonymity was preserved.

Colonoscopy. Colonoscopy was performed for patients with abdominal symptoms, anemia or a positive fecal occult blood test result. Colonoscopy was also performed for screening. The colonoscopes used were CF-Q260 and PCF-Q260AI (Olympus, Tokyo, Japan). The withdrawal time of colonoscopy ranged from 10 to 30 min. The diameter of the smallest polyps detected was 2 mm.

Laboratory variables. The variables analyzed as potential predictors of CP included white blood cell count, hemoglobin, C-reactive protein, platelet count, total protein, albumin, total bilirubin, alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase, lactate dehydrogenase, uric acid (UA), blood urea nitrogen, creatinine, total cholesterol, triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, blood glucose, HbA1c, carcinoembryonic antigen, carbohydrate antigen 19-9, body mass index, and BMI.

Statistical analysis. One-way analysis of variance (ANOVA) was performed to analyze the association between each variable and the presence of CP. The mean UA level was analyzed, according to age group, with one-way ANOVA. A χ² test was also performed to analyze the correlation between the percentage of patients with UA >7 mg/dl and CP prevalence. The χ² test was applied to investigate the performance of the regression equation. P<0.05
was considered to indicate a statistically significant difference. JMP 10.0.2 (SAS Institute Inc., Cary, NC, USA) was used for statistical analysis.

Results

Associations between laboratory variables and presence of CP. The associations between each laboratory test variable and the presence of CP is presented in Table I. Not all the patients were subjected to each laboratory test. Patients with CP were of a more advanced age compared to those without CP (P<0.0001). Serum UA levels were higher in patients with CP, compared with those without CP (P=0.0007). These results suggest that age and UA level were strongly associated with the presence of CP; these variables were chosen for further analysis.

Association between age and prevalence of colorectal polyps (CP). The association between the percentage of patients with CP and age is illustrated in Fig. 1; the presence of CP increased with age. This association was statistically significant (P=0.0001) (Table II). The number of patients in their 20s and 90s were 3 and 5, respectively. As these ages were significantly fewer in number compared with the other age groups, these patients were omitted from further analysis.

Serum UA level and the presence of CP. The serum UA level was correlated with the presence of CP; however, there was a possibility that this association was confounded by an association of UA level with age. Fig. 2 indicates that there was no association between a higher UA level and age.

The χ² test confirmed an absence of correlation between UA level and age (P=0.6279).

The above data indicated that the presence of CP correlated with aging and UA. To investigate the possibility that age and UA level could predict the presence of CP, logistic regression analysis was performed (P=0.0008) (Table III). The regression equation was as follows: ln(p/1 - p) = 2.79015 - 0.01836 x age - 0.28542 x UA level (mg/dl), where p represents the presence of CP.

The likelihood ratio χ² test showed a P-value for age and UA level of 0.1083 and 0.0011, respectively, indicating a strong correlation between UA level and the presence of CP.

Receiver-operator characteristic analysis. To investigate how well the regression equation predicted the presence of CP, receiver-operator characteristic analysis was applied (Fig. 3).
The area under the curve was 0.62092. The threshold value of P was 0.4370, and the sensitivity and specificity of the threshold value were 77.6 and 44.2%, respectively.

Discussion

Previous investigations into the correlation between laboratory test results and the presence of CP have focused on components of metabolic syndrome (17), and the literature regarding the association between UA level and the presence of CP is limited. Orannapalai et al (18) analyzed the correlation between laboratory test results and the presence of CP. Patients were divided into 2 groups, based on UA level; >7 and ≤7 mg/dl. The presence of CP was higher in the group with a UA level of >7 mg/dl. In the present study, the average level of UA was higher in patients with CP compared with patients without CP, which is consistent with the results of the previous report. The underlying reason for this association is unknown. Notably, Karaman et al (19) found that the average UA level was higher in patients with neoplastic CP, as compared to those with non-neoplastic CP. Patients with a higher UA level are also prone to cancer of the colon, liver and lung (20). These results suggest that a raised serum UA level may be involved in tumorigenesis (21).

There is limited information available on the CP predictors. Eisner et al (22) performed urinary metabolomics in search of such a predictor and reported that nicotinate and nicotinamide metabolites and the degradation of ketone bodies are associated with the presence of CP. They proposed a tool involving the use of urinary metabolomics to select patients at risk of CP, who would undergo further investigation with colonoscopy. The performance of this tool is more efficient than that of fecal occult blood testing. In the present study, age and UA level were associated with the presence of CP. It has previously been reported that advanced age is associated with the presence of CP (23). UA levels are also higher in patients with CP, as discussed above. The present data are therefore consistent with previous reports. Fecal occult blood testing is intended to select patients with colorectal cancer, rather than pre-cancerous CP (24). Eisner et al (22) analyzed fecal occult blood testing as a tool for the detection of CP. Fecal occult blood testing has been shown to have a sensitivity of 2.6-15.1% and a specificity of 94.5-99.4%. In terms of the detection of CP using UA level, the present regression equation showed a greater sensitivity, but a poorer specificity.

In conclusion, advanced age and higher serum UA levels are associated with the presence of CP. Logistic regression analysis obtained a regression equation with a greater sensitivity and poorer specificity for the detection of CP, compared with fecal occult blood testing.

References