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Journal of the Chinese Medical Association xx (2018) 1−7

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Original Article

The factors associated with negative colonoscopy in screening subjects with positive immunochemical stool occult blood test outcomes

Po-Hsiang Ting [a,c], Xi-Hsuan Lin [a,c], Jeng-Kai Jiang [b,e], Jiing-Chyuan Luo [a,c,*], Ping-Hsien Chen [a,d], Yen-Po Wang [a,d], I-Fang Hsin [a,d], Chin Lin Perng [a,c,d], Ming-Chih Hou [a,c], Fa-Yauh Lee [a,c]

[a] *Department of Medicine, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC*
[b] *Department of Surgery, National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC*
[c] *Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[d] *Endoscopic Center for Diagnosis and Therapy, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[e] *Division of Colorectal Surgery, Department of Surgery, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*

Received August 3, 2017; accepted November 14, 2017

Abstract

Background: The immunochemical fecal occult blood test (iFOBT) is an alternative method to colonoscopy that can be used for colorectal cancer (CRC) screening. If the iFOBT result is positive, a colonoscopy is recommended. In this retrospective study, we identify factors associated with negative colonoscopy and positive iFOBT results obtained during CRC screening.
Methods: We collected data for subjects who received a colonoscopy at Taipei Veterans General Hospital after receiving a positive iFOBT result during CRC screening from January 2015 to December 2015. Subjects' baseline data, medications, and co-morbidities as well as colonoscopy and histological findings were recorded. A negative colonoscopy result was defined as no detection of any colorectal neoplasia including non-advanced adenoma, advanced adenoma, and adenocarciona. Multivariate logistic regression analysis was conducted to identify the associated factors in screening subjects with positive iFOBT but negative colonoscopy results.
Results: 559 (46.3%) out of 1207 eligible study subjects received a colonoscopy with a negative result. Multivariate logistic regression analysis revealed that the use of antiplatelets [odds ratio (OR) = 0.654; 95% confidence interval (CI), 0.434−0.986], occurrence of hemorrhoid (OR = 0.595; 95% CI, 0.460−0.768), and the existence of colitis/ulcer (OR = 0.358; 95% CI, 0.162−0.789) were independent factors associated with negative colonoscopy but positive iFOBT results during CRC screening. The colon clean level, underlying diseases of gastrointestinal bleeding tendency (e.g., chronic kidney disease, cirrhosis), and the use of anticoagulant or nonsteroidal anti-inflammatory agents were not associated with negative colonoscopy and positive iFOBT results.
Conclusion: The use of antiplatelet agents and the presence of hemorrhoids and colitis/ulcers were factors associated with negative colonoscopy and positive iFOBT results.

Keywords: Antiplatelet agents; Colonoscopy; Colorectal neoplasia; Hemorrhoid; Immunochemical fecal occult blood test

1. Introduction

The incidence and mortality related to colorectal cancer (CRC) is rising in Asia.[1] The detection and removal of pre-cancerous lesions through CRC screening with colonoscopy can reduce CRC incidence and mortality.[2] However, previous

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Dr. Jiing-Chyuan Luo, Division of Gastroenterology and Hepatology, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC.
E-mail address: jcluo@vghtpe.gov.tw (J.-C. Luo).

https://doi.org/10.1016/j.jcma.2017.11.015

studies showed significantly lower adherence to colonoscopy compared with the fecal occult blood test (FOBT) during CRC screening.[3] The immunochemical fecal occult blood test (iFOBT), which is differentiated from the guaiac FOBT (gFOBT), is a valid and alternative method to colonoscopy in CRC screening.[4,5] If the iFOBT result is positive, a colonoscopy is recommended.[6] Though a meta-analysis study showed that iFOBTs are moderately sensitive, highly specific, and have high overall diagnostic accuracy for detecting CRC,[7] some false-positive results exist. Therefore, some risk factors and scoring systems − with or without iFOBT − have been established to increase the accuracy of advanced neoplasia detection during screening.[8−10] Age, personal history of colon adenomatous polyp and inflammatory bowel disease, family history of CRC, smoking, lack of physical activity, and obesity are all risk factors for CRC.[11] Previous studies have also shown that age, male gender, current or past smoking status, personal history of colon adenoma, and metabolic syndrome (MS) were associated with colorectal neoplasia.[12−14] However, only some studies have evaluated the predictors of negative colorectal neoplasia by colonoscopy in screening subjects with positive iFOBT results,[15] and few studies considered whether hemorrhoid or underlying co-morbidities comprise a confounding factor for positive iFOBT results.

In this study, we tried to identify the factors associated with negative colonoscopy results after positive iFOBT outcomes during CRC screening.

2. Methods

The iFOBT test has been used for CRC screening in Taiwan since 2003. Most of the screening subjects in this study who were 50−75 years old were included in the national CRC screening program. The program was directed by the Health Promotion Administration, Ministry of Health and Welfare of Taiwan. Some of the screening subjects in this study received their CRC screening from their physician's clinical practice at outpatient clinics. No specific diets or medications were restricted in screening subjects. All fecal samples were analyzed at a single central laboratory (Taipei Veterans General Hospital, Taipei, Taiwan), and the iFOBT was processed without rehydration using an automated reading technique (HM-Jack, Kyowa, Japan). The positivity cut-off value was set at $\geq$ 12 ng Hb/mL buffer according to the results of a pilot trial in a CRC screening setting.[16] A colonoscopy was recommended to subjects with positive iFOBT results.

We retrospectively collected the data of subjects who were given a colonoscopy at the Endoscopy Center for Diagnosis and Treatment of Taipei Veterans General Hospital due to a positive iFOBT result during CRC screening from January 2015 to December 2015. This study has been approved by the Institutional Review Board (IRB) of Taipei Veterans General Hospital (No: 2016-08-020BC), a tertiary medical center that provides medical services for part of the million habitants living in northern Taiwan. The following information were gathered for all of the subjects: age; gender; smoking behavior (current, past, ever smoking, or non); alcohol drinking (80 g or more weekly)[17]; family history of CRC defined as having one or more first-degree relatives with a previous diagnosis of CRC[8]; current medications (taking them regularly within 2 weeks before iFOBT) including antiplatelets (aspirin, clopidogrel, ticlopidine), nonsteroidal anti-inflammatory drugs (NSAIDs) including cyclooxygenase-2 inhibitors, anticoagulants (warfarin, dabigatran, and rivaroxaban), steroids, selective serotonin reuptake inhibitors (SSRIs), dipyridamole, and bisphosphonates; underlying co-morbidities including hypertension, diabetes mellitus (DM), cirrhosis, chronic kidney disease (CKD) (baseline serum creatinine >1.5 mg/dl or estimated glomerular filtration rate <60 ml/min/1.73 m^2),[18] coronary artery disease, heart failure, peptic ulcer disease, and chronic obstructive pulmonary disease (COPD). Subjects who had past history of colorectal polyps after polypectomy, history of CRC, clinical symptoms of gastrointestinal (GI) bleeding, and with a known pre-existing pathology that could account for a positive FOBT result—for example, underlying colorectal neoplasia, inflammatory bowel disease, hematuria, and menstruation at the time of stool sample collection for the iFOBT and who had incomplete data collection including regarding the colonoscopy were excluded.

The laxative Klean-Prep® (containing polyethylene glycol 59.0 g, sodium sulphate 5.68 g, sodium bicarbonate 1.68 g, NaCl 1.46 g, potassium chloride 0.74 g and aspartame 0.04 g) was used for bowel preparation before colonoscopy.[19,20] Colonoscopy (CF-H260 AZI and CF-H290 AZI; Olympus, Tokyo, Japan) was performed by experienced gastroenterologists and colorectal surgeons. The withdrawal time was at least 6 min to minimize any chance of missing lesions. Detailed colonoscopic findings including angiodysplasia, diverticula, hemorrhoid, inflammation/ulcer, size and morphology of the neoplastic lesions (polypoid and non-polypoid, Paris classification), their numbers and location as well as cecal or terminal ileal intubation and colon clean level were recorded.[20] Experienced pathologists confirmed the diagnosis of hyperplastic polyp, adenomatous polyp (tubular, tubulovillous, villous, sessile adenoma), advanced adenoma, or adenocarcinoma after reviewing the histologic examination. Advanced adenoma was defined as adenoma size >10 mm, with villous or tubule-villus architecture, or with high-grade dysplasia.[19] Advanced neoplasia included advanced adenoma and adenocarcinoma.The location of the adenoma/neoplasia was regarded as distal if a single lesion (non-advanced adenoma, advanced adenoma, or adenocarcinoma) or the major lesion (in the case of multiple lesions) was found from the rectum to the splenic flexure. The location was regarded as proximal if the single lesion or the major lesion (in the case of multiple lesions) was found proximal from the splenic flexure. If subjects exhibited non-advanced adenoma at both sides without advanced neoplasia or advanced adenoma at both sides without adenocarcinoma, we defined that they had both side lesions. Colon preparation was scored by the Boston bowel preparation scale (BBPS) ranging from 0 to 9; good clean was defined as BBPS score $\geq$ 5 and poor clean was defined as BBPS score < 5.[20] A negative colonoscopy result was defined as no detection of any colorectal neoplasia including non-advanced adenoma,

Please cite this article in press as: Ting P-H, et al., The factors associated with negative colonoscopy in screening subjects with positive immunochemical stool occult blood test outcomes, Journal of the Chinese Medical Association (2018), https://doi.org/10.1016/j.jcma.2017.11.015