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Research Article

Are Upper Gastrointestinal Endoscopies Necessary in Patients who have a Negative Colonoscopy but a Positive Fecal Occult Blood Test?

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Abstract

There is currently no recommendation regarding the necessity of performing colonoscopy in asymptomatic patients with positive fecal occult blood test and negative colonoscopy. A person performs an endoscopy. Patient records, endoscopic records and pathology reports were reviewed. Occult upper gastrointestinal bleeding was diagnosed in 67 patients (13%), and the most common cause was peptic ulcer (8%). Four patients were diagnosed with lung cancer and one patient was diagnosed with lung cancer. Additionally, 74 patients (15%) had lesions that were not considered occult bleeding; The only variable associated with identifying significant disease was anemia (multivariable odds ratio = 5.0; 95% confidence interval, 2.9 to 8.5; P < 0.001). The proportion of asymptomatic patients was found to be significant. Our data show that endoscopic evaluation of the gastrointestinal tract should be considered, especially in patients with diabetes.

Introduction

Colon cancer is the second leading cause of cancer in the United States (1). In 1998, approximately 130,000 new cases of cancer were diagnosed and 57,000 patients died from the disease (1). Recent studies have provided convincing evidence that annual screening with fecal occult blood tests reduces the risk of colon cancer (2,3,4). The American Cancer Society recommends that patients at average risk of colon cancer undergo an annual fecal occult blood test and sigmoidoscopy starting from the age of 50 and every 5 years (5). Colonoscopy is often the first diagnostic procedure in asymptomatic patients whose fecal occult blood test is shown to be positive during screening (6). A fecal occult blood test will be marked "inconclusive" when the source of occult bleeding cannot be determined on colonoscopy. Only a few studies have examined the diagnosis of upper endoscopy in patients with a positive fecal occult blood test (7 , 8 , 9 , 10 , 11 , 12), and only one of these studies focused on upper endoscopy in completely asymptomatic patients. Findings (9).

The aim of this study is to determine the predictive value of a positive fecal occult blood test for bowel pathology after negative colonoscopy in a large group of asymptomatic patients with cancer risk and

determination. Which patient and clinical characteristics are associated with the lesions detected in upper gastrointestinal endoscopy.

Methods

Patients

We identified consecutive asymptomatic patients under age 50 at high risk for colon cancer who tested positive for fecal occult blood at colon cancer screening and were referred to Bell over a 5-year period (January 1992). Patients with documented or suspected iron deficiency were excluded from the study. Iron deficiency data is defined as saturation change <15% or ferritin <20 μg/L. In the absence of iron deficiency studies, we use the mean corpuscular volume available for each patient (mean body volume) to exclude patients with suspected iron deficiency. <80 fl). Additionally, we did not include all patients with abdominal signs or symptoms determined by reviewing the patient's disease, health advice to drink clean, and record data at the time of endoscopy. All patients were evaluated by a gastroenterologist before each endoscopic procedure. Intermediate-risk patients were defined as individuals with no previous history of colon or rectal cancer and no family history of colon cancer or gastrointestinal disease. Since there was no bleeding event in the large intestine (adenocarcinoma or adenoma ≤1 cm) among these patients, we identified patients diagnosed with upper gastrointestinal disease. The decision to perform upper gastrointestinal endoscopy is at the discretion of the endoscopist. Colon endoscopy is not routinely performed on asymptomatic patients with occult bleeding detected during colonoscopy.

Data Collection

Data were collected by reviewing endoscopic records, patient files and pathology reports. Age, gender, race, patient location (inpatient vs. outpatient), comorbidities, history of peptic ulcer disease, history of gastrointestinal bleeding, alcohol consumption, aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), anticoagulants, and smoking. We took it into consideration. and diabetes. Comorbidity was defined as any of the following: heart disease (congestive heart failure, recurrent angina, or endocarditis), lung disease (pneumonia, pulmonary embolism, or chronic obstructive pulmonary disease), liver disease (hepatic or liver or cirrhosis), renal. disease (serum creatinine > 2 mg/dL), neurological disease (meningitis or deficient central nervous system disease), metastatic cancer, or bacterial or fungal infection. Anemia is defined as heme level

<14 g/dL in men and <12 g/dL in women. Testing for fecal occult blood was performed by testing fecal samples or feces obtained during digital rectal examination without backwashing using the Hemocult II test. The presence of occult blood is confirmed by positive examination of at least one slide.

Endoscopy

Upper endoscopy was performed by gastroenterology fellows with an experienced faculty member in attendance. Informed consent was obtained from all patients. All endoscopic abnormalities were noted and biopsied multiple times. No complications directly related to endoscopy were noted. Lesions that were considered to be a source of occult upper gastrointestinal blood loss included erosive esophagitis, gastritis or duodenitis, gastric or duodenal ulcers ≥1 cm, carcinoma, gastric polyps ≥1 cm, and multiple vascular ectasias. Clinically important lesions included gastric polyps ≥1 cm, gastric cancer, and esophageal carcinoma. Hiatal hernias and esophageal varices were not considered a source of gastrointestinal blood loss. Ulcer size was estimated using the open-forceps technique.

Statistical Analysis

Continuous variables were compared using the Student's t test or a nonparametric test, as appropriate. Categorical variables were compared using Fisher's exact test. Multivariate analysis was performed using forward stepwise logistic regression to determine which patient and clinical characteristics were associated with having a source of occult bleeding identified by upper endoscopy. Continuous data are expressed as mean ± SD. A two-tailed P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 7.5 for Windows (SPSS Inc, Chicago, Illinois).

Results

During the 5-year study period, approximately 1,100 patients were evaluated by colonoscopy for a positive fecal occult blood test. Among these, 672 were asymptomatic patients at average risk for colorectal cancer, 538 (80%) of whom did not have a clinically important neoplasm (adenocarcinoma or adenoma ≥1 cm) identified by colonoscopy. Of these 538 patients, 498 (93%) were evaluated by upper endoscopy. There were no significant differences between the 498 patients who underwent upper endoscopy and the 40 individuals

who did not with regard to age; race; inpatient status; comorbid disease; history of peptic ulcer disease or gastrointestinal hemorrhage; use of alcohol, NSAIDs, aspirin, or anticoagulants; smoking; or anemia.

Slightly more men than women underwent upper endoscopy (Table 1). A majority of the patients underwent endoscopy as outpatients. Fecal occult blood was tested in spontaneously passed stools in 288 patients (58%); the remaining 210 patients (42%) had fecal occult blood testing following a digital rectal examination.

Table 1: Characteristics of the 498 Asymptomatic Patients with Positive Fecal Occult Blood Tests and Negative Colonoscopy Who Were Evaluated by Upper Endoscopy

Characteristic	**Number (percent) or Mean ± SD**
Age	62.8 ± 9.5
Male sex	272 (55)
Race	-
Hispanic	148 (30)
Caucasian	140 (28)
Black	88 (18)
Asian	81 (16)
Other	41 (8)
Outpatient	442 (89)
Comorbid illness	98 (20)
Prior peptic ulcer disease	33 (7)
Prior upper gastrointestinal bleed	14 (3)
Prior lower gastrointestinal bleed	10 (2)
Alcohol use	61 (12)
NSAID or aspirin use	122 (24)
Anticoagulant use	32 (6)
Current smoker	119 (24)
Anemia	133 (27)

A source of occult upper gastrointestinal bleeding was found in 67 patients (13%), with clinically important lesions noted in 12 patients (2%). Duodenal and gastric ulcers were the most common lesions identified (Table 2). Four patients had gastric carcinomas and 1 had an esophageal carcinoma. Of these 5 patients, 1 patient with a gastric carcinoma had evidence of metastatic disease on computerized tomographic (CT) scan of the abdomen. One of the gastric cancers was early (stage 1); the remaining two gastric cancers and the esophageal cancer were more advanced (stage 2). In the 7 patients with gastric polyps ≥1 cm, 4 were hyperplastic and 3 were adenomatous.

Table 2: Distribution of 67 Upper Gastrointestinal Tract Lesions Identified by Endoscopy

Lesion	Number Percent
Duodenal ulcer ≥1 cm	25 (5)
Gastric ulcer ≥1 cm	15 (3)
Multiple vascular ectasias	9 (2)
Gastric polyp ≥1 cm	7 (1)
Erosive gastritis	4 (1)
Gastric cancer	4 (1)
Erosive duodenitis	2 (0.4)
Esophageal cancer	1 (0.2)

The diagnostic yield of upper endoscopy in patients who had a positive fecal occult blood test obtained by digital rectal examination was no different from that obtained by testing spontaneously passed stools (15% vs 12%; P = 0.35).

Seventy-four patients (15%) had other types of abnormalities noted in the upper gastrointestinal tract. These findings included nonerosive gastritis (n = 26), nonerosive duodenitis (n = 16), gastric or duodenal ulcers <1 cm (n = 10), nonerosive esophagitis (n = 9), Barrett's esophagus (n = 6), nonbleeding esophageal varices (n = 5), and gastric polyps <1 cm (n = 2). These findings prompted a change in clinical management in 56 patients (11%).

We compared the demographic and clinical characteristics of patients with and without a clinically important upper gastrointestinal lesion (Table 3). Anemia was the only variable that was significantly associated with

having a clinically important lesion identified by upper endoscopy (multivariate odds ratio = 5.0; 95% confidence interval, 2.9 to 8.5; P <0.001).

Table 3: Comparison of Patients with and without a Clinically Important Upper Gastrointestinal Lesion

	Lesion (N = 12) Number (percent) or Mean ± SD	**No Lesion (N = 486) Number (percent) or Mean ± SD**	***P* Value**
Age (years)	64.3 ± 10.6	62.8 ± 9.5	0.58
Men	8 (67)	264 (54)	0.56
Outpatient	11 (92)	431 (89)	1.0
Comorbid illness	2 (17)	96 (20)	1.0
Prior peptic ulcer disease	1 (8)	32 (7)	0.57
Prior upper gastrointestinal bleed	0 (0)	14 (3)	1.0
Prior lower gastrointestinal bleed	0 (0)	10 (0)	1.0
Alcohol use	3 (25)	58 (12)	0.17
NSAID or aspirin use	3 (25)	119 (24)	1.0
Anticoagulant use	2 (17)	30 (6)	0.17
Smoker	3 (25)	116 (24)	1.0
Anemia	8 (67)	125 (26)	0.004

Duodenal and gastric ulcers were significantly more common in patients with anemia than in those who were not anemic (Table 4). Overall, the diagnostic yield of upper endoscopy was significantly greater in anemic patients than in those in whom anemia was absent (29% vs 8%, P <0.001).

Table 4: Comparison of the Lesions Identified in Patients with and without Anemia

	Anemia (N = 133) Number (percent)	**No Anemia (N = 365) Number (percent)**	**P value**
Duodenal ulcer ≥1 cm	14 (11)	11 (3)	0.002
Gastric ulcer ≥1 cm	9 (7)	6 (2)	0.006
Multiple vascular ectasias	5 (4)	4 (1)	0.06
Gastric polyp ≥1 cm	4 (3)	3 (1)	0.09
Erosive gastritis	2 (2)	2 (1)	0.29
Gastric carcinoma	3 (2)	1 (0.3)	0.06
Erosive duodenitis	1 (1)	1 (0.3)	0.46
Esophageal carcinoma	1 (1)	0	0.27
Total	39 (29)	28 (8)	<0.0001

Discussion

Hemoccult II is the fecal occult blood test that is most widely used to screen for colorectal cancer (6, 13, 14). This guaiac-based test detects the pseudoperoxidase activity of hemoglobin (14). Two slides are prepared from two sites on each of three successive stool samples, and a positive test is defined as one or more slides with a blue-color reaction within 30 to 60 seconds after the addition of developing solution (14). The procedure of obtaining multiple stool samples from multiple sites stems from the belief that colorectal neoplasms may bleed only intermittently and that the blood may not be evenly distributed throughout a bowel movement, thereby making the sensitivity of any single fecal occult blood test low (6). In addition, the bleeding patterns of colorectal neoplasms are thought to be related to the size and location of the lesion, again limiting the sensitivity of fecal occult blood testing (15). Estimates of the sensitivity of Hemoccult II range from 22% to 92% for asymptomatic neoplasms, with the wide range of estimates reflecting different study designs and whether the test was rehydrated (6, 14, 16, 17).

The specificity of Hemoccult II is also limited by dietary factors and medication use. Several foods, such as red meat, as well as fresh fruits and vegetables that have peroxidase activity (eg, turnips and horseradish), can cause a false-positive guaiac test (6). In addition, such medications as aspirin and other NSAIDs can act as gastrointestinal irritants, leading to a positive fecal occult blood test (6). Estimates of the specificity of Hemoccult II range from 88% to 98% for asymptomatic colorectal neoplasms (6, 14, 17, 18, 19). Thus, as many as 12% of positive fecal occult blood tests may be "false-positives," leading to diagnostic procedures that are both expensive and not without risk.

There are no formal recommendations regarding further evaluation of the gastrointestinal tract after a negative colonoscopy in patients with a positive fecal occult blood test. Six previous studies have evaluated the yield of upper endoscopy in patients with a positive fecal occult blood test (7, 8, 9, 10, 11, 12). However, the results have not been consistent. Four studies found that upper endoscopy had a high diagnostic yield in these patients (8, 9, 10, 12). In contrast, one study recommended endoscopy only in patients with upper gastrointestinal symptoms (7) and a sixth study found no benefit of upper endoscopy (11). These differences may be explained by differences in the design of the studies as well as the patients evaluated. Furthermore, only three of these studies evaluated the role of upper endoscopy in patients with a positive fecal occult blood test after a negative colonoscopy (7, 9, 11).

To our knowledge, only one previous study has focused on the yield of upper endoscopy in completely asymptomatic patients with positive fecal occult blood test and negative colonoscopy (9). In that study, Hsia and Al-Kawas (9) prospectively evaluated 70 patients with upper endoscopy, excluding patients with symptoms of gastrointestinal disease, and found important upper gastrointestinal lesions in 19 patients (27%). Of these patients, 8 had peptic ulcer disease, 5 had arteriovenous malformations, 3 had esophageal or gastric varices, 2 had multiple erosions, and 2 had biopsy-proven Barrett's esophagus. The authors recommended that upper endoscopy be considered for all asymptomatic patients with occult bleeding and a negative colonoscopic examination.

In our study, we also found clinically important upper gastrointestinal pathology in asymptomatic patients. Of the 498 patients who underwent upper endoscopy, 67 (14%) had a source of occult gastrointestinal bleeding identified. Peptic ulcer disease was the most common lesion. In contrast to Hsia and Al-Kawas (9), who found no malignancies, we identified 4 patients with gastric cancer and 1 patient with esophageal carcinoma. In addition, 74 patients had abnormalities detected in the upper gastrointestinal tract that were not considered a cause of occult bleeding, and these findings prompted a change in clinical management in

56 patients.

In their study of 70 patients, Hsia and Al-Kawas (9) found the diagnostic yield of upper endoscopy to be 38% in patients with anemia and 25% in those without anemia. They concluded that there was no significant difference in the diagnostic yield of upper endoscopy between these two groups of patients (9). In contrast, we found that anemia was an independent predictor of having a clinically important upper gastrointestinal lesion (polyp ≥1 cm or carcinoma). The failure to detect a difference in the yield of endoscopy in the previous study may have been a result of the small number of patients evaluated. In our patients with anemia, the diagnostic yield of upper endoscopy was significantly greater than in those who were not anemic (29% vs 8%).

Overall, the frequency of upper gastrointestinal lesions in our study was lower than that reported by Hsia and Al-Kawas. This difference may be explained by the inclusion of patients with iron deficiency anemia in their study. We excluded patients with iron deficiency anemia, because the need for upper endoscopy after a negative colonoscopy in these patients is clear, and their inclusion would have overestimated the frequency of upper gastrointestinal lesions in asymptomatic patients. Interestingly, 94 (71%) of the 133 patients who were anemic did not have a source of occult bleeding identified by colonoscopy or upper endoscopy. In these patients, occult gastrointestinal bleeding may have been caused by a small bowel source or by a lesion that was missed by our endoscopic investigation. Alternatively, the positive guaiac test may have been falsely positive.

The utility of fecal occult blood testing obtained at the time of digital rectal exam is controversial. Some authors argue that obtaining stool for fecal occult blood testing by digital rectal examination leads to an increased number of false-positive results (20). In addition, the sensitivity of a single stool sample may be lower than that of multiple spontaneously passed stools (6, 20). In contrast, other studies have shown that screening for colorectal cancer at the time of digital rectal examination does not increase the rate of false-positive results and recommend that a single test result should prompt further diagnostic evaluation of the colon (12, 21, 22, 23). In our study, the diagnostic yield of upper endoscopy in patients who had a positive fecal occult blood test obtained by digital rectal examination was no different from that obtained by the traditional method of testing spontaneously passed stools (15% vs 12%).

Currently, screening for colorectal cancer is hampered by the limited sensitivity and specificity of the Hemoccult II test. New immunochemical tests, such as HemeSelect and FlexSureOBT (both from SmithKline Diagnostics, Inc., San Jose, California), that react with the globin portion of human hemoglobin

are available, thus reducing the number of tests that are false-positive as a result of dietary factors (6, 24, 25, 26). These tests are more specific for detecting bleeding from a colonic source, because hemoglobin from the upper gastrointestinal tract may be degraded before reaching the colon (26). A new combination approach to fecal occult blood testing, involving a guaiac-based test followed by confirmation with an immunochemical test, provides greater sensitivity and specificity than Hemoccult II alone (18, 25). If this method were widely implemented as a tool for colorectal cancer screening, clinically important upper gastrointestinal lesions that are currently picked up by the Hemoccult II test would remain undetected. Thus, although the number of "false-positive" tests would decrease, occult bleeding from the upper gastrointestinal tract would be missed.

This study is limited by its retrospective design. Not every patient at our hospital with a positive fecal occult blood test was referred for endoscopy. These patients may have been evaluated by barium enema or upper gastrointestinal series, may not have received any evaluation, or may have been lost to follow-up. In addition, it is possible that not all patients were completely asymptomatic. Although the gastroenterologists who evaluated the patients before endoscopy routinely asked all patients about abdominal symptoms, they may not have recorded every symptom in the consultation note. The inclusion of symptomatic patients would overestimate the diagnostic yield of endoscopy. These limitations emphasize the need for prospective studies to evaluate this important clinical problem.

Conclusion

We found clinically important upper gastrointestinal lesions in asymptomatic patients with a positive fecal occult blood test and a negative colonoscopy. An endoscopic evaluation of the upper gastrointestinal tract should be seriously considered in these patients, especially in those with anemia. Prospective studies are warranted to validate our findings.

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