

Advantages of Routine Upper-Gastrointestinal Endoscopy in Positive Fecal Occult Blood Tests with Negative Colonoscopy Results

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Background: Fecal occult blood test [FOBT] is a popular use for colorectal cancer screening. When positive results are found, colonoscopy is necessary to find pathologic lesion. However, in many patients, nothing can be identified in the colon or rectum. In this situation some surgeons prefer to perform bidirectional endoscopy to search for the source of the bleeding. Currently, there is no standard guideline or recommendation to support this, nor is there evidence against it.

Objective: To determine the predictive value of upper gastrointestinal pathology and benefits of routine use of esophago-gastroduodenoscopy [EGD] after negative colonoscopy in positive FOBT.

Materials and Methods: A retrospective medical records review between January 1, 2015 and December 31, 2016. All patients who had FOBT for screening colorectal cancer and positive results were included in the present study. Patients had undergone colonoscopy and EGD on the same day in the surgery unit and had negative finding in complete colonoscopy. The exclusion criteria were active gastrointestinal bleeding, pre-existing gastrointestinal disease, and previous gastrointestinal tract surgery.

Results: From the method, 185 patients with negative colonoscopy were enrolled. The mean age was 62.57 years. There were 145 females (78.38%) and 40 males (21.62%). In 160 patients who had pathological lesion from EGD, we found 117 cases (73.13%) with gastritis and no patients with gastric cancer. In 160 patients, there were 25 cases (15.63%) with dyspepsia. Of the 25 dyspepsia patients, there were 18 cases (69.23%) who had *Helicobacter pylori* infection.

Conclusion: EGD has a higher yield for diagnosing benign lesions, but not for gastric cancer, in FOBT-positive patients. Dual endoscopy may be cost effective in terms of early treatment and the reduced chance of future problems. In some patients, we diagnosed and eradicated *H. pylori*, therefore reducing the risk of gastric cancer.

Keywords: Esophagogastroscope, Negative colonoscopy, Fecal occult blood positive

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Fecal occult blood test [FOBT] is a convenient and low-cost procedure for screening colorectal cancer in general practice. The FOBT technique is well-known and used in many regions of Thailand. FOBT is highly sensitive for screening investigation, with up to 83.3% detection rate for all neoplasms in the colon and rectum^(1,2) but test results after 10 years of annual screening show 23.0% negative colorectal cancer⁽³⁾. However, when using fecal immunochemical test [FIT], results show more than 50% negative colonoscopy^(4,5). In cases of negative colonoscopy, surgeons who refer to false positive test results may actually just be unable

to identify the source of bleeding. Although no standard guidelines or recommendations use upper endoscopy for this situation, and some studies disagree with its use due to its low detection rate of gastric cancer⁽⁶⁾, some studies advocate its use for its high-detection yield for benign gastric disease that can then be treated appropriately^(7,8). Currently, there is no consensus for the routine use of upper endoscopy in this case⁽⁹⁾. Our study wants to determine the predictive value of upper gastrointestinal pathology and the benefits of the routine use of esophagogastroduodenoscopy [EGD] after negative colonoscopy in positive FOBT.

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Materials and Methods

We retrospectively reviewed data from medical records between January 1, 2015 and December 31, 2016, and this was approved by the ethical committee

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of The Faculty of Medicine, Ramathibodi Hospital, Mahidol University.

Patients

All patients had FOBT for screening colorectal cancer and positive results were included in the present study. Patients had undergone colonoscopy and EGD on the same day in the surgery unit and had negative finding in complete colonoscopy. We used the sedative technique by an endoscopist, with 2 to 5 mg of Midazolam and 20 to 50 mg of Pethidine in dual endoscopy. The exclusion criteria were active upper or lower gastrointestinal bleeding, pre-existing gastrointestinal disease, such as colitis, cancer etc, and previous gastrointestinal tract surgery, such as bariatric surgery, colectomy.

Fecal occult blood test

Ramathibodi Hospital used the immunochemical method for FOBT.

Endoscopy

We used EVIS EXERA III CV-190 Olympus in both colonoscopy and EGD. All endoscopies were performed by experienced surgeons. Complete colonoscopy was defined by cecum or terminal ileum intubation. Negative colonoscopy was defined by no visual evidence of abnormal lesion in the colon or rectum by the endoscopist. Esophagoduodenoscope was used with systematic screening protocol for the stomach [SSS]⁽¹⁰⁾.

Data collection

Results of endoscopic findings and pathological report were collected in the hospital database. The demographic data and subgroups were analyzed with Stata version 14.

Results

During this period, 2,629 patients had positive FOBT from screening colorectal cancer. Eight hundred ninety-four patients underwent colonoscopy with EGD in the same day and 529 patients did not meet the exclusion criteria. One hundred eighty-five patients had negative colonoscopy, and were included in our study (Figure 1) for analysis. The demographic data is shown in Table 1. The mean age was 62.57 years and hemoglobin 12.3 g/dL. There were 145 females and 40 males. There were 160 patients (86.49%) who had pathological lesion and 25 patients (13.51%) who had negative colonoscopy and normal EGD results. The

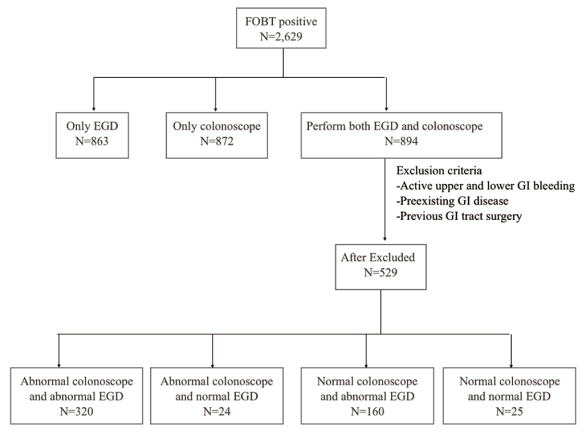


Figure 1. The methodology of study.

Table 1. Result of EGD and Colonoscopy in patients FOBT positive

Colonoscopy	EGD, n (%)		Total
	Abnormal	Normal	
Abnormal	320 (93.02)	24 (6.98)	344
Normal	160 (86.49)	25 (13.51)	185

EGD = esophagogastroduodenoscopy; FOBT = fecal occult blood test

Table 2. The demographic data of patients who had FOBT positive with negative colonoscopy

Diagnosis	n (%)
Total	185 (100)
Age (years), mean ± SD	62.57±13.05
Sex	
Female	145 (78.38)
Male	40 (21.62)
Hb (g/dL), mean ± SD	12.30±1.84

FOBT = fecal occult blood test; Hb = hemoglobin

Table 3. The detail of abnormal EGD finding when negative colonoscopy

Diagnosis	n (%)
Total	160 (100)
<i>Helicobacter pylori</i> positive	23 (14.37)
Gastritis (acute or chronic)	117 (73.13)
Gastric polyp	15 (9.38)
Gastric ulcer	14 (8.75)
Hiatal hernia	6 (3.75)
Duodenal ulcer	3 (1.86)
Duodenitis	2 (1.25)
Telangiectasis	1 (0.63)
GAVE	1 (0.63)
Esophageal web	1 (0.63)
Gastric cancer	0 (0.00)

EGD = esophagogastroscopy; GAVE = gastric antral vascular ectasia

Table 4. Symptom of EGD patients who had normal colonoscopy

EGD finding	Asymptomatic, n (%)	Dyspepsia, n (%)	Bowel habit change, n (%)	Anemia, n (%)	Weight loss, n (%)	Total, n (%)
Abnormal	107 (66.88)	25 (15.63)	10 (6.25)	14 (8.75)	4 (2.50)	160 (100)
Normal	17 (68.00)	0 (0.00)	2 (8.00)	4 (16.00)	1 (4.00)	25 (100)

EGD = esophagogastroduodenoscopy

Table 5. Pathologic proven for *H. pylori* infection in patients who had negative colonoscopy with symptom dyspepsia

Diagnosis	n (%)
Total	25 (100)
Positive for <i>H. pylori</i>	18 (69.23)
Negative for <i>H. pylori</i>	7 (26.92)

EGD pathological findings of 160 patients are shown in Table 2. We found 117 cases (73.13%) with gastritis, 15 cases (9.38%) with gastric polyp, 14 cases (8.75%) with gastric ulcer, six cases (3.75%) with hiatal hernia, three cases (1.86%) with duodenal ulcer, two cases (1.25%) with duodenitis, and one case each (0.63%) with telangiectasia, gastric antral vascular ectasia [GAVE], and esophageal web. There was no gastric cancer. Patients who were diagnosed with gastritis were tested by biopsy then send for pathological report.

In 160 patients who had pathological lesion we found the majority had no symptoms in clinical presentation (Table 3). There were 107 cases (66.88%) which had no symptoms, 25 cases (15.63%) with dyspepsia, 10 cases (6.25%) with bowel habit change, 14 cases (8.75%) with anemia, and 4 cases (2.5%) with weight loss (Table 4). The pathological report of 25 dyspepsia patients who had normal colonoscopy is shown in Table 5. Of the 25 dyspepsia patients, there were 18 cases (69.23%) who had *Helicobacter pylori* infection. However, from the 185, we found 23 patients (14.37%) who had *H. pylori* infection.

Three hundred forty-four patients from 529 were not included in our study due to finding lesions during colonoscopy (positive colonoscopy). We found 320 cases (93.02%) with pathological lesion in EGD. The diagnosis yields in upper gastrointestinal endoscopy after a positive FIT result, regardless of colonoscopy result, was 90.73%. In cases of positive FIT results with negative colonoscopy results the diagnostic yield was 86.48%.

Discussion

FOBT is used extensively in Thailand for screening colorectal cancer, due to its cost effectiveness and ease of use in rural areas. However, many reports found positive results, but colonoscopy could not identify

pathology in the colon or rectum^(4,5). This situation has led to the concept of bidirectional endoscopy (performing both EGD and colonoscopy)⁽¹¹⁾. However, there are no consensus or standard guideline recommendations to use EGD in cases of positive FOBT. Allard et al reported in a systematic review insufficient evidence for or against the recommendation of EGD in this condition⁽⁹⁾. Occasionally, endoscopists perform EGD in these situations to discover the source of occult bleeding in the stomach, especially for gastric cancer, but several reports disagree because gastric cancer is a rare condition in FIT-positive patients^(5,6,12,13). Ali et al⁽¹⁴⁾ reported dual endoscopy in 260 cases that had positive FOBT with negative colonoscopy. In the 260 cases, 16 (6.1%) had positive findings on EGD but none of these 16 cases had gastric cancer. He concluded that performing EGD after negative colonoscopy should be based on the clinical condition and risk factors of each patient. Hisamuddin et al⁽⁶⁾ reported 70 from 99 cases had positive FOBT with negative colonoscopy. He found 25 cases (36%) had abnormal EGD findings but no cases of gastric cancer. Some authors reported they can detect gastric cancer in dual endoscopy. Choi et al reported 3 cases (1.2%) with gastric cancer from EGD⁽⁸⁾. Zappa et al⁽⁵⁾ found the 4-times higher gastric cancer risk in FOBT-positive patients with negative colonoscopy. Beyond the oncologic outcome, numerous benign lesions in the upper gastrointestinal tract were found in dual endoscopy. Velez et al⁽¹⁵⁾, Choi et al⁽⁸⁾, and Ng et al⁽⁷⁾ advocated EGD in this scenario because we can treat benign conditions before they become advanced. We found that *H. pylori* infection in EGD is a risk factor of gastric cancer. Chronic gastritis can develop into intestinal metaplasia and lead to carcinoma in situ of stomach⁽¹⁶⁾. Both can be treated and need follow-up. In addition, EGD has a very low complication and mortality rate 0.004%^(17,18) and is not a difficult or time-consuming procedure. In our division, when we performed the dual procedure on patients they were sedated, but when only performing EGD, we used local anesthesia. This can cause some discomfort for the patient. Patients did not feel uncomfortable when we perform the dual procedure.

In our study, the aim was to find a conclusion of performing EGD in patients of positive FOBT with negative colonoscopy. From 529 patients included in the study, we found 185 patients with negative colonoscopy findings. In 160 patients (86.49%) we found lesions in EGD and the majority were gastritis (117, 73.13%), proven by pathological results. The pathological results of gastritis are subjective and depend on the pathologist. Although we did not find gastric cancer, we found *H. pylori* infection in 23 patients (14.37%), which is a risk factor in gastric cancer. Our study shows that we cannot use EGD in FOBT-positive patients for screening gastric cancer, but it has a higher yield in detecting benign conditions. The diagnosis yield is 90.73% for EGD in colonoscopies with both positive and negative results. In cases of positive FIT results with negative colonoscopy results the diagnostic yield was 86.48%. This study represents that dual endoscopy may be cost effective because it can reduce the cost of treatment before benign conditions become advanced, and EGD in Thailand is not expensive when compared to other countries. However, this study has limitations due to the study design and low study population. In the future, we hope our study can lead to randomized control trials to reduce our limitations.

Conclusion

From our study, the EGD has a higher yield for diagnosing benign lesions, but not for gastric cancer in FOBT-positive patients. Dual endoscopy may be cost effective in terms of early treatment and the reduced chance of future problems. In some patients, we diagnosed and eradicated *H. pylori*, therefore, reducing the risk of gastric cancer.

What is already known on this topic?

Many studies do not have any conclusion about the role of EGD after negative colonoscopy in FOBT-positive patients. Some studies encourage the use of EGD to identify early stages of gastric cancer. However, others do not agree with this type of diagnosis because gastric cancer is a rare condition and is not screened by fecal blood count.

What this study adds?

This study suggest that dual endoscopy should be done in patients who had FOBT positive because it is cost effective in terms of early treatment and it can reduce the chances of benign conditions becoming advanced. EGD in Thailand is not expensive when

compared to other countries.

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Potential conflicts of interest

None.

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ข้อดีของการส่องกล้องทางเดินอาหารส่วนบนในผู้ป่วยที่ตรวจพบเลือดในอุจจาระแล้วผลส่องกล้อง ทางเดินอาหารส่วนล่างปกติ

ชลลดา คุรุทศรี, ไชยรัตน์ ทรัพย์สมุทรชัย, ปิติโชติ หิรัญเทพ, พงศศิษฏ์ สิงห์ทัศน์, ธาวัน ธรรมพงษา, จักรพันธ์ จิริสิริธรรม

ภูมิหลัง: เนื่องจากการตรวจหาเลือดในอุจจาระเป็นวิธีที่นิยมใช้ในการคัดกรองมะเร็งลำไส้ใหญ่ในปัจจุบัน เมื่อผลตรวจเป็นบวก คือ พบเลือดในอุจจาระ ผู้ป่วยทุกรายควรได้รับการส่องกล้องตรวจลำไส้ใหญ่เพื่อหาสาเหตุ อย่างไรก็ตามมีผู้ป่วยจำนวนหนึ่งที่ได้รับการส่องกล้องตรวจลำไส้ใหญ่แล้วไม่พบความผิดปกติ จึงมักจะได้รับการส่องกล้องตรวจทางเดินอาหารส่วนบนร่วมด้วยเลยในวันเดียวกันเพื่อหาสาเหตุเพิ่มเติมของเลือดที่ตรวจพบในอุจจาระ ซึ่งในปัจจุบันยังไม่มีแนวทางที่สนับสนุนหรือคัดค้านอย่างชัดเจนในเรื่องนี้

วัตถุประสงค์: เพื่อศึกษาถึงความจำเป็นและประโยชน์ในการส่องกล้องตรวจทางเดินอาหารส่วนบนร่วมด้วย ในผู้ป่วยที่ตรวจพบเลือดในอุจจาระและผลส่องกล้องตรวจลำไส้ใหญ่ปกติ

วัสดุและวิธีการ: เก็บข้อมูลย้อนหลังจากประวัติผู้ป่วยที่ได้รับการตรวจเลือดในอุจจาระเป็นผลบวก และเข้ารับการส่องกล้องตรวจลำไส้ใหญ่และส่องกล้องตรวจทางเดินอาหารส่วนบนร่วมด้วยในวันเดียวกัน โดยที่ผลส่องกล้องตรวจลำไส้ใหญ่ปกติ โดยคัดผู้ป่วยที่มีโรคทางเดินอาหารอยู่เดิม เคยรับการผ่าตัดทางเดินอาหาร และกำลังมีเลือดออกในทางเดินอาหารออก ทำการเก็บข้อมูลทั่วไปและผลการส่องกล้องในช่วงวันที่ 1 มกราคม พ.ศ. 2558 ถึง 31 ธันวาคม พ.ศ. 2559

ผลการศึกษา: หลังจากได้ทำการคัดเลือกตามวิธีการศึกษาข้างต้นแล้วมีผู้ป่วย 185 ราย ที่พบผลส่องกล้องลำไส้ใหญ่เป็นปกติ โดยมีอายุเฉลี่ย 62.57 ปี เป็นเพศหญิง 145 ราย (78.38%) เพศชาย 40 ราย (21.62%) ในจำนวนนี้มี 160 ราย ที่พบผลการส่องกล้องทางเดินอาหารส่วนบนผิดปกติร่วมด้วย พบมีกระเพาะอาหารอักเสบ 117 ราย (73.13%) และไม่พบว่ามึะเร็งกระเพาะอาหารใน 160 ราย ที่ผลการส่องกล้องทางเดินอาหารส่วนบนผิดปกติ พบผู้ป่วยมีอาการจุกแน่นท้อง 25 ราย (15.63%) และมีการติดเชื้อ *Helicobacter pylori* 18 ราย (69.23%)

สรุป: ในผู้ป่วยที่ตรวจพบเลือดในอุจจาระและส่องกล้องตรวจลำไส้ใหญ่ไม่พบความผิดปกติ การส่องกล้องตรวจทางเดินอาหารส่วนบนจะให้ผลดีในการตรวจหาสาเหตุทั่วไป โดยเฉพาะกระเพาะอาหารอักเสบและการติดเชื้อ *H. Pylori* ซึ่งเป็นปัจจัยเสี่ยงสำคัญของมะเร็งกระเพาะอาหาร ดังนั้นการส่องกล้องลำไส้ใหญ่ร่วมกับส่องกล้องทางเดินอาหารส่วนบนในผู้ป่วยที่ตรวจพบเลือดในอุจจาระมีความคุ้มค่าในแง่ของการตรวจพบและให้การรักษาการติดเชื้อ *H. Pylori* ตั้งแต่เนิ่นเพื่อลดปัจจัยเสี่ยงหนึ่งของการเป็นมะเร็งกระเพาะอาหารได้