Original Article

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Evaluation of Gastrointestinal Lesions by Bidirectional Endoscopy in Thai Patients with Iron Deficiency Anemia

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ABSTRACT

Background: Occult bleeding from the gastrointestinal (GI) lesions is a common cause of iron deficiency anemia (IDA). The information concerning the prevalence and the appropriate strategy of GI evaluation in Thai IDA patients is scant. The aim of this study is to prospectively evaluate Thai patients with IDA for GI lesions with bidirectional endoscopy.

Method: One hundred and three consecutive patients with IDA were investigated by esophagogastroduodenoscopy (EGD) and colonoscopy. Any significant GI lesion was identified. Clinical data from history and physical examination and results of the fecal occult blood testing (FOBT) were collected to determine factors associated with the presence of GI lesions.

Results: The age of the 103 patients was 63.6 ± 15.2 years. Significant GI lesions were detected in 58 patients (56%), 43% from EGD, 25% from colonoscopy. Twelve patients (12%) had dual lesions from both EGD and colonoscopy. The most common lesions were peptic ulcers (22%) and colonic carcinoma (13%). Anti-platelet used and positive FOBT were associated with significant GI lesions, with odds ratios of 2.37 (95% CI 1.05-5.36, p = 0.036) and 2.83 (95% CI 1.05-7.68, p = 0.038), respectively. The sensitivity, specificity, PPV and NPV of FOBT for significant GI lesions were 81%, 40%, 68% and 66%, respectively. Site-specific symptoms correctly guided the route of endoscopy in only half of the patients.

Conclusion: The prevalence of GI causes of IDA in Thai patients as evaluated by bidirectional endoscopy is 56%. Peptic ulcers and colorectal cancer are the two most common causes. EGD has a higher yield than colonoscopy, and is the preferred initial endoscopy unless there are suggestive lower GI symptoms. Dual lesions are common. Bidirectional endoscopy is required in most patients unless cancer is detected by the initial endoscopy. No factors, including FOBT, can reliably predict the presence of GI lesions.

Key words : iron deficiency anemia, endoscopy, esophagogastroduodenoscopy, colonoscopy, bidirectional, fecal occult blood test

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INTRODUCTION

Iron deficiency anemia (IDA) is an important health problem worldwide. In patients without obvious causes of blood loss, the gastrointestinal (GI) tract is the most common site of occult blood loss, and the etiology can vary from benign to malignant diseases. Therefore, the standard work-up in patients with IDA is evaluation of GI tract for GI lesions. The British Society of Gastroenterology guideline[1] and the American Gastroenterology Association guideline[2] advocate both esophagogastroduodenoscopy (EGD) and colonoscopy based on evidences from many studies, which have shown that EGD could detect lesions in 28-56% (average 38%), colonoscopy 14-30% (average 24%) and dual lesions by both endoscopies in 0-29% (average 10%)[3-8]. However, there are remained some controversies.

The sequence of the endoscopy routes is a matter of debate. Some suggest using symptoms as a guide for the initial route of endoscopy[6], whereas others and most guidelines conclude that symptoms are not predictive[1,2,5]. In the absence of site-specific symptom, some have advised starting with colonoscopy[2], while some prefer EGD[1].

In Thailand, there have been 2 studies investigating the causes of GI tract lesions in patients with IDA. In a study by Ovartlarnporn[9], 44 patients were investigated with EGD and barium enema. GI lesions were detected in 50%. A recent study by Sophonthanasiri[10] involving 69 IDA patients employed bidirectional endoscopy and detected GI lesions in only 17%. The differing results may reflect differences in the inclusion criteria and definitions of the lesions considered as a cause of IDA. In the meantime, although most guidelines concluded that guiac-based fecal occult blood tests (FOBT) is neither sensitive nor specific for predicting GI lesions, the test is still commonly used by general practitioners in the work-up of IDA. Whether the results of FOBT may help predict GI lesions and decision to perform endoscopy in Thailand is not known.

The present study aims to (1) elucidate the prevalence and the sites and types of GI lesions as identified by bidirectional endoscopy that may be causative of IDA in Thai patients, and (2) identify variables including the FOBT that may help predict the presence of GI lesions or indicate the appropriate initial route of endoscopy.

MATERIALS AND METHODS

Outpatients with IDA who were referred to the gastroenterology service at Siriraj Hospital from December 2005 to December 2006 were prospectively enrolled into the study. IDA was defined as a hemoglobin concentration ≤ 13 g/dl for men and ≤ 12 g/dl for women, accompanied by at least one of the following laboratory values consistent with IDA: a serum iron ≤ 45 μg/dl with a transferrin saturation ≤ 15%, a serum ferritin concentration ≤ 20 μg/l for men and ≤ 10 μg/l for women, peripheral blood smear revealing hypochromic microcytic red cells with normal hemoglobin typing, anemia responding to iron supplement (i.e., increased hemoglobin level of at least 1 g/dl per week). Exclusion criteria were an obvious cause of blood loss within 3 months, hypermenorrhea, vegetarian diet, history of gastrectomy, concurrent diagnosis of GI cancer, chronic kidney disease, pregnancy, thrombocytopenia (platelets < 50,000/mm^3), age under 18, and inability to give informed consent for endoscopy.

Based on the above criteria, 103 consecutive patients were enrolled into the study, and underwent complete evaluation of the upper and lower GI tract irrespective of the presence of GI symptoms. Informed consent was obtained from all patients.

Data collection

Clinical data

Before the endoscopic procedures, patients were clinically evaluated by gastroenterology fellows at the time of patient's presentation. A detailed structured questionnaire was completed, including age, sex, presence of upper GI symptoms (upper abdominal pain, dyspepsia, nausea, vomiting, dysphagia, heartburn, reflux) or lower GI symptoms (lower abdominal pain, change of bowel habit, diarrhea, constipation), use of aspirin and non-steroidal anti-inflammatory drugs, use of alcohol and/or tobacco within 3 months before endoscopy, and FOBT (nonrehydrated hemooccult II; Hema-screen, Stabiolab, Taxas).

Laboratory data

Standard hematologic tests (CBC, iron study) were obtained. The results of FOBT were available in 82 patients. The results of all clinical and laboratory data were recorded in a computerized database.

Endoscopic data

The initial route of endoscopy was chosen according to patient's symptoms. In the absence of sugges-

tive GI symptoms, EGD was performed first. If significant lesions considered likely to be the cause of IDA were not found, the other route of endoscopy was subsequently performed. In patients older than 50 years, bidirectional endoscopies were performed in all cases, unless the initial endoscopy revealed carcinoma.

The definition of a significant lesion for EGD included: carcinoma, esophagitis with erosions or ulceration involving > 10% of the distal 5 cm of esophagus, erosive gastritis or duodenitis (defined by at least 50 erosions ≥ 1 mm diameter with white bases encircled by erythema), single duodenal or gastric ulcer ≥ 1 cm in diameter or two ulcers ≥ 0.5 cm in diameter, adenomatous polyp over 1.5 cm in diameter, vascular ectasia numbering five or more or at least 8 mm in diameter. Significant lesions for colonoscopy were: carcinoma, adenomatous polyps over 1.5 cm in diameter, vascular ectasia numbering five or more or at least 8 mm in diameter, active colitis, and colonic ulcer more than 1 cm in diameter[6].

Statistical analysis

Statistical analysis was done by SPSS version 13. Data were presented as numbers and percentages. Descriptive statistic was used where appropriate. Sensitivity, specificity, and accuracy were calculated for FOBT. Univariate analysis of the correlation between clinical parameters and significant GI lesions was performed. Chi-square test for categorical variable and student t-test for continuous variable data were employed. Statistical significance was considered when $p < 0.05$.

The present study was approved by the Ethics Committee of Siriraj Hospital.

RESULTS

During the study period, 133 patients were referred to the GI division for the evaluation of IDA. Thirty patients were excluded; 27 did not meet the criteria for IDA and 3 underwent incomplete endoscopic evaluation. Therefore, 103 patients were finally included in the study.

Baseline information

The baseline information of 103 patients and the numbers and types of endoscopies performed are shown in Table 1. Two-thirds of the patients were female, with a mean age of 64 years. GI symptoms were present in 39 patients (38%) including dysphagia (1), nausea/vomiting (1), heartburn (1), dyspepsia (12), abdominal pain (6), diarrhea (2), constipation (14), and lower abdominal pain (4).

Endoscopic findings

Significant GI lesions were detected in 58 of the 103 patients (56%). EGD demonstrated significant lesions in 44 patients (43%) whereas colonoscopy demonstrated significant lesions in 26 patients (25%). Dual lesions from both EGD and colonoscopy were noted in 12 patients (12%), while 45 patients (44%) had insignificant lesions or normal findings (Table 2).

Details of the endoscopic findings in all patients were shown in Table 3. Peptic ulcer diseases and colonic carcinoma were the most common lesions detected by EGD (22%) and colonoscopy (13%), respectively.

Predictors of significant GI lesions

Univariate analysis of the possible factors associated with significant GI lesions is shown in Table 4. The use of anti-platelet medications and the positive

Table 1. Baseline data of 103 patients.

Age, mean ± SD (years)	63.6 ± 15.2
Sex, n (M:F)	33:70
Hemoglobin, mean ± SD (g/dl)	7.61 ± 2.12
GI symptoms, n (%)	39 (38)
Upper alone	21 (20)
Lower alone	9 (9)
Upper and lower	10 (10)
Endoscopy, n (%)	
EGD alone	4/103 (4)
Colonoscopy alone	13/103 (13)
Bidirectional endoscopy	86/103 (84)

Table 2. Prevalence of significant GI lesions in 103 patients.

Lesions	Number of patients (%)
Significant lesions	58 (56)
Single lesion	46 (45)
By EGD	32 (31)
By colonoscopy	14 (14)
Dual lesions	12 (12)
Insignificant lesions	26 (25)
Normal	19 (18)

Table 3. Endoscopic findings of 103 patients.

EGD (n = 90)		Colonoscopy (n = 99)	
Findings	**n (%)**	**Findings**	**n (%)**
Significant lesions		*Significant lesions*	
GU, DU (≥ 1 cm or ≥ 2 ulcers ≥ 0.5 cm)	20 (22)	Colonic carcinoma	13 (13)
Erosive gastritis	18 (20)	Polyp ≥ 1.5 cm	4 (4)
GERD LA grade C-D	1 (1)	Ulcer	8 (8)
Gastric carcinoma	4 (4)	Angiodysplasia	1 (1)
Insignificant lesions		*Insignificant lesions*	
Small esophageal varices	5 (6)	Polyp < 1.5 cm	6 (6)
Small ulcer	4 (4)	Diverticulum	6 (6)
Hyperplastic polyp	2 (2)	Lipoma	1 (1)
GERD LA grade A-B	8 (9)	Parasites	2 (2)
Submucosal mass	1 (1)	Hemorrhoids	7 (7)
Nonerosive gastritis	8 (9)		

Table 4. Univariate analysis of factors associated with significant GI lesions.

Factors	Significant lesions (n = 58)	Insignificant lesions or normal (n = 45)	Odds Ratio (95% CI)	*p-value*
Age, mean ± SD (year)	65.2 ± 14.1	61.6 ± 16.4	-	0.231
Male gender	19 (33)	14 (31)	0.93 (0.40-2.14)	0.859
Hemoglobin level (g/dl)				
Mean ± SD	7.51 ± 2.11	7.75 ± 2.14	-	0.562
< 10, n (%)	53 (91)	38 (84)	1.95 (0.58-6.62)	0.277
GI symptoms, n (%)	26 (45)	13 (29)	2.20 (0.81-4.98)	0.098
Anti-platelet used, n (%)	30 (52)	14 (31)	2.37 (1.05-5.36)	0.036
Positive FOBT, n (%)*	34/42 (81)	24/40 (60)	2.83 (1.05-7.68)	0.038

*FOBT was done in 82 patients

FOBT were the only two predictors for significant GI lesions (OR 2.37 and 2.83, respectively). However, the sensitivity, specificity, PPV and NPV of FOBT for significant GI lesions were 81%, 40%, 68% and 66%, respectively. The presence of GI symptoms did not predict the presence of GI lesions.

The values of site-specific GI symptoms

Thirty-one patients had upper GI symptoms, and significant lesions were found in 26 (84%). However, EGD could detect lesions in only 14 cases (54%), whereas 12 had lesions in the colon. Likewise, lower GI symptoms were present in 19 patients, of which 14 (74%) had significant GI lesions. Colonoscopy could detect lesions in only 7 cases (50%), and missed 7 cases (50%) with upper lesions.

DISCUSSION

IDA in adult patients without obvious cause of blood loss is often considered a consequence of occult GI blood loss. Bidirectional endoscopy (i.e., EGD and colonoscopy) is therefore the mainstay investigation. However, the appropriateness of this strategy for IDA patients in Thailand is not known, because the sites and types of GI lesions may differ and the prevalence of colorectal carcinoma is lower than in Western countries. In an attempt to establish an appropriate guideline, the authors prospectively studied 103 patients with IDA using bidirectional endoscopy.

The present study identified significant GI lesions in 56% of patients. This prevalence is comparable to the results from Western studies (40-84%)[3-8] and from

Ovartlanporn's study[9] (49%), but differs markedly from the 17% from Sophonthanasiri's study10. The different criteria of IDA as well as geographic differences may contribute to the differing prevalences of GI lesions. The use of less strict criteria of IDA (e.g. low transferrin iron saturation alone) as used in the previous study, as well as and the different geography[10], may have led to the inclusion of some patients with anemia of chronic disease, and thus resulted in the low prevalence of GI lesions.

The present study confirms the results of most previous studies that EGD has higher yield than colonoscopy, 43% and 25%, respectively, while dual lesions were found in 12%. The most commonly identified lesion from EGD and from colonoscopy were peptic ulcers and colonic carcinoma, respectively. These are very similar to the observations from Western studies[3-8].

The value of using site-specific symptoms to guide the route of endoscopy is controversial. The present study suggests that these symptoms are not helpful in guiding the initial route of endoscopy. Nevertheless, in the 64 patients without GI symptoms, the authors found significant upper GI lesions in 25 patients (39%) and lower GI lesions in 11 patients (17%). From these results, EGD may be more appropriate as the initial endoscopy in Thai patients without guiding GI symptoms.

The present study could identify 2 predictors for the presence of significant GI lesions, namely antiplatelet use and positive FOBT. However, the associations were not strong, and the predictive value for GI lesions, particularly in the case of FOBT, was not good enough to alter the clinician's decision on performing endoscopy. Endoscopy is eventually required in every case of IDA, regardless of the result of FOBT.

There were some limitations in the present study. Firstly, the study was conducted in the university hospital setting, thus the results may not extrapolable to other outlying hospitals, where the prevalence of diseases may differ. A large multicenter study is needed to clarify the true prevalence. Secondly, the present study did not further investigate the small intestine in patients with negative bidirectional endoscopy, e.g. by capsule endoscopy (CE) or double-balloon enteroscopy (DBE). It has been shown that CE and DBE may uncover small intestinal causes of IDA in about 50-60% of patients investigated[11]. Thus, the true prevalence of GI lesions in IDA patients should infact be higher.

In conclusion, the prevalence of GI tract lesions in Thai IDA patients as evaluated by bidirectional endoscopy is 56%. Peptic ulcers and colorectal cancer are the two most common causes. EGD has a higher yield than colonoscopy, and is the preferred initial endoscopy unless there are suggestive lower GI symptoms. Dual lesions are not uncommon, thus bidirectional endoscopy is required in most (particularly elderly) patients, if cancer is not detected in the initial endoscopy. No predictors can reliably rule in or rule out patients for an endoscopy examination.

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