Original Article

Upper Gastrointestinal Endoscopy Findings in Patients Presenting with Dyspepsia

Piyaporn Choomsri, MD
Wanichya Bumpenboon, RN
Yodying Wasuthit, MD
Chakkrapan Euanorasetr, MD
Preeda Sumritpradit, MD
Weerapat Suwanthunma, MD
Panuwat Lertsithichai, MD

Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Abstract   *Objective:*   To determine the prevalence of important upper gastrointestinal (UGI) lesions in patients with dyspepsia and to determine the associated risk factors.

Methods: A prospective cohort study on dyspeptic patients undergoing UGI endoscopy during the period between May 2006 and October 2008 was conducted. A questionnaire was administered to all patients who consented to participate in the study. Endoscopic findings were defined as important if lesions seen were gastric or duodenal ulcers, moderate to severe gastritis, severe esophagitis, adenomatous polyps or cancer. Histological examination results were obtained for patients who also underwent endoscopic biopsy.

Results: A total of 291 dyspeptic patients were enrolled. Only 19% (54/291) of patients had important endoscopic lesions. No clinical findings including age and alarm symptoms were related to important endoscopic lesions. In 132 patients, 23% (30/132) of the endoscopic biopsies showed evidence of *H. pylori* infection. In patients with endoscope biopsy results, *H. pylori* infection was not associated with important endoscopic findings.

Conclusion: Dyspeptic patients had a low prevalence of important endoscopic lesions. The presence of these lesions could not be reliably predicted using clinical data and *H. pylori* infection status. Empirical anti-acid therapy was recommended as the initial screening therapeutic test prior to endoscopic evaluation for most patients.

Keywords: upper gastrointestinal endoscopy, dyspepsia, *H. pylori*

INTRODUCTION

Patients presenting with uncomplicated dyspepsia often have minor or no detectable gastroduodenal lesions as seen on conventional upper gastrointestinal (UGI) endoscopy. Approximately 40% of dyspeptic patients have some organic cause, and only 20% of patients with dyspepsia have significant gastroduodenal lesions, such as peptic ulcer.[1-3] Guidelines for the management of dyspepsia therefore recommend UGI endoscopy for patients with a higher risk of harboring serious UGI lesions.[4,5] There are currently no evidence-based criteria for categorizing a dyspeptic patient as

Correspondence address : *Panuwat Lertsithichai, MD, Department of Surgery, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand; Telephone: 066 2 2011315; Fax: 066 2 2011316; E-mail: raplt@mahidol.ac.th*

being at high risk.[3,4] The objective of the present study was to determine the prevalence of important endoscopic lesions in patients presenting with dyspepsia who underwent UGI endoscopy, and to identify significant clinical risk factors associated with the presence of such lesions.

PATIENTS AND METHODS

During the period between May 2006 and October 2008, data on patients presenting with dyspepsia - defined as one or more of the following symptoms: epigastric discomfort or pain, postprandial fullness, epigastric burning, and early satiety, persisting for more than 3 months[5] - and scheduled for UGI endoscopy, were prospectively collected. All patients gave informed consent to participate in the study. The hospital's research ethics committee approved the study. Patients who underwent UGI endoscopy for UGI hemorrhage, patients with documented chronic liver disease or who had advanced cancer were excluded from the study.

After informed consent was obtained, a questionnaire was administered to each patient. After completion of the questionnaire, UGI endoscopy was performed. The data acquired via the questionnaire consisted of demographic data, presenting symptoms, alarm symptoms, other illnesses, information concerning caffeinated and alcoholic beverage consumption, drugs used, and smoking history. In addition, reports of available laboratory and radiologic investigations were also obtained. To estimate the rate of *Helicobacter pylori (H. pylori)* infection, identified histologically, data on biopsies of the gastric or duodenal mucosa were collected. Endoscopic biopsy was done at the discretion of the endoscopist.

Endoscopic findings were categorized as "important" or "not important". Important findings included cancer, adenomatous polyps, peptic ulcer, moderate to severe gastritis, and severe esophagitis. Other findings, in particular the less severe forms of gastritis (in the absence of other important lesions), were regarded as not important. Grading of endoscopic gastritis was consistent with the Sydney Criteria.[6]

Continuous data were summarized as mean and standard deviation (SD) or median and range as appropriate. Categorical data were summarized as counts and percentages. Tests for differences in continuous data between patients with and without important endoscopic findings were done using unpaired t-test or Wilcoxon rank-sum test as appropriate. Tests for categorical data were performed using chi-square or Fisher's exact test as appropriate. Stata Statistical Software version 9 (Stata Corp, College Station, TX, USA) was used for all statistical analyses. Statistical significance was defined as a p-value of 0.05 or less.

RESULTS

There were 291 patients who completed questionnaires in the present study. Data from the first endoscopic examinations at our hospital were chosen for analysis. The patients' ages were 41 years on the average (SD = 14 years), of whom 68% were women, and who presented most often (52%) with chronic epigastric fullness. A comparison of demographic, clinical, and laboratory findings between patients with and without important endoscopic findings are presented in Tables 1 and 2. The frequencies of the endoscopic lesions and pathological diagnoses are shown in Table 3.

There was a low prevalence of each alarm symptom such as unintentional weight loss (13%), repeated vomiting (8%), dysphagia (3%), anemia (3%), or abdominal mass (1%) in the present samples of patients, although in combination 20% (57/291) of patients had at least one alarm symptom. A small percentage of patients were current smokers (5%), and a moderate percentage consumed coffee (22%), carbonated drinks (18%), and alcohol (10%) with any regularity. One in five (20%) were current users of NSAIDs but one third (32%) were regular users of anti-acid medications. Some patients had a history of UGI endoscopy performed elsewhere (14%), confirming the chronic nature of the presenting problems. The majority of patients (68%) reported leading stressful lives.

Laboratory reports in selected patients revealed that most were within normal range, except for a few outliers. Sonographic examination of the liver revealed non-specific parenchymatous abnormalities in 23% of patients; the rest were normal. Endoscopic examination showed important findings in only 19% (54/291) of patients; most of these findings were moderate to severe gastritis (67%, 36/54). Although peptic ulcers were found in 31% of the patients with important

Table 1. Clinical characteristics of patients

Characteristics	All patients N = 291		No important findings N = 237		Important findings N = 54		p-value*
Age (years): Mean (sd)	51	(13.6)	50.5	(13.6)	53.4	(13.6)	0.160
Gender (female)	198	(68%)	167	(70%)	31	(57%)	0.075
Epigastric discomfort, pain	16	(6%)	15	(6%)	1	(2%)	0.193
Abdominal bloating, fullness	150	(52%)	125	(53%)	25	(46%)	0.392
Abdominal masses	2	(1%)	0	2	(1%)	0.999	
Nausea & vomiting	39	(13%)	32	(14%)	7	(13%)	0.916
Repeated vomiting	23	(8%)	18	(8%)	5	(9%)	0.682
Food intolerance	29	(10%)	24	(10%)	5	(9%)	0.848
Weight loss, unintentional	38	(13%)	31	(13%)	7	(13%)	0.982
Dysphagia	9	(3%)	8	(3%)	1	(2%)	0.559
Undocumented GI bleeding	8	(3%)	5	(2%)	3	(6%)	0.162
Anemia needing iron supplement	9	(3%)	8	(3%)	1	(2%)	0.559
Hx of smoking	14	(5%)	11	(5%)	3	(6%)	0.777
Regular caffeinated beverage	65	(22%)	56	(24%)	9	(17%)	0.268
Regular alcoholic beverage	29	(10%)	21	(9%)	8	(15%)	0.187
Carbonated soft drinks	52	(18%)	42	(18%)	10	(19%)	0.890
Stressful life	197	(68%)	165	(70%)	32	(59%)	0.142
Hx of UGI malignancy	6	(2%)	6	(3%)	0		0.237
Hx of previous UGI endoscopy	40	(14%)	33	(14%)	7	(13%)	0.853
Use of NSAIDS	59	(20%)	47	(20%)	12	(22%)	0.693
Use of PPI & H2 antagonists	92	(32%)	79	(33%)	13	(24%)	0.187

*p-values according to t-test, chi-square test or Fisher's exact test as appropriate; Hx: history; UGI: upper gastrointestinal; NSAIDS: non-steroidal anti-inflammatory drugs; PPI: proton pump inhibitors

Table 2. Laboratory and radiologic findings

Laboratory and radiologic investigation	All patients	No important findings	Important findings	p-value**
WBC*: Median (range)	6800 (2400-16400)	6800 (2400-16400)	7200 (2460-11800)	0.107
Hct*: Mean (SD)	38.3 (4.6)	38.3 (4.0)	38.3 (6.5)	0.945
Platelets* (per 10,000): Median (range)	27.3 (3.3 to 71.9)	27.5 (3.3 to 50.7)	26.1 (18.0 to 71.9)	0.823
Albumin (g/L): Mean (SD)	42.1 (4.3); n = 106	42.2 (4.2); n = 86	41.8 (4.6); n = 22	0.689
Alkaline phosphatase (U/L): Median (range)	77 (37-501); n = 107	72.5 (37-501); n = 84	92 (48-228); n = 23	0.103
Aspartate aminotransferase (U/L): Median (range)	20 (10-179); n = 107	19.5 (9-179); n = 84	22 (13-93); n = 23	0.354
Alanine aminotransferase (U/L): Median (range)	35 (22-156); n = 107	35 (22-156); n = 84	39 (22-219); n = 23	0.165
Gamma glutamyl transferase (U/L): Median (range)	38 (15-416); n = 105	36 (13-416); n = 83	43 (19-200); n = 22	0.048
Liver sonography				
Normal findings	98/127 (77%)	85/109 (78%)	13/18 (72%)	0.590
Parenchymatous disease	29/127 (23%)	24/209 (22%)	5/18 (28%)	

*sample size = 150; 120 in the no significant findings group and 30 in the other; **p-values according to t-test or chi-square test as appropriate; WBC: white blood cell; Hct: hematocrit

Table 3. Endoscopic and pathologic findings

Characteristics	All patients N = 291	No important findings N = 237	Important findings N = 54	p-value*
Ulcers and masses				
Gastric ulcer	14 (5%)	0	14 (26%)	-
Duodenal ulcer	3 (1%)	0	3 (6%)	
Fungating mass & polyps	5 (2%)	0	5 (9%)	
Small hyperplastic polyps	5 (2%)	5 (2%)	0	
Endoscopic gastritis				
None	140 (48%)	126 (53%)	14 (26%)	-
Mild	115 (40%)	111 (47%)	4 (7%)	
Moderate-severe	36 (12%)	0	36 (67%)	
Histological gastritis; n = 129				
None	4/129 (3%)	4/90 (4%)	0	0.052
Mild	86/129 (67%)	64/90 (71%)	22/39 (56%)	
Moderate-severe	39/129 (30%)	22/90 (24%)	17/39 (44%)	
H. pylori infection (histology)	30/132 (23%)	18/90 (20%)	12/42 (29%)	0.274
Gastric cancer	3 (1%)	0	3 (6%)	-

*p-values according to chi-square test; "-" refers to tests not performed because of inappropriateness

lesions (17/54); they constituted only 6% of all findings (17/291). Gastric cancer was seen in only 3 patients (1% of all patients or 6% of those with important findings).

Only 45% of patients (132/291) had endoscopic biopsy performed. Of these, only 23% (30/132) were positive for helicobacter pylori infection. There seemed to be no significant difference in the prevalence of *H. pylori* infection between patients with important and those without important endoscopic findings, 29% (12/42) and 20% (18/90), respectively, with p-value = 0.274. Similarly, the difference in the prevalence of *H. pylori* between patients with peptic ulcers and cancer and those without were also not statistically significant: 9% (2/22) and 25% (28/110), respectively.

The comparison of the demographic, clinical, laboratory, and pathological findings (Tables 1 to 3) between patients with important and those without important endoscopic findings did not show any significant differences beyond those expected by chance. Similarly, combinations of alarm symptoms (from 1 to 5 symptoms) did not relate to significant findings. No further multivariable analyses were done because the simple univariable analyses presented should be sufficient to demonstrate the lack of evidence for any significant predictive factor related to important endoscopic lesions in the present study.

DISCUSSION

Most patients with dyspepsia have no detectable organic disease.[1-5] Dyspepsia with no evidence of organic disease is termed non-ulcer or functional dyspepsia.[4-7] For this reason, diagnosis and management of dyspepsia often go hand in hand, because an extensive diagnostic investigation to detect organic disease prior to therapy is not cost-effective and might even be harmful.[5] Initial management strategies include a trial treatment with various medications such as prokinetics, antacids, H2-receptor antagonists and proton pump inhibitors (PPI)[8-12]; initial endoscopy followed by treatment according to findings[10-13]; and the "test and treat" strategy of non-invasive testing for *H. pylori* infection to identify patients needing *H. pylori* eradication or endoscopy.[3,10-13] Currently the most cost-effective strategy, in the absence of alarm symptoms, is probably to either empirically treat dyspeptic patients with medications or to "test and treat" *H. pylori* infection and proceed to endoscopy in a stepwise manner.[5-13]

Many dyspeptic patients continue to be sent for endoscopic evaluation as the initial step in management, even though guidelines recommend endoscopic evaluation for older patients (older than 55 years), those with alarm symptoms, those taking NSAIDS, and those resistant to medications and *H. pylori* eradica-

tion.[4-7] Even at institutions where non-invasive testing of *H. pylori* is not readily available, an initial trial of anti-acid medications is probably warranted.[10-12] But because the prevalence of important lesions seen on UGI endoscopy is low even in selected patients, it might be useful to identify risk factors that could help predict the presence of important UGI lesions in some of these patients. This information might be used to stratify patients into risk groups; for example, to help identify those in need of urgent endoscopy rather than a trial of medications.[3]

From the perspective of clinicians, important lesions in the UGI tract are those needing specific treatment or are life threatening. In this sense, cancer, peptic ulcer, severe esophagitis and similar lesions must be considered important.[3] Mild chronic gastritis, diagnosed histologically, is a frequent finding in all patients who underwent UGI endoscopy for any reason.[14] Sometimes these lesions are related to *H. pylori* infection.[14,15] The clinical significance of these lesions in the absence of other important findings is not clear, but since the majority of such lesions are not currently known to be a precursor of gastric cancer,[15,16] we consider them unimportant from a therapeutic point of view.

The findings of the present study confirmed that the majority of patients with dyspepsia had no important endoscopic lesions. However, no clinical factors addressed in the present study could be used to predict the presence of important endoscopic lesions. In particular, "alarm symptoms", singly or in combination, were not significant predictors. Previous studies have also emphasized the nonspecific nature of many UGI symptoms and their lack of association with organic disease.[1,2,5,7,17] Another possible risk factor was the presence of *H. pylori* infection.[15,16] But non-invasive determination of *H. pylori* infection was not available in our institution at the time of study. Therefore, we used the histological method of determination, which was available only for patients who underwent endoscopic biopsy. Nonetheless, in patients on whom endoscopic biopsy was performed, *H. pylori* infection was not a significant risk factor for important endoscopic lesions.

Alarm symptoms, which usually include weight loss, GI bleeding, persistent vomiting, persistent pain and dysphagia,[2,4-7] are usually not predictive of UGI malignancy unless viewed from a screening perspective on a large number of patients, usually targeting male

patients older than 65 years.[17] In addition, an increased risk can only be detected after repeated follow up.[18] Some of these malignant lesions will not be found in the UGI tract.[18] It was therefore not surprising that in the present study we did not find alarm symptoms to be significant predictors of UGI malignancy, or other important lesions as seen on endoscopy. The low prevalence of gastric cancer in the present study, 1% (3/291), although similar to that of other studies,[3,7] contributed to the lack of a significant statistical relationship.

At our institution, *H. pylori* infection can only be diagnosed based on endoscopic mucosal punch biopsy. From a practical point of view, histological identification of *H. pylori* was the only viable method, as the CLO (campylobacter-like organism) test and culture methods were either more expensive, or took too much time, or both. The sensitivity of biopsy-based methods is known to be relatively low,[19,20] because of sampling errors and inadequate histological examination techniques. The prevalence of *H. pylori* as determined in the present study was only 23% (30/132), much lower than expected from the results of similar studies on dyspeptic patients elsewhere.[19,20] The low prevalence in the present study could have been due to inadequate biopsy technique, and the use of hematoxylin & eosin stain to examine the biopsy specimens instead of the more sensitive Genta or modified Giemsa stain.[20]

The findings of the present study supported selective UGI endoscopy in patients with dyspepsia, because the prevalence of important lesions was very low, although this was similar to the prevalence seen in other studies. Since no clinical findings - including alarm symptoms - in the present study could help select high-risk patients, selection by empirical treatment seemed to be the most cost-effective option, with or without the availability of non-invasive *H. pylori* tests.[11,12] Endoscopic biopsy and histological examination to detect *H. pylori* infection should not be done, unless proper techniques are used.[20]

Limitations of the present study included a relatively small sample size, and hence a small number of important lesions, resulting in a low power to detect significant differences in clinical and endoscopic findings between the two outcome groups. The questionnaire used for determining UGI symptoms was never validated and may have misclassified patients

as having or not having certain symptoms. Standardized criteria for the diagnosis and classification of symptoms (such as the Rome III criteria)[5] were not consistently used, and might have limited the external validity of the present study.

Conclusion

There was no evidence that some potentially significant predictive factors, such as age and alarm symptoms, were related to important endoscopic lesions. From the available evidence, it was recommended that an empirical treatment with anti-acid medications be used prior to endoscopic evaluation in most patients. *H. pylori* infection should not be determined by endoscopic biopsy and histology unless appropriately done.

REFERENCES

1. Fisher RS, Parkman HP. Management of nonulcer dyspepsia. N Engl J Med 1998;339:1376-81.

2. Spiller RC. Anorexia, nausea, vomiting, and pain. Br Med J 2001;323:1354-7.

3. Valle PC, Breckan RK, Amin A, et al. "Test, score and scope": a selection strategy for safe reduction of upper gastrointestinal endoscopies in young dyspeptic patients referred from primary care. Scand J Gastroenterol 2006;41: 161-9.

4. The American Gastroenterological Association. American Gastroenterological Association medical position statement: evaluation of dyspepsia. Gastroenterology 2005;129:1753-55.

5. Tack J, Talley NJ, Camilleri M, Holtman G, Hu PJ, Malagelada JR, Stanghellini V. Functional gastroduodenal disorders. Gastroenterology 2006;130:1466-79.

6. Rugge M, Meggio A, Pennelli G, et al. Gastritis staging in clinical practice: the OLGA staging system. Gut 2007;56:631-6.

7. Talley NJ, Phung N, Kalantar J. Indigestion: when is it functional? Br Med J 2001;323:1294-7.

8. Moayyedi P, Shelly S, Deeks JJ, Delaney B, Innes M, Forman D. Pharmacological interventions for non-ulcer dyspepsia. Cochrane Database of Syst Rev 2006, Issue 4. Art. No.: CD001960. DOI: 10.1002/14651858. CD001960.pub3.

9. van Marrewijk C, Mujakovic S, Fransen GAJ, et al. Effect and cost-effectiveness of step-up versus step-down treatment with antacids, H2-receptor antagonists, and proto pump inhibitors in patients with new onset dyspepsia (DIAMOND study): a primary-care-based randomized controlled trial. Lancet 2009;373:215-25.

10. Duggan AE, Elliot CA, Miller P, Hawkey CJ, Logan RFA. Clinical trial: a randomized trial of early endoscopy, *Helicobacter pylori* testing and empirical therapy for the management of dyspepsia in primary care. Aliment Pharmacol Ther 2008;29:55-68.

11. Ford AC, Moayyedi P, Jarbol DE, Logan RFA, Delaney BC. Meta-analysis: *Helicobacter pylori* "test and treat" compared with empirical acid suppression for managing dyspepsia. Aliment Pharmacol Ther 2008;28:534-44.

12. Delaney BC, Qume M, Moayyedi P, et al. *Helicobacter pylori* test and treat versus proton pump inhibitor in initial management of dyspepsia in primary care: multicentre randomized controlled trial (MRC-CUBE trial). Br Med J 2008;336:651-4.

13. Arents NLA, Thijs JC, van Zwet AA, et al. Approach to treatment of dyspepsia in primary care: a randomized trial comparing "test-and-treat" with prompt endoscopy. Arch Intern Med 2003; 163: 1606-12.

14. Peura DA, Haber MM, Hunt B, Atkinson S. *Helicobacter pylori*-negative gastritis in erosive gastritis, nonerosive reflux disease or functional dyspepsia patients. J Clin Gastroenterol 2010;44:180-5.

15. Stabile BE, Smith BR, Weeks DL. *H. pylori* infection and surgical disease - part II. Curr Probl Surg 2005;42:796-862.

16. Hartgrink HH, Jansen EPM, van Grieken NCT, van de Velde CJH. Gastric cancer. Lancet 2009;374:477-90.

17. Vakil N, Moayyedi P, Fennerty MB, Talley NJ. Limited value of alarm features in the diagnosis of upper gastrointestinal malignancy: systematic review and meta-analysis. Gastroenterology 2006;131:390-401.

18. Jones R, Latinovic R, Charlton J, Guilliford MC. Alarm symptoms in early diagnosis of cancer in primary care: cohort study using General Practice Research Database. Br Med J 2007;334:1040-11.

19. Logan RPH, Walker MM. Epidemiology and diagnosis of *Helicobacter pylori* infection. Br Med J 2001; 232: 920-2.

20. Stabile BE, Smith BR, Weeks DL. *H. pylori* infection and surgical disease - part I. Curr Probl Surg 2005;42:756-89.