

Discriminant value of dyspeptic symptoms in peptic ulcer and non-ulcer dyspepsia

*M.V. Kudva, MBBS (Malaya), MRCP (UK), MRCP (Ire)
Lecturer

*Mazlam Zawawi, MB ChB, BAO, LRCP & SI, MRCP (UK)
Lecturer

**Najib Rafee, MSc
Assoc. Prof.

*Omar Ismail, MD (UKM)
Medical Officer

*Department of Medicine
Faculty of Medicine
University Kebangsaan Malaysia
Jalan Raja Muda,
50300 Kuala Lumpur,

**Department of Statistics,
Centre for Quantitative Studies,
Universiti Kebangsaan Malaysia
43600 Bangi, Selangor.

Summary

The objective of the study was to determine whether discriminant analysis of characteristics of dyspepsia can differentiate peptic ulcer from non-ulcer dyspepsia in a Malaysian population. Two hundred and twenty six patients with dyspepsia were interviewed using a standard history questionnaire before undergoing upper gastrointestinal endoscopy. Forty seven patients had peptic ulcer while 149 others were classified as having non-ulcer dyspepsia. Stepwise logistic regression analysis was done on 25 variables. The study showed that only five of these variables could differentiate peptic ulcer from non-ulcer dyspepsia, namely, nocturnal pain, pain before meals or when hungry, absence of nausea, age and sex. A scoring system was devised based on these discriminant symptoms. At a sensitivity of 51%, the specificity for peptic ulcer was 83%, but only prospective studies will determine if this scoring system is of actual clinical value.

Key words: Dyspepsia, peptic ulcer, non-ulcer dyspepsia, discriminant analysis, nocturnal pain.

Introduction

Dyspepsia is a common symptom and the prevalence of dyspepsia has been estimated to be about 30% in the Western population.¹ We had shown earlier that 72% of our patients with dyspepsia do not have an endoscopically diagnosed organic disease.² These patients are labelled as having non-ulcer dyspepsia. About 21% of patients will have peptic ulcer. Several studies have shown that the diagnostic accuracy of differentiating peptic ulcer from non-ulcer dyspepsia can be enhanced by the use of a structured history questionnaire.³⁻⁶ However there have been no such studies done in the Malaysian population. We undertook this study to determine whether the features of dyspepsia can discriminate peptic ulcer from non-ulcer dyspepsia in a Malaysian population.

Materials and methods

This prospective case controlled study was conducted at the gastrointestinal unit, Department of Medicine, National University of Malaysia, over a six month period (July to December 1988). All patients with dyspepsia were interviewed personally by one of the investigators (MK, MZ, OI) using a standard history questionnaire, which enquired about symptoms in a standard fashion. Dyspepsia was defined as any pain, discomfort or nausea referable to the upper alimentary tract which may be intermittent or continuous, has been present for one month or more, and is not precipitated by exertion and not relieved within five minutes by rest.^{3,7}

The patients with dyspepsia were then subjected to a fiberoptic upper alimentary endoscopy. The endoscopy was performed by two of the authors (MK, MZ). As far as possible, the endoscopy was performed by the author who did not interview the patient. This precaution was carried out to reduce any bias which might affect endoscopic interpretation. After endoscopy the patients with dyspepsia were divided into two groups:—

- (1) Peptic ulcer (PU) — where the endoscopy showed gastric or duodenal ulcer, or both.
- (2) Non-ulcer dyspepsia (NUD) — where the endoscopy was normal or there was only visual evidence of non-erosive gastritis or non-erosive duodenitis. Patients with histories of gallstones, gastric surgery, or endoscopic or XRay proof of peptic ulcer in the past were excluded from the NUD group.

The history questionnaire consisted of 22 symptoms and three co-variables (Table I). Sixteen of these symptoms had been previously used by Talley³ in their study on the discriminant value of dyspeptic symptoms. They had arbitrarily selected these symptoms based on studies which had shown these to be of value as discriminants of dyspepsia. We included an additional six symptoms; pain aggravated by chillies or spices, heartburn, symptoms suggestive of the irritable bowel syndrome, visible abdominal distension, hematemesis and/or meleana, and the duration of dyspepsia. Irritable bowel syndrome was defined as dyspepsia associated with three or more of the six criteria of Manning,⁸ namely, loose stools at onset of abdominal pain, more frequent bowel movements at onset of abdominal pain, pain eased after bowel movements, visible abdominal distension, mucus per rectum and feeling of incomplete bowel evacuation.

The data from the questionnaire and endoscopic findings was fed into a mainframe computer at the Computer Centre, Medical Faculty, NUM, and analysed using an SAS software package.⁹ The mean values and ranges for symptoms in each diagnostic group (PU or NUD) was calculated. A discriminant function based on stepwise logistic regression was used to compare the two diagnostic groups. The logistic regression model was built by including all variables. However the variables were entered in the order of its strength of association with the dependent variable based on medical and biological grounds. Any variables that were not significant at the 0.05 level were excluded, and the analysis was repeated until a final model was established. The alpha level of 0.05 was taken so as not to exclude important discriminant symptoms.

The significant coefficients obtained from the logistic regression analysis were used to calculate a diagnostic score, by multiplying the regression coefficient by ten and rounding. This weighted score consisted of a weighted combination of relevant symptoms. The score of a particular patient was then obtained by multiplying these weights by the patient's responses to the corresponding symptoms, summing these components, and adding 50. A weighted score was obtained for each patient. The sensitivity and specificity of the scores were then calculated. The sensitivity of a test is defined as the proportion of subjects with a disorder who have a

Table I
Predefined variables assessed for predictive value in
each diagnostic category (peptic ulcer, non-ulcer dyspepsia)

A. SYMPTOMS

1. Classical ulcer symptoms (0 or 1)
Criteria: 3 or more of the following:
 - i) Epigastric pain relieved by food, milk or antacids
 - ii) Periodicity of epigastric pain
 - iii) Post prandial epigastric pain
 - iv) Nocturnal epigastric pain
2. Pain localised to the epigastrium only (0 or 1)
3. Pain severity (0–4)
 - 0 Nil
 - 1 Mild: can be ignored if the patient does not think about it
 - 2 Moderate: cannot be ignored but does not influence daily activities
 - 3 Severe: influences concentration on daily activities
 - 4 Very severe: markedly influences daily activities and/or requires rest
4. Intermittent vs continuous pain (any site) (1 or 2)
5. Length of attack of pain (0–3)
 - 0 Nil
 - 1 < 1/2 hour
 - 2 ≥ 1/2 hour to < 6 hours
 - 3 ≥ 6 hours
6. Pain radiating to the back (0 or 1)
7. Night pain – that is, pain at any site which wakes the patient from sleep (0 or 1)
8. Pain occurring before meals or when hungry (at any site) (0 or 1)
9. Pain half to three hours after meals (any site) (0 or 1)
10. Pain aggravated by food or milk (0 or 1)
11. Pain aggravated by chillies/spicy food (0 or 1)
12. Pain relieved by food, milk or antacids (any site) (0 or 1)
13. Pain relieved by vomiting (0 or 1)
14. Nausea (0 or 1)
15. Vomiting (0 or 1)
16. Anorexia (0 or 1)
17. Weight loss (>3 kg) (0 or 1)
18. Heartburn (0 or 1)
19. Symptoms suggestive of the Irritable bowel syndrome (0 or 1)
20. Visible abdominal distension (0 or 1)
21. History of hematemesis and/or melena (0 or 1)
22. Duration of symptoms (continuous variable in months)

B. COVARIABLES

1. Age (continuous variable in years)
2. Sex
3. Race (Chinese, Malay, Indian, Others)

positive or abnormal test for the disorder, whilst the specificity is the proportion of subjects without the disorder who have a negative or normal test.

Results

There were 47 patients with peptic ulcer (PU) [24 gastric ulcer (GU) 22 duodenal ulcer (DU), 1 GU + DU]. One hundred and forty nine patients had non-ulcer dyspepsia (NUD). The mean age for PU and NUD patients was 47.4 and 40.9 years respectively. The male to female ratio of PU and NUD was 2.1:1 and 1:1 respectively. Thirty other patients were excluded from the study. (9-erosive gastritis, 15-past history of peptic ulcer but without current evidence of active lesions, three reflux esophagitis, 2-Carcinoma stomach, 1-Carcinoma esophagus).

The mean values and ranges for symptoms in NUD and PU are given in Table II. The five commonest symptoms with PU (mean values in brackets) were pain localised to the epigastrium (0.80) hunger pain (0.75) pain relief with food, milk or antacids (0.71), night pain (0.58) and pain aggravated by chillies or spicy food (0.54).

For NUD the five commonest symptoms were pain localised to the epigastrium (0.72), pain relief with food, milk or antacids (0.62), pain before meals (0.58), pain aggravated by chillies and spices (0.54) and nausea (0.54).

Heartburn was noted in approximately the same number of patients with PU and NUD (35% and 40% respectively). Symptoms suggestive of the irritable bowel syndrome was commoner in NUD than PU (18% versus 8% respectively) but this was not statistically significant. There was no significant difference in the duration of dyspepsia in the two groups (PU: 63 months, NUD: 55 months). Analysis of the 22 symptom variables (Table III) showed that a diagnosis of peptic ulcer was more likely if (1) there was a history of night pain waking the patient from sleep ($p = 0.012$) (2) pain occurred before meals or when hungry ($p = 0.041$) and (3) there was no nausea ($p = 0.028$). A diagnosis of peptic ulcer was also more likely in the presence of two covariables; sex (male) and age.

Using the data in Table II, the score function for diagnosing ulcer is thus

$$50 + 9 (\text{Nocturnal pain}) + 9 (\text{Pain before meals}) \\ + 0.3 (\text{age}) - 9 (\text{Nausea}) - 8 (*\text{Sex}).$$

(Adding 50 gives diagnostic scores greater than zero)
(*Value for sex; Male = 1, Female = 2)

For a 60 year old male patient with nocturnal pain, but without pain before meal or nausea, the score would be 69 [ie $50 + 9 (1) + 9 (0) + 0.3 (60) - 9 (0) - 8 (1)$]. For a 30 year old female with nausea but without nocturnal pain or pain before meals, the score would be 34 [ie. $50 + 9 (0) + 9 (0) + 0.3 (30) - 9 (1) - 8 (2)$]. A score of 65 points or more would give a diagnosis of peptic ulcer with a specificity of 83% and a sensitivity of 51% (Table IV). A score of 55 points or more would give a diagnosis of peptic ulcer with specificity of 51% and a sensitivity of 83%. A score of less than 55 would give a diagnosis of non ulcer dyspepsia with a specificity of 83% and a sensitivity of 51%.

Discussion

Dyspepsia is a very common presenting symptom. Although there are many definitions of dyspepsia, we choose the definition that has been commonly used in several recent studies.

Table II
Mean values for symptoms (as defined in Table I)
in non-ulcer dyspepsia (NUD) and peptic ulcer (PU)

	NUD (n=149)	PU (N=47)	Min. value	Max. value
Classical ulcer symptoms	0.30	0.37	0	1
Pain localised to epigastrium	0.72	0.80	0	1
Pain severity	2.52	2.69	1	4
Intermittent vs continuous	1.20	1.17	1	2
Length of pain	1.60	1.45	1	3
Radiation to back	0.24	0.31	0	1
Night pain	0.40	0.58	0	1
Pain before meals	0.58	0.75	0	1
Post prandial pain	0.41	0.46	0	1
Pain aggravated by food or meals	0.49	0.33	0	1
Pain aggravated by chillies/spices	0.54	0.54	0	1
Pain relieved by food, milk, antacids	0.62	0.71	0	1
Pain relieved by vomiting	0.17	0.13	0	1
Nausea	0.54	0.29	0	1
Vomiting	0.23	0.15	0	1
Anorexia	0.26	0.33	0	1
Weight loss	0.15	0.19	0	1
Heartburn	0.40	0.35	0	1
Irritable bowel syndrome	0.18	0.08	0	1
Visible abdominal distension	0.23	0.15	0	1
Hematemesis/Melena	0.03	0.06	0	1
Duration of dyspepsia (months)	55	63	1	480

Table III
Stepwise logistic regression of symptoms, age, sex and
race of peptic ulcer vs non-ulcer dyspepsia; significant variables

Variables	Regression coefficient	P value
(1) Nocturnal pain	0.94	0.012
(2) Age	0.03	0.014
(3) Sex	-0.84	0.031
(4) Nausea	-0.87	0.028
(5) Pain before meals or when hungry	0.87	0.041

It is estimated that only half of patients with dyspepsia are correctly diagnosed when first seen in the hospital. It has been said that 'dyspepsia often defeats diagnosis'.¹⁰ However studies have been done which show that the diagnostic accuracy can be increased by 20–30% with the use of a predefined structured history questionnaire.¹¹ The importance of this would be

Table IV
Diagnostic scores for peptic ulcer: sensitivity and specificity

Diagnostic score	Peptic ulcer (N=47)	Non-ulcer dyspepsia (N=149)	Sensitivity	Specificity
0 – 54	8	76	17%	49%
55 – 64	15	48	32%	68%
>65	24	25	51%	83%

to predict which patient with dyspepsia has peptic ulcer or non-ulcer dyspepsia and so enhance the cost-effectiveness of subjecting him for endoscopy. We did not analyse gastric and duodenal ulcer separately, as our numbers were too small. To reduce bias, the author who interviewed a particular patient was separate from the one who performed the endoscopy. Ideally, the interview should be carried out by a single person. However we were not able to do so for practical reasons. The random allocation of PU and NUD patients to the three interviewers, would have reduced any particular bias of the interviewers:

Non-ulcer dyspepsia (NUD) includes gallbladder, liver, pancreatic, small intestinal or even colonic disease. In many others, no organic disease will be found even after extensive investigations. The term essential dyspepsia³ has been used to describe NUD patients without organic lesions. There have been very few reports on the use of discriminant analysis of dyspeptic symptoms to help to differentiate the various subsets of non-ulcer dyspepsia. Our study did not attempt to do so, and considered non-ulcer dyspepsia as a single diagnostic category. We have shown in our previous study on dyspepsia that 21% of the patients would have peptic ulcer while 75% would have non-ulcer dyspepsia.² The remaining 5% have other endoscopic lesions eg. esophagitis, gastric and esophageal malignancies. No studies have been done in Malaysia regarding the discriminating value of symptoms in distinguishing peptic ulcer from non-ulcer dyspepsia. Our study showed that out of 22 foregut symptoms, only three were reliable enough to distinguish PU from NUD. These were the presence of nocturnal pain, hunger pain and absence of nausea. The first two symptoms comprise the traditional classical ulcer symptoms,^{5,6,12-14} and our results appear to support this. Nocturnal pain is probably related to the maximal acid output that occurs around 11pm – 7am. This traditional concept of pain pattern in peptic ulcer is based on the assumption that gastric acid produces pain and acid neutralization relieves it. However controlled blinded experiments do not support this.¹⁵ In one study, instillation of 0.1 M HCL into the stomach of patients with active ulcers often did not produce pain. Under experimental condition, single and multiple doses of antacids were no more effective in degree or duration of pain relief than placebo liquids that looked and tasted like antacids.

The majority of the symptoms of PU appear to overlap with that of NUD such as site, radiation, periodicity, intensity, duration and aggravating and relieving factors. There are conflicting reports as to whether food aggravates pain in peptic ulcer and non-ulcer dyspepsia.^{3,6,16} However this variation may be due to differences in the definition of non-ulcer dyspepsia in the various studies.

Male sex and age were the other significant co-variables, and similar findings have been noted in our previous study.² Using a weighted score system for scores 65 and above, the sensitivity and specificity for peptic ulcer was 51% and 83% respectively. Conversely for non-ulcer

dyspepsia, the sensitivity and specificity for scores below 55, was 51% and 83% respectively. However only prospective studies will determine if this scoring system is of clinical value.

Conclusion

Our study shows that the majority of dyspeptic symptoms cannot differentiate peptic ulcer from non-ulcer dyspepsia. Only three out of 22 symptoms, namely, nocturnal pain, pain before meals or when hungry, and absence of nausea, were significantly commoner in peptic ulcer. Coupled with two other significant variables (age, sex) we calculated a diagnostic score for peptic ulcer. However, only prospective studies will determine if this scoring system is of actual clinical value.

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