
Discriminant Value of Symptoms in Patients with Dyspepsia

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Background. Family physicians encounter many pitfalls in managing and treating dyspeptic patients, most of whom are treated in family practice based solely on their signs and symptoms.

Methods. A computer literature search followed by a systematic methodological appraisal was performed to identify studies that evaluated clinical symptomatology in dyspeptic patients.

Results. Ten studies, none of which took place in a family practice, fulfilled our inclusion criteria. The main conclusion drawn from outpatient populations and patients referred for open-access endoscopy was that certain clusters of symptoms have a negative predictive

value for organic causes of dyspepsia. Higher age, male sex, pain at night, relief by antacids or food, and previous history of peptic ulcer disease were identified as predictors of organic causes for abdominal symptoms.

Conclusions. These findings can be helpful to family physicians in determining the need for endoscopy referral. However, since the diagnostic values of tests in family practice may differ from those in referred populations, there is a need for prospective studies in primary care.

Key words. Dyspepsia; predictive value of tests; family practice; endoscopy, gastrointestinal; endoscopy, digestive system; endoscopy. (*J Fam Pract* 1994; 38:139-143)

Family physicians must assess the likelihood of serious diseases in populations in which these diseases have a low prevalence. The positive predictive value of certain symptoms and signs in office practice is generally less than in hospital medicine.¹ Johnsen et al² showed that, in patients who saw their family physician for dyspepsia, the symptoms of dyspepsia did not correlate well with endoscopic or histologic findings. Nevertheless, dyspepsia is a common problem, and in the Netherlands, the prevalence of dyspepsia in family practice is about 32/1000 registered subjects per year.³

On the basis of signs and symptoms, family physicians must decide when to refer patients for endoscopy or when to commence treatment.⁴ This article is a review of

studies that have evaluated the diagnostic value of signs and symptoms in patients with upper abdominal complaints.

Methods

To identify all diagnostic studies using clinical symptomatology that have been published in the English language, the authors conducted a manual and computer search of the medical literature from January 1980 to July 1993 using *Index Medicus*, *Family Medicine Literature Index*, and MEDLINE. An additional manual search was performed in *Current Contents* from 1992 to date. Key words used in the search were "dyspepsia," "abdominal pain," "diagnosis" and "symptomatology." Reference sections of the studies found were examined for further research. By these methods, several hundred studies were identified.

Studies used in the analysis had to meet the following criteria: (1) they had to include at least two different

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groups of patients, one with an organic and one with a nonorganic upper gastrointestinal disease, (2) at least one of the diagnostic variables had to be a symptom, and (3) the patients must not have been experiencing acute abdominal pain necessitating immediate hospital admission.

Based on our inclusion criteria, most studies we found had to be excluded. The most frequent reasons were lack of clinical symptomatology assessment and lack of patient control groups with either an organic or nonorganic cause (criteria 1 and 2). Whenever possible, only the prediction of serious organic disease (malignancy, ulcer, complicated esophagitis) was assessed in the studies found.

A criteria-based analysis was performed to assess the diagnostic value of signs and symptoms of patients with dyspeptic abdominal complaints. A standardized method was used to review the selected studies. The assessment of the methodological quality of the studies was done with the aid of a list of criteria based on literature.^{5,6} The following nine criteria were formulated:

1. The study population consists of primary care patients.
2. The diagnoses are clearly defined (eg, esophagitis, ulcer).
3. The enrollment of patients is not restricted to the more severe cases to avoid a selection bias.
4. The selection of the patients is adequately described.
5. An acceptable reference standard has been used (eg, endoscopy).
6. There is a blind comparison of the diagnostic test (history) with the reference standard.
7. The intra/inter-observer variability of recorded symptoms has been measured.
8. The symptoms are clearly described to ensure study reproducibility.
9. The diagnostic value of the signs and symptoms is assessed in one population (learning population) and tested in a separate one (test population).

Diagnostic Value

The diagnostic value of symptom clusters is expressed in sensitivity, specificity, and positive or negative predictive value.⁷ These values were partly calculated from the data. *Sensitivity* refers to the probability that a symptom is present in patients with organic disease. *Specificity* refers to the probability that a symptom is absent in patients with no organic disease. When both of these probabilities are close to 100%, the symptom is of high value. Whenever possible, sensitivity, specificity, and predictive values

were calculated for a cluster of several symptoms simultaneously.

Results

Several hundred studies were retrieved, but only 10 met the inclusion criteria⁸⁻¹⁷ regarding patients, clinical symptomatology, and organic/nonorganic disease (Table 1). A wide range in percentages of organic disease (18% to 69%) was found in these studies. None of the studies were executed in family practice, although some^{11,14,16,17} included patients referred directly by their family physician to an open-access endoscopy service. In one study, only three specific diagnoses (peptic ulcer, symptomatic gallstones, and nonulcer dyspepsia) were considered an inclusion criterion.⁸ The remaining studies prospectively included all patients visiting an outpatient department or endoscopy unit. All patients had complaints for more than 1 month. An acceptable reference standard for diagnosing peptic ulcers, gastric malignancies, complicated esophagitis, and gallstones (eg, endoscopy, ultrasound) is present in all studies, but a blind comparison of the collected symptoms using this reference standard is performed in only four studies.^{10,11,16,17} Four studies tested an already existing set of clinical symptoms based on earlier consensus.^{11,13,14,16} The other studies lacked validation of their findings in other populations.

Table 2 includes the clinical prediction models of variables with an independent discriminatory value. All anamnestic items are easily elicitable by a family physician. In three studies,⁸⁻¹⁰ more than one organic outcome is predicted. The symptom complexes found for predicting peptic ulcer or gallstones are different from those for serious organic dyspepsia. The diagnostic values of these sets of symptoms are summarized in Table 3. The negative predictive values for dyspepsia caused by organic gastrointestinal diseases and specifically for peptic ulcer and gallstones are high. For nonulcer dyspepsia, high positive predictive values are found.⁸

Discussion

A review of the studies reveals that little research has been done in the field of diagnostic assessment of clinical symptoms in dyspepsia. This is remarkable considering how extensively traditional textbooks describe "typical" symptoms of conditions such as peptic ulcer disease.¹⁸ The studies found do not show optimistic results: a prediction of organic upper abdominal disease is generally inaccurate on the basis of symptoms alone. The main impact of scoring models of symptoms in dyspepsia is

Table 1. Characteristics of 10 Diagnostic Studies of Specific Symptoms in Patients with Upper Abdominal Complaints

Study (Principal Author)	No. of Patients	Inclusion Symptoms	Exclusion Symptoms	Organic Diseases, %	Diagnostic Reference Standard
Talley ⁸	221	All nonulcer dyspepsia, proven peptic ulcer, and symptomatic gallstone disease without other diagnosis in outpatients, prospectively	Jaundice, dysphagia or bleeding for less than 1 mo, irritable bowel syndrome, gastroesophageal reflux	49	Endoscopy or laparotomy
Johannessen ⁹	930	All patients visiting an endoscopy unit for upper abdominal symptoms, prospectively	Jaundice, gastrointestinal hemorrhage, acute abdominal pain, previous gastric surgery, endoscopy in preceding 6 mo	29	Endoscopy
Galatola ¹⁰	282	All abdominal pain in gastroenterological outpatients, prospectively	—	73	Ultrasound or endoscopy or radiography
Holdstock ¹¹	1279	All patients attending endoscopy, partly from open-access service and partly outpatients, prospectively	Repeat examination within 2 y History of gastric surgery	58	Endoscopy
Kudva ¹²	196	All outpatients with dyspepsia, prospectively	Complaints of less than 1 mo No relation to exertion and no relief by rest Erosive gastritis Reflux esophagitis Carcinoma (stomach, esophagus) History of peptic ulcer	24	Endoscopy
Lindberg ¹³	467	Patients referred for gastroscopy, prospectively	Jaundice, rectal bleeding	19	Endoscopy, two cases of radiography
Mann ¹⁴	235	Patients referred for open-access gastroscopy, prospectively	—	20	Endoscopy
Naji ¹⁵	483	All elective upper gastrointestinal endoscopy, retrospectively	—	69	Endoscopy
Bytzer ¹⁶	878	Referred for open-access gastroscopy	Gastric surgery, gastrointestinal bleeding	18	Endoscopy
Mansi ¹⁷	2253	All referred for upper gastrointestinal endoscopies, including open-access	Complaints of less than 2 wk duration, jaundice, bleeding, alarming symptomatology, previous surgery	43	Endoscopy

their high negative predictive value for organic disease and high positive predictive value for nonorganic dyspepsia. A comparison between these studies is severely hampered, however, by differences in predicted diseases and the different clinical symptoms used.

For a family physician, the models are clinically attractive. They contain anamnestic items that can be easily elicited during normal history taking. However, generalizing the results of these studies directly to family practice may be difficult. Because of the lower prevalence of serious disease in primary care, the diagnostic value of symptoms is different: in general, a lower positive predictive and a higher negative predictive value of diagnostic tests can be expected here.^{7,19}

Another differentiated mechanism of selection may

influence generalizability. If a family physician refers to outpatient departments only the patients with atypical upper abdominal complaints (ie, those not corresponding to textbook descriptions), studies of this population will show low predictive value, whereas studies in a population with more typical symptoms may show better results. These hypotheses have yet to be tested in a study of patients who are treated for dyspepsia by a family physician.

The use of endoscopy as a reference standard in the selected studies may be questionable. A recent paper that suggested that histologic abnormalities can be detected in a substantial proportion of apparently healthy people³ generated a flurry of correspondence about what constitutes a normal upper gastrointestinal tract. In the 10

Table 2. Overview of Clinical Prediction Models of 10 Diagnostic Studies in Patients with Upper Abdominal Complaints

Study (Principal Author)	Predicted Diagnoses		Other Serious Organic Causes (eg, Malignancies, Ulcers, Complicated Esophagitis)
	Peptic Ulcer	Gallstones	
Talley ⁸	Night pain, pain relief with ingestion of food, milk, antacids; short episodes of pain; higher age	More severe pain, <i>not</i> localized only to epigastrium; food, milk, antacids do <i>not</i> relieve pain; <i>no</i> pain before meals; higher age	Food or milk aggravates; pain less severe; <i>no</i> night pain, <i>no</i> vomiting, <i>no</i> weight loss; lower age (this model predicts the <i>absence</i> of ulcers or gallbladder disease)
Johannessen ⁹	Previous peptic ulcer; pain relief with ingestion of antacids or food; age >40; smoker	—	Pain relieved by antacids; age >40 y; previous peptic ulcer disease; male; symptoms provoked by berries; night pain relieved by antacids or food
Galatola ¹⁰	Pain radiating to the back <i>not</i> related to peptic ulcer	Classic biliary colic; pain radiating to the back	—
Holdstock ¹¹	—	—	Vomiting, smoking, previous peptic ulcer or hiatal hernia; higher age, male
Kudva ¹²	—	—	Night pain, pain before meals or when hungry; <i>absence</i> of nausea; higher age, male
Lindberg ¹³	Frequent night pain; total duration >2 years; ability to eat <15 minutes after vomiting; pointing sign positive*; smoker; family history of ulcer; pain relief with ingestion of food or antacids; episode duration >10 days; male; episodic pain; less pronounced in winter	—	—
Mann ¹⁴	—	—	Age >55; vomiting; male; history of smoking; previous peptic ulcer disease or hiatal hernia
Naji ¹⁵	—	—	Endoscopy is a review of a previous one; aged ≥55 y uncommon indication for endoscopy; diffuse epigastric pain (this model predicts the presence of <i>any</i> pathology in the upper abdomen)
Bytzer ¹⁶	—	—	Higher age; vomiting; male; smoking; previous ulcer or hiatal hernia
Mansi ¹⁷	—	—	Dysmotility dyspepsia in patients aged <50 y points to nonorganic dyspepsia

*Patient uses one finger to show the site of the pain.

studies included in the current review, endoscopy was used to assess whether gastrointestinal malignancies, peptic ulcer, or gastroesophageal reflux disease were present according to international criteria. When reflux disease was suspected despite normal endoscopy, further manometric and pH registrations was indicated, but because these diagnostic methods were not always used, there is a chance that reflux disease might not have been detected. For general practice research, a standardized follow-up period in which symptoms and clinical events are closely monitored is considered an alternative reference standard.²⁰

We conclude that there is a need for further validation of the prediction models in family practice populations. Future studies that fulfill the methodological criteria mentioned in the Methods section should include a study of all new patients consulting a family physician for upper abdominal complaints. Symptoms and signs indicative of any upper abdominal disorder should be included in the study. After a 1-year follow-up, the fate of these patients should be analyzed, taking all investigations into consideration. The predictive value of signs and symptoms offered at inclusion can then be assessed, assuming that fol-

Table 3. Diagnostic Value of Prediction Models at the Optimal Cutoff Point

Study (Principal Author)	Diagnosis Predicted	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Prevalence of Predicted Diagnosis
Talley ⁸	No gallstones or peptic ulcer	57	94	90	67	51
Johannessen ⁹	Organic dyspepsia	84	51	41	88	29
	Peptic ulcer	90	55	27	93	17
Galatola ¹⁰	Gallstones					
	Biliary colic	22	98	69	88	15
	Pain radiating to back	83	74	36	95	15
	Peptic ulcer					
	Pain radiating to back	25	69	18	79	20
Holdstock ¹¹	Organic dyspepsia*	97	31	34	97	58
Kudva ¹²	Peptic ulcer	51	83	49	84	24
Lindberg ¹³	Peptic ulcer	†	†	†	†	19
Mann ¹⁴	Organic disease	98	75	51	99	20
Naji ¹⁵	Any pathology	95	28	79	49	31
Bytzer ¹⁶	Organic disease	72	50	25	89	18
Mansi ¹⁷	Organic disease	†	†	†	†	43

*Organic dyspepsia refers to serious organic disorders: malignancies, ulcers and complicated esophagitis.

†No predictive values can be calculated from the original data.

low-up data reveal relevant conditions at the moment of inclusion.

References

1. Taking risks in family practice [editorial]. *Lancet* 1991; 336:541.
2. Johnsen R, Bernersen B, Straum B, et al. Prevalences of endoscopic and histological findings in subjects with and without dyspepsia. *BMJ* 1991; 302:749-52.
3. Van der Velden J, De Bakker DH, Claessens AAMC, Schellevis FG. Een nationale studie naar ziekten en verrichtingen in de huisartspraktijk. Basisrapport: morbiditeit in de huisartspraktijk. Utrecht: Nederlands Instituut voor onderzoek van de eerstelijnsgezondheidszorg (NIVEL), 1991.
4. Nyren O. Therapeutic trial in dyspepsia: its role in the primary care setting. *Scand J Gastroenterol* 1991; 26(suppl 182):61-9.
5. Ter Riet G, Kleijnen J, Knipschild P. De meta-analyse als reviewmethode. *Huisarts Wet* 1989; 32:176-81.
6. Knottnerus JA. De evaluatie van diagnostische technieken. In: Habbema JDF, Casparie AF, Mulder FFH (red.). *Medische technologie assessment en gezondheidsbeleid*. Samson, Stafleu, Alphen aan de Rijn, 1989.
7. Sackett D, Haynes RB, Guyatt GH, Tugwell P. *Clinical epidemiology. A basic science for clinical medicine*. Boston, Mass: Little, Brown Co, 1991.
8. Talley NJ, McNeil D, Piper DW. Discriminant value of dyspeptic symptoms: a study of the clinical presentation of 221 patients with dyspepsia of unknown cause, peptic ulceration, and cholelithiasis. *Gut* 1987; 28:40-6.
9. Johannessen T, Petersen H, Kleveland PM, et al. The predictive value of history in dyspepsia. *Scand J Gastroenterol* 1990; 25: 689-97.
10. Galatola G, Jazrawi RP, Kupfer RM, et al. Value of different

symptom complexes for clinical diagnosis of gallstones in outpatients presenting with abdominal pain. *Eur J Gastroenterol Hepatol* 1991; 3:623-5.

11. Holdstock G, Harman M, Machin D, Patel C, Lloyd RS. Prospective testing of a scoring system to improve case selection for upper gastrointestinal investigation. *Gastroenterology* 1986; 90: 1164-9.
12. Kudva MV, Zawawi M, Rafee N, Ismail O. Discriminant value of dyspeptic symptoms in peptic ulcer and non-ulcer dyspepsia. *Med J Malaysia* 1989; 44:236-42.
13. Lindberg G, Scensalu R, Nilsson LH, et al. Transferability of a computer system for medical history taking and decision support in dyspepsia. A comparison of indicants for peptic ulcer disease. *Scand J Gastroenterol* 1987; 22(suppl 128):190-6.
14. Mann J, Holdstock G, Harman M, Machin D, Lochry CA. Scoring system to improve cost effectiveness of open access endoscopy. *BMJ* 1983; 287:937-40.
15. Naji SA, Brunt PW, Hagen S, et al. Improving the selection of patients for upper gastrointestinal endoscopy. *Gut* 1993; 34:187-91.
16. Bytzer P, Schaffalitzky de Muckadell OB. Prediction of major pathologic conditions in dyspeptic patients referred for endoscopy. A prospective validation study of a scoring system. *Scand J Gastroenterol* 1992; 27:987-92.
17. Mansi C, Savarino V, Mela GS, Picciotto A, Mele MR, Celle G. Are clinical patterns of dyspepsia a valid guideline for appropriate use of endoscopy? A report on 2253 dyspeptic patients. *Am J Gastroenterol* 1993; 88:1011-5.
18. Wilson JD, Braunwald E, Isselbacher KJ, et al, eds. *Harrison's principles of internal medicine*. New York: McGraw-Hill, 1991.
19. Knottnerus JA. Interpretation of diagnostic data. An unexplored field in general practice. *J R Coll Gen Pract* 1985; 35:270-4.
20. Feinstein AR. *Clinical epidemiology. The architecture of clinical research*. Philadelphia, Pa: WB Saunders, 1985:622-3.