Clinical and Economic Assessment of the Omeprazole Test in Patients With Symptoms Suggestive of Gastroesophageal Reflux Disease

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Objective: To evaluate the diagnostic accuracy of a trial of a high-dose proton pump inhibitor (the omeprazole test) in detecting gastroesophageal reflux disease (GERD) in patients with heartburn symptoms.

Design: A randomized, double-blind, placebo-controlled, crossover trial.

Patients and Setting: Forty-three consecutive patients with symptoms suggestive of GERD were enrolled at a Veterans Affairs medical center.

Main Outcome Measures: Symptom response to the omeprazole test vs placebo in GERD-positive and GERD-negative patients; sensitivity, specificity, and positive and negative predictive values of the omeprazole test; and cost per correct diagnosis achieved with the omeprazole test compared with traditional diagnostic strategies.

Results: Of 42 patients (98%) who completed the study, 35 (83%) were classified as GERD positive and 7 (17%) as GERD negative. Twenty-eight GERD-positive and 3 GERD-negative patients responded to the omeprazole test, providing a sensitivity of 80.0% (95% confidence interval, 66.7%-93.3%) and a specificity of 57.1% (95% confidence interval, 20.5%-93.8%). Economic analysis revealed that the omeprazole test saves $348 per average patient evaluated, and results in a 64% reduction in the number of upper endoscopies performed and a 53% reduction in the use of pH testing.

Conclusions: The omeprazole test is sensitive and fairly specific for diagnosing GERD in patients with typical GERD symptoms. This strategy could result in significant cost savings and decreased use of invasive diagnostic tests.

Arch Intern Med. 1999;159:2161-2168

Gastroesophageal reflux disease (GERD), usually defined as symptoms or tissue damage related to esophageal exposure to gastric contents, is common in the US adult population. Heartburn and acid regurgitation are considered typical symptoms of GERD and the basis for initiating medical treatment in many patients. The prevalence of heartburn or acid regurgitation experienced at least annually or weekly is 58.7 or 19.8, respectively, per 100 people. Less than half of all patients with typical GERD symptoms have erosive esophagitis on upper endoscopy. Moreover, up to 20% of patients with typical heartburn have normal upper endoscopy and ambulatory 24-hour esophageal pH monitoring results. Using Rome criteria, this group of patients has been categorized as having functional heartburn. The cause of symptoms, natural course, and response to treatment of this large group of patients remains to be fully elucidated.

An accurate diagnosis of GERD often requires a variety of tests, most of which are invasive and costly, and some of which are not readily available to community-based primary care physicians. In addition, many physicians now practice in an environment that emphasizes cost-containment, in which referrals to a gastroenterologist or for a diagnostic procedure may be discouraged. Thus, a simpler, accurate, and cost-effective approach to diagnosing GERD would be beneficial to physicians who treat patients with GERD.

The aim of this study was to evaluate the diagnostic accuracy of a trial of a high-dose proton pump inhibitor (the omeprazole test) in detecting GERD. Validating the accuracy of this test would result in improvement in the diagnostic capability of primary care and specialty physicians, and in cost savings compared with more traditional diagnostic strategies for GERD (upper endoscopy and ambulatory 24-hour esophageal pH monitoring).
PATIENTS, MATERIALS, AND METHODS

PATIENTS

Forty-two patients (32 men and 10 women; mean ± SD age, 55.2 ± 2.0 years; age range, 26-75 years) with at least 3 episodes of heartburn per week for a minimum of 3 months completed this study between January 1, 1996, and December 31, 1996. Patients were recruited from primary care and gastroenterology outpatient clinics and were excluded if they had a medical contraindication to omeprazole therapy, had already been empirically treated with an antireflux medical regimen, reported a history of peptic ulcer disease or gastrointestinal surgery, or were unwilling or unable to provide informed consent. In addition, patients who were unable to fully complete all stages of the study were excluded.

This study was approved by the Human Subjects Committee of the University of Arizona, Tucson.

STUDY PROTOCOL

All enrolled patients underwent an initial diagnostic evaluation with upper endoscopy and ambulatory 24-hour esophageal pH monitoring, and were classified as GERD-positive or GERD-negative. Any patient with a duodenal or gastric ulcer was excluded from further study. The presence of erosive esophagitis (defined in “Upper Endoscopy” subsection) or abnormal ambulatory 24-hour esophageal pH monitoring results was used to define GERD. Otherwise, patients were considered to be GERD negative. Using a stratified block randomization scheme (with a block size of 4), patients in the 2 groups were randomly assigned to receive either omeprazole (40 mg in the morning and 20 mg in the evening) for 7 days followed by a comparable dose of placebo at a similar schedule for 7 days, or placebo initially followed by omeprazole. The study was carried out in a double-blind fashion. Omeprazole and placebo were administered in identical capsules so that neither the patient nor the study personnel could identify the treatment arm (Figure 1). In addition, patients were notified about the results of the upper endoscopy and ambulatory 24-hour esophageal pH monitoring only at study completion.

During the first study week, all patients completed a daily symptom diary as part of baseline symptom assessment. During the second treatment, week 1 was taken and daily symptoms were recorded by the patient. A weeklong washout period occurred in the third study week, followed by completion of another baseline symptom diary during the fourth week. Treatment 2 was taken during the fifth week, again with daily symptoms recorded. Patients were seen at the end of the first, second, fourth, and fifth study weeks to return their symptom records and any unused medications, which were used for a pill count to assess compliance.

UPPER ENDOSCOPY

After informed consent was obtained, patients underwent standard upper endoscopy. The stomach and the duodenum were inspected to exclude possible lesions. The distal portion of the esophagus was carefully evaluated to determine the presence of mucosal injury. The extent of esophageal mucosal damage was assessed using the Hetzel-Dent grading system. Grades 2 through 4 were considered diagnostic of erosive esophagitis and GERD for the purpose of this study.

AMBULATORY 24-HOUR ESOPHAGEAL pH MONITORING

After an overnight fast, a pH probe with a lower esophageal sphincter identifier (Digitrapper, MK III; Synectics Medical, Stockholm, Sweden) was inserted via the nose into the stomach. The pH probe was then placed 5 cm above the upper margin of the lower esophageal sphincter and was connected to a digital portable recorder. A reference electrode was attached to the upper chest. Patients were instructed to keep a diary to record meal times, position changes, and time and type of their symptoms. Patients were encouraged to pursue their everyday activities and maintain their usual diet. At the beginning and end of the study, the electrode and the system were calibrated in standard solutions of pH 1 and 7. Reflux was defined as pH less than 4, and reflux time as the interval until pH rose above 4 again. The presence of GERD was defined as greater than 4.2% of total time that pH was less than 4. Analysis of the recorded data was performed using standard commercially available computer software (Synectics Medical). In GERD-negative patients (pH < 4 < 4.2% of the time), a symptom index (SI) (number of symptoms with pH < 4 × 100/total number of symptoms) was calculated using patients’ diary and event marker. An SI greater than 30% was considered positive.

SYMPTOM ASSESSMENT

Patients kept a daily record of the frequency and severity of each symptom experienced. Symptoms such as heartburn and acid regurgitation were evaluated. A scale was used to determine the severity of each symptom: (1) mild symptoms were easily tolerated and did not last long, (2) moderate symptoms caused some discomfort but did not interfere with usual activities, (3) severe symptoms caused much discomfort and interfered with usual activities, and (4) disabling symptoms were unbearable and interfered considerably with usual activities.

Symptom score was calculated by adding the reported daily severity values (mild, 1; moderate, 2; severe, 3; and disabling, 4) and multiplying by the reported daily frequency values obtained during each week of symptom recording.

STATISTICAL ANALYSIS

Results are presented as mean ± SEMs. Because the heartburn score was not normally distributed, nonparametric methods of analysis were used. Mann-Whitney tests were done to investigate a baseline difference between GERD-positive and GERD-negative patients on the heartburn score. A Mann-Whitney test was also done to investigate an age
difference between GERD-positive and GERD-negative patients. Spearman correlation coefficients were calculated to examine the correlation between heartburn score and both upper endoscopy score and ambulatory 24-hour esophageal pH monitoring. The hypothesis H0: \( \rho = 0 \) was also tested.

A Fisher exact test was used to examine the association between GERD (positive and negative) and complete resolution of heartburn with therapy, defined as a score of 0 after treatment with omeprazole.

The treatment effect was tested using methods described by Fleiss\(^{12}\) for nonnormal quantitative data using a crossover design. First, a period effect was examined (assessing the effect of initiating placebo or medication administration). If the period effect was determined to not be significant, the treatment effect was examined using data from both periods. If the period effect was statistically significant, the treatment effect was examined using data from only the first period. Period and treatment effects were investigated using the Mann-Whitney test. This analysis was repeated separately for GERD-positive and GERD-negative patients.

When we tested for a difference between the 2 baseline measurements for heartburn using a Wilcoxon signed rank test, there was no significant difference (\( P = .30 \)). Because the measurement for heartburn after washout did not significantly differ from the first baseline measurement, we proceeded under the assumption that the carryover effect was negligible relative to the direct treatment effect.\(^{13}\)

Sensitivity, specificity, positive and negative predictive values, and accuracy of the omeprazole test to detect GERD-positive patients were calculated, along with 95% confidence intervals. The omeprazole test was considered positive if the heartburn score improved more than 50% from the first baseline score after treatment with omeprazole, ie, the heartburn score after treatment with omeprazole decreased by at least 50%.

Sensitivity, specificity, positive and negative predictive values, and accuracy were also calculated using symptom improvement ranging from 30% to 90%.

A McNemar test was done to test for any difference between the proportion of positive scores on the omeprazole and placebo tests for all patients and for GERD-positive patients alone. Placebo tests were considered positive if the heartburn scores improved at least 50% after placebo treatment.

**ECONOMIC ANALYSIS**

Decision analysis is a quantitative method for estimating the financial costs and clinical outcomes of alternative management strategies under conditions of uncertainty. To evaluate the potential economic impact of an initial noninvasive diagnostic strategy using the omeprazole test compared with a traditional invasive diagnostic strategy for patients with heartburn, we developed a decision analytic model using DATA decision analysis software.\(^{14}\) Our analysis considered patients with heartburn who required a diagnostic evaluation. We described the decision analysis using base-case estimates of the most likely clinical scenarios, and evaluated the strategies over a range of cost and probability estimates in a process known as sensitivity analysis. The model estimated financial and clinical outcomes for 1 year.

In traditional diagnostic strategy, patients with GERD underwent diagnostic upper endoscopy; if esophagitis was found they were given proton pump inhibitor therapy once daily for 8 weeks followed by maintenance therapy at the same dose for the remainder of 1 year. If the endoscopy result was negative, patients would then undergo ambulatory 24-hour esophageal pH monitoring. Patients found to have GERD by pH testing were treated with a proton pump inhibitor once daily for the remainder of 1 year (healing and maintenance). If the pH test result was normal, the diagnostic evaluation was complete and it was assumed that the patient did not have GERD.

In modeling the omeprazole test strategy, we assumed that the results of the omeprazole test are believed, and clinicians treat for GERD if positive and pursue alternative diagnoses if negative. Thus, patients with positive omeprazole test results were treated with a proton pump inhibitor once daily for the remainder of 1 year (healing and maintenance). If the omeprazole test result was negative, patients underwent diagnostic upper endoscopy followed by ambulatory 24-hour esophageal pH monitoring if they did not have erosive esophagitis. Patients with false-positive test results were assumed to have recurrent symptoms within 1 month. Patients with false-positive test results at the end of sequential diagnostic testing incurred the cost of undergoing once-daily proton pump inhibitor therapy for the remainder of 1 year.

**DATA SOURCES**

Probability estimates for the model (Table 1) were derived from published reports listed in the MEDLINE computerized bibliographic database. When the literature offered a range of probabilities, we chose estimates to bias the model in favor of the traditional invasive diagnostic strategy. Probabilities regarding the sensitivity, specificity, and predictive diagnostic values of the omeprazole test were derived from this prospective, placebo-controlled, double-blind, crossover trial of the omeprazole test in GERD. Bayesian analysis was used to revise the predictive values of diagnostic tests based on the pretest probability of GERD before and after diagnostic testing.\(^{15}\)

Cost estimates for the model were taken from the perspective of a third-party payer and were derived from the 1998 Medicare Fee Schedule and the 1998 Red Book of Average Wholesale Prices for Pharmaceuticals (Table 2). Because long-term outcomes in GERD are not likely impacted by the initial diagnostic strategy, we performed a cost-effectiveness analysis to evaluate the diagnostic efficiency (cost per correct diagnosis) of alternative strategies for 1 year.

We evaluated the model base-case estimates of the most likely clinical scenarios, and evaluated the strategies over a range of cost and probability estimates (sensitivity analysis). For the purposes of this analysis, the measure of cost-effectiveness is the cost per correct diagnosis of competing strategies.
Forty-three patients were enrolled and 42 (98%) completed the study. All 42 patients reported experiencing daytime heartburn, and 36 (86%) also experienced nighttime heartburn. Acid regurgitation was reported by 30 patients (71%). One patient was excluded from the analysis because of substantial deficiency of daily recorded symptoms. Thirty-five patients (83%) were classified as GERD positive: only 13 (37%) had abnormal ambulatory 24-hour esophageal pH monitoring and upper endoscopy results, while 14 (40%) had only an abnormal ambulatory 24-hour esophageal pH monitoring result, and 8 (23%) had only erosive esophagitis. The remaining 7 patients with heartburn (17%) had normal upper endoscopy and ambulatory 24-hour esophageal pH monitoring results and thus, were classified as GERD negative; only 2 (29%) of them had an SI greater than 50%.

Table 3 summarizes the baseline characteristics of both groups. There was no age difference between GERD-positive and GERD-negative patients (P = .83). However, 6 GERD-positive (17%) vs 4 GERD-negative (56%) patients were women.

Adverse effects during therapy were noted in 2 GERD-positive and 1 GERD-negative patients. Two patients developed diarrhea, and 1 developed diarrhea and abdominal pain. No patients discontinued treatment. Compliance, as measured by pill count, was 100% with both medication and placebo.

BASELINE

Symptom assessment scores for heartburn differed significantly between GERD-positive and GERD-negative patients (P = .006). Patients with GERD had high symptom assessment scores for daytime and nighttime heartburn. However, only daytime heartburn was significantly higher (P = .003), whereas the trend for nighttime heartburn was toward statistical significance (P = .07). There was no significant difference at baseline between GERD-positive and GERD-negative patients for acid regurgitation (P = .75). There was a significant correlation between symptom assessment score for heartburn and 24-hour esophageal pH monitoring results (percent total time pH < 4) (r = 0.33; P = .04). However, a significant correlation was not found between heartburn assessment score and esophageal mucosal injury, as assessed by upper endoscopy.

GERD-POSITIVE PATIENTS

Overall symptom assessment score for heartburn in the GERD-positive group improved significantly during omeprazole compared with placebo administration (P = .001). Twenty-eight GERD-positive patients (80%) had a positive response to the omeprazole test. Fourteen patients (40%) had complete resolution of heartburn during treatment; an additional 14 patients (40%) had at least 50% improvement in heartburn intensity score (Figure 2). No patient had complete resolution of heartburn when placebo was administered; however, 9 patients (26%) had at least 50% improvement. A period effect was not observed for heartburn in the GERD-positive group (P = .92).
GERD-NEGATIVE PATIENTS

In GERD-negative patients, there was no significant treatment effect for heartburn (P = .64). Two patients (29%) had complete resolution of heartburn with omeprazole therapy, and I had at least 50% improvement in heartburn assessment score. When placebo was administered to the GERD-negative group, 1 patient (14%) had complete resolution of symptoms and another had a 50% reduction in heartburn assessment score. Of 2 patients who had a positive SI, neither responded to the omeprazole test. For the GERD-negative group, no period effect was identified (P = .99).

SENSITIVITY, SPECIFICITY, AND PREDICTIVE VALUES

Twenty-eight of 35 GERD-positive patients responded to the omeprazole test vs 3 of 7 GERD-negative patients. Calculated sensitivity by 2 × 2 tables for the omeprazole test was 80% (95% CI, 66.7%-93.3%), and specificity was 57.1% (95% CI, 20.5%-93.8%). Of 31 patients with a positive omeprazole test result, 28 were GERD positive, resulting in a positive predictive value of 90.3% (95% CI, 79.9%-100%). Of 11 patients with a negative omeprazole test result, 4 were GERD negative, resulting in a negative predictive value of 36.4% (95% CI, 7.9%-64.8%). Overall test accuracy was 76.2%.

The receiver operating curve was obtained by varying the percentage reduction in heartburn while taking the response to the omeprazole test as a predictor of GERD. When using different reductions in heartburn, the optimal predictor of GERD was a 75% reduction. This cutoff point provided 85.7% sensitivity, 90.9% positive predictive value, and 81.0% accuracy.

Only 7 (23%) of 31 patients who had a positive omeprazole test result also had a positive placebo test result. None of the 7 patients with a positive placebo test result had a negative omeprazole test result. This was a statistically significant difference (P < .001), and indicates that a positive omeprazole test result significantly differs and may be easily distinguished from a positive placebo test result.

Only 6 of 28 GERD-positive patients who had a positive omeprazole test result also had a positive placebo test result, none of whom had a negative omeprazole test result. This was a statistically significant difference (P < .001), and indicates that a positive omeprazole test result differs from chance or from a positive placebo test result in GERD-positive patients.

ECONOMIC ANALYSIS

The potential impact of implementing a noninvasive strategy using the omeprazole test rather than a traditional invasive diagnostic strategy was estimated in this cost-effectiveness analysis. Results reveal that the omeprazole test saves $348 per average patient with heartburn undergoing a diagnostic evaluation (Table 4). This savings is achieved in conjunction with an improvement of 84% to 94% in diagnostic accuracy of the sequential testing strategy. The omeprazole test strategy results in an average cost-effectiveness ratio of $1634 per correct diagnosis compared with $2234 per correct diagnosis by the traditional invasive diagnostic strategy (Table 4).

Cost savings attributable to the omeprazole test strategy result from a 64% reduction in the number of upper endoscopies performed and a 53% reduction in the use of ambulatory 24-hour esophageal pH monitoring. Such reductions are attributed to the high positive predictive value of the omeprazole test for GERD in patients with heartburn.

We performed sensitivity testing to examine the effect of varying the cost and probability estimates in our model on the results of analysis. If the prevalence of GERD in the population of patients with heartburn fell below 20%, then the traditional diagnostic strategy would become the preferred strategy. We found that the cost of the 7-day omeprazole test must be greater than $627 for the traditional diagnostic strategy to be equally cost-effective. This represents an 825% increase from our base-
In our study, the omeprazole test seemed to be a sensitive, cost-effective diagnostic tool for detecting GERD as the cause of heartburn symptoms in 80% of patients. Maintenance of antireflux treatment in these patients with the lowest effective dose of antisecretory medication is the natural next step, which will spare patients from a variety of invasive diagnostic tests.15

Although the omeprazole test has been shown to be an accurate diagnostic test, the duration of treatment and the optimal dose remain issues of controversy in the literature. Some authors17-19 suggested that 6 to 8 weeks of treatment is necessary for diagnostic accuracy. However, it is impractical and expensive to have patients complete a full 2 months of antireflux treatment before it is determined whether the medication is of benefit. Schindlbeck et al20 treated patients with nonerosive esophagitis for 1 week with 40 mg of omeprazole twice a day and demonstrated a sensitivity of 83%. These investigators demonstrated that, for the omeprazole test to be an effective tool, a higher dosage than the standard once-daily dose of omeprazole is necessary. Further conclusions from their study are hampered by the absence of a placebo arm, inclusion of patients solely with nonerosive esophagitis, and the assumption that upper endoscopy is readily available and usable in symptomatic patients with GERD. The objective of our study was to include all patients with typical GERD symptoms, regardless of the presence or absence of mucosal injury. This approach attempts to capture the typical clinical challenge that a treating physician faces on a daily basis.

In a Scandinavian multicenter study,21 20 mg of omeprazole was administered twice daily to patients with typical symptoms of GERD and revealed a sensitivity of 71% to 81%, which is again similar to our findings. This study was the first to address the response rate to the omeprazole test in patients with typical GERD symptoms but without objective evidence of the disease (negative upper endoscopy and 24-hour esophageal pH monitoring results). Although they accounted for only 9.4% of the patients—a lower prevalence than is expected in the general population—they tended to respond to the omeprazole test, reducing its specificity. In another European multicenter study,22 patients with GERD were randomly assigned to receive either omeprazole, 40 mg/d, or placebo for 2 weeks. Patients with esophageal mucosal injury were excluded, and 24-hour esophageal pH monitoring served as the gold standard. The omeprazole test was found to have positive and negative predictive values of 68% and 63%, respectively.

Although heartburn is considered a typical symptom of GERD, up to 20% of patients with heartburn have no objective evidence of GERD, and are considered to have functional heartburn.6 In our study, the functional heartburn group accounted for only 16% of patients and was too small to provide valid and generalizable results regarding the specificity and negative predictive value of the omeprazole test. However, this is the group of patients that we hope to identify with the omeprazole test without the need for invasive tests. In our study, the response of the functional heartburn group to the omeprazole test was lower than that of the GERD-positive group. Similarly, Schenk et al22 demonstrated a 68.2% response to the omeprazole test in GERD-positive patients vs only 36.8% in the functional heartburn group. The underlying mechanism of functional heartburn remains to be elucidated, but, at least from the omeprazole test data, acid seems to have only a partial role. Similar to other functional bowel disorders, there was a female predominance in the functional heartburn group in our study. The mechanisms responsible for the observed sex difference remain to be elucidated.

In addition, it has been suggested that GERD-negative patients with a positive SI may yet represent a subgroup of GERD-positive patients.10 For this reason, indication of a positive SI has become a method for iden-
tifying false-negative 24-hour esophageal pH monitoring results. None of the aforementioned studies of the omeprazole test calculated the SI for the GERD-negative group. However, 2 GERD-negative patients in our study had a positive SI, and neither responded to the omeprazole test. Because of the small number of these patients in our study, it is difficult to draw conclusions about their response to the omeprazole test. Future studies are needed that specifically address this group.

A known limitation of crossover trials is the carryover effect. Young et al23 randomly assigned patients to receive either a single dose of 80 mg of omeprazole or placebo, and then crossed the patients over to the opposite arm. Although a sensitivity of 90% for the omeprazole test was reported, a carryover effect might have confounded the results of that study. In our study, we attempted to ensure a negligible carryover effect by introducing a washout period between treatments and by demonstrating a similar baseline symptom recording for heartburn at baseline and after washout.

As with any diagnostic test, the optimal cutoff value is critical in defining optimal test accuracy. Although we used 50% symptom reduction as the cutoff value for a positive omeprazole test result, when a range of cutoff values was evaluated, the optimal preoff value for a positive omeprazole test result, when a A known limitation of crossover trials is the carryover effect. Young et al23 randomly assigned patients to receive either a single dose of 80 mg of omeprazole or placebo, and then crossed the patients over to the opposite arm. Although a sensitivity of 90% for the omeprazole test was reported, a carryover effect might have confounded the results of that study. In our study, we attempted to ensure a negligible carryover effect by introducing a washout period between treatments and by demonstrating a similar baseline symptom recording for heartburn at baseline and after washout.

As with any diagnostic test, the optimal cutoff value is critical in defining optimal test accuracy. Although we used 50% symptom reduction as the cutoff value for a positive omeprazole test result, when a range of cutoff values was evaluated, the optimal preoff value for a positive omeprazole test result, when a value of the omeprazole test, symptom assessment cutoff values were chosen arbitrarily, and no attempt was made to explore ranges of cutoff values. Several authors20,23 used a 75% reduction in heartburn symptoms as the cutoff value, and others2 used a 50% cutoff value, perhaps explaining in part the variation in sensitivity of the omeprazole test.

Ambulatory 24-hour esophageal pH monitoring, with a sensitivity of 79% to 96% and a specificity of 85% to 100%, is considered the gold standard for diagnosing GERD.24-27 However, in our study, 22% of patients had a normal test result, despite evidence of erosive esophagitis on upper endoscopy, which is a relatively high false-negative rate. Schenk et al22 found that 26% of patients with endoscopically proven erosive esophagitis had a normal ambulatory 24-hour esophageal pH monitoring result. Thus, it seems that the sensitivity of the 24-hour esophageal pH monitoring test is likely closer to the lower end of the previously reported sensitivity range.

Our economic analysis revealed that the omeprazole test provides cost savings superior to the traditional diagnostic strategy: $348 per average patient and reduced use of upper endoscopy and ambulatory 24-hour esophageal pH monitoring by 64% and 53%, respectively. Moreover, by using the noninvasive omeprazole test strategy, we demonstrated an increase in diagnostic accuracy, resulting in an even more cost-per-correct diagnosis. By using sensitivity analysis, we found our economic model to be robust. Only if the prevalence of GERD is below 20%, the omeprazole test sensitivity is less than 12%, or the cost of the 7-day omeprazole test is greater than $627 would the traditional diagnostic strategy for GERD become more cost effective.

Kahrilas28 raised the concern that, amid attempts to initiate therapeutic trials by primary care providers, the role of upper endoscopy in GERD might be forgotten. He and others have argued that upper endoscopy is the best way to minimize the associated risks of either misdiagnosis or a missed diagnosis. Although these arguments are valid, in an era of cost-containment, the value of any diagnostic test is often closely scrutinized. Obviously, patients presenting with alarm symptoms such as bleeding, dysphagia, or weight loss should undergo upper endoscopy as the initial step. The cost-effectiveness of endoscopic screening for Barrett’s esophagus has not been established, and there is currently no consensus as to at what point patients with GERD should be screened, although recommendations by the American College of Gastroenterology have recently been published.20 The decision analysis model used estimated cost and outcome for 1 year and did not preclude subsequent endoscopy as clinically indicated.

The utility of the omeprazole test is to provide the primary care physician with a diagnostic tool in an environment where invasive, costly tests are not always readily available. In addition, the test is a simple, relatively sensitive, and clinically practical method of diagnosing GERD as the cause of heartburn.

The cost-effectiveness of the omeprazole test strategy may suffer, however, if patients who respond are not stepped down to less expensive medical therapy such as generic H2 receptor antagonists. Moreover, it remains to be seen how many of these responders ultimately require invasive testing with endoscopy or ambulatory 24-hour esophageal pH monitoring to tailor therapy or evaluate therapeutic failures.

Although many questions about the utility of the omeprazole test in GERD remain unanswered, it seems to be a valid and reliable initial test for patients who present with symptoms suggestive of GERD. Use of the omeprazole test as the initial step can provide the simplicity, diagnostic accuracy, and cost savings that patients and physicians are seeking when establishing the diagnosis of GERD.

Accepted for publication February 15, 1999.

This study was supported in part by a research grant from Astra Pharmaceuticals, Wayne, Pa.


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