Evaluation of Noncardiac Chest Pain: Toward a Positive Diagnosis

Case Study, Michael P. Jones, MD, FACP
Commentary, Michael P. Jones, MD, FACP, Thangam Venketesan, MD, and Lawsun R. Wulsin, MD

INSTRUCTIONS

The following case study, “Evaluation of Noncardiac Chest Pain: Toward a Positive Diagnosis,” is accompanied by a continuing medical education (CME) evaluation that consists of 5 multiple-choice questions. After reading the case study, carefully consider each of the questions in the CME evaluation on page 52. Then, circle your selected answer to each question on the CME evaluation form on page 53. In order to receive one CME credit, at least 3 of the 5 questions must be answered correctly. The estimated time for this CME activity is 1 hour.

OBJECTIVES

After participating in the CME activity, primary care physicians should be able to:
1. Appreciate the impact of noncardiac chest pain on quality of life and health care resource utilization
2. Know the etiology of noncardiac chest pain
3. Understand the importance of ruling out cardiac etiologies of noncardiac chest pain and establishing a positive diagnosis
4. Understand the utility and drawbacks of modalities available for determining an esophageal cause of noncardiac chest pain
5. Develop a rational approach to treating noncardiac chest pain

INTRODUCTION

Angina-like chest pain is a common reason patients seek evaluation in both acute care and office-based settings. Many patients who present with chest pain are subsequently diagnosed with symptomatic coronary artery disease (CAD). However, a large percentage of individuals presenting with chest pain will not exhibit evidence of symptomatic heart disease.

Angina-like chest pain in the absence of a demonstrable cardiac abnormality is termed noncardiac chest pain and is a clinical problem frequently encountered by primary care physicians, gastroenterologists, and cardiologists. Because the pathophysiology may vary and is often elusive, the evaluation and management of patients with noncardiac chest pain is problematic. The combination of an anxiety-provoking condition with an often unsystematic and inconclusive physician evaluation frequently results in visits to multiple physicians, ongoing use of acute care services, and both patient and physician dissatisfaction.

The magnitude and cost of this problem should not be underestimated. Annually, over 1 million people undergo cardiac catheterization because of chest pain, and approximately 30% of these patients have normal coronary arteries [1,2]. Although the subsequent cardiac mortality in these patients is low, many have persistent chest pain, continue to feel disabled, and continue to consume health care resources [3,4]. These individuals receive an average of 1.2 prescription medications per month, visit a physician or emergency room 2.2 times yearly, and are hospitalized 0.8 times yearly for further evaluation of their chest pain [5]. The evaluation and treatment of these patients has been estimated to cost $350 million annually [4].

Clinical outcomes data are lacking in this area, and pathways for the evaluation and treatment of these individuals are not well defined. This case study presents a rational clinical approach to the problem of noncardiac chest pain, identifying areas where further research is needed.

CASE STUDY

Initial Presentation

A 52-year-old man presents to the emergency department (ED) with squeezing substernal chest pain that woke him from sleep 2 hours earlier. The pain is steady, does not radiate to the neck or arms, and is not associated with light-headedness, palpitations, nausea, or vomiting.

Michael P. Jones, MD, FACP, Assistant Professor of Medicine, Division of Digestive Diseases, Director, Digestive Motility Center, University of Cincinnati School of Medicine, Cincinnati, OH; Thangam Venketesan, MD, Fellow, Division of Digestive Diseases, University of Cincinnati School of Medicine; and Lawsun R. Wulsin, MD, Associate Professor of Psychiatry, Department of Psychiatry, University of Cincinnati School of Medicine.
NONCARDIAC CHEST PAIN

History
The patient’s father died of a heart attack at age 62 years, and the patient reports that within the past year he was diagnosed with mild hypertension and hyperlipidemia. He is currently being treated with medications for both conditions. He has a 30 pack-year history of smoking. The patient is married, has 3 children, and works approximately 55 hours per week; he is also renovating a second home himself. He reports that he recently experienced several episodes of pain that were qualitatively similar to this presenting episode but not as severe. He does not associate the pain with activity, meals, or recumbency.

Physical Examination
Physical examination reveals a mildly obese man who appears anxious and is mildly diaphoretic. His blood pressure is 150/98 mm Hg, and his pulse is 104 bpm. The remainder of his physical examination is unremarkable. An electrocardiogram reveals sinus tachycardia and nonspecific ST-T wave changes. Chest radiograph is normal.

• What are initial steps in the evaluation of patients with chest pain?

Evaluation of Recurrent Chest Pain
CAD is the leading cause of death in the United States, and nearly 25% of all deaths in the United States are due to symptomatic CAD. The evaluation of patients with recurring chest pain always begins with the exclusion of significant cardiac disease. However, differentiating cardiac and noncardiac etiologies of chest pain is not always possible on clinical grounds alone. Additionally, CAD and many of the etiologies of noncardiac chest pain commonly coexist. For example, Davies and colleagues reported that certain clinical features were helpful in distinguishing esophageal etiologies of angina-like chest pain, but they also noted that as many as 50% of patients with anginal pain were found to have 1 or more symptoms of esophageal pain [6]. Thus, suspicion for symptomatic CAD must always be high, and its presence must be firmly established or excluded.

The extent of the cardiac evaluation is chiefly determined by the patient’s age, family history, and other risk factors for cardiac disease (eg, hypertension, hyperlipidemia, diabetes mellitus, smoking). Various modalities are used to evaluate for myocardial ischemia, including resting electrocardiograms, exercise electrocardiography and echocardiography, various forms of stress scintigraphy, and coronary angiograms. Selection of appropriate diagnostic modalities largely depends on pretest suspicion for symptomatic CAD, the patient’s ability to participate in the studies, availability of diagnostic tests, and the physician’s experience and preference.

Because of interest in providing more accurate diagnoses and more cost-efficient allocation of diagnostic resources, there is focused attention on increasing the accuracy of risk stratification for patients presenting to acute care services [7]. These strategies frequently include 6- or 8-hour observation periods during which cardiac enzymes and resting electrocardiograms are monitored, as well as noninvasive testing for myocardial ischemia in patients at low risk for CAD. Although outcomes studies evaluating these methods are not yet available, their use in clinical settings is increasingly common.

Results of Cardiac Evaluation
In the ED, the patient undergoes a 6-hour rule-out protocol for myocardial infarction and demonstrates symptom resolution, normal cardiac enzymes, and a stable electrocardiographic pattern. Following this, he undergoes a graded exercise tolerance test that discloses no abnormalities suggestive of myocardial ischemia. He is told that his chest pain is unrelated to CAD and is discharged.

Over the next 2 months, he continues to have episodes of chest pain, both with exertion and while at rest, resulting in 2 additional visits to the ED. During the second visit, the patient is admitted and undergoes cardiac catheterization. The procedure discloses normal coronary arteries, and the patient is again reassured that his chest pain is noncardiac and is discharged. One week later, he presents to his primary care physician complaining of persistent chest discomfort, asking again for an explanation of his symptoms as well as relief from the episodic pain.

• What is the natural history of noncardiac chest pain?

Several studies show that patients with noncardiac chest pain have an excellent prognosis with respect to mortality but continue to experience considerable morbidity [8–10]. In an important study by Ockene and colleagues [3], 57 patients with chest pain and normal coronary angiograms were informed that their pain was noncardiac in nature and that their activity need not be limited because of the pain. Although after an average follow-up of 16 ± 7.7 months there was no mortality, 47% of study subjects still described their activity as limited by the pain (compared with 74% prior to catheterization). Additionally, 51% of subjects were still unable to work due to the pain (compared with 63% prior to catheterization). Use of medical facilities was significantly reduced after catheterization. During follow-up, physicians were more likely than patients to believe that the symptoms had improved.
Although a normal coronary angiogram is reassuring to physicians, it clearly leaves something to be desired from the patient’s point of view. Establishing a positive diagnosis is critical for improving the quality of life and reducing the health care resource consumption of patients with noncardiac chest pain. Ward and colleagues [8] have shown that patients whose noncardiac chest pain was found to have an esophageal etiology were less likely to feel disabled by their pain and less likely to require continued physician evaluation than patients whose chest pain was not specifically diagnosed. Interestingly, although establishing an esophageal etiology for these subjects’ chest pain did not result in a significant decrease in symptoms, it did significantly reduce the number of subjects who felt that their pain was cardiac in nature, felt disabled by their symptoms, and sought continued evaluation for the ongoing chest pain.

• What are common causes of noncardiac chest pain?

### Noncardiac Causes of Chest Pain

After exclusion of epicardial CAD and other more obvious noncardiac etiologies, the differential diagnosis of chronic, unexplained noncardiac chest pain includes microvascular angina, esophageal disorders, psychiatric disorders, and musculoskeletal causes (Table 1). Importantly, these conditions frequently overlap and may be fundamentally linked. For example, approximately 33% of patients with documented microvascular angina will have esophageal motility disorders, and 25% to 33% will fulfill diagnostic criteria for panic attacks [11,12]. At least 50% of noncardiac chest pain syndromes are attributable to gastroesophageal reflux disease (GERD) or panic or depressive disorders.

#### Microvascular Angina

Although the existence of microvascular angina as a specific syndrome remains controversial and its pathophysiology remains elusive, it may be a cause of myocardial ischemia in patients with normal epicardial coronary arteries. Cannon and colleagues [13] demonstrated that a subset of patients with exertional chest pain and normal coronary arteries appeared to have abnormalities of coronary vasodilator reserve. These patients developed pain as a result of exercise, and many had evidence of cardiac wall motion abnormalities and reduced left ventricular ejection fraction. Despite the ominous findings, these individuals usually enjoy a benign course, with no significant increase in cardiovascular mortality [14,15].

#### Esophageal Disorders

Esophageal motility disorders. Although esophageal dysmotility is historically an important touchstone for diagnosing noncardiac chest pain [16,17], more recent evidence suggests that it is a much less common etiology of chest pain [18]. Initial observations suggested that esophageal dysmotility and spasm caused pain as a result of high amplitude contractions and possible concomitant esophageal ischemia [16]. As shown in Table 2, nonspecific esophageal motility disorders, such as the nutcracker esophagus and hypertensive lower esophageal sphincter, occur with similar frequencies across a variety of patient subsets. Achalasia, arguably the 1 motility disorder with a definable pathophysiology, is found with increased frequency only in patients with dysphagia. These observations suggest that, in the absence of other esophageal symptoms, particularly dysphagia, esophageal motility disorders are uncommon etiologies for noncardiac chest pain [19,20].

### Table 1. Common Etiologies of Chest Pain

<table>
<thead>
<tr>
<th>Cardiovascular</th>
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<tbody>
<tr>
<td>Aortic aneurysm</td>
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<td>Coronary artery disease</td>
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<td>Microvascular angina</td>
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<td>Mitral valve prolapse</td>
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<td>Abnormal visceral nociception</td>
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<tr>
<td>Cholelithiasis</td>
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<tr>
<td>Esophageal dysmotility</td>
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<tr>
<td>Gastroesophageal reflux disease</td>
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<tr>
<td>Nonpeptic esophagitis</td>
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<tr>
<td>Pernic ulcer disease</td>
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<tbody>
<tr>
<td>Depression</td>
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<tr>
<td>Panic and anxiety disorders</td>
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<tr>
<td>Somatization</td>
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<tbody>
<tr>
<td>Asthma</td>
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<td>Pleural effusion</td>
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<td>Pneumothorax</td>
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<tr>
<td>Pulmonary embolism or infarction</td>
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<tr>
<td>Pulmonary hypertension</td>
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<table>
<thead>
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<td>Cervical and thoracic radiculopathy</td>
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<tr>
<td>Chest wall trauma</td>
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<tr>
<td>Costochondritis</td>
<td></td>
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<tr>
<td>Fibromyalgia</td>
<td></td>
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<tr>
<td>Varicella-zoster virus reactivation</td>
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</tbody>
</table>
**NONCARDIAC CHEST PAIN**

Table 2. Manometric Abnormalities in Patients with Chest Pain or Dysphagia

<table>
<thead>
<tr>
<th>Study Population</th>
<th>n</th>
<th>Achalasia (%)</th>
<th>DES (%)</th>
<th>Nutcracker Esophagus (%)</th>
<th>Total Nonspecific Disorders (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAD and suspected esophageal disease</td>
<td>251</td>
<td>0.0</td>
<td>4.3</td>
<td>13.5</td>
<td>26.6</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>251</td>
<td>19.0</td>
<td>7.0</td>
<td>5.0</td>
<td>27.0</td>
</tr>
<tr>
<td>Noncardiac chest pain</td>
<td>1372</td>
<td>4.3</td>
<td>2.4</td>
<td>12.6</td>
<td>24.0</td>
</tr>
<tr>
<td>Unselected manometry</td>
<td>2811</td>
<td>5.8</td>
<td>3.6</td>
<td>16.4</td>
<td>32.4</td>
</tr>
</tbody>
</table>

CAD = coronary artery disease; DES = diffuse esophageal spasm. (Adapted with permission from Kahrilas PJ, Clouse RE, Hogan WJ. American Gastroenterological Association technical review on the clinical use of esophageal manometry. Gastroenterology 1994;107:1865–84.)

Table 3. Results of Ambulatory pH and Pressure Monitoring in Patients with Presumed Esophageal Chest Pain

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Motility</th>
<th>Reflux</th>
<th>Neither</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peters et al</td>
<td>22</td>
<td>3</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Ghillebert et al</td>
<td>21</td>
<td>4</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Soffer et al</td>
<td>15</td>
<td>0</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Hewson et al</td>
<td>45</td>
<td>6</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Breumelhof et al</td>
<td>25</td>
<td>2</td>
<td>2</td>
<td>17</td>
</tr>
<tr>
<td>Nevens et al</td>
<td>8</td>
<td>1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Total (%)</td>
<td>136</td>
<td>16 (12)</td>
<td>40 (29)</td>
<td>59 (43)</td>
</tr>
</tbody>
</table>


**GERD.** A large body of evidence supports the role of GERD in noncardiac chest pain. Pooled analysis of studies using simultaneous ambulatory monitoring of both esophageal pH and motor function have identified dysmotility in only 12% of patients studied, whereas abnormal esophageal acid exposure was documented in 29% (Table 3) [20]. These data are consistent with additional reports that have documented abnormal degrees of esophageal acid exposure in patients with noncardiac chest pain, with a prevalence of 25% to 60% [21–25].

Abnormal visceral nociception. Patients with chest pain of undetermined origin may have a lowered threshold to visceral sensation, or abnormal visceral nociception. In this condition, pain may not arise in a particular end organ, but rather in the nociceptive afferent nerves and the modulatory, perceptual, and localizing pain pathways of the central nervous system [26,27]. In this condition, chest pain could be caused by a noxious stimulus involving the thoracic viscera, decreased threshold of visceral nociceptors, or an intrinsic disorder of nociceptive pathways.

**Psychiatric Disorders**

Psychiatric disorders are also quite common in patients with noncardiac chest pain. In evaluating 229 patients presenting to the ED of a large urban hospital, Yingling and colleagues identified panic disorder in 17.5% of patients and depression in 23.1% of patients [28]. Similar prevalence rates for these disorders have also been reported by other researchers [29,30]. Importantly, patients found to have panic or depressive disorders are much more likely to make multiple visits to acute care facilities, and their use of these costly resources exceeds that of patients with symptomatic CAD [28]. Identifying psychiatric disorders associated with noncardiac chest pain is clearly important both for resolving patient symptoms and for ensuring that resources are used efficiently.

**Rheumatologic Disorders**

Rheumatologic disorders may also present as noncardiac chest pain. Chest wall syndromes, including costochondritis, are reported in approximately 15% of patients, although the pain found on palpation does not always reproduce the presenting chest pain [31]. Additionally, fibromyalgia or fibrositis has been reported in up to 30% of patients with noncardiac chest pain [32].

* What is the approach to the patient with noncardiac chest pain?

**Evaluating Noncardiac Chest Pain**

Determining whether the chest pain is truly noncardiac in etiology is the critical first step in the evaluation of noncardiac chest pain. Symptomatic CAD and other cardiac abnormalities must be excluded to the satisfaction of both the
physician and patient. After the exclusion of cardiac and other thoracic conditions, patients should be evaluated for panic disorder (Figure 1).

Screening for Psychiatric Disorders

Our practice is to screen patients with noncardiac chest pain for panic disorder using a self-administered checklist (Figure 2) derived from the PRIME-MD Patient Problem Questionnaire [33] and based on criteria from the Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV). (Similar questionnaires to evaluate for depressive and somatoform disorders in primary care settings are also available [34,35].) Individuals with a positive screen for panic disorder should be promptly treated or referred for specialist evaluation and care. Because the presence of panic or depressive disorders strongly affects acute care resource use, prompt diagnosis and initiation of effective therapy are critical in achieving satisfying clinical and economic outcomes [28].

Screening and Evaluation for Esophageal Disorders

Patients with noncardiac chest pain also need to be screened for esophageal disorders. Although a valid questionnaire for GERD exists, it is principally a research study tool and is somewhat cumbersome for use in a busy private practice or acute care setting [36]. At the very least, physicians evaluating patients with noncardiac chest pain should determine whether heartburn, regurgitation, dysphagia, odynophagia, and epigastric pain are present. Although these symptoms are frequently present in patients with an esophageal etiology for chest pain, approximately 11% of patients with an esophageal cause of chest pain will have no other esophageal symptoms [22]. Therefore, the absence of other esophageal symptoms should not necessarily preclude further evaluation.

Upper gastrointestinal (UGI) endoscopy. Strategies for evaluating suspected esophageal chest pain continue to evolve. Patients with chest pain syndromes and dysphagia or other “alarm symptoms” (eg, weight loss, gross or occult bleeding, anemia) warrant prompt anatomic evaluation with UGI endoscopy and other studies as clinically indicated. The utility of UGI endoscopy and radiography as first-line investigative modalities in patients with noncardiac chest pain is quite limited, because both tests are insensitive for diagnosing GERD and most patients with GERD-induced chest pain do not have esophagitis[37].

Esophageal pH monitoring. Ambulatory esophageal pH monitoring has become the gold standard for evaluating esophageal acid exposure and diagnosing GERD [38]. In addition to documenting overall esophageal acid exposure (which is the most reliable test parameter for establishing a diagnosis of GERD), esophageal pH monitoring also allows for direct correlation of chest pain episodes with acid reflux episodes. This correlation is important because individuals with overall esophageal acid exposure within normal limits may still experience symptoms associated with isolated reflux events [22,39].

The procedure is performed by transnasally placing a 2-mm pH probe 5 cm above the lower esophageal sphincter and connecting it to a small recording device that the patient wears on his or her belt. While the test is being performed, patients are able to eat a normal diet, exercise, and perform activities generally without restriction. The procedure is generally well tolerated. Meal periods and symptoms are recorded in a diary and may later be correlated with esophageal acid exposure levels.

Despite the quantitatively useful aspects of ambulatory esophageal pH monitoring, it is not a perfect diagnostic modality. Its overall sensitivity and specificity for diagnosing GERD is approximately 81% to 85% and 85% to 100%, respectively [40,41]. Additionally, when patients without esophagitis are compared to asymptomatic controls, the test’s sensitivity is reduced to 60% to 70% [38]. These factors significantly limit the utility of the procedure because the predictive value of the test is weakest in the clinical subset in which it is most needed.

Proton pump inhibitors as diagnostic modality. The limited sensitivity of pH monitoring has led some investigators to suggest use of a therapeutic trial of proton pump inhibitors, with pH monitoring reserved for patients who have partial or no response to treatment [38]. Several recent studies have demonstrated the efficacy of an empiric trial of high-dose proton pump inhibitors in patients with noncardiac chest pain [21,42–44]. In these studies, investigators used omeprazole in doses ranging from 40 to 60 mg per day, administered as a single or split dose for 1 to 8 weeks.

In perhaps the best designed of these trials, Fass and colleagues [21] administered omeprazole (40 mg every morning and 20 mg nightly) for 1 week to 37 subjects with noncardiac chest pain. All subjects underwent endoscopy and pH monitoring before treatment, which was conducted in a double-blind, placebo-controlled, crossover design. Patients were considered GERD-positive if they had either a positive esophageal pH study or an endoscopy demonstrating esophagitis. Of 23 GERD-positive patients, 18 responded to omeprazole; only 2 of the 14 GERD-negative patients responded positively to omeprazole. Sensitivity for the “omeprazole test” was 78.3%, and the specificity was 85.7%. An economic decision analysis was performed for a 1-year period comparing the omeprazole test to conventional evaluation for suspected GERD. Empiric omeprazole was shown to save $573 per average patient and resulted in a 59% reduction in the number of diagnostic procedures.

OUTCOMES AND THE PATIENT

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Although further study regarding this approach is needed, proton pump inhibitors, given in high doses for a brief period of time, appear to represent a useful tool in the evaluation and treatment of noncardiac chest pain. We presently employ proton pump inhibitors, given twice daily for a 2-week period. Patients returning with persistent or incompletely relieved symptoms then undergo esophageal pH monitoring while on medication. This approach allows for assessment of therapeutic efficacy as well as correlation of symptoms with esophageal pH levels. And, although the omeprazole test requires further evaluation, the data clearly show that it has a sensitivity and specificity comparable to pH monitoring for patients with noncardiac chest pain, without the hassle or expense; in fact, this diagnostic strategy may actually be cost-saving if the patient is completely responsive to the omeprazole.

**Esophageal acid perfusion test.** Because GERD is the most common esophageal etiology of noncardiac chest pain [19-23], initial investigative efforts should address this consideration. The esophageal acid perfusion test, introduced by Bernstein and Baker in 1958, was long used to identify esophageal acid exposure as a mechanism of pain in subjects with noncardiac chest pain. However, this test has largely
been replaced by esophageal pH monitoring and empiric trials of acid suppressive therapy. Although this test has good diagnostic specificity, it lacks sensitivity when compared with ambulatory esophageal pH monitoring. In a study of 75 patients with noncardiac chest pain who underwent both esophageal acid perfusion and pH monitoring, “Bernstein’s test” was found to have a specificity of 90% but a sensitivity of only 36% [45].

Esophageal manometry: Esophageal motility disorders are uncommon causes of chest pain in the absence of dysphagia or other esophageal symptoms [18,19]; therefore, esophageal manometry has little use as a first-line diagnostic modality in the evaluation of noncardiac chest pain in these cases. However, esophageal manometry can be used in cases of noncardiac chest pain to localize the lower esophageal sphincter to facilitate accurate pH probe placement in the further evaluation of GERD.

Initial Treatment and Further Evaluation

After a negative screen for panic disorder, the patient is placed on oral omeprazole (20 mg twice daily). He returns in 2 weeks reporting a 30% reduction in his symptoms.

While still taking the omeprazole, the patient is referred for esophageal manometry and pH monitoring. Manometry fails to disclose significant esophageal dysmotility; pH monitoring demonstrates that esophageal acid exposure is within normal limits. The patient has a single episode of chest pain during the study, which is not associated with an acid reflux event.

- What are appropriate next steps in establishing a diagnosis in this patient?

Some individuals with no evidence of psychiatric disorders, GERD, or esophageal dysmotility will have persistent chest pain with no obvious etiology. At this stage of investigation, many physicians empirically administer psychoactive medication because of the high prevalence of psychiatric disorders in patients with noncardiac chest pain; the recognized psychophysiological effects of depression and anxiety on esophageal motor function, and the potential benefits of these medications for managing chronic pain syndromes [46]. Trazodone and imipramine have both been shown to be effective in this setting, with an approximately 50% improvement in self-reported symptom scores versus placebo [47,48] (Figure 3).
Esophageal Provocative Testing
Alternatively, patients at this stage may be referred for esophageal provocative testing to determine whether they have abnormal visceral nociception that may respond favorably to agents used to treat chronic pain syndromes. Additionally, patients who reach this level of evaluation are likely experiencing frequent symptoms and are often highly motivated to determine the cause of their problem. These provocative studies offer an opportunity for a positive diagnosis, which is the most critical determinant of a successful clinical outcome.

The fundamental principle of these provocative tests is that an esophageal stimulus, which is generally not perceived as adverse by asymptomatic individuals, is adverse to patients with abnormal visceral nociception. Similar observations have been made at angiography in patients with chest pain and normal coronary arteries. Right-heart catheter manipulation, pacing, and intracoronary injection of contrast medium were more likely to evoke chest discomfort in these individuals than in patients with valvular heart disease or cardiomyopathy [49]. Recognition of this entity allows initiation of useful therapies (e.g., imipramine or trazodone) in the management of chronic pain syndromes [47, 48].

Edrophonium infusion (the “Tensilon test”) and graded esophageal balloon distension are most commonly used. In our practice, these studies are performed in addition to pH monitoring after the patient has failed a trial of omeprazole. Administration of the cholinesterase inhibitor edrophonium chloride increases the amplitude and duration of esophageal contractions in all patients and reproduces pain in 18% to 55% of patients with noncardiac chest pain, but not in asymptomatic controls [50–53]. Graded intraesophageal balloon distension also identifies individuals with noncardiac chest pain who develop pain in response to distension at volumes not perceived as adverse by asymptomatic controls (Figure 4) [54]. Further study in this area is needed, most importantly to determine whether response to provocative esophageal testing predicts a response to neuromodulatory agents. Clearly, it would be advantageous to further identify subsets of patients with noncardiac chest pain who would respond to specific therapeutic agents. At present, the greatest value of provocative testing is providing the patient with a positive diagnosis.

Further Testing and Clinical Course
The patient undergoes provocative esophageal testing with both edrophonium and balloon distension. He develops typical chest pain after infusion of edrophonium, but not after a saline placebo; typical chest pain also develops at 7 mL of balloon distension. The patient is happy that “somebody finally found something” and is relieved that “it’s not all in [his] head.” Because of its demonstrated benefits in reducing noncardiac chest pain symptoms, he is started on oral trazodone 150 mg 4 times daily.
At a follow-up visit 6 weeks later, the patient reports that his pain still occurs but with less frequency and severity. He has not missed work and has resumed recreational activities. He has not sought medical care in the interim. Overall, the patient feels that his quality of life has significantly improved.

SUMMARY

Noncardiac chest pain is a common and costly problem. After exclusion of cardiac disease, a careful interview and evaluation should be performed to determine the presence of disorders of other thoracic viscera. In the absence of positive findings, patients should be evaluated and treated for panic or depressive disorders. Additionally, the high prevalence of esophageal disorders, particularly GERD, also warrants evaluation. In the absence of other esophageal symptoms, the omeprazole test is a reasonable and possibly cost-saving strategy. Individuals failing a trial of proton pump inhibitors should be referred for esophageal pH monitoring while on medication to determine esophageal acid exposure and association of symptoms with acid reflux events. In the absence of reflux as an obvious cause, esophageal manometry, either stationary or ambulatory, should be performed to exclude motility disorders. Ideally, provocative testing should be performed simultaneously, because it helps the physician make a positive diagnosis and identify patients with abnormal visceral nociception. Patients whose chest pain does not have an obvious etiology, and perhaps those with positive provocative studies in particular, should receive a trial of trazadone or imipramine.

There is a need for formal outcomes evaluation in this area. Favorable outcomes (ie, decreased resource consumption and improved patient functioning) have been shown to occur not only by excluding mortal conditions such as CAD but also by rendering a positive diagnosis [3,8]. This case study offers a concise, practical diagnostic strategy that does not depend heavily on inpatient services or endoscopy.

Our approach emphasizes the detection and treatment of common and treatable causes of noncardiac chest pain, including panic disorder and abnormal visceral nociception. The former condition has been shown to be a major determinant of acute care resource utilization, and the latter is a treatable entity not commonly considered. We are presently conducting outcomes studies to determine the predictive value of provocative testing with regard to response to imipramine, to develop an esophageal screening questionnaire for use in the ED, and to determine the predictive value and efficacy of the omeprazole test.

References

NONCARDIAC CHEST PAIN


1. The most appropriate first step in the evaluation of angina-like chest pain is
   (A) Trial of a proton pump inhibitor for suspected GERD
   (B) Evaluation for possible panic or anxiety disorder
   (C) Esophageal manometry to evaluate for esophageal spasm or other esophageal dysmotility
   (D) Exclusion of cardiac etiology for chest pain

2. Agents most likely to decrease symptoms in a patient with noncardiac chest pain and no evidence of cardiac, esophageal, rheumatologic, or psychiatric disease include
   (A) Proton pump inhibitors
   (B) Nitrates and calcium channel blockers
   (C) Trazodone and imipramine
   (D) Benzodiazepines

3. All of the following statements about psychiatric disorders in noncardiac chest pain are true EXCEPT
   (A) The most common psychiatric disturbances are panic disorder and depression
   (B) Establishing a psychiatric diagnosis obviates the need for further evaluation of noncardiac chest pain
   (C) The presence of panic disorder or depression is a major determinant of frequency of acute care service utilization
   (D) Psychiatric disturbances may be present in approximately 30% to 40% of patients with noncardiac chest pain

4. Which of the following tests may identify patients with noncardiac chest pain who have abnormal visceral nociception?
   (A) Omeprazole test
   (B) Bernstein’s test
   (C) Tensilon test
   (D) Upper gastrointestinal endoscopy

5. Diagnostic options for suspected GERD-related noncardiac chest pain include all of the following EXCEPT
   (A) Trial of proton pump inhibitors
   (B) Upper gastrointestinal endoscopy
   (C) Esophageal pH monitoring
   (D) Esophageal manometry
To receive CME credit for this case study, read the case study and then answer the multiple-choice questions on page 52. Circle your answers below. Also, please respond to the four questions that follow. Then, detach the evaluation form and mail or FAX to:

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Circle your answer to the CME questions below:
1. A  B  C  D
2. A  B  C  D
3. A  B  C  D
4. A  B  C  D
5. A  B  C  D

Please answer the following questions:
1. In general, how do you rate the information presented in the case study?
   ❑ excellent   ❑ good   ❑ fair   ❑ poor
2. Do you find the information presented in this case study to be fair, objective, and balanced?
   ❑ yes   ❑ no
3. Name three clinical conditions that, in your experience, lead to less than optimal patient outcomes:
   Condition 1: ________________________________________
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Note: CME credit letter and correct responses will be sent to the above-named person.

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