

Approach to managing undiagnosed chest pain

Could gastroesophageal reflux disease be the cause?

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ABSTRACT

OBJECTIVE To highlight gastroesophageal reflux disease as a common cause of undiagnosed chest pain.

SOURCES OF INFORMATION Diagnostic considerations are based on information in peer-reviewed articles retrieved from MEDLINE. Studies had to be in English and involve at least 30 subjects. Population-based studies had to have a sample size of at least 300 and a response rate of at least 60%. Thirty-seven relevant articles were found.

MAIN MESSAGE Clinical management of patients presenting with diagnostically challenging chest pain starts with a careful search for coronary artery disease and other potentially life-threatening causes. Investigations must continue until the underlying disease is identified and symptoms have been effectively controlled. Ongoing symptoms of undiagnosed chest pain cause considerable suffering, impair quality of life, and add unnecessary costs to the health care system. In more than half the patients with undiagnosed chest pain, symptoms are caused by gastroesophageal disease. Empirical acid-suppressive therapy with a proton pump inhibitor can assist clinicians in identifying patients whose symptoms are acid-related.

CONCLUSION Many patients with undiagnosed chest pain can be managed in primary care, minimizing the need for referrals and costly investigations.

RÉSUMÉ

OBJECTIF Mettre en évidence que le reflux gastro-œsophagien est une cause fréquente de douleur thoracique d'étiologie indéterminée.

SOURCES DE L'INFORMATION Les considérations d'ordre diagnostique proviennent d'articles révisés par des pairs recensés dans MEDLINE. Les études devaient être en anglais et porter sur au moins 30 sujets. Dans les études démographiques, la taille des échantillons devait être d'au moins 300 et le taux de réponse d'au moins 60%. Trente-sept articles pertinents ont été retenus.

PRINCIPAL MESSAGE Chez un patient qui présente une douleur thoracique d'origine incertaine, on doit d'abord rechercher soigneusement une maladie coronarienne ou toute autre cause potentielle de mort. L'investigation doit se poursuivre jusqu'à ce qu'on ait identifié la maladie causale et obtenu un contrôle adéquat des symptômes. Des douleurs thoraciques d'étiologie indéterminée entraînent à la longue d'importantes souffrances, une perte de qualité de vie et des coûts inutiles pour le système de santé. Dans plus de la moitié des cas de douleur thoracique non diagnostiquée, les symptômes sont causés par le reflux gastro-œsophagien. Un traitement empirique d'inhibition de la sécrétion acide par un inhibiteur de la pompe à protons peut aider le médecin à identifier les patients dont les symptômes sont reliés à l'acidité.

CONCLUSION Plusieurs patients présentant des douleurs thoraciques d'origine indéterminée peuvent être traités adéquatement en soins de première ligne, réduisant ainsi le recours à des consultations ou investigations coûteuses.

This article has been peer reviewed.

Cet article a fait l'objet d'une révision par des pairs.

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This article presents an approach to management of undiagnosed chest pain, focusing on the importance of gastroesophageal reflux disease (GERD) once physicians have determined that cardiac causes are unlikely. The management plan is based on a review of the literature by a group of experienced family physicians, a gastroenterologist, and a cardiologist. Using this management plan, family physicians can resolve most cases.

Bob's case

Bob, a stressed entrepreneur with unexplained chest pain, is a 48-year-old businessman with a sedentary lifestyle (Table 1). He is increasingly troubled by chest pain that started more than a year ago and is getting more frequent as his work stress increases. He came to the emergency ward recently with a particularly severe episode of chest pain. After performing the usual cardiac tests, the emergency physician and the cardiologist concluded that there was a low probability of symptomatic coronary artery disease and advised Bob to visit his family doctor. Bob has made an appointment to talk to you. He remains concerned because he continues to experience chest pain and

Table 1. Case profile

48-year-old man
Sedentary lifestyle
Stressful job
Body mass index of 31
Central obesity
Nonsmoker
Slightly elevated low-density lipoprotein cholesterol
Normoglycemic
Eats a predominantly "fast food" diet
Consumes 2 units of alcohol daily

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has not been given an explanation for his symptoms. He suspects something is seriously wrong, and he trusts your opinion. What will you do?

Sources of information

MEDLINE was searched from 1966 to June 2005 using the terms "chest wall tenderness or chest pain" and "myocardial infarction or coronary or gastroesophageal reflux" or "non-cardiac chest pain." Inclusion criteria were that articles were in English and that clinical studies included at least 30 subjects. Population-based studies were required to have a sample size of at least 300 and a response rate of at least 60%. This search identified 37 relevant articles. Evidence supporting recommendations was graded using the Strength Of Recommendation Taxonomy (SORT), where level I was the highest and level III the lowest grade.¹ Conclusions are based primarily on meta-analyses, systematic reviews, high-quality cohort studies, and large population-based studies. By SORT criteria, most of these studies provided level II evidence.

Undiagnosed chest pain

Chest pain can be one of the most challenging problems managed by primary care physicians. Chest pain is a common symptom in the community, with an estimated prevalence of between 10% and 30%,²⁻⁶ yet it accounts for only about 2% of primary care consultations.⁷ Chest pain can be an indication of potentially life-threatening coronary artery disease (CAD), but cardiac causes account for fewer than 20% of chest pain cases in the community and primary care settings.^{2,7,8} Unfortunately, investigation of many patients stops once CAD has been ruled out, bypassing the critical steps needed for an accurate diagnosis and effective management of their symptoms.⁹ Patients whose history, physical examination, and basic diagnostic tests have not revealed the cause of their chest pain are said to have undiagnosed chest pain, because they do not appear to have cardiovascular disease or other obvious causes of their symptoms.

Investigating the cause of chest pain

Common causes of chest pain include those of musculoskeletal, gastrointestinal, cardiac, pulmonary, and psychiatric origin (Table 2). Regardless of where care is given, the critical first step in managing patients with chest pain is to explore the possibility of potentially life-threatening causes of the symptoms. This often requires a few key investigations to search for evidence of CAD.

Careful assessment of patients' history is often the most helpful starting point. Historical features generally of greatest value include the quality, duration, and timing of pain, as well as its association with trauma, meals, respiration, or exertion. Unfortunately, physicians are often unable to make an accurate diagnosis based

Table 2. Potential causes of chest pain
CARDIAC CAUSES

Atherosclerotic coronary artery disease
 Congenital coronary artery disease
 Coronary spasm
 Systemic hypertension
 Pulmonary hypertension
 Aortic stenosis
 Aortic insufficiency
 Hypertrophic cardiomyopathy
 Severe anemia
 Severe hypoxia
 Polycythemia
 Aortic dissection
 Aortic aneurysm
 Pericarditis
 Mitral valve prolapse
 Myocarditis
 Cardiomyopathy

GASTROINTESTINAL CAUSES

Nutcracker esophagus
 Diffuse esophageal spasm
 Nonspecific motility disorder
 Achalasia
 Gastroesophageal reflux
 Mallory–Weiss syndrome
 Esophagitis
Candida infection
 Herpes
 Irradiation-induced pain
 Esophageal foreign body
 Peptic ulcer disease
 Pancreatitis
 Biliary disease
 Splenic infarction
 Gaseous bowel distention

NEUROMUSCULOSKELETAL CAUSES

Thoracic outlet syndrome
 Anterior scalenus hypertrophy
 Cervical rib syndrome
 Cervical disc disease
 Costochondritis or Tietze's syndrome
 Chest wall trauma or rib fracture
 Malignancy
 Herpes zoster
 Precordial catch syndrome
 Entrapment of nerves by sternal wire sutures
 Xiphodynia
 Slipping rib syndrome
 Ostealgia due to neoplasm
 Intercostal neuritis
 Costovertebral joint dysfunction

PULMONARY CAUSES

Pulmonary embolism
 Pneumothorax
 Pneumonia
 Pleuritis
 Bronchospasm
 Pulmonary hypertension
 Tracheitis or tracheobronchitis
 Intrathoracic tumour

PSYCHIATRIC CAUSES

Depression
 Anxiety
 Panic attacks
 Malingering

OTHER CAUSES

Cocaine use
 Lymphoma
 Diabetes
 Uremia
 Renal stones
 Mondor's syndrome
 Mediastinitis
 Mediastinal emphysema
 Mediastinal neoplasm

solely on history because, for example, descriptions of chest pain of cardiac, upper gastrointestinal, or gallbladder origin can be identical.¹⁰ Hence, although patients' history is a valuable starting point, it often fails to provide a definite diagnosis because symptoms generally have poor specificity in diagnosis of chest pain (level I evidence).^{11,12}

Similarly, physical examination rarely reveals clinical signs sufficiently specific to support an accurate diagnosis (level II evidence).¹¹ The most common finding during examination of patients with chest pain is chest wall tenderness,⁸ but this is another clinical feature of low value in excluding cardiac causes of symptoms.^{11,13,14} It has been reported that 51% of patients with proven acute myocardial infarction have chest wall tenderness.¹⁵ Diaphoresis, a third heart sound, or hypotension might support the presence of ischemic heart disease, but have insufficient sensitivity and specificity to be helpful in most cases.¹¹

Cardiac risk stratification is of little use, given that even in the highest risk groups, most patients' chest pain is not caused by cardiac conditions (level II evidence).^{2,7,8} Only 30% of patients admitted to hospital for chest pain are found to have cardiac origins of their symptoms.^{16,17} Patients consulting primary care physicians for nonurgent assessment of chest pain are even less likely to have CAD. A few carefully chosen diagnostic tests are often needed to support or refute a developing diagnosis. The importance of CAD as a cause of chest pain means clinicians often need to order electrocardiograms, serum troponin assays, and exercise stress tests when carefully searching for symptomatic CAD.

Need for a definite diagnosis

Managing patients with undiagnosed chest pain is a real challenge. Once a cardiac cause for the pain is judged unlikely, patients are often dismissed without further diagnostic efforts.⁹ Undiagnosed chest pain results in ongoing anxiety because patients continue to experience pain and often continue to believe there is a cardiac origin for their symptoms.⁹ These patients need

a diagnosis and access to appropriate treatment.^{18,19} Chest pain can be perpetuated by secondary anxiety and this, together with avoidance behaviour,²⁰ results in a substantially diminished quality of life for undiagnosed patients.^{21,22}

The psychological and physical suffering of patients with undiagnosed chest pain costs the health care system a great deal. In 1989, an American study calculated that initial treatment of a patient with undiagnosed chest pain cost approximately \$3500 (US) per year.²³ This added to a total in excess of \$315 million (US) for all noncardiac cases diagnosed per year in the United States. Now, 16 years later, these costs are likely much higher.

Role of gastroesophageal reflux disease

What are the next steps for clinicians committed to providing high-quality health care for their patients with chest pain? Some population-based studies have found undiagnosed chest pain to be associated with GERD^{2,4,5,24,25} as well as anxiety and depression (level II evidence).^{2,26} The prevalence of GERD in those with undiagnosed chest pain is estimated to be greater than 50%.^{2,5,6,26} Prevalence of GERD is 10% to 20% in

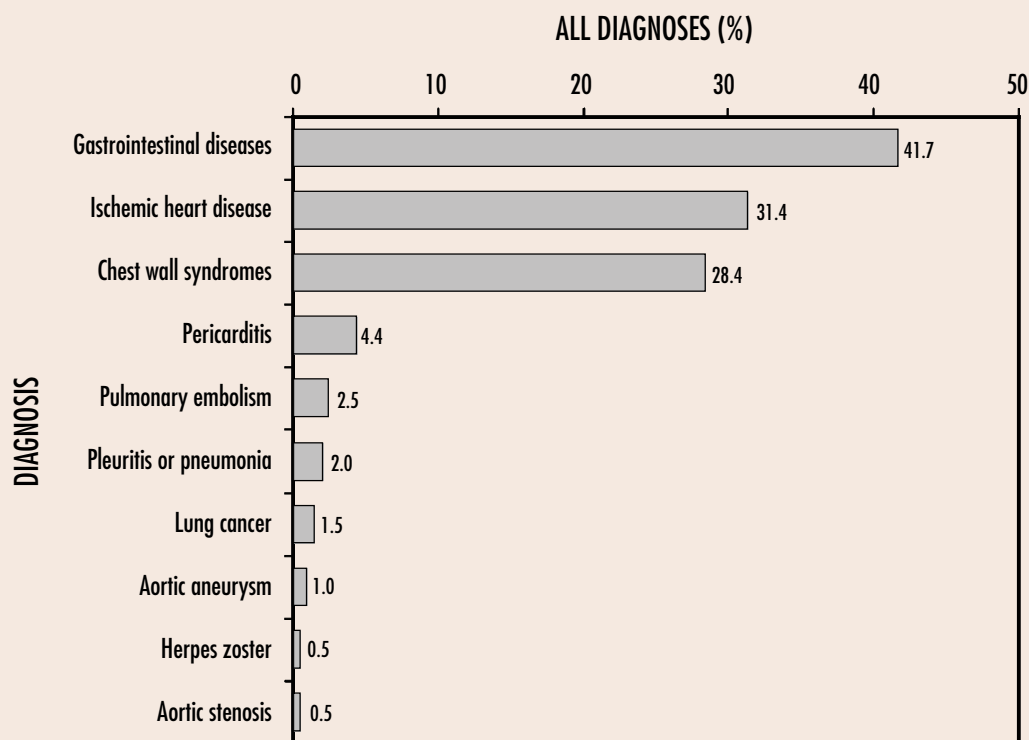
the general population.^{5,27} Fruergaard and colleagues¹⁶ reported the frequency of diagnoses in patients who were admitted to a coronary care unit in Denmark with unexplained chest pain. They showed that the most common causes of undiagnosed chest pain were gastrointestinal diseases, among which GERD was by far the most prominent (level II evidence) (Figure 1¹⁶).

Diagnosis of gastroesophageal reflux disease

The next logical step in management of patients with undiagnosed chest pain is to consider a diagnosis of GERD. There are many ways to diagnose GERD, including pH testing, manometry, upper gastrointestinal radiography, and endoscopy.²⁸ All the tests have limitations, such as suboptimal sensitivity, specificity, or availability, so no single test can be considered a criterion standard for diagnosing GERD.

The practical approach of symptom-based diagnosis minimizes the need for costly investigations that are often difficult to access and sometimes add little information (level I evidence).²⁹ Symptom-based approaches use the typical features of heartburn and regurgitation to identify patients thought to have GERD. It is important to bear in mind, however, that this approach often

Figure 1. Frequency of diagnoses in patients admitted with acute chest pain who have not had myocardial infarctions



Adapted from Fruergaard et al.¹⁶

fails to identify patients whose GERD presents predominantly as chest pain rather than typical GERD. In the Canadian Adult Dyspepsia Empiric Treatment–Prompt Endoscopy (CADET–PE) study of 1040 primary care patients with dyspepsia (level II evidence), endoscopy was carried out within a few days of entry into the study to identify clinically significant lesions that could explain each patient's symptoms.³⁰ The investigators found that the dominant symptoms of many patients with esophagitis were similar to symptoms of ulcer or dysmotility rather than reflux symptoms indicative of GERD. These findings confirmed earlier observations that the typical symptoms of heartburn and regurgitation can be absent in many GERD patients, including those presenting with chest pain.

For now, the inclusion of atypical symptoms, such as chest pain, as possible markers of GERD should be in the context of a careful initial assessment, close follow up, and monitoring for response to empirical treatment. A logical strategy would be to use a proton pump inhibitor (PPI) to test patients for response to effective acid suppression,^{31,32} an approach supported by recent meta-analyses (level I evidence).^{33,34} It is recommended that PPIs be used for such tests because the effectiveness of diet and lifestyle advice and H₂-receptor antagonists for patients with undiagnosed chest pain remains unsupported by data from randomized controlled trials. Response to PPI therapy would support the clinical hypothesis of an acid-related upper gastrointestinal disorder as the cause of the undiagnosed chest pain; the CADET–PE study identified GERD as the cause of almost all acid-related disorders in Canadian primary care dyspepsia patients.³⁰

Issues in clinical management

Patients with undiagnosed chest pain need close follow up when they are tested with PPIs, as upper gastrointestinal symptoms can, on rare occasions, indicate serious diseases, such as cancer. Care should always be taken to identify patients who might benefit from further investigations, such as upper gastrointestinal endoscopy, because they have alarm features (Figure 2²⁹) or are

advanced in age (risk of upper gastrointestinal malignancy increases each year after age 50).

Clinicians also need to remain alert for coexisting common conditions. Coronary artery disease and GERD are both common^{5,27,35,36} and can coexist in the same patient. There might even be some poorly understood connection between these 2 conditions that results in an unusually common coexistence.^{37,38} Identifying GERD as a cause of undiagnosed chest pain does not, therefore, exclude other causes.

Other causes of undiagnosed chest pain

In the absence of evidence for cardiac or gastrointestinal causes of undiagnosed chest pain, further investigations might be necessary. A careful history can suggest possible alternative causes in some patients; physical examination might help diagnose such causes as pneumothorax or herpes zoster. Investigations, such as oxygen saturation testing, blood-gas measurements, chest x-ray scans, ventilation or perfusion scanning, or computed tomography, might be required to identify vascular, pulmonary, and more obscure causes of chest pain. Abdominal ultrasound or CT scan might be requested for patients whose symptoms or physical findings suggest other abdominal diseases, such as gallbladder disease, as the cause.

Case resolution

Results of Bob's cardiovascular disease investigations indicated that he was unlikely to have CAD as a cause for his symptoms. His family physician prescribed a PPI because a careful history and physical examination failed to reveal the diagnosis. This strategy was based on the working hypothesis that Bob could be experiencing atypical symptoms of GERD. Two weeks later, Bob reported nearly complete relief of his symptoms, and he was no longer worried that his symptoms were from an impending heart attack. Bob and his family physician discussed the health benefits of eating a more balanced diet and taking regular exercise, and Bob continued the course of PPI therapy. Bob and his family doctor are pleased with the outcome and remain in contact periodically to monitor Bob's progress.

Conclusion


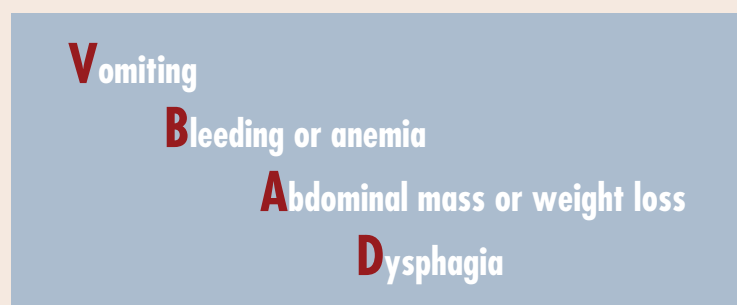
While managing undiagnosed chest pain can be a great challenge for primary care physicians, it is also an opportunity to provide optimal care with minimal need for costly investigations or referrals. A careful search for symptomatic cardiovascular disease followed, if necessary, by a clinical assessment for atypical GERD will provide a solid foundation for managing patients with undiagnosed chest pain. 

Figure 2. Alarm features prompting further investigation by endoscopy²⁹



Competing interests

None declared

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EDITOR'S KEY POINTS

- The causes of chest pain are many, but family doctors need to first rule out life-threatening diagnoses when patients present with symptoms.
- Once cardiac or other serious illnesses have been ruled out, physicians should consider gastroesophageal reflux disease as most likely, because it has the highest prevalence as a cause of undiagnosed chest pain.
- Unless patients have "red flags," such as vomiting, bleeding, anemia, abdominal mass, weight loss, or dysphagia (and possibly are older than 50 years), a trial of a proton pump inhibitor will often eliminate symptoms and confirm the diagnosis.
- Gastroesophageal reflux disease can present without a sense of reflux, but rather as ulcerlike pain or with dysmotility symptoms. A trial of proton pump inhibitors helps confirm the diagnosis.

POINTS DE REPÈRE DU RÉDACTEUR

- Compte tenu des nombreuses causes de douleur thoracique, le médecin doit d'abord éliminer les problèmes pouvant menacer la vie du patient.
- Après avoir exclu les problèmes cardiaques et autres maladies graves, le médecin doit penser au reflux gastro-œsophagien comme étant le diagnostic le plus probable, cette maladie étant la cause la plus fréquente de douleur thoracique d'étiologie indéterminée.
- Sauf en présence de signes évidents tels que vomissements, hémorragie, anémie, masse abdominale, perte de poids ou dysphagie (et peut-être aussi quand le patient a plus de 50 ans), l'essai d'un inhibiteur de la pompe à protons pourra souvent soulager les symptômes et confirmer le diagnostic.
- Dans le reflux gastro-œsophagien, il peut ne pas y avoir de sensation de reflux, mais plutôt de la douleur de type ulcère ou des troubles de motilité. Un essai avec un inhibiteur de la pompe à protons aidera à confirmer le diagnostic.

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