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An Algorithm for the Diagnosis and Management of Chest Pain in Primary Care

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KEYWORDS

• Chest pain • Algorithm • Diagnosis • Evidence

BACKGROUND AND SIGNIFICANCE

In response to the demands that chest pain assessment has placed on the health system, chest pain assessment protocols and services have been established in several countries to provide more effective and cost-efficient methods of dealing with the assessment and management of chest pain. Many of them are focused on risk stratification for life-threatening causes of chest pain, for example the Rouan decision rule for myocardial infarction (MI)¹ or the Wells score for pulmonary embolism (PE).² These protocols are mostly oriented toward use in the emergency department setting. They need some adaptation to make them relevant to the primary care setting, in which the spectrum of causes of chest pain is different to that in the emergency setting.³ The emergency department protocols generally do not venture into the diagnosis of other causes of chest pain that are not life threatening, commonly referred to as noncardiac chest pain (NCCP).⁴

The diagnosis of NCCP is challenging as it is a condition with many causes; individuals may have more than 1 cause of NCCP or have chest pain from cardiac and noncardiac causes simultaneously. History, examination, and investigations all have limited sensitivity and specificity and a definitive pathology often difficult or impossible to define. The noncardiac causes of chest pain have been classified broadly as

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gastroenterologic, soft-tissue, musculoskeletal, pulmonary, and psychiatric.⁵ The morbidity in this group with NCCP is considerable.^{4,5} There has been a debate in the literature about how to deal with these patients once coronary artery disease (CAD) has been excluded. Some propose that providing a definitive diagnosis may be less important than addressing the patients' fears by providing an explanation and reassurance.⁶ They call for the development of better, noninvasive algorithms for use by general practitioners to avoid unnecessary referrals to hospital. Others strongly endorse the importance of a definitive diagnosis and argue that the inability to provide a definitive diagnosis may relate to the psychological and psychiatric complications of chest pain.⁷ They claim that it is possible to achieve this in up to 85% of cases. If this is indeed possible, there may be opportunities to develop better algorithms for positive diagnosis coupled with good-quality explanation, reassurance, and medical management of chest pain to reduce the physical and psychological morbidity of NCCP and the associated costs to the individual and the health system.

Few algorithms are designed to guide practitioners on all major causes of chest pain, particularly in the outpatient primary care setting. Cayley⁸ has devised an algorithm derived from the best available evidence, incorporating the Rouan rule for MI,¹ the Wells score for PE,² a 2-question screen for panic disorder,⁹ and selective symptoms and signs with the best, albeit limited, diagnostic usefulness. However, it does not fully address diagnosis of gastroenterologic, musculoskeletal, soft-tissue, and psychological causes of chest pain. This article updates and expands this algorithm to provide the primary care practitioner with a flexible, efficient, and evidence-based approach to the primary care patient with chest pain. The algorithm covers the common causes and the rare but life-threatening causes and is based on several principles that translate evidence into practice and that also recognize the realities of working in primary care.

PRINCIPLES UNDERPINNING THE CHEST PAIN ALGORITHM

Given the large number of potential causes of chest pain in primary care and multiple clinical features and investigations used for the diagnosis or exclusion of each cause, the authors have devised an algorithm that guides the diagnostic processes for chest pain in primary care. This algorithm combines problem-solving and decision-making approaches.¹⁰ In the problem-solving approach, clinical features lead to a limited number of hypotheses based on pattern recognition, spot diagnosis, and clinical experience. These hypotheses inform subsequent information gathering. In the decision-making process, the diagnosis is refined using probabilistic reasoning.¹¹ Probabilistic reasoning is based on knowledge of the pretest probability or prevalence of a condition and how this translates to the posttest probability based on knowledge of the diagnostic accuracy of the clinical feature or test. This principle is often not applied explicitly by exact computation of posttest probabilities, but in a more informal, implicit manner following 2 basic rules in deciding between 2 possible causes with a positive diagnostic test result:

- 1. If the 2 possible causes have equal prevalence, but the diagnostic tests differ in their accuracy, prioritize the cause with the better test.
- 2. If the 2 diagnostic tests have equal accuracy, prioritize the cause with the higher prevalence.

The algorithm presented in **Fig. 1** describes a logical order to diagnosis that is safe, efficient, and comprehensive. A key consideration for safety in diagnosis is to start by assessing conditions that have the potential to threaten life. Similar to the assessment

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Fig. 1. Algorithm for assessment of chest pain in primary care. The key elements for use in the algorithm are summarized in **Tables 6**, **7** and **8**. The algorithm proposed here, although based on available evidence, does not constitute a validated decision rule.

of low back pain, indicators of life-threatening physical causes are labeled as red flags, indicators of non–life-threatening physical causes as green flags, and psychosocial indicators as yellow flags.¹² The assessment of red flags takes priority over green and yellow flags. The assessment of green flags comes next, and it is the step in which the principle of probabilistic reasoning is most prominent. As all potential green flag conditions are of equal medical importance (in the sense of their need to be treated), and as the diagnostic elements of the green flags can be easily performed, it is reasonable to consider these potential causes simultaneously and to select the most likely causes for further consideration. Although assessment of yellow flags may occur throughout the consultation, decisions about their contribution to the sensation of chest pain are left until after the green flags have been adequately assessed, with the intention of increasing the diagnostic confidence about psychogenic causes or factors.

The key diagnostic elements used in the processes of the algorithm are described and tabulated later in this article. Here, the term "element" includes various symptoms, signs, and investigations or diagnostic rules or scores based on pieces of diagnostic information. A diagnostic element may also include a pragmatic trial of treatment, in which the response may support or refute a provisional diagnosis.

In choosing the elements for use in the algorithm, several properties of the elements in the primary care setting have been considered. These elements include their diagnostic performance, risks, benefits, cost, and usefulness.

Diagnostic Performance

Single history, examination, and investigation elements

The diagnostic performance of single elements with positive or negative results is variously described by the properties of sensitivity and specificity, positive and negative likelihood ratios (LRs), positive and negative predictive values, and odds ratios. Definitions of these terms can be viewed at http://www.cebm.utoronto.ca/glossary/index. htm#s. Positive predictive value expresses the probability that the disease is present when the test is positive. A high positive predictive value is desirable in the early phase of the algorithm to make quick and accurate decisions about treatment; however, a lower positive predictive value is acceptable later in the algorithm when making decisions about therapeutic trials for low-risk conditions. The negative predictive value expresses the probability that the disease is absent when the test is negative. This factor is most important for ruling out red flag causes confidently early in the algorithm but also later to rule out additional diagnoses.

Clinical prediction rules

Clinical prediction rules (CPRs), also called diagnostic rules or diagnostic scores, aim to quantify the contribution of history, physical examination and diagnostic tests and stratify patients into levels of probability of having a condition.¹³ A validated CPR offers more diagnostic confidence than an unvalidated rule.

Accessibility

The following considerations affect the accessibility of elements to primary care physicians.

Cost

Lower cost elements, such as clinical assessment and simple surgery tests, are preferred but when an expensive investigation has a high diagnostic accuracy that leads to definitive diagnosis, this may be incorporated.

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Time

Because of the time constraints in primary care, elements that are simpler and more rapidly administered are favored. With respect to tests or treatments, elements with a more rapid response time are more useful diagnostically.

Resources

Equipment, if needed for the element, should be available in primary care. If it is not widely available, such as bedside troponin testing, an alternative, such as laboratory testing, should be considered.

Level of training required

The element should be able to be performed in primary care. If the level of training is higher than that generally present in the primary care setting, the element should be included only as an option with an alternative.

Risks Versus Benefits

Risks

The risk of adverse events is balanced against the potential benefits of diagnostic and treatment elements of the algorithm. Higher risks are more acceptable for red flag causes than for green or yellow flag causes. The risk of missing a red flag cause by not including an element is also a consideration.

Benefits

Benefits include reassurance as well as relief of symptoms and reduction of risk of future events. With therapeutic trials, the size of the treatment effect and the predictive value of a response to treatment, if available, will influence their inclusion in the algorithm.

Diagnostic Confidence

In the process of applying the algorithm, there will be branching points with decisions about the use of an expensive or high-risk test or therapeutic trial that will be affected by the diagnostic confidence at that point. For example, patients who are categorized as at high risk of acute coronary syndrome (ACS) will have a strong indication for referral for coronary angiography.

Quality of Evidence

This article uses the strength of recommendation taxonomy (SORT) for clinical review articles based on the quality and consistency of available evidence (http://www.aafp. org/online/en/home/publications/journals/afp/afpsort.html).¹⁴

- A = consistent, good-quality patient-oriented evidence
- B = inconsistent or limited-quality patient-oriented evidence
- C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series for studies of diagnosis, treatment, prevention, or screening.

In the interests of efficiency, we have limited the choice of elements to those with the best evidence or at least some evidence supporting them. Despite this the level of evidence for many elements, particularly those related to NCCP, is still only at level C.

The Epidemiology of Chest Pain in Primary Care

Patients with chest pain place a considerable burden on the health systems of many countries. The proportion of general practice consultations for chest pain varies from at least 1% in the United Kingdom¹⁵ to 1.5% in Sweden¹⁶ and 2.7% in Switzerland.¹⁷

In the British general practice setting the rate of new diagnoses of chest pain has been estimated at 15.5 per 1000 person-years.¹⁸

The diagnostic probabilities across the spectrum of causes depend on the setting. The prevalences of diagnostic categories for chest pain in primary care have been defined for at least 3 countries, based on studies of often unvalidated medical diagnoses from medical records and patient questionnaires (**Table 1**). In Belgium they have been compared with the spectrum of chest pain diagnoses in a hospital emergency department setting, highlighting some major differences. Cardiac diagnoses accounted for 54% in hospital compared with 13% in primary care.³ Of the noncardiac causes, musculoskeletal chest pain comprised 6% of hospital diagnoses compared with 21% in primary care. Pulmonary diagnoses accounted for 12% in hospital compared but only 20% of the latter were serious diagnoses (ie, pneumonia, pleuritis, pneumothorax, and lung cancer) and the remainder were for tracheitis or bronchitis. Over the 3 countries, musculoskeletal diagnoses comprised 21% to 51% of totals, making them the most common amongst the noncardiac categories.^{3,17,19} The prevalence of gastroenterologic diagnoses was 8% to 19% and of psychogenic diagnoses was 8% to 17%.

The key diagnostic elements for specific causes of chest pain are outlined in the following section. In the spirit of probabilistic reasoning we have addressed them in order of decreasing prevalence within each diagnostic category. However, as we were unable to find comparative data on the prevalence of many of these specific causes, the estimates of prevalence for some causes are based on our clinical experience.

DIAGNOSTIC ELEMENTS FOR COMMON CAUSES OF CHEST PAIN IN PRIMARY CARE Cardiovascular Causes

ACS

Three key clinical features of chest pain can help predict the risk of CAD: (1) location (is it substernal chest pain?), (2) aggravating factors (is it exertional?), and (3) alleviating factors (is it relieved by rest or nitroglycerin?). Chest pain with all 3 characteristics is considered angina chest pain, and is high risk for CAD in all age groups. If only 2 of

Table 1

The prevalence of diagnostic categories for chest pain in patients with chest pain in the primary care setting versus the emergency department setting

Diagnosis	Primary Care (USA) ¹⁸ (%)	Primary Care (Switzerland) ¹⁶ (%)	Primary Care (Belgium) ³ (%)	Emergency Department (Belgium) ³ (%)
Cardiovascular ^a	16	16	13	54
Musculoskeletal	36	51	21	6
Pulmonary	5	10	20	12
Gastroenterologic	19	8	10	3
Psychogenic	8	11	17	9
Total noncardiac	68	80	68	30
Other			10	10
Uncertain/not specified	16	4	1	5

^a Including pulmonary embolism.

the 3 characteristics are present, chest pain is considered atypical angina, which carries intermediate risk for CAD in women older than 50 years and in all men. Nonanginal chest pain, with only 1 of the 3 characteristics present, carries intermediate risk for CAD in women older than 60 years and men older than 40 years.²⁰

Patients whose chest pain puts them at moderate to high risk of CAD deserve prompt assessment for the risk of ACS. ACS includes acute myocardial infarction (AMI) and unstable angina. However, studies in emergency department settings show that only a few features of angina chest pain have adequate usefulness to meaningfully increase or decrease the diagnostic likelihood of AMI. Exertional chest pain (LR 2.35) and pain radiating to the shoulder or both arms (LR 4.07) increase the likelihood of AMI. Similarly, exertional chest pain (LR 2.06), and pain radiating to the shoulder, the left arm, or both arms (LR 1.62) are the features most predictive of any ACS.²¹ Symptoms that are not predictive for either ACS or AMI include the site or nature of the pain and the presence of nausea, vomiting, or diaphoresis.²² The only physical finding that is helpful in diagnosis of ACS or MI is chest wall tenderness. Presence of chest wall tenderness (LR 0.3) or reproduction of chest pain with palpation (LR 0.23) both significantly decrease the likelihood that chest pain is caused by ACS or AMI.^{22,23}

The most important initial test for the patient at risk of ACS or AMI is an electrocardiogram (ECG). Electrocardiographic findings that most strongly suggest ACS or AMI are new ST segment increase (LR 16), new Q waves (LR range, 8.7), and a new conduction defect (LR 6.3). Although a normal ECG result markedly decreases the likelihood of an MI (LR range, 0.1–0.3), no ECG abnormality is sensitive enough for AMI or ACS that its absence completely excludes the diagnosis.²⁴

The Rouan decision rule can help predict which patients with chest pain and a normal or nonspecific ECG are at higher risk for MI (**Table 2**).¹ However, emergency department data indicate that up to 3% of patients initially diagnosed with a noncardiac cause of chest pain suffer death or MI within 30 days of presentation; thus patients with cardiac risk factors such as male sex, greater age, diabetes, hyperlipidemia, previous CAD, or heart failure warrant close follow-up.²⁵

The most common markers of myocardial damage are creatine kinase (CK), its MB subform (CKMB), troponin T (TnT), and troponin I (TnI). A CKMB level greater than 6.0 ng/mL within 9 hours of presentation for emergency care modestly increases the likelihood of MI or death in the next 30 days.²⁶

Increased levels of either troponin (TnT > 2 ng/mL or TnI > 1 ng/mL) support the diagnosis of MI or ACS and increase the likelihood of death or recurrent MI within 30 days. Increase of troponin takes 4 to 6 hours and may remain increased for 5 to 14 days.²⁷

Table 2 Rouan decision rule: clinical characteristics and risk of MI					
Clinical Characteristics	No. of Factors Present	Risk of MI (%)			
Age > 60 years	0	Up to 0.6			
Male gender	1	Up to 3.4			
Pain described as pressure	2	Up to 4.8			
Pain radiates to arm, shoulder, neck or jaw	3	Up to 12			
Diaphoresis	4	Up to 26			
History of previous MI or angina					

Data from Rouan GW, Lee TH, Cook EF, et al. Clinical characteristics and outcome of acute myocardial infarction in patients with initially normal or nonspecific electrocardiograms (a report from the Multicenter Chest Pain Study). Am J Cardiol 1989;64:1087–92. A survey of New Zealand general practitioners found that the majority ordered troponins at least once monthly and would be more likely to use this test if the likelihood of AMI was less than 5%, or the pain was more than 12 hours ago.²⁸ One study of 773 patients presenting to an emergency department with chest pain and an essentially normal ECG found that for detection of AMI, the sensitivity of TnT was 94% and of TnI was 100%. The specificity of the 2 assays was 99.7% and 98.9%, respectively (ie, only 0.3% with a normal TnI and 1.1% with a normal TnT at 6 hours died or had acute MI in the next 30 days).²⁹

In the detection of MI in the emergency department without ST segment increase on presentation, a normal level of TnT and of TnI between 6 and 72 hours after the onset of chest pain is strong evidence against MI or ACS, particularly if the ECG is normal or near normal.^{30,31} Thus, individuals with chest pain and a low-risk history, a normal or near-normal ECG, and normal troponins can safely be evaluated as outpatients.

Potential hazards of using troponin in the primary care setting include possible delays in appropriate referral of patients with ACS to an emergency department setting,²⁸ and a false-negative result if the test is performed too early.²⁷

Several studies in the emergency department setting have found that the response of chest pain to administration of nitroglycerin does not reliably predict the presence or absence of cardiac chest pain, CAD, or myocardial ischemia.^{32–35}

ΡΕ

No individual signs or symptoms can reliably diagnose PE, but a validated clinical prediction rule can help determine which patients have low, moderate, or high likelihood of PE, which then guides further evaluation. The Wells clinical prediction rule (**Table 3**) has been subjected to more than 10 years of testing and development, and validated in numerous settings.^{36–39} Other clinical prediction rules have been developed and validated, but to date the Wells rule is the most widely tested.

Table 3 Simplified Wells scoring system for PE			
Clinical Finding			Score
Symptoms of DVT (objectively measured leg sw of leg veins)	velling or pain witl	n palpation	3.0
No alternate diagnosis more likely than PE			3.0
Heart rate >100 beats per minute			1.5
Immobilization (bed rest, except for access to a consecutive days) or surgery in past 4 weeks	oathroom, for 3 or	more	1.5
Previous objectively diagnosed DVT or PE			1.5
Hemoptysis			1.0
Malignancy (patients receiving treatment of cancer, those with cancer and cessation of treatment in past 6 months, those with cancer receiving palliative care)			1.0
Interpretation			
<2 points = low probability of PE 2–6 points = moderate probability of PE >6 = high probability of PE	(1%–28%) (28%–40%) (38%–91%)	(LR 0.13) (LR 1.82) (LR 6.75)	

Data from Wells PS, Anderson DR, Rodger M, et al. Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: increasing the models utility with the SimpliRED D-dimer. Thromb Haemost 2000;83:416–20. D-dimer testing has also become an important part of the evaluation for PE and deep vein thrombosis (DVT), but not all assays are the same; quantitative enzymelinked immunosorbent assay (ELISA) D-dimer assays are more sensitive, and have been more thoroughly tested in clinical settings, than whole-blood agglutination assays.⁴⁰ A low clinical suspicion for PE (eg, a Wells score <2) plus a normal quantitative ELISA D-dimer assay safely rules out PE with a negative predictive value greater than 99.5%. Helical computed tomography (CT) can be combined with clinical suspicion and other testing such as lower extremity ultrasound to rule in or rule out PE if further testing is needed.^{36,40–43}

Several different sequential testing protocols have been proposed that all involve essentially the same elements:

- 1. For patients with low clinical suspicion for PE (Wells score <2) and a normal D-dimer, no further evaluation or treatment;
- 2. For patients with moderate or high clinical suspicion for PE (Wells score 2 or greater), and abnormal CT or venous ultrasound, treat for PE or DVT regardless of D-dimer
- 3. For patients with an abnormal D-dimer, plus a normal CT and venous ultrasound, consider serial ultrasound if clinical suspicion is low to moderate and pulmonary angiography if clinical suspicion is high.

Patients who are initially diagnosed as free of PE by such an approach, and are not treated, have a less than 1% chance of PE in the subsequent 3 months.^{42,44,45}

Heart failure

Heart failure by itself is unlikely to cause chest pain, but it may accompany ACS, valvular disease, MI, or other critical cardiac conditions. A displaced apical impulse and a previous history of MI support this diagnosis. Because virtually all patients with heart failure have exertional dyspnea, its absence is helpful at ruling out this diagnosis.⁴⁶ An abnormal ECG and cardiomegaly on chest radiograph can increase the likelihood of heart failure among patients with chest pain, and increased b-type natriuretic peptide (BNP) levels have been found reliable for detecting heart failure in patients presenting with acute dyspnea.^{47–49} For any patient suspected of having heart failure based on clinical examination or laboratory testing, echocardiography is crucial to making the final diagnosis.^{50,51}

Aortic dissection

Dissection of the thoracic aorta is a rare, red flag condition that occurs at a rate of only 6 to 10/100,000 patient years.⁵² Left untreated, it has a mortality of 50% at 48 hours. The acute/sudden severe onset of pain is the cardinal feature of aortic dissection, with a sensitivity of 84%. The description of the pain as ripping or tearing has an LR for aortic dissection from 1.2 to 10.8.⁵² Hypertension is the most common predisposing factor, being present in 78% of patients.⁵³

Pulmonary Causes of Chest Pain

Acute bronchitis and pneumonia

It is important to differentiate bronchitis from pneumonia, as the latter is a more severe infection that may require more aggressive treatment, including hospitalization.⁵⁴ Chest radiograph is considered the reference standard test for patients suspected to have pneumonia, and is the standard against which clinical evaluations for pneumonia are compared.⁵⁵ When deciding whether to proceed to chest radiograph, the presence of fever or focal chest signs such as increased vocal resonance or dullness

to percussion are the most useful clinical tools in differentiating these 2 conditions.⁵⁵ In 1 sample of patients with acute cough and a 5% to 10% prevalence of pneumonia, in whom focal auscultatory signs were present, the chance of pneumonia increased to 39%, and reduced to only 2% when the signs were absent.⁵⁶ The absence of focal chest findings does not completely rule out pneumonia in the patient with chest pain and cough.⁵⁵ A large study in 1984 developed a decision rule (**Table 4**) using 7 clinical findings to predict the likelihood of pneumonia.⁵⁷

A Cochrane review has shown modest benefits for treating acute bronchitis with antibiotics, including reduction in cough, days feeling unwell, and days of limited activity.⁵⁸ There is a stronger indication for treating those subgroups at high risk of complications including those aged more than 75 years, and those with insulin-dependent diabetes, preexisting chronic obstructive pulmonary disease, cardiac failure, and serious neurologic disorders.⁵⁸

Lung cancer

Chest pain is a presenting symptom in 53% of patients with lung cancer.⁵⁹ Respiratory symptoms with a higher frequency at presentation include dyspnea (86%), cough (81%), hoarseness (54%), and hemoptysis (26%). None of these symptoms are diagnostic of lung cancer, but other common symptoms, such as tiredness (86%) and lack of appetite (76%), are too general to indicate lung cancer, let alone a respiratory cause of any kind.

Smoking is the major risk factor for lung cancer, with hazard ratios (compared with those who have never smoked) ranging from 2 for former smokers to 55 for heavy smokers.⁶⁰ One review has summarized that the relative risk of developing lung cancer in ever-smokers is 24.2 for men and 12.5 for women.⁶¹

Sputum cytology, a test that can readily be arranged in primary care, has a specificity of 99% and a sensitivity of 66% in the detection of lung cancer.⁶² Further investigation requires referral for bronchoscopy, cytobrushing, transbronchial biopsy, or transthoracic needle aspirate.

Pneumothorax

Pneumothorax is a rare, red flag cause of chest pain, with an incidence of 14 per 100,000 person-years in men and 3 per 100,000 years in women.^{63,64} Spontaneous

Table 4 Diehr diagnostic rule for pneu	monia in ac	dults with	acute cougl	า	
			In	terpretatior	ı
			L	R	Probability of
Finding	Points	Score	LR (+)	LR (—)	Pneumonia (%)
Rhinorrhea	-2				
Sore throat	-1				
Night sweats	1	-3	1.1	0	5
Myalgia	1	_1	2.5	0.37	12
Sputum all day	1	0	4.9	0.47	21
Respiratory rate >25 breaths per minute	2	1	8.3	0.70	30
Temperature >100°F	2	3	11	0.90	37

Data from Diehr P, Wood RW, Bushyhead J, et al. Prediction of pneumonia in outpatients with acute cough—a statistical approach. J Chronic Dis 1984;37:215–25.

pneumothorax may be primary (usually in the 20- to 40-year age-group) or secondary to underlying pulmonary disease (usually in the 60 years and older age-group). Other causes of pneumothorax are chest trauma and medical procedures. Acute, pleuritic chest pain and dyspnoea occur together in 64% to 85% of patients.⁶⁴ Signs of tachy-cardia are most common followed by tachypnea and hypoxia. Diagnosis is by chest radiograph, ultrasound, or CT scan.

Musculoskeletal Chest Wall Pain

Most musculoskeletal chest wall pain is labeled by an umbrella term chest wall syndrome, which encompasses a range of diagnostic labels including anterior chest wall syndrome, atypical chest pain, musculoskeletal chest pain syndrome, cervico-thoracic angina (CTA), and costochondritis.¹⁷ All of these diagnoses are clinically based and lack a true reference standard for diagnosis, such as a radiological or pathologic test. The cause of chest wall syndrome is poorly understood. Musculoskeletal chest pain caused by trauma is discussed separately to the chest wall syndrome, as is that associated with the generalized pain syndrome labeled fibromyalgia.

Chest wall syndrome

In a Swiss primary care cohort study of 672 patients with chest pain,¹⁷ using a standardized history and examination protocol, 45% were diagnosed with conditions that fell within the broad category of chest wall syndrome. The clinical characteristics that best discriminated this syndrome from other causes of chest pain were chest wall pain reproducible by palpation, chest pain that was neither squeezing nor oppressive, pain localized to left chest wall, nonexercise-induced chest pain, pain influenced by mechanical factors or simply well localized on the chest wall (**Table 5**). Diagnoses were not validated by other clinicians or investigations.

In an Australian study of musculoskeletal signs comparing patients from primary care with pain in the chest or abdomen with pain-free controls, the prevalence of pain with cervical and thoracic spinal movements was 60% to 70% versus 20% to 35% and thoracic spinal tenderness was 65% versus 25%.⁶⁵

Further useful information on clinical features of musculoskeletal pain comes from hospital studies of patients with chest pain undergoing coronary angiography. In an early study of patients with chest pain and negative coronary angiography, chest wall tenderness was found in 69% of patients compared with none of a control group without chest pain.⁶⁶ However, there was a correlation between the sites of tenderness and pain in only 23% of the case group. Christensen and colleagues⁶⁷ have

Table 5The 6 most discriminative clinical characteristics of chest wall syndrome versus the otherconditions causing chest pain				
Clinical Characteristic	Odds Ratio (95% CI)			
Pain is				
 Not squeezing or oppressive 	2.53 (1.21–5.28)			
 Localized on the left or median-left part of the chest wall 	2.28 (1.58–3.28)			
 Well localized on the chest wall 	2.10 (1.37–3.22)			
 Nonexercise-induced chest pain 	1.58 (1.00–2.49)			
 Influenced by movement or posture 	1.54 (1.06–2.24)			
 Reproducible by palpation 	5.72 (1.20–5.28)			

Data from Verdon F, Burnand B, Herzig L, et al. Chest wall syndrome among primary care patients: a cohort study. BMC Fam Pract 2007;851.

made a diagnosis of musculoskeletal chest pain labeled as CTA in 18% of a cohort of patients with known or suspected stable angina referred to a hospital for coronary angiography. This diagnosis was based on a detailed history and spinal/chest wall palpation findings and produced a group in which 80% had negative myocardial perfusion scintigraphy compared with 50% in the remaining non-CTA group. They found that combining several clinical features may be more accurate in making a musculoskeletal diagnosis than using 1 feature alone. The diagnosis of CTA is most closely associated with:

- The grading of angina by a physician as noncardiac or atypical angina (Canadian Cardiovascular Society [CCS] guidelines)
- The presence of neck pain
- Reduced motion palpation of the T3 to T5 vertebrae
- The presence of spinal tenderness.

Indirect support for the diagnosis of musculoskeletal chest pain in the CTA group came from improvements in pain and general health with a trial of manual therapy compared with no change in these parameters in those without CTA treated by other means.⁶⁸ The same research team is about to publish a similar analysis of a cohort of patients with acute chest pain but with a more rigorous assessment of manual therapy using randomized clinical trial design.⁶⁹

Costochondritis

Costochondritis, also called costosternal syndrome, is a condition characterized by pain and tenderness at the costochondral or chondrosternal articulations without a notable swelling as in the less common condition of Tietze syndrome.⁷⁰ Usually multiple levels are affected and they lack swelling or induration. Pain is reproduced by palpation of the affected cartilage segments and may radiate on the chest wall.

Corticosteroid injections have been used as a treatment of costochondritis with sulfasalazine added for recurrent cases. This approach has been shown in a retrospective case series to reduce investigation and hospitalizations for chest pain.⁷¹ Otherwise there is little research in this area. Trial of analgesics or antiinflammatory medication, rest, and reassurance has been recommended, but there are no data about their efficacy.⁷²

Trauma

Chest pain may arise from ribs and muscles that have suffered direct or indirect trauma.⁷⁰ This trauma is usually clear from the history. Less obvious may be rib fractures resulting from repetitive strain of coughing and also as stress fractures in sports such as golf, rowing, pitching, and bodybuilding.⁷¹ Clinical features include pain on inspiration and chest or upper limb movements and localized tenderness at the site of the strain or fracture. Not all fractures may be detected by plain radiographs, so if a clinical suspicion of fracture remains, bone scintigraphy, CT scanning,⁷³ or ultrasonography⁷⁴ may be necessary.

Fibromyalgia

Fibromyalgia is a syndrome characterized by widespread chronic muscle pain and tenderness in multiple discrete points.⁷⁰ The pain must be present on both sides of the body and above and below the waist, including part of the spine or anterior chest.⁷⁵ Fatigue, insomnia, and joint pains further help to characterize fibromyalgia, as they are present in more than 70% of patients. Common muscle tender points in the chest are in the pectorals, the rotator cuff, rhomboids, and trapezius. There are no serologic or histologic markers of inflammation or other pathology in this condition. Coexisting anxiety and depression may add to the pain and suffering. The key to

screening for fibromyalgia as the cause of chest pain is to check if pain is present outside the chest and then assess if its distribution and an examination of the designated points for tenderness fit the pattern for fibromyalgia. Other rheumatologic causes of widespread pain should be excluded before diagnosing fibromyalgia.

Gastroenterologic Causes of Chest Pain

In assessing possible gastroenterologic causes of chest pain, attention should first be paid to several important symptoms that may herald serious conditions: the so-called alarm symptoms. These symptoms include repeated vomiting, decreased appetite, weight loss, dysphagia, odynophagia (pain on swallowing), hematemesis, anemia, and melena (**Box 1**).⁷⁶

Differentiating cardiac pain from esophageal pain is difficult, but features that are more indicative of esophageal pain in the emergency department setting are an atypical response to exercise, pain that continued as a background ache, retrosternal pain without lateral radiation, pain that disturbed sleep, and the presence of certain esophageal symptoms.⁷⁷ These esophageal symptoms include dysphagia and odynophagia, heartburn, and regurgitation, Of these symptoms, the only 3 significantly more common in patients with NCCP with gastroesophageal reflux disease (GERD) versus those without GERD are heartburn (57% vs 21%) and regurgitation (49% vs 16%) and pain relieved by antacid (43% vs 16%).⁷⁷ These translate to sensitivities of 40% to 49% and specificities of 81% to 84%.

Although upper gastrointestinal (GI) endoscopy or 24-hour esophageal pH monitoring have been used as reference standards for the diagnosis of GERD,^{78,79} neither shows a perfect correlation with symptoms. The cheaper and more accessible alternative in primary care is an empiric trial of high-dose acid suppression using a proton pump inhibitor (PPI). The range for the sensitivity of this test is 65% to 90% and for the specificity, 75% to 88%, using upper GI endoscopy or 24-hour esophageal pH monitoring as a reference standard.^{78,80} Treatment success at 12 months is also higher than for endoscopy or monitoring (84% vs 74%).⁸¹ Several schedules of therapeutic trials of PPIs ranging from 1 day to 4 weeks have been tested but the one with the best balance between accuracy and usefulness is a 7-day trial of lansoprazole (60 mg in the morning and 30 mg in the evening).⁷⁶ At the threshold of 50% reduction in symptoms, this test has a sensitivity of 78% and specificity of 82% in

Box 1 Alarm symptoms requiring endoscopic investigation for gastroenterologic conditions in patients with NCCP
Repeated vomiting
Decreased appetite
Weight loss
Dysphagia
Odynophagia (pain on swallowing)
Hematemesis
Anemia
Melena
Data from Faybush EM, Fass R. Diagnosis of noncardiac chest pain: In: Fass R, Eslick GD, editors. Noncardiac chest pain: a growing medical problem. San Diego: Plural Publishing; 2007.

the diagnosis of GERD and is able to diagnose most of the responders within the first 48 hours. Others recommend a longer PPI trial period of 1 to 2 months before investigating for other causes of chest pain (see the article by Oranu and Vaezi elsewhere in this issue for further explanation of this topic).

Failing a clear response to the PPI test, if the primary care practitioner still suspects an esophageal cause for the pain, referral is needed to a gastroenterologist for investigation of esophageal motility with esophageal manometry or visceral hyperalgesia with an intraesophageal balloon distension test.⁷⁶ Alternatively, the practitioner should revisit the history and examination to check for causes other than gastroesophageal disorders.

Skin and Soft-Tissue Causes

In assessment of skin and soft tissue as a cause of chest pain, the detection of a tender skin lesion at the site of pain may uncover an obvious cause of the pain. Skin lesions such as glomus tumors, eccrine spiradenomas, leiomyomas, angiolipomas, and traumatic neuromas are unlikely to cause diagnostic uncertainty (see the article by Muir and Yelland elsewhere in this issue for further explanation of this topic). Painful breast lesions including cancer and fibrocystic disease are somewhat more difficult to detect and require deeper palpation and special tests for diagnosis.^{82,83} The main difficulty is in the exclusion of herpes zoster as a cause in the prodromal period of about 4 days before the emergence of skin lesions in a dermatomal distribution. The commonest symptoms in this period are dermatomal pain (41%), itching (27%), and paresthesia (12%).⁸⁴ Antiviral therapies given before the emergence of the rash may reduce pain during treatment and for a month after this, but have no effect on pain at 3 months and beyond.⁸⁵

Psychogenic Chest Pain

The proportion with a primary diagnosis of psychogenic chest pain is difficult to estimate with any accuracy. The precise contribution of the psychiatric disorder to the chest pain is difficult to define. In an article elsewhere in this issue on psychological causes of chest pain, White avoids labeling certain types of chest pain as purely psychogenic; rather she discusses the increased likelihood of psychiatric problems in patients with NCCP, showing nearly twice the prevalence of psychiatric impairment compared with in patients with CAD⁸⁶ and 2 to 3 times the prevalence of anxiety compared with patients with cardiac disease and with the general population. The situation is made more complex by the association between stress and myocardial ischemia. In patients without documented CAD, mental stress can induce myocardial ischemia in 16% to 21%.⁸⁷ Furthermore, in patients with documented CAD, mental stress-induced transient myocardial ischemia has been found in 34% to 74%.⁸⁷ Therefore it is prudent to view psychological disorders as contributors to the sensation of chest pain rather than the cause per se. It is also prudent to remember that psychological and physical conditions commonly coexist.

An assessment of the contribution of psychological factors to chest pain commences with a thorough assessment of the physical causes of chest pain outlined in this article followed by an assessment for panic, anxiety, and depression. Panic disorder has a reported prevalence of 8% in primary care patients with NCCP.⁸⁸

Given the time constraints of primary care, the use of 2 questions as a brief diagnostic screen for panic disorder in primary care⁹ has been suggested to screen for underlying panic disorder. These are:

• "In the past 6 months, have you ever had a spell or an attack when all of a sudden you felt frightened, anxious, or very uneasy?"

• "In the past 6 months, have you ever had a spell or an attack when for no reason your heart suddenly began to race, you felt faint, or you couldn't catch your breath?"

A positive response to either item is a positive screen. In a primary care setting, this brief questionnaire has good sensitivity (94%–100%) and negative predictive value (94%–100%) so it is useful for excluding panic disorder. However, its low specificity (25%–59%) and positive predictive value (range 18%–40%) mean that a positive result requires more thorough assessment.

Similarly, there is a rapid screen for depression using the following 2 questions⁸⁹:

- "During the past month have you often been bothered by feeling down, depressed, or hopeless?"
- "During the past month have you often been bothered by little interest or pleasure in doing things?"

As with the screen for panic disorder, a positive response to 1 or both questions is regarded as positive screen. In the primary care setting this screen has a sensitivity of 97% (95% confidence interval [CI], 83%–99%) and a specificity of 67% (95% CI, 62%–72%). The associated positive LR of 2.9 (2.5–3.4) and negative LR of 0.05 (0.01–0.35)⁸⁹ make it a useful screening tool for depression.

A therapeutic trial of treatment of anxiety or depression is not only desirable to reduce the episodes of chest pain, but may act as a diagnostic tool. Several psychological interventions for NCCP are discussed elsewhere in this issue in the article by White on psychological causes of chest pain. These include cognitive behavioral therapy (CBT), hypnotherapy, relaxation training, and biofeedback. Of these, the best evidence for effectiveness in the short- and long-term is for CBT.⁹⁰

Other evidence from therapeutic trials for psychological disorders is not specific to patients with chest pain, but may give some guide to treatment. For panic disorder, combined psychotherapy and antidepressant therapy is more effective than either therapy alone.⁹¹ When appropriate psychological interventions are not available or have been unsuccessful, there is a role for a trial of selective serotonin reuptake inhibitors for depression. These drugs have evidence for effectiveness compared with placebo in the primary care setting.⁹² They may be preferred to tricyclic antidepressants in patients with chest pain because of their lower cardiotoxicity in overdose.⁹³

Applying the Algorithm in Practice

The chest pain algorithm shown in **Fig. 1** acts as a guiding framework for the clinical application of the diagnostic elements described in the body of this article. The diagnostic elements relating to history, examination, and investigation are summarized in **Tables 6** and **7** and those relating to therapeutic trials in **Table 8**.

Early in the red flag algorithm it is important to take a brief history and check the vital signs to assess if emergency treatment and referral to an emergency department are necessary. If the patient seems stable, a more detailed assessment for red flag conditions can be performed, with urgent treatment and referral if red flags are found.

Not all cardiac and pulmonary causes are red flags. Certain cardiac and pulmonary causes can be safely managed in the community and may depend on the availability of community-based treatments and the ability to refer for complex investigations and specialist review if indicated. For example, a patient with stable angina can be managed with medication and referral to a cardiologist for coronary angiography.

Table 6 Cardiac and pulmor (the evidence for e:	ary causes of che ach element is cla	st pain, their flag status, and associated diagnostic elements derived from histor ssified according to SORT)	y, examination, and in	ivestigation
Condition	Flag Status	Element	Evidence Rating	References ^a
Cardiovascular				
ACS	Red	Classification of chest pain as anginal, atypical anginal, or nonanginal helps determine cardiac risk	U	20
		Exertional chest pain and pain radiating to the shoulder or both arms increases the risk of ACS	В	21
		The Rouan decision rule aids risk stratification for MI	U	1
		ECG findings of new ST segment increase, Q waves, and conduction defects strongly suggest ACS or AMI	U	22
		Serum troponin is an accurate predictor of AMI of death or recurrent MI within 30 days	υ	29
		Patients with chest pain and a negative initial cardiac evaluation should have further testing with stress ECG, perfusion scanning, or angiography depending on their level of risk	C	20
Heart failure	Red or	The absence of exertional dyspnea makes heart failure unlikely	υ	46
	green	An abnormal ECG and cardiomegaly on chest radiograph suggest heart failure in patients with chest pain	U	47
		Increased BNP levels suggest heart failure in patients with acute dyspnea	U	47–49

PE	Red	A Wells score of less than 2 plus a normal D-dimer assay should rule out PE In patients with an abnormal D-dimer assay or a Wells score indicating moderate to high risk, helical CT and lower extremity venous ultrasound examination should be used to rule in or rule out PE	4 4	2,9,42 42,45
Dissecting aortic aneurysm Pulmonary	Red	Sudden severe onset of pain Pain described as ripping or tearing	υυ	52 52
Pneumonia	Red or green	Focal chest signs in lower respiratory tract infections increase the likelihood of pneumonia The Diehr diagnostic rule predicts the likelihood of pneumonia based on clinical findings	A B	56 56
Lung cancer	Red	The most common respiratory symptoms in patients presenting with lung cancer are dyspnea, cough, hoarseness, and hemoptysis Smoking is a risk factor for lung cancer Sputum cytology has a specificity of 99% and a sensitivity of 66% in the detection of lung cancer	8 4 4	59 59,60 62
Pneumothorax	Red	Acute, pleuritic chest pain with dyspnea, tachycardia, tachypnea, and hypoxia are suggestive of pneumothorax	υ	63,64
^a The evidence for eac	h alamant is class	fied according to SORT		

ITTLE EVIQUETICE TOT EACT ELEMENT IS CLASSIFIED ACCOTORING TO SURT. Data from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69(3):548–56.

Table 7 Noncardiac causes of chest pain, for each element is classified acc	, their flag status, a cording to SORT)	and associated diagnostic elements derived from history, examination,	and investigation (t	he evidence
Condition	Flag Status	Element	Evidence Rating	References
Musculoskeletal				
Chest wall syndrome	Green	Pain is not squeezing or oppressive Pain is well localized	88	17 17
		Musculoskeletal chest pain is more likely in patients with chest	пœ	65,66
		wan tenuerness Presence of paraspinal tenderness	В	65,67
		CTA most closely predicted by	В	67
		 The grading of angina by a physician as noncardiac or atypical angina (CCS guidelines) 		
		 The presence of neck pain 		
		 Reduced motion palpation of T3–T5 The presence of spinal tenderness 		
Costochondritis	Green	Tenderness to palpation of costochondral junctions; reproduces patient's pain; usually multiple sites on same side of chest	C	72,95
Chest trauma	Green	History of direct trauma or repetitive trauma Localized pain and tenderness	C	73,95
Fibromyalgia	Green	Widespread pain and tenderness	C	75
Gastrointestinal				
Life-threatening GI conditions	Red	 Alarm symptoms for investigation Repeated vomiting Decreased appetite Weight loss Wysphagia Odynophagia (pain on swallowing) Hematemesis Anemia 	U	76

GERD	Green	Patients with heartburn and regurgitation are more likely to have C abnormal esophageal pH results than those without these	77
		symptoms Symptoms significantly more common in patients with NCCP who B have GERD are heartburn, regurgitation, and pain relieved by antacid	96
Skin and soft tissue			
Herpes zoster	Green	Dermatomal pain, itching, or paresthesia	84
Skin tumor	Red or green	Skin or soft-tissue lump	
Breast lesion	Red or green	Anterior chest pain \pm breast lump C	82,83
Psychogenic chest pain			
Panic disorder	Yellow	A 2-question screen can accurately exclude panic disorder if negative but requires further evaluation if positive	6
Depression	Yellow	A 2-question screen for depression is a valid screening tool	68
			: :

Data from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69(3):548–56.

Table 8
Conditions causing chest pain and associated diagnostic elements derived from therapeutic
trials (the evidence for each element is classified according to SORT)

Condition	Element	Evidence Rating	References
Cardiovascular			
ACS	Administration of nitroglycerin does not reliably predict the presence or absence of cardiac chest pain, CAD, or myocardial ischemia	В	32–35
Pulmonary			
Acute bronchitis	Antibiotics have modest benefits Stronger indication for antibiotics in groups with a high risk of complications from infection	A C	58 54
Musculoskeletal			
Chest wall syndrome	Manual therapy in patients with clinical features of musculoskeletal chest pain	с	67
Costochondritis	Local anesthetic injections Analgesics or antiinflammatory medication, rest, and reassurance	В	71,72
Gastrointestinal			
GERD	PPI for reflux esophagitis	В	76
Skin and soft tissue			
Herpes zoster	Antiviral agents for herpes zoster (not specific to chest pain patients)	В	85
Skin tumor or breast lesion	Excision of tumors (not specific to chest pain patients)	С	
Psychogenic			
Panic disorder	CBT Combined behavioral therapy and antidepressants in panic disorder (not specific to chest pain patients)	A A	90 91
Depression	SSRIs for depression (not specific to chest pain patients)	A	92

Data from Ebell MH, Siwek J, Weiss BD, et al. Strength of recommendation taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. Am Fam Physician 2004;69(3):548–56.

Once red flags have been assessed as unlikely, the assessment can switch to green flags. If a green flag is found, basic investigations that can be performed quickly and locally may be performed, often to deal with any remaining uncertainty about red flags. If green flags are unlikely, the brief screening questionnaires for panic disorder and depression can be used to screen for these conditions, and a more detailed assessment of the mental health status performed if they are positive. If this screening process is negative, further investigation, at least at a basic level, may be indicated to exclude green flags with more certainty. These assessments should lead to a provisional diagnosis and an appropriate therapeutic trial. This trial may require referral, depending on the skills of the practitioner. The response to the trial is used as a weak form of evidence to confirm or refute the provisional diagnosis. If the trial is successful, but the underlying condition is likely to continue, then follow-up should be arranged for monitoring and secondary prevention. If the trial is unsuccessful or only partly successful, the options are to search for a different cause or a second cause or to refer for further investigation and/or specialist review.

A Word of Caution

Trials of treatment are incorporated within this algorithm not only to provide treatment per se but also for their diagnostic benefit. However, throughout this process the practitioner should be mindful of investigating any symptoms suggestive of serious causes. Patients may have more than 1 cause of chest pain. Discovery of a noncardiac cause is no reason to be complacent about cardiovascular risk factors. In the emergency department setting, predictors of adverse cardiac events after an initial diagnosis of NCCP include hypercholesterolemia, diabetes, history of CAD, and history of congestive heart failure.²⁵ These features can act as a guide to primary care practitioners for patients, and further testing to exclude cardiac causes of chest pain is warranted when these predictors are present.

The algorithm proposed here, although based on available evidence, does not constitute a validated decision rule. It warrants testing in a clinical trial in primary care, where it could be compared with usual care for chest pain.

SUMMARY

It is apt to conclude with a quote from Anthony Komaroff, who, in 1982, wrote about the concern that algorithms would threaten the art of clinical medicine, leading to regimentation and mediocrity in decision making.⁹⁴ In their defense, he wrote:

In our view, algorithms can help us to articulate how we make decisions, to clarify our knowledge and to recognize our ignorance. They can help us to demystify the practice of medicine, and to demonstrate that much of what we call the "art" of medicine is really a scientific process, a science which is waiting to be articulated.

Although the science behind the assessment of chest pain into an algorithm has progressed considerably since 1982, this article illustrates that there is still a lot left to be validated about many of the diagnostic elements used in this assessment process. Nonetheless, there is now a lot of science that can inform the art of dealing with patients presenting with chest pain. The algorithm and its diagnostic elements presented should be used with discretion to guide, rather than replace, clinical decision making.

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