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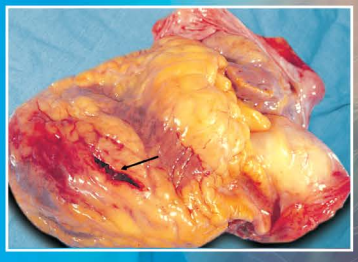
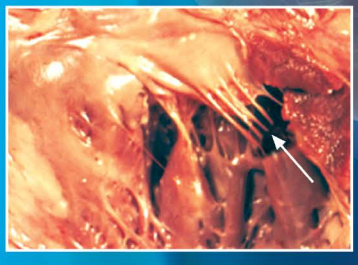
Manual of
CORONARY HEART DISEASES





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CHAPTER

Evaluation of Chest Pain

3

Kirsten E Fleischmann, Raveen Pal

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- Scope
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SCOPE

Chest pain is a common presenting symptom for patients visiting family physicians, general internists, cardiologists and emergency physicians. In 2009, there were 8 million visits to the emergency room alone due to chest pain.[1] Although chest pain is most often benign,[2] it may represent the symptoms of a life-threatening process, such as myocardial infarction (MI) or aortic dissection, so a low threshold for prompt investigation is prudent. Indeed, heart disease is the leading cause of death in the United States. In 2009, an estimated 785,000 had a new heart attack, while approximately 470,000 had a recurrent heart attack.[3] This high incidence has resulted in the development of programs directed to both the general public and the general medical practitioners to promote awareness of the signs and symptoms of heart disease and the indications for further investigation of chest pain. Fortunately, through increased awareness and improved therapies, mortality from heart disease has decreased steadily in the last few decades.[4]

This chapter reviews the history and differential diagnosis of chest pain, the physical findings associated with cardiac ischemic pain and the role of various investigations in the further investigation and management of chest pain.

HISTORY

Chest pain has an extensive differential diagnosis, so the clinical history is critical in establishing the pre-test probability of any given diagnosis and to guide subsequent test decisions. Testing then refines this risk further into a post-test risk. Finally, the history is an important part of the physician patient interaction that helps patients to establish trust and provides the physician with important social information about the patient that may impact their management.

DIFFERENTIAL DIAGNOSIS

Chest pain has an extensive differential diagnosis. It may be useful to think of the differential diagnosis of chest pain by system **(Table 1)**.

The first step in the management of chest pain is to rule out an immediate life-threatening cause. Once stable vitals have been established and if the patient is not in extremis, it is reasonable to proceed with a more detailed history and physical examination, helping to differentiate among the various etiologies. The history includes the description of the pain itself and the patient's medical history and risk factors.

PATIENT'S DESCRIPTION

Description of patient's presenting symptoms should include details of location, radiation, quality, intensity, onset, duration, and exacerbating and alleviating factors.

Location

Location of pain (retrosternal, epigastric, shoulder) can be useful to determine the source. A discrete location of pain, especially if reproducible with palpation, makes a musculoskeletal origin more likely. Epigastric pain more commonly has a gastrointestinal (GI) etiology, although ischemia, particularly in the inferior distribution, can sometimes mimic GI symptoms.

Table 1 Differential diagnosis of chest pain by system

- Cardiac
  - Angina
  - MI
  - Pericarditis/myocarditis
  - Aortic dissection
- Musculoskeletal
- Gastrointestinal
  - Esophageal spasm
  - Reflux
  - Cholecystitis
  - Pancreatitis
- Pulmonary
  - Pulmonary embolus
  - Pneumothorax
  - Pneumonia
  - Pulmonary hypertension
- Neuropathic
  - Shingles
  - Costochondritis
  - Cervical spine
- Psychiatric

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Pain that follows a nerve distribution may be attributable to shingles. In general, location of pain is a poor discriminator.[5]

Radiation

Radiation of pain to the jaw, neck, shoulders, arms or back can be useful in assessing the likely cause of chest pain. Pain radiating to the jaws or neck or arms is classically associated with cardiac ischemia. Radiation to the back is classically associated with aortic dissection. This feature can be used to rule in cardiac ischemia with a greater likelihood.[6]

Quality

Description of chest pain by the patient can be helpful. Angina may be described in many ways. However, most often it is described as a dull ache, squeezing or heaviness. Pain that is sharp or stabbing in nature is less likely to be ischemic in origin. Pain that is referred to as burning is more suggestive of a GI etiology. Classically, the pain of aortic dissection has been described as a tearing sensation. These various descriptors can help raise or lower suspicion for various causes of pain.

Intensity

Pain severity is typically graded on a scale of 1 to 10. However, recent data suggest that pain due to myocardial ischemia has a wide range of intensities and that severity is not useful to discriminate source of chest discomfort.[7] Thus, pain severity is most useful to grade relief from pain or change from previous episodes.

Associated Symptoms

Shortness of breath, diaphoresis, nausea and dizziness are symptoms that often accompany cardiac ischemia.

Onset of Pain

Sudden onset versus gradual onset is a useful differentiating feature. Aortic dissection and pulmonary embolism tend to have sudden onsets. More gradual and escalating pain is more typical of cardiac ischemia. Cardiac ischemic pain tends to occur with activity. Also, cardiac pain has been reported to occur more frequently in the morning when sympathetic tone is highest.

Duration

The length of symptoms is a useful piece of information. Pain that is brief and sharp, and conversely pain that is prolonged

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and unremitting for days, are both less likely to be ischemic in origin.

Alleviating and Aggravating Factors

Pain with a pleuritic component that worsens with position or with respiration suggests a pericardial or respiratory etiology. Pain that worsens following meals, or at night after lying down, and is relieved with oral antacid preparations, suggests a GI etiology. Pain that is exacerbated by exertion or strong emotion is more typical of cardiac ischemia. While it is classically taught that pain relieved with nitroglycerin is suggestive of cardiac ischemia, it can also be esophageal in origin, limiting its usefulness as a distinguishing feature.[8]

It is important to recognize that, while pain descriptors make various etiologies of pain more or less likely, there is no perfect discriminator. Various studies have shown a wide range of likelihood ratios for different symptoms and signs.[9,10] Furthermore, elderly,[11] female[12,13] and diabetic[14] patients have been found to have more atypical symptoms. Thus, while the medical history can help to narrow the differential diagnosis and determine the next most appropriate steps in management, no one symptom is definitive.

ANGINA

Angina is a medical term derived from the classical Greek word "ankhon" meaning to strangle or choke. Angina pectoris is chest pain due to lack of blood flow to the heart, or cardiac ischemia. The first ischemic chest pain was described by Heberden in 1798; a painful sensation in the chest accompanied by a strangling sensation. This description remains largely unchanged today. Angina is still classically described as a dull, heavy, pressure-like sensation in the retrosternal area. Since angina is caused by inadequate blood flow to the myocardium, which is innervated by the vagus nerve, there is a visceral nature to the pain that does not allow clear localization. It is broadly localized to the central chest area. Occasionally, patients will make a fist on top of their retrosternal area; this has been given the moniker the Levine sign, and may be associated with ischemia. Pain can radiate to the jaw, neck or shoulders. The intensity varies quite significantly and lasts for a few minutes to half an hour. (Please see the section "History").

Angina is due to a fixed coronary artery stenosis, less commonly dynamic coronary artery stenosis and spasm or small vessel disease, that does not allow adequate blood flow, and thus oxygen delivery, to the myocardium. Therefore, it is usually brought on by exercise, emotional exertion, or even after large meals; states that result in increased heart

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rate (HR) and/or blood pressure (BP) and, therefore, have increased myocardial oxygen demands. Coronary blood flow is increased during exercise, but oxygen extraction is not, since it is already at maximal levels. Therefore, oxygen delivery to the myocardium is directly proportional to vessel size. If there is a fixed coronary artery stenosis that limits blood flow, it, in effect, limits oxygen delivery to the myocardium. Thus, in states requiring increased myocardial oxygen, there is an imbalance between oxygen delivery and demand.

Double product (HR times BP) is an indirect marker of myocardial oxygen consumption in patients with fixed coronary stenosis, because it incorporates two variables that affect oxygen consumption. First, the systolic pressure developed by the ventricular wall (Laplace's law tension = pressure × radius/wall thickness) and second, the HR which determines diastolic filling time, during which the majority of coronary blood flow occurs. Since the degree of stenosis determines the amount of blood flow, the amount of physical activity that elicits angina appears to be related to the severity of stenosis rather than the number of stenoses.

Diurnal variation in angina has been reported. It can sometimes be reported consistently with sleep. It is speculated that this is due to the increased venous return to the heart in the supine position, which results in increased LV size, and therefore LV wall tension (Laplace's law), resulting in increased oxygen demand. Angina can also classically be reported as a morning phenomenon. It is thought that this is related to increased sympathetic activity following waking which results in increased HR and BP. These variables together result in increased oxygen demand with less delivery, resulting in angina. Angina is classically relieved with rest or the use of sublingual nitroglycerin. Nitroglycerin relaxes the vascular tone resulting in dilation of coronary vasculature, resulting in increased flow to the myocardium. This, at least temporarily, alleviates the oxygen delivery imbalance and relieves pain. It also decreases myocardial oxygen demand resulting from decreased left ventricular (LV) end-diastolic volume.

Diamond and Forrester [15] developed a simple classification scheme to determine the pre-test likelihood that a patient's pain was cardiac ischemic in origin. Patient's age and sex was recorded and their symptoms were divided into typical, atypical, non-cardiac and asymptomatic. Typical angina (definite) was described as: (1) substernal chest discomfort with a characteristic quality and duration; (2) provoked by exertion or emotional stress and (3) relieved by rest or NTG. Atypical angina (probable) met two of the above characteristics, and so-called noncardiac chest pain met one or none of the typical anginal characteristics. Based on age, gender and symptom description,

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the pre-test likelihood of angina was determined. This system continues to provide a rapid and reasonably reliable estimate of the likelihood that a patient's symptoms are reflective of coronary artery disease (CAD).

PAST MEDICAL HISTORY

Once the chest pain description has been clearly classified, risk factors for the development of CAD should be determined. Large population studies, like Framingham, followed participants prospectively and determined their risk of developing CAD depending on their medical conditions. From this cohort study, currently established cardiac risk factors include age, cigarette smoking, hyperlipidemia, diabetes and hypertension.[16,17] These clinical features are incorporated into a risk score **(Fig. 1)** that determines if a patient is at low (< 10%), intermediate (10% to < 20%) or high (≥ 20%) risk for the development of atherosclerosis over the next 10 years.[18] In addition, pre-established histories of kidney disease and coronary vascular, cerebrovascular or peripheral vascular disease are high-risk indicators. An alternate, revised risk score is the Reynolds risk score. This score incorporates all of the Framingham risk factors, but adds family history of CAD and requires a high sensitivity CRP determination.[19]

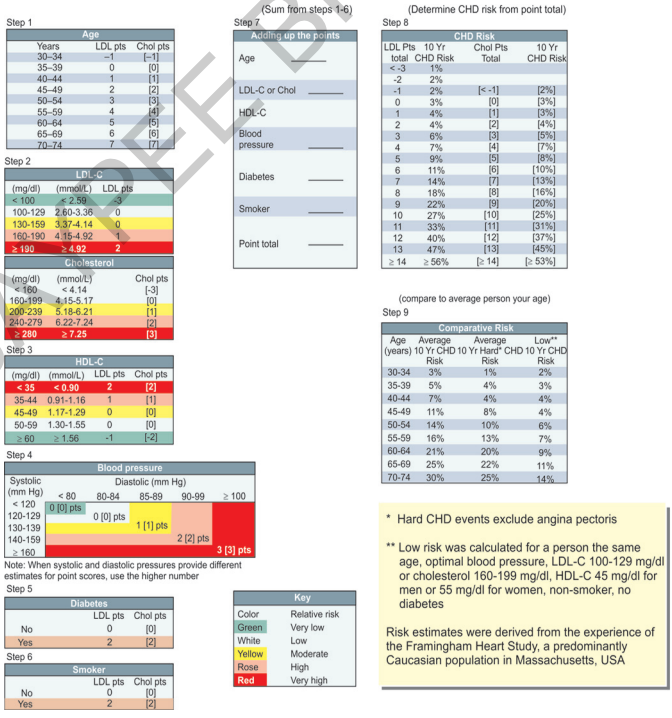

Figure 1: Framingham risk score calculation (*Source:* Wilson, et al. Circulation. 1998;97:1837-47)

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While risk factors increase the risk of underlying CAD, they have not been shown to predict whether an individual presentation of chest pain is or is not cardiac ischemic in origin.[20-22] A classic history, ECG finding and/or biomarker findings supersede clinical risk factor prediction.

PHYSICAL EXAMINATION

Following a history, the next step is to incorporate the patient's physical examination findings into a clinical decision making process. The physical examination starts with a general assessment of appearance. It is important to observe if the patient is in distress, diaphoretic, working hard to breath, pale or cyanotic. Concurrently vital signs, such as HR, BP and rhythm, should be recorded. Normal sinus rhythm is regular and between 60 and 100 beats per minute. The BP should be performed in both arms to detect discrepancies that may heighten suspicion for dissection or peripheral vascular disease. Respiratory rate and oxygen saturation should all be done routinely. An anatomical approach with review of the patient's head and neck area may reveal signs of hypercholesterolemia—specifically arcus senilis in patients under 50, xanthelasma and xanthomas in the feet. A fundoscopic exam may reveal signs of longstanding hypertension (pruning of arterioles distally, arteriovenous nicking, flame-shaped hemorrhages, optic head edema) or diabetes (hard exudates, microaneurysms, retinopathy).

A complete cardiovascular examination including inspection, palpation and auscultation should be completed. The carotid pulsation is palpated for volume and contour. Then all of the peripheral pulses (brachial, radial, renal, femoral, popliteal and dorsalis pedis) are palpated and areas overlying the carotid and femoral pulses auscultated for bruits. The jugular venous pressure (JVP) is examined for height and contour.

Auscultation of the patient with chest pain usually reveals normal sounding first and second heart sounds. The S2 may demonstrate paradoxical splitting during active myocardial ischemia for the same reason as a left bundle branch block (LBBB); the delayed LV ejection time due to dysfunctional myocardium results in a later aortic component resulting in lack of splitting or paradoxical splitting of S2. The S3 can be heard, if there is associated heart failure, due to rapid and high volume LV filling. Actively ischemic myocardium also has decreased ventricular compliance, resulting in an audible S4.

Auscultation for systolic and diastolic murmurs is important in the aortic, tricuspid, pulmonic and mitral areas. The most common murmur heard in patients with CAD is one of mild mitral regurgitation due to ischemia and papillary muscle dysfunction. In particular, the murmurs secondary to acute

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complications of MIs, including acute mitral regurgitation, ventricular septal defect and free wall rupture, are important to seek. Also, the murmur of aortic regurgitation, which may suggest an aortic dissection, is important to rule out and may be accentuated by auscultation at end expiration with the patient sitting forward. Finally, the discovery of a pericardial rub may lend support to an alternate diagnosis of chest pain namely pericarditis.

The respiratory exam is an important part of a chest pain examination. There may be crepitations or crackles heard in the lower lung fields or throughout the lung fields depending on the degree of edema present. Crepitations localized to one focal area with evidence of consolidation may be more representative of an infectious process such as pneumonia. Active wheeze may represent bronchoconstriction, although pulmonary edema can present with wheezing as well. Finally an examination of the abdomen, searching for liver capsule tenderness, abdominal aorta size and epigastric pain on palpation should be completed (please see the section "Physical Examination").

Most commonly, the physical exam of a patient with stable CAD is quite benign. In the routine investigation of chest pain, the physical exam is most important in ruling out an imminent life-threatening cause requiring immediate investigation or intervention.

INVESTIGATIONS

Chest X-ray

The chest radiograph is a routine diagnostic test in the assessment of patients with chest pain. The cardiac silhouette may be enlarged due to LV chamber enlargement, resulting in a high cardiac:thoracic (C:T) ratio. Longstanding hypertension or LV dysfunction can lead to left atrial enlargement, suggested by flattening of the left heart border, splaying of the left and right bronchus, or by a double right heart border. The right ventricle (RV) may also be enlarged due to infarction, volume overload or pulmonary hypertension and is marked by loss of the retrosternal airspace in the lateral projection. Right atrial enlargement is seen by a prominent right heart border.[23] Aortic arch, aortic valve and mitral valve calcification can be viewed on plain radiographs and are associated with increased risk of atherosclerosis.[24] Coronary artery calcification is difficult to visualize on plain radiographs, but if present is also a high-risk indicator of coronary atherosclerosis. There may be signs of congestive heart failure; plethoric pulmonary arteries, peribronchiolar cuffing, interstitial edema, Kerley B lines and blunting of the costophrenic angles with pleural effusions.

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There may be signs of pulmonary hypertension, prominent pulmonary arteries with rapid pruning, with right atrial and/or RV enlargement.

Chest radiograph is most commonly normal in a patient with anginal chest pain, but may be helpful in identifying a non-cardiac diagnosis or to diagnose complications of acute cardiac ischemia. In patients with aortic dissection, there may be a wide mediastinum, pericardial effusion or displacement of calcium from the soft tissue border of the aorta. In pulmonary embolus, there may be RV and pulmonary artery enlargement, a Westermark sign (a zone of avascular tissue), or Hampton's hump (wedge-shaped density along the periphery consistent with infarction).[25] Clear signs of an infiltrative process, a pneumothorax or a mediastinal mass may also help to direct the diagnosis.

ECG

The resting electrocardiogram (ECG) is normal in up to half of individuals who present with undifferentiated chest pain. A normal ECG is very useful in reducing the probability of acute coronary syndromes (ACS).[26,27] However, a retrospective series of patients presenting to an outpatient cardiology clinic for evaluation of recent chest pain showed that up to 30% of patients ultimately diagnosed with unstable angina (UA) had a normal ECG.[28]

An abnormal ECG may reveal the presence of Q waves suggesting a previous MI. However, it is important to note that prior MI may not result in the presence of a Q wave and that the presence of Q waves is not pathognomic of infarction, particularly if seen in leads III, V1 and V2.

Changes in the ST segment are important to pursue. Elevation of more than 1 mm in two or more consecutive leads is highly concerning for acute transmural infarction and requires immediate evalution for possible intervention. ST flattening and ST depression are also commonly witnessed and are also highly suggestive of ischemia. The only changes seen on an ECG may be T-wave flattening or inversion. Deep symmetric T-wave inversion in the anterior precordial leads is referred to as Wellen's sign, a marker of LAD territory ischemia. The presence of ST elevation, Q waves, ST depression, T-wave inversion or new conduction defects all significantly increase the risk of chest pain being cardiac ischemic in origin.[27,29]

Comparison with a prior ECG and serial ECGs are very helpful in the interpretation of ECG changes. Patients may have longstanding non-specific ST segment flattening. The presence of the same findings during an episode of chest pain in a patient with a previously normal ECG is far more concerning. Subtle

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ECG changes which are transient during an episode of chest discomfort are highly suspicious for cardiac ischemic changes. Finally alternate causes of ST and T waves changes, such as pericarditis, metabolic states, digitalis effect or hypertrophic cardiomyopathy, should always be considered.

Laboratory Investigations

Laboratory biomarkers can be useful for determining diagnosis as well as prognosis in cardiac disease. In addition to this, biomarkers help to identify the subset of patients most likely to benefit from more aggressive therapeutic interventions. As myocardium becomes ischemic and necrotic, the myocardial cell membrane integrity is compromised resulting in leakage of intracellular enzymes. While there are multiple enzymes (myoglobin, creatine kinase, troponins) that are specific to muscle cell compromise, there are only a few enzymes, such as troponins T and I, that are specific to cardiac muscle cells. The presence of these enzymes in the blood stream implies loss of specifically cardiac muscle.

Creatine kinase (CK) has multiple isoforms such as MM, BB and MB. The MB form is most concentrated in cardiac muscle. In the past, unfractionated CK or CK-MB were the primary cardiac markers used in the evaluation of ACS. The CK-MB is limited by its specificity since it can also be released by strain or damage to skeletal muscles and it is occasionally present in normal healthy individuals.[30] Troponin detection is the current key tool in the diagnosis of MI. The troponin complex is composed of troponin T, I and C. The troponin I (TnI) and troponin T (TnT) of cardiac myofibrils are distinct from those of skeletal muscles. Therefore, if cardiac myofibrils undergo damage, cardiac-specific TnI or TnT is released into the bloodstream.[31] Troponins have both greater specificity and greater sensitivity for small amounts of cardiac damage than CK-MB.[32] Troponin elevation without CK-MB elevation has been found to be associated with evidence of focal myocardial necrosis. One study estimated that 30% of patients who presented with rest pain, and without ECG changes, would have been diagnosed as having UA rather than non ST elevation myocardial infarction (NSTEMI), based on CK-MB alone versus TnI or TnT. It is important to distinguish between detection of myocardial damage and the cause of myocardial damage. While myocardial strain or damage can be inferred by the release of TnI or TnT into the bloodstream, myocardial strain can be secondary to many causes other than ACS and underlying CAD. Congestive heart failure, chronic kidney disease, LV hypertrophy and extreme exercise are all common alternate explanations for an elevated troponin. Elevated levels of TnI or

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TnT also provide useful prognostic information. Patients with elevated levels of TnI or TnT are at increased risk of death, irrespective of whether the troponin elevation is identified as having a cardiac cause or not.[33,34] When elevated troponin is due to CAD, the amount of troponin released is related to the amount of damaged myocardium. Larger amounts of troponin release are associated with increased risk of death.[35,36] Troponin elevation can also help to identify the subset of patients presenting with ACS who will benefit from GpIIb/IIIa inhibitor treatment[37] and LMWH treatment.[38] Only patients who were biomarker positive showed a lower risk of death or MI when treated with these more aggressive medications. Cardiac biomarkers have varying kinetics with respect to their release into the bloodstream and, thus, their availability to detection. Therefore, it is critical to correlate the presence or absence of a particular biomarker in the blood stream with the onset of the patient's symptoms. While myoglobin is the earliest detectable biomarker, its lack of specificity limits its utility. CK is present in the bloodstream as quickly as 2–4 hours after the onset of damage. As compared with troponins, CK levels peak more quickly (24 hours) and clear much more quickly. Troponins are typically not present until 6 hours after the onset of damage, they take 5–7 days to peak and can persist for 10–14 days. These timelines are important in determining presence of damage and whether or not recurrence of pain is associated with recurrence of damage. Thus, if troponin is negative immediately after, or within the first 6 hours after, an episode of pain, it must be repeated, so that it is being measured at least 8–10 hours after pain in order to ensure that it is in fact negative. Furthermore, it is important to understand that troponin levels may be persistently elevated after an episode of cardiac damage. Thus, if a patient has an MI on day 1 and then experiences more pain on day 5, a single elevated troponin may simply represent residual biomarker from the incident MI, not a recurrent MI. If serial troponin levels are increasing, however, this would be consistent with a recurrent ischemic event.

ESTIMATION OF RISK

As aforementioned, the Framingham and Reynolds risk scores are population based risk scores that predict an individual's risk of having a heart disease event in the longer term.

However, other scores have been developed that address the more acute risk of adverse events in patients with ACS. Risk of death or other adverse outcome based on initial presentation has been assessed in multiple large trials. The thrombolysis in myocardial infarction (TIMI) risk score is one score that assesses 7 aspects of the history and physical examination to predict the

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risk of adverse outcome. Age more than 64 years, greater than 3 CAD risk factors (family history, hypertension, increased cholesterol, diabetes, smoking), known CAD (stenosis > 50%), aspirin use in the last 7 days, recent (< 24 hours) severe angina, increased cardiac markers and ST deviation on ECG greater than or equal to 0.5 mm are each assigned a single point. The risk of death, MI or urgent revascularization by 14 days based on this score ranges from 5% to 41%.[39]

Another score, the Grace risk score, derived from a population with undifferentiated chest pain, incorporates age, HR, systolic BP, Killip class (degree of pulmonary edema/shock), presence of ST deviation on ECG, cardiac arrest, creatinine and elevated cardiac biomarkers to predict in-hospital mortality. It has been shown to be predictive of both shorter (30 days) and longer term (1 year) mortality.[40]

One limitation of these scores is that they have been derived from trial populations that tend to exclude very high and very low risk patients. So, their application to all patients is unclear. Also, known high-risk indicators, such as kidney dysfunction, are not included since these patients tend to be excluded from the clinical trials from which these scores are derived. Finally, regression models used to derive these prediction scores can result in statistical significance, but not necessarily clinical meaning.

Thus, while these scores can be used to determine, how aggressively a patient should be treated with medications and interventions, clinical judgment must always be factored in.

DIAGNOSTIC TESTING

Several testing modalities are available to help determine whether an individual patient's chest pain is due to CAD or ischemia. The main distinction among testing modalities is functional versus anatomic testing. Functional tests investigate the effect of stress on the myocardium, while anatomic tests image the coronary arteries that provide blood flow to the myocardium. Functional tests generally employ stress in the form of exercise (treadmill or bicycle) or pharmaceutical agents (dipyridamole, dobutamine and adenosine). There are many combinations of these stress and imaging modalities. The most commonly applied stress test is the treadmill electrocardiogram test (ETT), which involves stress in the form of ambulation and electrocardiography as the main assessment tool. It is important to understand that each test has its own sensitivity and specificity for the detection of CAD. Thus, depending on the pre-test likelihood of a patient's having CAD, a test will further increase or decrease that probability.

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Manual of
CORONARY HEART DISEASES

Key Features

- The title covers coronary heart diseases in detail with the discussion focusing on our current understanding and the recent advances that are happening at a fast pace in the field
- The title highlights the global burden of CHD and discusses in detail the risk factors for CHD
- The text starts with the basic approach to a patient with chest pain highlighting the importance of history and physical examination in making the diagnosis
- Discusses in detail the pathophysiologic mechanisms and treatment of acute coronary syndrome
- The new therapeutic modalities for the management of CHDs have also been covered
- Various acute complications in CHDs have also been highlighted
- Surgical management for CHDs has also been discussed
- Easy-to-follow, providing practical advice on how to diagnose cardiac diseases with a focus on hands-on therapeutic guidance for the clinicians
- Contributions from leading international experts, each chapter contains additional comments and guidelines from reputed international bodies
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Kanu Chatterjee is currently Professor of Medicine, the Carver College of Medicine, University of Iowa and Emeritus Professor of Medicine, University of California, San Francisco, USA. He is an internationally recognized expert in heart failure and coronary artery disease. He has received numerous awards including "Gifted Teacher Award" of the American College of Cardiology; the Legacy Award, University of California San Francisco; Melvin Marcus Distinguished Fellowship Award, International Academy of Cardiology; Lewis E January Clinical Teaching Award, University of Iowa; Cardiovascular Distinguished Scientist Award, University of Iowa; and American Heart Association Professional Education Award. He is a Fellow of the Royal College of Physicians of London and of Edinburgh, American Heart Association, American College of Cardiology and a Master of the American College of Physicians. He is listed in the "Best Doctors in America" and in "America's Top Cardiologists".



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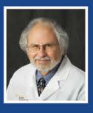

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