9. Curry SC, Vance MV, Ryan PJ, et al: Envenomation by the scorpion Centruroides sculpturatus. J Clinical Toxicology 1983-84; 21
10. Freire-Maia L, Campos JA, Amaral CF: Approaches to the treatment of scorpion envenoming. Toxicon 1994, 32
11. Gueron M, Ilia R, Sofer S: The cardiovascular system after scorpion envenomation. A review. J Clinical Toxicology 1992; 30
12. Diekema DS, Reuter DG: Environmental Emergencies: Arthropod Bites and Stings . Clinical Pediatric Emergency Medicine 2001, 2
13. Kelley TD 3rd, Wasserman G: The dangers of pet tarantulas: experience of the Marseilles Poison Centre. J Clinical Toxicology, 1998, 36
14. Saucier JR: Arachnid envenomation. Emergency Medicine Clin North Am 2004 May; 22
15. Waggoner TL, Nishimoto JH, Eng J: Eye injury from tarantula. J American Optom Assocciation 1997, 68

MANAGEMENT OF ACUTE CORONARY SYNDROME

The review of the medical literature in English

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Approximately 8 million patients present annually to the emergency room with symptoms of acute chest pain. Of these, 2 million turn out to have a cardiac cause resulting in hospitalization. Fewer than 10% of these patients have ST segment elevation on the electrocardiogram. Since the diagnostic sensitivity and specificity of the electrocardiogram are poor in this setting, there is a strong impetus for effective emergency room stratification.

The spectrum of "Acute coronary syndromes" includes unstable angina and non-ST segment elevation myocardial infarction as the clinical presentations. The distinction between these syndromes is usually made retrospectively based on biochemical markers, and hence, initial treatment strategies are identical. The diagnosis of primary unstable angina excludes external factors that may exacerbate the symptoms of coronary ischemia, such as severe anemia, thyrotoxicosis, and tachyarrhythmias.

An approach to management must take into account the severity of symptoms, the circumstances in which they are occurring, and indicators of the risk of such catastrophic events as death or myocardial infarction.

Clinical Presentations of Unstable Angina

1. Rest angina
2. New onset angina of CCSC class III or IV within 4 wk of presentation
3. Increasing frequency and intensity of previously stable angina to CCSC class III or IV
4. Angina within 6 wk of myocardial infarction (CCSC, Canadian Cardiovascular Society Classification).

Braunwald Classification of Unstable Angina

Severity

Class I New-onset, severe, or accelerated angina

Patients with angina of less than 2 month duration, severe or occurring three or more times per day, or angina that is distinctly more frequent and precipitated by distinctly less exertion; no rest pain in the last 2 month.

Class II Angina at rest; subacute.

Patients with one or more episodes of angina at rest during 3 preceding months but not within the preceding 48 hours.

Class III Angina at rest; acute.

Patients with one or more episodes at rest within the preceding 48 hours.

Clinical Circumstances

Class A Secondary unstable angina.

A clearly identified condition extrinsic to the coronary vascular bed that has intensified myocardial ischemia, e.g., anemia, infection, fever, hypotension, tachyarrhythmia, thyrotoxicosis, hypoxemia secondary to respiratory failure.

Class B Primary unstable angina.

Class C Postinfarction unstable angina (within 2 week of documented myocardial infarction).

Intensity of Treatment

1. Absence of treatment or minimal treatment.

2. Occurring in presence of standard therapy for chronic stable angina (conventional doses of oral beta-blockers, nitrates, and calcium antagonists).

3. Occurring despite maximally tolerated doses of all three categories of oral therapy, including nitroglycerin.

The term "unstable angina" is currently falling into disuse and is being replaced with the term "Acute coronary syndrome without ST segment elevation" or, more simply, "Acute coronary syndrome."

This new nosology has developed for three reasons. First, the syndromes that do and do not cause ST segment elevation both have a common pathology, namely vascular inflammatory changes leading to disruption of a previously stable atherosclerotic plaque, and subsequent thrombosis. The second reason for the adoption of the new terminology reflects the development of increasingly "sensitive" markers of myocardial necrosis. Patients with small amounts of myonecrosis as well as those with recent, rather than acute, episodes of necrosis who were previously classified as having "unstable angina" are now recognized as having myocardial infarction using the modern classification scheme espoused by the joint European Society of Cardiology/American College of Cardiology guidelines. Third, effective forms of therapy do not differ between patients with or without biochemical indications of necrosis, but rather are distinguished according to risk score and to the presence or absence of ST segment elevation on the surface electrocardiogram.

The majority of patients presenting with non-ST segment elevation acute coronary syndromes have multiple plaques in the coronary arteries. However, in most studies, approximately 20% of patients with suspected acute coronary syndromes are found to have minimally obstructed or normal coronary arteries when coronary angiography is performed. This proportion is somewhat lower in studies that use more stringent entry criteria. The precipitating event of myocardial ischemia is most commonly coronary plaque disruption or erosion. Plaques vulnerable to this process tend to be relatively soft and lipid-rich, and have abundant extracellular matrix and smooth muscle cells.

Following disruption of the fibrous cap, platelets are activated by local thrombogenic and inflammatory factors such as lipid and inflammatory mediators from lipid-laden macrophages. As a result thrombosis may occur. The final component of arterial damage involves local vasoconstriction, most likely in response to secretion of platelet-derived serotonin and thromboxane A2.

Thrombolytic therapy has been shown to be ineffective, and potentially detrimental in non-ST segment elevation acute coronary syndromes. Treatment is based primarily on antithrombotic and antiplatelet agents.

The initial diagnosis of acute coronary syndrome (ACS) is based entirely on history, risk factors, and, to a lesser extent, ECG findings. The symptoms are due to myocardial ischemia, the underlying cause of which is an imbalance between supply and demand of myocardial oxygen.

Patients with ACS include those whose clinical presentations cover the following range of diagnoses: unstable angina, non–ST-elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI). This ACS spectrum concept is a useful framework for developing therapeutic strategies.

Pathophysiology of ACS

Myocardial ischemia is most often due to atherosclerotic plaques, which reduce the blood supply to a portion of myocardium. Initially, the plaques allow sufficient blood flow to match myocardial demand. When myocardial demand increases, the areas of narrowing may become clinically significant and precipitate angina. Angina that is reproduced by exercise, eating, and/or stress and is subsequently relieved with rest, and without recent change in frequency or severity of activity that produce symptoms, is called chronic stable angina. Over time, the plaques may thicken and rupture, exposing a thrombogenic surface upon which platelets aggregate and thrombus forms.

The patient may note a change in symptoms of cardiac ischemia with a change in severity or of duration of symptoms. This condition is referred to as unstable angina. Patients with STEMI have a high likelihood of a coronary thrombus occluding the infarct artery. Angiographic evidence of coronary thrombus formation may be seen in more than 90% of patients with STEMI but in only 1% of patients with stable angina and about 35-75% of patients with unstable angina or NSTEMI. However, not every STEMI evolves into a Q-wave MI; likewise, a patient with NSTEMI may develop Q waves.

The excessive mortality rate of coronary heart disease is primarily due to rupture

and thrombosis of the atherosclerotic plaque. Inflammation plays a critical role in plaque destabilization and is widespread in the coronary and remote vascular beds. Systemic inflammatory, thrombotic, and hemodynamic factors are relevant to the outcome. Evidence indicates that platelets contribute to promoting plaque inflammation as well as thrombosis. A new theory of unbalanced cytokine-mediated inflammation is emerging, providing an opportunity for intervention.

A less common cause of angina is dynamic obstruction, which may be caused by intense focal spasm of a segment of an epicardial artery (Prinzmetal angina). Coronary vasospasm is a frequent complication in patients with connective tissue disease. Other causes include arterial inflammation and secondary unstable angina. Arterial inflammation may be caused by or related to infection. Secondary unstable angina occurs when the precipitating cause is extrinsic to the coronary arterial bed, such as fever, tachycardia, thyrotoxicosis, hypotension, anemia, or hypoxemia. Most patients who experience secondary unstable angina have chronic stable angina as a baseline medical condition.

Spontaneous and cocaine-related coronary artery dissection remains an unusual cause of ACS and should be included in the differential diagnosis, especially when a younger female or cocaine user is being evaluated. An early clinical suspicion of this disease is necessary for a good outcome. Cardiology consultation should be obtained for consideration for urgent percutaneous coronary intervention.

Irrespective of the cause of unstable angina, the result of persistent ischemia is myocardial infarction (MI).

History of the ACS:

Typically, angina is a symptom of myocardial ischemia that appears in circumstances of increased oxygen demand. It usually is described as a sensation of chest pressure or heaviness that is reproduced by activities or conditions that increase myocardial oxygen demand.

Not all patients experience chest pain. Some present with only neck, jaw, ear, arm, or epigastric discomfort. Other symptoms, such as shortness of breath or severe weakness, may represent anginal equivalents.

A patient may present to the ED because of a change in pattern or severity of symptoms. A new case of angina is more difficult to diagnose because symptoms are often vague and similar to those caused by other conditions (e.g., indigestion, anxiety).

Patients may have no pain and may only complain of episodic shortness of breath, weakness, lightheadedness, diaphoresis, or nausea and vomiting.

Patients may complain of the following: palpitations; pain, which is usually described as pressure, squeezing, or a burning sensation across the precordium and may radiate to neck, shoulder, jaw, back, upper abdomen, or either arm; exertional dyspnea that resolves with pain or rest; diaphoresis from sympathetic discharge; nausea from vagal stimulation; decreased exercise tolerance; patients with diabetes and elderly patients are more likely to have atypical presentations and offer only vague complaints, such as weakness, dyspnea, lightheadedness, and nausea.

Stable angina: involves episodic pain lasting 5-15 minutes; provoked by exertion; relieved by rest or nitroglycerin.

Unstable angina. Patients have increased risk for adverse cardiac events, such as MI or death. Three clinically distinct forms exist, as follows: new-onset exertional angina; angina of increasing frequency or duration or refractory to nitroglycerin; angina at rest; variant angina (Prinzmetal angina); occurs primarily at rest; triggered by smoking; thought to be due to coronary vasospasm.

Elderly persons and those with diabetes may have particularly subtle presentations and may complain of fatigue, syncope, or weakness. Elderly persons may also present with only altered mental status. Those with preexisting altered mental status or dementia may have no recollection of recent symptoms and may have no complaints whatsoever.

As many as half of cases of ACS are clinically silent in that they do not cause the classic symptoms described above and consequently go unrecognized by the patient. Maintain a high index of suspicion for ACS especially when evaluating women, diabetics, older patients, patients with dementia, and those with a history of heart failure.

Physical findings:

Physical examination results are frequently normal. If chest pain is ongoing, the patient usually will lie quietly in bed and may appear anxious, diaphoretic, and pale. Hypertension may precipitate angina or reflect elevated catecholamines due to either

anxiety or exogenous sympathomimetic stimulation. Hypotension indicates ventricular dysfunction due to myocardial ischemia, infarction, or acute valvular dysfunction. It is possible to find out signs of congestive heart failure (CHF) and jugular venous distention. Sometimes one can hear third heart sound (S3). A new murmur may reflect papillary muscle dysfunction. Rales on pulmonary examination are suggesting left ventricular (LV) dysfunction or mitral regurgitation. Presence of a fourth heart sound (S4) is a common finding in patients with poor ventricular compliance due to preexisting ischemic heart disease or hypertension.

Causes of the ACS:

1. Atherosclerotic plaque is the predominant cause. Coronary artery vasospasm is less common.

2. Alternative causes of angina include the following: ventricular hypertrophy due to hypertension, valvular disease, or cardiomyopathy; embolic occlusion of the coronary arteries; hypoxia, as in carbon monoxide poisoning or acute pulmonary disorders; cocaine and amphetamines, which increase myocardial oxygen demand and may cause coronary vasospasm; underlying coronary artery disease, which may be unmasked by severe anemia; inflammation of epicardial arteries; coronary artery dissection.

Risk factors for ACS should be documented and include the following: male gender; diabetes mellitus (DM); smoking history; hypertension; increased age; hypercholesterolemia; Hyperlipidemia; prior cerebrovascular accident (CVA) - these patients constitute 7.5% of patients with ACS and have high-risk features; inherited metabolic disorders; methamphetamine use; occupational stress; connective tissue disease.

Laboratory studies and findings:

Troponin I is considered the preferred biomarker for diagnosing myocardial necrosis. Troponins have the greatest sensitivity and specificity in detecting MI, and elevated serum levels are considered diagnostic of MI. They also have prognostic value. For early detection of myocardial necrosis, sensitivity of troponin is superior to that of the creatine kinase–MB (CK-MB). Troponin I is detectable in serum 3-6 hours after an MI, and its level remains elevated for 14 days. Troponin is a contractile protein that normally is not found in serum. It is released only when myocardial necrosis occurs. Troponin should be used as the optimum biomarkers for the evaluation of patients with ACS who have coexistent skeletal muscle injury.

Troponin T has similar release kinetics to troponin I and remains elevated for 14 days. False-positive results may occur in patients with renal failure. Minor elevations in troponin T also identify patients at risk for subsequent cardiac events. Elevated troponin levels may also point to minor myocardial injury due to other causes.

CK-MB levels begin to rise within 4 hours after MI, peak at 18-24 hours, and subside over 3-4 days. A level within the reference range does not exclude myocardial necrosis. The upper limit of normal for CK-MB is 3-6% of total CK. A normal level in the ED (Emergency Department) does not exclude the possibility of MI. A single assay in the ED has a 34% sensitivity for MI. Serial sampling over periods of 6-9 hours increases sensitivity to approximately 90%. Serial CK-MB over 24 hours detects myocardial necrosis with sensitivity near 100% and a specificity of 98%. Occasionally, a very small infarct will be missed by CK-MB; therefore, troponin levels should be measured for patients suspected to have MI who have negative results from serial CK-MB tests.

Myoglobin, a low-molecular-weight heme protein found in cardiac and skeletal muscle, is released more rapidly from infarcted myocardium than troponin and CK-MB and may be detected as early as 2 hours after MI. Myoglobin levels, although highly sensitive, are not cardiac specific. They may be useful for early detection of MI when performed with other studies.

Cardiac markers should be used liberally to evaluate patients with prolonged episodes of ischemic pain, with new changes on ECG, or with nondiagnostic or normal ECGs in whom the diagnosis of ACS or MI is being considered.

Complete blood count is indicated to determine if anemia is a precipitant. Transfusion with packed red blood cells may be indicated.

Chemistry profile: Obtain a basic metabolic profile, including a check of blood sugar level, renal function, and electrolytes levels, for patients with new-onset angina. Potassium and magnesium levels should be monitored and corrected. Creatinine levels must be considered before using an angiotensin-converting enzyme (ACE) inhibitor.

Imaging Studies:

Chest radiograph may demonstrate complications of ischemia, such as pulmonary edema, or provide clues to alternative causes of symptoms, such as thoracic aneurysm or pneumonia.

Echocardiogram often demonstrates wall motion abnormalities due to ischemia. It is of limited value in patients whose symptoms have resolved or in those with preexisting wall motion abnormalities. However, echocardiogram may be useful in identifying precipitants for ischemia, such as ventricular hypertrophy and valvular disease.

ECG is the most important ED diagnostic test for angina. It may show changes during symptoms and in response to treatment, which would confirm a cardiac basis for symptoms. It also may demonstrate preexisting structural or ischemic heart disease (left ventricular hypertrophy, Q waves). A normal ECG or one that remains unchanged from the baseline does not exclude the possibility that chest pain is ischemic in origin.

Treatment of the ACS

Prehospital Care: Generally, patients transported with chest pain should initially be managed under the assumption that the pain is ischemic in origin. Prehospital interventions should be guided by the nature of the presenting complaint, individual risk factors, and associated symptoms (e.g., breathing difficulty, hemodynamic instability, appearance of ectopy). Airway, breathing, and circulation should be rapidly assessed with institution of CPR, ACLS-guided interventions, or other measures as indicated for the unstable patient.

Management:

1. Obtain IV access.
2. Administer supplemental oxygen.
3. Aspirin should be given in the field, 162-325 mg chewed and swallowed.
4. Prehospital ECG, if available, may be helpful in selected circumstances.
5. Perform pulse oximetry.
6. Administer sublingual or aerosolized nitroglycerin if chest pain is ongoing and is felt to be cardiac in origin.

Emergency Department Care:

Antithrombin therapy and antiplatelet therapy should be administered to all patients with an ACS regardless of the presence or the absence of ST-segment elevation. Patients presenting with persistent ST-segment elevation are candidates for reperfusion therapy (either pharmacological or catheter based) to restore flow promptly in the occluded epicardial infarct-related artery. Patients presenting without ST-segment elevation are not candidates for immediate pharmacological reperfusion but should receive anti-ischemic therapy when appropriate.

Management:

1. Goals of ED care are rapid identification of patients with STEMI, exclusion of alternative causes of nonischemic chest pain, and stratification of patients with acute coronary ischemia into low- and high-risk groups.
2. Obtain IV access, administer supplemental oxygen, and provide telemetry monitoring if these procedures have not already been accomplished in the prehospital phase. In addition, obtain a 12-lead ECG as soon as possible after arrival.
3. Complete a history and physical examination, with focus on risk factors for coronary ischemia; onset, duration, and pattern of symptoms; and early identification of complications of myocardial ischemia (e.g., new murmurs, cardiac congestive failure).
4. Perform frequent reassessment of vital signs and symptoms in response to administered therapies.
5. Serial ECGs and continuous ST segment monitoring may be useful.
6. Medical therapy.

The goals of treatment are to preserve patency of the coronary artery, augment blood flow through stenotic lesions, and reduce myocardial oxygen demand. All patients should receive antiplatelet agents, and patients with evidence of ongoing ischemia should receive aggressive medical intervention until signs of ischemia, as determined by symptoms and ECG, resolve.

Drug Category:

Antiplatelet agents - Inhibit the cyclooxygenase system, decreasing the level of thromboxane A2, which is a potent platelet activator. Antiplatelet therapy has been shown to reduce mortality by reducing the risk of fatal strokes and fatal myocardial infarctions.

Nitrates - These agents oppose coronary artery spasm and reduce myocardial oxygen demand by reducing both preload and afterload.

Analgesics – These agents reduce pain, which decreases sympathetic stress, in addition to providing some preload reduction.

Anticoagulants – These agents are

used to prevent recurrence of clot after a spontaneous fibrinolysis.

Beta-adrenergic blockers - These agents have antiarrhythmic and antihypertensive properties as well as the ability to reduce ischemia. They minimize the imbalance between myocardial supply and demand by reducing afterload and wall stress. In patients with acute MI, they have been shown to decrease infarct size as well as short- and long-term mortality, which is a function of their anti-ischemic and antiarrhythmic properties.

Low molecular weight heparin (enoxaparin) has been shown to reduce cardiac ischemic events and death by as much as 15% in patients with unstable angina. These clinical effects have been reported with all patients also receiving aspirin.

Direct thrombin inhibitors - hirudin is the prototype of direct thrombin inhibitors. Hirudin binds directly to the anion binding site and the catalytic sites of thrombin to produce potent and predictable anticoagulation.

Adenosine diphosphate (ADP) receptor antagonists - two thienopyridines, ticlopidine and clopidogrel, are ADP antagonists that are approved for antiplatelet activity. Both have irreversible antiplatelet activity but take several days to become manifest. A potential additive benefit exists when ADP antagonists are used in conjunction with aspirin. These drugs may be considered alternatives to aspirin in patients intolerant or allergic to aspirin.

High-risk criteria include the following:

1. Symptoms refractory to medical management
2. Hemodynamic instability, cardiogenic shock
3. New or worsening mitral regurgitant murmur
4. Known or suspected severe aortic stenosis

Complications:

1. Acute myocardial infarction
2. Cardiogenic shock
3. Ischemic mitral regurgitation
4. Arrhythmias: a) supraventricular arrhythmias (rare complication of ischemia, may actually precipitate ischemic events); b) ventricular arrhythmias; simple and complex premature ventricular contractions (PVCs), and nonsustained ventricular tachycardia.
5. Atrioventricular nodal blockade: usually transient in setting of reversible ischemia; treatment guided by location of block and hemodynamic stability.
6. Ventricular rupture occurs in the interventricular septum or the LV free wall. This represents a catastrophic event with mortality rates greater than 90%. Prompt recognition, stabilization, and surgical repair are crucial to any hope of survival. An echocardiogram usually will define the abnormality, and a right heart catheterization may show an oxygenation increase with septal rupture.

References:

1. Bartholomew BA, Sheps DS, Monroe S, et al: A population-based evaluation of the thrombolysis in myocardial infarction risk score for unstable angina and non-ST elevation myocardial infarction. Clinical Cardiology, 2004 Feb.
2. Libby et al. Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine, 8th ed., 2007
3. Cardiovascular Emergencies. Edited by Crispin Davies and Yaver Bashir. BMJ, 2001
4. Cardiovascular Medicine. Edited by Willerson et al. Springer, 2007
5. Coronary Heart Disease in Clinical Practice. Satish Mittal. Springer, 2005
6. Gandhi MM, Lampe FC, Wood DA: Incidence, clinical characteristics, and short-term prognosis of angina pectoris. Britain Heart Journal, 1995 Feb.
7. Heart Disease. Diagnosis and Therapy. Khan. Humana Pres, 2005.
8. Hamm CW, Ravkilde J, Gerhardt W, et al: The prognostic value of serum troponin T in unstable angina. New England Journal Medicine, 1992 Jul 16.
9. Hasdai D, Haim M, Behar S, et al: Acute coronary syndromes in patients with prior cerebrovascular events: lessons from the Euro-Heart Survey of Acute Coronary Syndromes. American Heart Journal, 2003 Nov.
10. Hurst's the Heart. Ed. Valentin Fuster et al. McGraw-Hill, 2004
11. Lindahl B, Venge P, Wallentin L: Relation between troponin T and the risk of subsequent cardiac events in unstable coronary artery disease. The FRISC study group. Circulation 1996 May 1.
12. Management of Acute Coronary Syndromes. Ed. Cannon. Humana Press. 2003
13. Roig S, Gomez JA, Fiol M, et al: Spontaneous coronary artery dissection causing acute coronary syndrome: an early diagnosis implies a good prognosis. American Journal Emergency Medicine, 2003 Nov.
14. Taylor's Cardiovascular Diseases. Taylor et al. Springer, 2005
15. Textbook of Cardiovascular Medicine. Ed. Topol et al. Williams-Wilkins, 2007
16. Wu AH, Abbas SA, Green S: Prognostic value of cardiac troponin T in unstable angina pectoris. American Journal Cardiology, 1995 Nov 1.