

Coronary Artery Disease

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Introduction:

It is estimated that more than 16 million Americans have coronary artery disease (CAD) and 8 million have had a myocardial infarction (MI). Every year approximately 1 million will have a new myocardial infarction. Based on data from the Framingham trial nearly 50% of males and 30% of females over the age of 40 will develop coronary artery disease. Coronary artery disease is most commonly due to atherosclerotic occlusion of the coronary arteries. Atherosclerosis is a process that can involve many of the body's blood vessels with a variety of presentations. When it involves the coronary arteries it results in coronary artery disease, the cerebral arteries; cerebrovascular disease (transient ischemic attack, stroke), the aorta; aortic aneurysms, the ileo-femoral and popliteal arteries; peripheral vascular disease, the mesenteric arteries; intestinal ischemia. Half of all deaths in the developed world and a quarter of deaths in the developing world are due to Cardiovascular Disease which are comprised of hypertension and the diseases caused by atherosclerosis.

Coronary Blood Flow:

The heart is an aerobic organ that is dependent for its oxygen supply entirely on coronary perfusion. Under resting condition, the myocardium extracts the maximum amount of oxygen from the blood it receives. The O₂ saturation of blood returning from the coronary sinus to the right atrium has the lowest saturation of any body organ (30%). Interruption of coronary blood flow will result in immediate ischemia. Coronary blood flow is directly dependent upon perfusion pressure and inversely proportional to the resistance of the coronary vessel.

$$Q \propto \text{Perfusion pressure} / \text{Vessel resistance}$$

Coronary perfusion occurs in diastole hence diastolic pressure is more important than systolic pressure in determining coronary perfusion. Coronary vessels are divided into epicardial or conductance vessels (R1), pre capillary (R2) and microvascular vessels (R3). The epicardial vessels, the site most commonly affected by atherosclerosis, offer negligible resistance to coronary flow. Resistance to flow occurs in the pre capillary (R2), and microvascular (R3) vessels which are termed **resistance vessels**. The increase coronary blood flow in response to increase myocardial oxygen demand (MVO₂) is achieved by the dilatation of these resistance vessels. Three factors play a key role in modifying vascular tone; the accumulation of local metabolites, endothelial factors and neural tone. The accumulation of adenosine during ischemia is an example of local metabolic factors. The most important endothelial substance mediating *vasodilatation* is **nitric oxide (NO)**. Other important mediators are **bradykinin**, **endothelium derived**

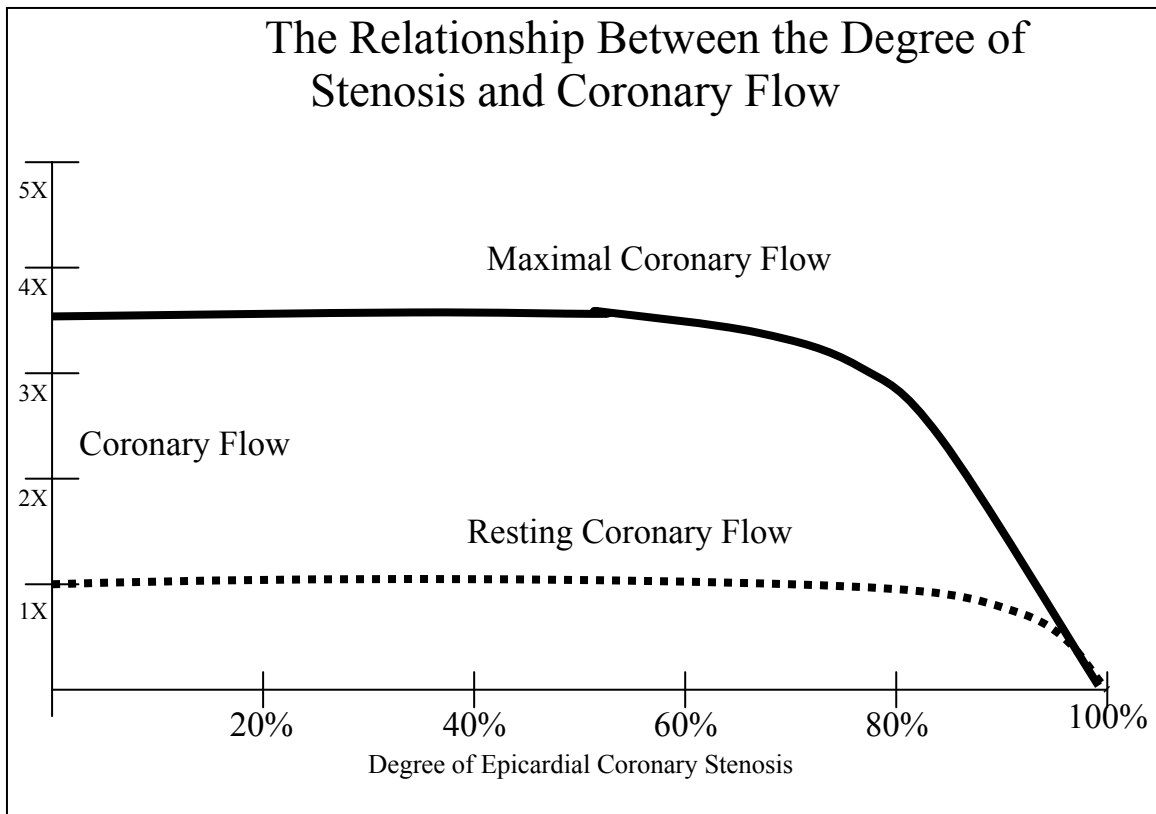
hyperpolarizing factor and **prostacyclin**. On the other hand, **endothelin-1 (ET-1)** is a well known *vasoconstricting* substance. **Angiotensin II** and **thromboxane A₂** are other well known endothelium derived constricting factors. Alpha receptor adrenergic stimulation results in coronary vasoconstriction whereas beta 1 receptor stimulation leads to vasodilatation.

Coronary vascular resistance can be reduced to 1/5th of baseline resistance leading to a five fold increase in the volume of perfusion in response to an increase in need.

Coronary reserve is the term used to reflect the amount of increase in coronary perfusion to accommodate increased demand. **Autoregulation**, mediated by changes in the vascular tone of the resistance vessels, allows distal coronary perfusion to remain unaltered in the face of changes in proximal perfusion pressures. Impaired endothelial function disrupts autoregulation and may lead to ischemia. Diseases known to impair endothelial function include atherosclerosis, dyslipidemias, diabetes mellitus, hypertension, smoking (both passive and active) and hyperhomocysteinemia.

Coronary arteries suffering from atherosclerosis lose the ability to release the vasodilating substances that allow the increase in coronary perfusion in the face of increased demand. Their coronary reserve is limited by the failure to dilate and reduce vascular resistance. Furchgott showed that acetylcholine, through the release of NO, results in vasodilation of the coronary vessel. However if the endothelium overlying the vascular smooth vessel was diseased (e.g. by atherosclerosis), the smooth muscle will paradoxically vasoconstrict.

Blockage of the epicardial coronary vessels (**coronary stenosis**) of up to 60% is compensated at rest and maximal exercise by vasodilation of the **resistance coronary vessels**. Blockage of epicardial coronary vessels in excess of 60% will result, under conditions of increases myocardial oxygen demand, in reduced perfusion and in turn **ischemia**. Clinically, this translates to **effort or exercise induced angina**. This is the basis for performing **exercise stress testing** in patients suspected of having coronary artery disease. When the severity of the blockage is greater than 90%, perfusion is compromised even at rest. Clinically, this may result in **resting angina**, a critical stage of coronary artery disease. **Ischemia** is the result of the coronary vessel's inability to meet the demand of the myocardium it supplies. The imbalance between supply and demand (↑ demand, ↓ supply) results in ischemia. Clinically this presents as chest discomfort and / or shortness of breath



The Determinants of Myocardial O₂ Consumption:

The major determinants of myocardial O₂ consumption (MVO₂) are **1) heart rate** **2) ventricular wall stress (afterload)** and **3) contractility (inotropy)**. Heart rate is the main determinant of MVO₂. Ventricular wall stress, as defined by Laplace's law, is the product of the left ventricular systolic pressure and the radius of the left ventricle divided by its wall thickness. Hence, processes such as aortic stenosis and hypertension, which increase systolic pressure, mitral and aortic regurgitation, which increase LV cavity size, increase myocardial oxygen consumption. During exercise stress testing MVO₂ can be described using the “**double product**,” the product of the maximal systolic pressure and heart rate attained during maximal exercise. This formula represents the two key components of myocardial oxygen demand.

The Pathogenesis of the Atherosclerotic Plaque:

Atherosclerosis is the main cause of coronary artery disease. The process begins as disruption of endothelial function due to the accumulation of lipoprotein droplets in the intima of the coronary vessels. *Water insoluble lipids are carried in the bloodstream attached to water soluble apolipoproteins (lipoproteins). High concentrations of low density lipoprotein (LDL) can permeate an already disrupted or dysfunctional endothelium where it undergoes oxidation and, in diabetics, glycation. Modified LDL attracts leukocytes into the intima and can be scavenged by macrophages leading to the formation of foam cells. These cells replicate giving rise to one of the earliest*

pathological lesions; the **fatty streak**. The fatty streak is the earliest visualized lesion of atherosclerosis.

Smooth muscle cells are then recruited and migrate to the site of the foamy cells. Smooth muscle cells proliferate and manufacture extracellular matrix. A large volume of the plaque is occupied by extracellular matrix (collagen and proteoglycan) secreted by the smooth muscle cells. The fatty streak is now transformed into the **fibrous plaque**. At this point the lesion begins to encroach on the lumen of the vessel. Small blood vessels form in these plaques (angiogenesis) and these plaques can subsequently calcify. Inflammation plays an important role in promoting smooth muscle cell migration and proliferation. The final lesion, the advanced **complicated lesion**, consists of a **fibrous cap** overlying a lipid rich core which also contains necrotic material, this core is highly thrombogenic.

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Risk Factors for Atherosclerotic Coronary Artery Disease:

1. Dyslipidemias; particularly high low density cholesterol (LDL-C) and low high density cholesterol (HDL-C). (ATP III classification of LDL, total and HDL cholesterol; **LDL**: Optimal < 100 mg/dL, Near or above optimal 100-139 mg/dL, Borderline high 140-159 mg/dL, High > 160 mg/dL. **Total cholesterol**: Desirable < 200, borderline high 200-239 mg./dL, High > 240 mg./dL. **HDL**: Low < 40 mg./dL. *JAMA*. 2001;285:2486-2497)
2. Hypertension (50 million in the US, 1/3 undiagnosed, 3/4 under treated). (Classification of HTN **Normal BP**: systolic < 120 mmHg AND diastolic < 80 mmHg, **Prehypertension**: systolic 120-139 OR diastolic 80-89 mmHg, **Hypertension**: systolic > 140 OR diastolic > 90 mmHg. The JNC 7 Report *JAMA*. 2003;289:2560-2571)
3. Diabetes mellitus (8% of US population). (Classification: Normal fasting glucose < 110 mg/dL, Impaired 110-≤ 126 mg/dL, Diabetes > 126 mg/dL)
4. Smoking (most important modifiable risk factor), CAD accounts for 35%-40% of all smoking related deaths
5. Family history of premature coronary artery disease (CAD); First degree male relatives < 55 years or females < 65 years.
6. Obesity (18% of US population) and lack of exercise
7. Male sex and advanced age
8. Others (20% of CAD occurs in individuals without any of the classical risk factors); homocysteinemia, high sensitivity C reactive protein (hs-CRP), Fibrinogen, Lipoprotein a (Lp_a), infection (? *Chlamydia pneumoniae*)

The **metabolic syndrome** is a recently identified entity that is associated with an increase in the risk of developing diabetes mellitus, cardiovascular disease and mortality from all causes. It is found in 22%-24% of the US population. Individuals with three or more of the following high risk features are defined as having the metabolic syndrome;

1. Abdominal obesity: waist circumference >102 cm in men and >88 cm in women
2. Hypertriglyceridemia: ≥ 150 mg/dL
3. Low high-density lipoprotein (HDL) cholesterol: <40 mg/dL in men and <50 mg/dL in women
4. High blood pressure: $\geq 130/85$ mm Hg
5. High fasting glucose: ≥ 110 mg/dL (≥ 6.1 mmol/L).

JAMA, Jan 2002; 287: 356 – 359

Consequences of Atherosclerosis

1. Calcification, rigidity and increased fragility
2. Rupture of the fibrous cap exposing thrombogenic material to circulating platelets and coagulants leading to thrombosis. This would result in vessel occlusion and distal myocardial infarction (necrosis). **Unstable angina and myocardial infarction**
3. Plaque hemorrhage further narrowing the vessel lumen and occluding distal flow
4. Distal embolization of fragmented atheromatous plaque
5. Weakening of the vessel wall, wall expansion and dilatation (**aneurysm**)

Consequences of Reduced Blood Flow to the Myocardium

The duration and severity of ischemia will determine the fate of the compromised myocardium. Diastolic and systolic dysfunction are one of the first consequences of ischemia. This is followed by elevation of filling pressures, electrocardiographic changes and then, pain. Myocardial necrosis (infarction) is the final outcome of prolonged cessation of blood flow. The extent of myocardial necrosis depends upon the size of the territory supplied by the compromised vessel and the duration of antecedent ischemia to that territory. A sudden occlusion of the proximal left anterior descending coronary artery (LAD) has very grave consequences (an occlusion anecdotally termed the “widow maker”) due to the large size of myocardium perfused by the LAD. The damage incurred by a more distal lesion would be less profound.

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Complete occlusion of a vessel that had a preceding tight occlusion may result in a smaller myocardial infarction than one occurring in the absence of a tight stenosis. This is partly due to the time dependent formation of **collateral circulation** that circumvents the site of stenosis and leading to a process known as **ischemic preconditioning**. Recurrent ischemia results in changes that attenuate the impact of the final complete occlusion.

The myocardium supplied by a tightly stenosed vessel may display impaired contractility even if it did not suffer irreversible injury. This is called **hibernating myocardium** and is important to identify. Restoration of blood flow would restore myocardial function and improve the overall ejection fraction. This should be distinguished from **stunned myocardium**. Stunned myocardium is myocardium with reversibly impaired contractility

that lies adjacent to irreversibly damaged myocardium immediately after an infarction despite restoration of coronary blood flow, resolution of pain and ischemic electrocardiographic changes. With time, myocardial contractility to the stunned segment returns to its former function.

Shortly after a myocardial infarction, the segment of infarcted myocardium undergoes **expansion** due to dilation and thinning *without* further loss of myocardium. This may result in **aneurysm** formation, and a shift in the hemodynamic forces to the healthier myocardial segments. This results in dilatation of the non infarcted segments where by increasing stretch, it compensates for the loss in inotropy caused by the loss of myocardial cells. These changes are collectively called **remodeling**. While short-term, these changes are using the Frank-Sterling laws to enhance cardiac output and compensate for the loss the heart has suffered, long-term these changes are detrimental. Many of the recently introduced interventions are aimed at preventing or minimizing the impact remodeling has on the heart. These include the early use of angiotensin converting enzyme inhibitors and early revascularization to minimize the size of infarcted myocardium.

Clinical Consequences of Coronary Artery Disease

Coronary artery disease can present in a variety of ways. The classical presentation is with chest discomfort. Chest discomfort resulting from myocardial ischemia secondary to coronary artery disease is called **angina pectoris** (squeezing of the chest). Discomfort is diffuse and not localized and may radiate down the arms, as low as the umbilicus and up to the lower jaw. This may be associated with shortness of breath (dyspnea). This discomfort is the result of myocardial ischemia however it is one of the last manifestations to appear. Due to the myocardium's complete reliance on coronary blood flow for energy supply, within a few beats of coronary occlusion, diastolic and systolic dysfunction set in and the electrocardiogram begins to register abnormalities before the patient begins to experience angina pectoris. This explains why patients may describe associated shortness of breath when they experience angina. The association of both symptoms together indicates that the myocardium fed by the narrowed vessel is sizable.

The following are the more frequent clinical consequences of coronary artery disease. These "scenarios" may progress from one to another and their recognition allows for their proper management to preclude any potential lethal consequence. The term **acute coronary syndrome** refers to unstable angina, non ST-segment elevation and ST-segment elevation myocardial infarction. One fourth of acute coronary syndrome patients are diagnosed with ST-segment elevation myocardial infarction, the remainders have unstable angina or non ST-segment MI (NSTEMI).

1. **Stable Angina:** Angina occurring predictably after exertion and relieved by rest. This is due to increased oxygen demand in the face of limited coronary flow. The more severe the narrowing, the less the amount of exertion required to induce ischemia and angina pectoris. As the narrowing becomes more severe, the amount of exertion required to precipitate angina becomes less. Certain types of exertion are classical in reproducing angina such as climbing stairs/slopes, walking in cold weather especially if accompanied

by wind and after meals. The discomfort is pressure-like and diffuse, it peaks over minutes and when relieved by rest or sublingual nitroglycerine, it does so within 5-10 minutes. Some patients display individual variability in the amount of effort required to precipitate angina. This is called **variable threshold angina** where a component of vasoconstriction may play a role in lowering the threshold for angina.

Cardiac catheterization has shown that 25% of patients with stable angina have single vessel disease, 25% have two and 25% have three-vessel disease (defined as luminal narrowing of > 70%). Five to ten percent have left main disease and 15% have no discernible obstruction. Treatment is by using beta-blockers to reduce myocardial O₂ requirements, Ca⁺⁺ channel blockers to vasodilate and reduce preload and afterload. Nitrates also vasodilate and reduce preload. When medical therapy fails, percutaneous intervention with balloon angioplasty or surgical revascularization may be required. Risk factor modification is equally important addressing dyslipidemia, hypertension, smoking, obesity and physical inactivity. The annual risk of death in this patient population is 1.7%-3% with a 1.4%-2.4% risk of a major ischemic event.

2. **Unstable Angina:** The diagnosis of unstable angina is a clinical one where patients with UA can present in one of three clinical scenarios; A) An acceleration from stable angina to one that occurs with less activity with more intensity and lasting longer. B) Angina at rest C) New onset angina usually with severe discomfort. Whereas the pathogenesis of ST-segment elevation myocardial infarction is total occlusion of the coronary vessel, the pathogenesis of UA is severe but not total occlusion of the culprit vessel. This is usually due to 1. plaque disruption with clot formation and interruption of distal blood flow, 2. Vasoconstriction, 3. mechanical occlusion, 4. inflammation, and 5. increased myocardial oxygen demand due to extracardiac causes (anemia, thyrotoxicosis) play variable roles in the pathogenesis of unstable angina.

One year progression to death or myocardial infarction is between 7% and 14%. Patients older than 70 yrs., diabetic patients, and patients with vascular disease have a worse prognosis. Electrocardiographic determinants of prognosis include the magnitude of ST-segment deviation as well as the presence of a left bundle branch block. Elevated serum troponin and C-reactive protein also portend a worse prognosis. The existence of these features should prompt a more aggressive approach.

Since thrombus formation is an integral component in the pathogenesis of unstable angina, anticoagulants such as aspirin, heparin and more recently glycoprotein IIB/IIIA inhibitors are critical ingredients of the therapeutic armamentarium. Reduction of oxygen consumption using beta-blockers and nitrates are also used. A rise in one of the serum cardiac markers, troponin, portends a worse prognosis. Such patients are treated more aggressively with glycoprotein IIB/IIIA inhibitors and early cardiac catheterization.

3. **Non-ST Elevated Myocardial Infarction.** If patients present with chest discomfort and / or symptoms of a myocardial infarction (nausea, vomiting, diaphoresis, shortness of breath), have positive biomarkers for myocardial necrosis (CPK, CPK-MB and troponin, but without ST-segment elevation in the electrocardiogram, the diagnosis is

non ST-elevated myocardial infarction (NSTEMI). Recent studies have shown that patients with NSTEMI constitute the majority (54%) of acute MIs patients admitted to the hospital. This study also showed that patients with NSTEMI had higher 1 year mortality (31%) than patients with ST-elevation MI (21%). Patients with NSTEMI tend to be older, have worse LV function, multi vessel disease and a history of acute coronary events. The pathophysiology of NSTEMI shares many of the features of UA i.e. clot on plaque, vasoconstriction, increased O2 demand, inflammation and progression of occlusive thrombus.

Management includes the use of heparin and glycoprotein IIB/IIIA inhibitors in addition to aspirin and beta-blockers. The importance of distinguishing ST-segment elevation from non ST-segment elevation myocardial infarction is that thrombolytic agents are **not** administered in NSTEMI and percutaneous intervention may be used acutely if the patient does not respond to medical therapy.

Severity		
Class	Definition	MI or Death in the next year
<i>Stable angina</i>		1.4%-3%
<i>Unstable angina / NSTEMI</i>		
Class I	New onset of severe angina or accelerated angina; no rest pain	7.3%
Class II	Angina at rest within past month but not within preceding 48 hr (angina at rest, subacute)	10.3%
Class III	Angina at rest within 48 hr (angina at rest, subacute)	10.8%
Clinical Circumstances		
A (secondary angina)	Develops in the presence of extracardiac condition that intensifies myocardial ischemia	14.1%
B (primary angina)	Develops in the absence of extracardiac condition	8.5%
C (post infarct angina)	Develops within 2 wks after acute myocardial infarction	18.5%

The prognosis of stable vs. unstable angina pectoris / NSTEMI

4. **ST-Segment Elevation Myocardial Infarction.** This is the other end of the spectrum of coronary syndromes. The etiology is complete occlusion of a coronary vessel from a clot developing on a recently ruptured plaque. These plaques are usually < 50% in diameter and are lipid rich. The ensuing activation of platelets and the coagulation cascade results in thrombus formation and occlusion of the vessel.

Patients describe chest discomfort that is severe and often associated with nausea and vomiting. Discomfort typically lasts more than twenty minutes and does not respond to nitroglycerine. Radiation may occur down either arm, the lower jaw and to the back. Discomfort due to an acute MI does not radiate below the umbilicus or above the earlobes. Shortness of breath may indicate a large sized infarction. Up to 25% of patients, may not experience any discomfort when they suffer an infarction. The elderly and diabetic patients are more prone to having a **silent myocardial infarction**. Acute MIs, particularly in patients not receiving beta blockers or aspirin, tend to cluster between 6AM and 12PM. This *circadian variation* is thought to be due to circadian variation in levels of circulating corticosteroids and catecholamines.

On examination, patients are uncomfortable and diaphoretic. They may exhibit pallor indicating decreased peripheral perfusion due to a drop in cardiac output and / or heightened sympathetic tone. Blood pressure may be normal, elevated due to discomfort and anxiety or reduced due to low cardiac output (especially if the right ventricle is involved) or the medications used to treat the patient's condition. Jugular venous distension indicates right sided heart failure, the commonest cause being left-sided heart failure. Râles heard over the lung bases suggests left heart failure and is an ominous finding in patients suffering a myocardial infarction.

The WHO criteria for diagnosing an acute myocardial infarction is: Chest pain, serial elevation of cardiac enzymes and typical electrocardiographic features. The fulfillment of two out of three of these criteria establishes the diagnosis. A more recent definition for an acute, evolving or recent myocardial infarction requires the typical rise and fall of cardiac enzymes (troponin, CK-MB) along with one of the four following criteria;

1. Typical ischemic symptoms
2. ST-segment elevation or depression
3. Development of Q waves
4. Acute percutaneous intervention

Myocardial necrosis results in the release of non-specific and more specific enzymes. An estimation of the magnitude of myocardial necrosis can be determined by the degree of enzyme elevation. One of the first enzymes to climb is myoglobin. It peaks and falls back to baseline within one day of the MI, however myoglobin is very non-specific. The more cardio specific enzymes CK-MB and Troponins then begin to rise, CK-MB reaches a peak in 1-1 ½ day and is down to baseline in 4 days. Troponins peak in two days and fall to baseline in 5-7 days. Hence, for the diagnosis of an MI that may have occurred 4-5 days ago, troponins are more helpful than CK-MB.

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Cardiac enzymes should display a characteristic rise followed by a fall back to baseline. The electrocardiogram displays characteristic changes. One of the first changes seen is elevation of the ST-segment and peaking of the T wave. The T wave then begins to invert and once irreversible myocardial necrosis sets in, Q waves begin to show. The ST-segment then descends to baseline and the T wave may or may not normalize with time. Persistent ST-segment elevation may indicate formation of an **aneurysm** in the underlying myocardium. Patients with angina of non ST-segment elevation myocardial infarction (NSTEMI) display ST-segment depression and T wave changes but not the characteristic ST-segment elevation.

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Where myocardial infarction is involved, time is salvageable myocardium and every minute from the inception of symptoms counts. Irreversible injury begins to set in < one hour after occlusion of the offending vessel takes place. However myocardium can be salvaged as late as 12 hours after symptoms begin. This sets the stage for prompt intervention by one of two available methods of revascularization; **thrombolytic (fibrinolytic) therapy** and **percutaneous intervention**.

Tissue plasminogen activator is released by endothelial cells in response to clot formation. Plasminogen is cleaved to plasmin which in turn lyses fibrinogen breaking up formed or forming clot. This agent is given intravenously, however it cannot discriminate between a clot causing a myocardial infarction and a clot preventing a catastrophic hemorrhage, in for instance, the GI tract or the central nervous system. The risk / benefit ratio increases as time goes by. It is most effective when given the first four hours however it may be administered as late as twelve hours after symptoms began. Up to 80% of occluded coronary vessels are reperfused with fibrinolytic therapy leading to enhanced survival, improving prognosis and lowering complication rates.

Recent studies have shown that acute percutaneous intervention with balloon tipped catheters (primary angioplasty) to revascularize occluded coronary vessels is equally as good as if not safer than thrombolytic therapy as long as its employment does not lengthen the critical time to intervention. Up to 30% of patients with myocardial infarction have a contraindication to receive fibrinolytic therapy and may benefit from primary angioplasty.

Adjunctive treatment includes aspirin, heparin, analgesics and beta blockers. Recently administration of afterload reducing agents angiotensin converting enzyme inhibitors (ACE-inhibitors) and cholesterol reducing hydroxymethylglutaryl coenzyme-A reductase inhibitors (statins) has been shown to portend favorably on patients with acute MI.

Mortality from ST-elevated MI has declined over the last 40 years. This is in part due to the introduction of coronary care units, use of invasive monitoring when appropriate, thrombolytic therapy and direct acute revascularization. Large studies report in-hospital

mortalities of 6.5%-7% whereas community based observation yield a 15%-20% mortality.

5. **Silent Ischemia.** Impaired coronary flow may occur without symptoms. This syndrome can be seen in up to 40% of patients with classical angina pectoris and in up to 10% of patients with no symptoms of angina at all. Diabetic patients have a higher incidence of silent ischemia. Angina is a warning symptom without which serious underlying coronary disease is often overlooked. Hence patients with silent ischemia have a worse prognosis than those with angina pectoris.

6. **Sudden Cardiac Death.** Patients with coronary artery disease can present for the first time with a lethal arrhythmia; ventricular fibrillation. The definition of Sudden Cardiac Death is *natural death due to cardiac causes, heralded by abrupt loss of consciousness within one hour of the onset of acute symptoms. Preexisting heart disease may or may not have been known to be present, but the time and mode of death are unexpected.* Ischemia plays an important role in generating ventricular fibrillation, the lethal arrhythmia that leads to sudden cardiac death. It may occur immediately as a result of plaque rupture and occlusion of a critical vessel or after the onset of a myocardial infarction. Patients with a history of a myocardial infarction and myocardial damage are also predisposed to ventricular arrhythmias (primary ventricular fibrillation arrest).

Clinical Consequences of Myocardial Infarction

A) Short Term

- i. **Cardiac Arrest;** accounts for most acute deaths complicating myocardial infarction and is due to ventricular fibrillation. Treatment is immediate defibrillation. Understanding that, this one of the most lethal complications of acute MI led to the introduction of ICU monitoring for acute MI patients. This risk is usually seen during the first 24 hours of an MI. While VF arrest within the first 48 hours of an MI does not portend an adverse long-term prognosis, VF arrest beyond the first 48 hours does, and reflects extensive myocardial injury and poor underlying myocardial function. It also predicts a high future likelihood of recurrence of VF arrest.
- ii. **Congestive Heart Failure;** A consequence of a sizeable myocardial infarction (> 25% cardiac muscle). The single most important determinant of prognosis after an acute STEMI. Carries a poor prognosis.
- iii. **Cardiogenic Shock;** Seen when > 40% of myocardial muscle is injured. Marked by hypotension, poor peripheral perfusion and drop in urine output. Portends a very poor prognosis (50%-60% mortality) and is the cause of death in 60% of STEMI. Systolic BP < 80 mmHg, high filling pressure > 18 mmHg, and low cardiac index < 1.8L/min/M²). May also be the consequence of ruptured papillary muscle or interventricular septum.

- iv. *Rupture*; Into the pericardial space resulting in immediate death due to pericardial tamponade. Usually complicating anterior or lateral wall MIs and in older individuals.
- v. *Pseudoaneurysm*; A pseudoaneurysm is a confined free wall rupture held up by clot formation. Once identified it should be surgically corrected urgently. The difference between a pseudoaneurysm and a true aneurysm is that the wall of a true aneurysm contains myocardial tissue whereas the wall of a pseudoaneurysm is composed of clot and pericardial tissue.
- vi. *Ruptured Papillary Muscle*; Resulting in acute mitral regurgitation. Seen more commonly after an inferior myocardial infarction. Requires urgent surgical repair.
- vii. *Ruptured Interventricular Septum*; Usually after an acute anterior wall MI. Results in heart failure and requires urgent surgical therapy
- viii. *Aneurysm formation*; This is an intermediate-term complication of a myocardial infarction. When a segment of myocardium becomes sluggish in its contraction secondary to a myocardial infarction it is described as **hypokinetic**. When the segment does not contract it is **akinetic**. When it bulges outward during systole; **dyskinetic**. This segment is aneurysmal and can lead to clot formation and ventricular arrhythmias.

B) Long Term

- i. *Heart failure*; Coronary artery disease is the commonest cause of congestive heart failure in the Western economies
- ii. *Sudden cardiac death*; Due to ventricular arrhythmias

Determinants of Prognosis in Patients with Coronary Artery Disease

- 1. Left ventricular dysfunction
- 2. Extent of coronary artery disease

Natural History of Coronary Artery Disease Based Upon Number of Stenosed Vessels Before Intervention	
Number of Stenosed Vessels	Annual Mortality (%)
1	<4
2	7-10
3	10-12
Left Main	15-25

Adapted from Gupta A et al; Ischemic Heart Disease. Pp. 131-156. Pathophysiology of Heart Disease. 3rd. edition. Leonard S. Lilly (ed). Lippincott Williams & Wilkins 2003

- 3. Arrhythmias
- 4. Advanced age
- 5. History of congestive heart failure
- 6. Diabetes mellitus
- 7. Accelerating symptoms

8. Resting ECG changes