CHAPTER I

INTRODUCTION

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The term "unstable angina" is said to be present when angina pectoris first begins, and has been present for less than 6 weeks; angina pectoris is increasing in frequency and duration; angina pectoris is provoked with less than usual stimuli or angina occurs at rest. Patients with such complaints are considered to be in jeopardy of having a coronary event such as myocardial infarction or sudden death within a few days, weeks or months.[1,2] Many synonyms were used for untable condition such as impending myocardial infarction,[2] coronary failure,[3] acute atypical coronary artery insufficiency,[4] the intermediate coronary syndrome,[5] impending acute coronary occlusion,[6] preinfarction angina,[7] acute coronary insufficiency,[8,11] status anginosus,[9] preinfarctional angina,[10,12] preinfarction syndrome,[13] accerlated angina pectoris.[14]

1. Histological review

Our current knowledge regarding the recognition, prognosis and treatment of atherosclerotic coronary artery disease is considerable. It is, at the present time, grossly deficient,because we know so little about the prevention of the disease or how to treat all the sequelae of it. These inadequacies assume even more importance because the disease continues to be the leading cause of death in this country.

1.1 Recognition of angina pectoris

William Heberden, M.D (1710 - 1801) originally mentioned angina pectoris in a lecture at the Royal College of Physicians in London in 1768. His observations were published in Medical Transactions in 1786.[15] He did not attribute angina pectoris to a decreased blood flow through obstructed coronary arteries. He actually did not know what disease his patient had.

John Hunter, M.D (1728-1793)

John Hunter recorded his observations on himself. He, more than anyone, emphasized that angina pectoris was precipitated by emotional stress.

1.2 Etiology of angina pectoris

Caleb Hillier Parry (1755 - 1822) and Edward Jenner (1749-1823)

Parry and Jenner are usually given the credit for recognizing that angina pectoris can be caused by coronary artery disease.

1.3 Pathophysiology of angina pectoris

Allan Burns (1781-1813)

He was anatomist and not a physician. He believed that coronary arteries can undergo spasm, and also understood that the decreased blood flow that resulted from obstructed arteries caused angina pectoris.

1.4 Recognition of Coronary thrombosis

James Herrick (1861-1954)[16,17]

Herrick described the clinical feature of coronary thrombosis (myocardial infarction) and stressed the need for a classification of numerous clinical syndromes that resulted from coronary disease.

1.5 "In Between" Syndromes

Arthur Master (1885-1973)

Master recognized that Heberden's angina

was at one extreme of the clinical spectrum and that Herrick's acute coronary thrombosis (MI) was at the other extreme of the clinical spectrum. [18] He emphasized that some patients exhibited a syndrome that was in between the two extremes. In 1944 he labeled this subset of patients as having "coronary insufficiency".

1.6 Variant angina

Myron Prinzmetal (1908-)

Prinzmetal's variant angina may occur in patients who have coronary spasm with normal coronary arteries, but it more commonly occurs in patients with obstructive coronary disease plus coronary spasm.[19] He postulated that the condition was caused by "temporary hypertonus of a large atherosclerotic artery."

2. Etiologic factor

A number of conditions and habits present more frequently in individuals who develop atherosclerosis than in general population, these factors have been termed "risk factors".

Risk factors for atherosclerosis

1. Not reversible

a) Aging

b) Male sex

c) Genetic traits - positive family history of premature atherosclerosis

2. Reversible

a) Cigarette smoking

b) Hypertension

c) Obesity

3. Potentially or partially reversible

a) Hyperlipidemia hypercholesterolemia and/or hypertriglyceridemia

b) Hyperglycemia and diabetes mellitus

c) Low levels of high density lipoprotein (HDL)

4. Other possible factors

a) Physical inactivity

b) Emotional stress and/or personality type

2.1 Hyperlypidemia

Both hypercholesterolemia and hypertriglyceridemia appear to be important risk factors for atherosclerosis

2.2 Hypertension

High blood pressure is an important risk factor for atherosclerosis, mainly ischemic heart disease

and cerebrovascular disease. The risk increases progressively with increasing blood pressure; in the Framingham study, ischemic heart disease incidence in middle - aged men with blood pressure exceeding 160/95 were more than five times that in normotensive men (blood pressure 140/9o or less). Hypertensive men and women are both affected with the diastolic pressure perhaps being more important. Conversely the risk for atherosclerosis appears diminished by therapeutic reduction of blood pressure.[20]

2.3 Cigarette smoking[21]

The incidence of ischemic heart disease increases 3-5 folds in men who smoke one pack of cigarettes per day compared with nonsmokers. In general, the increase in death rate is proportional to the amount smoked and decreases with age. The association of smoking and increase ischemic heart disease remains unexplained. Pipe and cigar smokers have a lesser increase in risk of ischemic heart heart disease, presumable because less smoke is inhaled. Those who stop smoking show a prompt decline in risk about 50 percent within 1 year. Therefore, the risk approaches that of nonsmokers is from 2 to 10 years, as report in different studies.[22-24]

2.4 Hyperglycemia and diabetes mellitus

Diabetes mellitus increases the susceptibility to coronary heart disease. Glucose intolerance doubles the occurrence of coronary disease in men, and triples to quadruples the incidence in women, particularly prior to age 50.[25] Diabetes may predispose to atherosclerosis by a variety of mechanism.[26,27] Control of hyperglycemia alone does not eliminate coronary risk: substantial multifactorial risk reduction appears necessary.

2.5 Other risk foctors

Genetic factors, obesity[28], physical inactivity, stress and personality type[29], trace elements, blood groups, coffee drinking, climate, noise, and air pollution are also possible risk factors[30,31].

Pathophysiology of myocardial ischemia

Myocardial ischemia is the result of a deficiency of arterial blood supply to the heart muscle. This deficiency must be evaluated in terms of the requirement of the heart muscle for oxygen and nutrients.

1. Primary causes of myocardial ischemia

The most frequently recognized cause of myocardial ischemia is obstructive coronary atherosclerosis, which either occludes or narrows the vessel lumen primarily or may secondarily induce a coronary thrombosis. Myocardial ischemia may also be caused by aortic valve diseases; hypertrophic cardiomyopathy; stenosis of the coronary ostia secondary to primary disease of the aorta; coronary embolism; inflammatory disease of the coronary arteries, including periarteritis and mucocutaneous lymph node syndrome (Kawasaki's disease); and congenital states such as anomalous origin of coronary arteries from the pulmonary artery.

1.1 Under normal circumstances, metabolic demands are closely paralleled by myocardial blood flow despite wide variations in oxygen consumption of the heart. Myocardial ischemia occurs when supply is insufficient for demand, and ischemia is normally avoid by a careful matching of blood flow to metabolism. The excessive demand is never a primary cause of ischemia.[32]

1.2 In the presence of coronary artery disease, however, the increased coronary blood flow will not be sufficient enough for increased cardiac demand and myocardial ischemia can be avoided only by

limiting the metabolism of the heart. [32]

2. Myocardial blood flow

A limited myocardial blood supply is common to both mild and severe ischemia, so that factors which determined blood flow will be a constant feature of myocardial ischemia. For this reason it is careful to place primary emphasis on the blood flow aspect of the supply/demand ratio.

2.1 Autoregulation of coronary blood flow.

One of the most striking features of regulation of the coronary circulation is the almost complete independence of coronary blood flow on changes in coronary perfusion pressure. Coronary perfusion pressure normally is identical to aortic pressure, and aortic pressure is maintained within narrow limits by powerful baroreceptor reflexes. Morever, any change in aortic pressure would produce a change in metabolic requirements of the heart and thus would have an indirect role in determining coronary blood flow. Thus when an atheroma progressively narrows a large coronary artery, pressure distal to the obstruction is reduced by the resistance of the obstruction but ischemia is avoided by a progressive decrease in resistance in the distal coronary arteriolar bed. Under this conditions flow will be maintained until the effective coronary perfusion pressure falls below the

flat portion of the autoregulatory curve.[32]

2.2 Effect of myocardial contraction on coronary blood flow. The beating heart inhibits its own supply.[33] Systole appears to inhibit blood flow in the layers nearer the endocardium more than in epicardial layers. Systole does not normally inhibit the blood supply to the right ventricle to the same extent that it does to the left ventricle. Right coronary flow occurs throughout the cardiac cycle, and the rate of systolic flow approximates diastolic flow. In right ventricular hypertension, however systolic blood flow is reduced and may even be absent.

2.3 Coronary perfusion pressure. Coronary perfusion pressure is reduced by proximal coronary obstruction and also can be reduced by decreases in aortic pressure. The reduction of coronary perfusion pressure is determined by the severity of the obstruction, but even an 80 percent decrease in the cross-sectional area of the lumen of a coronary artery may not reduce coronary perfusion pressure below the range in which autoregulation will maintain sufficient myocardial flow in all layers of the heart wall under resting conditions.[34] With severe obstruction, however, vasodilation may still be possible in epicardial layers, and the resultant increase flow will cause an increased pressure drop across the obstruction and

will further decrease coronary perfusion pressure.

3. Myocardial oxygen consumption

Although the primary cause of myocardial ischemia is a defect in arterial blood supply, ischemia does not occur until the tissue's demand for oxygen to support energy generation outstrips its supply of oxygen. Three factors can be identified as having important effect on myocardial oxygen consumption: heart rate, systolic wall tension and myocardial contractility.

3.1 Heart rate is the most easily measured and is likely to have the most direct relation to the rate of myocardial energy utilization.

3.2 Systolic wall tension is proportional to ventricular systolic pressure and ventricular radius. Wall tension is inversely proportional to wall thickness and consequently decreases with cardiac hypertrophy caused by pressure overload. A systemic vasodilator will reduce systolic ventricular pressure (afterload) and also ventricular filling pressure (preload); both effects tend to reduce systolic wall tension and consequently myocardial oxygen consumption.

3.3 Myocardial contractility is a concept with general utility but for which there is no agreed upon or easily obtained measure. Indices which on the rapidity of the contractile process, such as the rate of rise of pressure during isovolumic contraction, dP/dt, have been widely used and are helpful in estimating change in myocardial oxygen consumption.

Diagnosis

The diagnosis of unstable angina is made on the basis of the history and transient ST-segment changes, most commonly depressions, and/or T-wave invertions occurring during episodes of chest pain.

1. Clinical manifestations

This condition includes four groups of patients:[69] (1) patients with angina pectoris of new onset (within 6 weeks) that occur on exertion (1 A) and at rest (1 B); (2) Patients with chronic stable angina with increase in intensity, frequency, or duration of pain that occur on exertion (2 A) and at rest (2 B).

2. Physical examination

The physical examination is usually normal. The patients general appearance may reveal signs and risk

factors associated with coronary atherosclerosis such as xanthelasma, or diabetic skin lesions. There may also be signs of anemia, thyroid disease and nicotine stains on the fingertips from cigarette smoking. Palpitation can reveal thickened or absent peripheral arteries, sign of cardiac enlargement. Examination of the fundi may reveal increased light reflexed and arteriovenous nicking as evidence of hypertension, while auscultation can uncover arterial bruits, a third and/or fourth heart sound, and when acute ischemia or previous infarction impairs papillary muscle function, a late apical systolic murmur due to mitral regurgitation.

3. Laboratory examination

Although the diagnosis of unstable angina can be made with confidence from the typical history, a number of simple laboratory test can be most helpful. The urine should be examined for evidence of diabetes mellitus and renal disease, examination of the blood should include measurements of glucose, creatinine, hematocrit and lipids. The chest x-ray is an important test, since the consequences of ischemic heart disease, i,e., cardiac enlargement, ventricular aneurysm, or signs of heart failure may be evidence.

3.1 Electrocardiogram

A normal ECG does not exclude the diagnosis of ischemic heart disease; however, certain characteristic abnormalities in tracings obtained at rest can confirm it. Serial tracings are particularly useful to look for evolving signs of infarction.

3.2 Exercise Stress test

Patients with unstable angina pectoris should not, as a rule, have an exercise ECG stress test or an exercise radionuclide stress test.

3.3 Echocardiogram

The two-dimensional echocardiogram records cross sectional image of the left ventricle and can identify regional wall motion abnormalities resulting from myocardial infarction or during ischemia.

3.4 Coronary arteriography

This invasive diagnostic method outlines the coronary anatomy and can provide important evidence of coronary atherosclerosis or can exclude this condition. The severity of obstructive lesions and the global and regional function of the left ventricle can be

assessed. Coronary arteriography is indicated in patients with unstable angina who are refractory to medical therapy and who are being considered for revascularization, i.e., percutaneous transluminal coronary angioplasty or coronary artery bypass graft surgery.

Differential diagnosis

Conditions simulating atherosclerotic coronary heart disease

1. "Emotional" causes of chest discomfort.[34]
   - Anxiety states
   - Depression
   - Cardiac psychosis
   - Self-gain

2. Noncoronary cardiovascular causes of chest discomfort
   - Cardiac arrhythmia (premature beats)
   - Acute pericarditis
   - Dressler's syndrome (post - myocardial infarction syndrome)
   - Hypertrophic cardiomyopathy
   - Dilated cardiomyopathy
   - Valve disease
   - Right ventricular hypertension

. Dissecting aneurysm of the aorta

. Pulmonary embolism

. Superficial thrombophebitis of the precordial veins (Mondor's Syndrome)

. Vasoregulatory asthenia

. Paroxysmal hepatic engorgement

3. Gastrointestinal causes of chest discomfort[35]

. Reflux esophagitis

. Hiatal hernia

. Diffuse esophageal spasm [36,37]

. Esophageal rupture

. Cholecystitis and cholelithiasis

. Peptic ulcer

. Acutic pancreatitis[38]

. The "Cafe coronary"[39,40]

. Distension of the splenic flexure of the colon[41]

4. Pulmonary causes of chest discomfort

. Pulmonary hypertensive pain

. Pulmonary embolism

. Mediastinal emphysema (Hamman's disease)

. Spontaneous pneumothorax

5. Neuromuscular skeletal causes of chest discomfort

- Thoracic outlet syndrome [42]
- Tietze's syndrome
- Herpes zoster [43]
- Chest wall pain and tenderness

4. Management[32]

The patient should be admitted promptly to the hospital for observation, further diagnosis, and treatment. It is important immediately to identify and treat concomitant conditions which can intensify ischemia such as uncontrolled hypertension and diabetes, cardiomegaly, heart failure, arrhythmias, and any acute febrile illness. Acute myocardial infarction should be rule out using serial ECG and measurements of cardiac enzyme activity. Continuous ECG monitoring should be carried out and the patients should receive reassurance and sedation.

4.1 Sublingual nitroglycerin should be used to relieve and prevent angina pectoris. Nitroglycerin ointment should be used several times daily, and isosorbide dinitrate should be given orally. An intravenous drip of nitroglycerin is often needed in

patients with frequent and recurrent unstable angina pectoris.[70] Diltiazem or nifedipine can be added to the treatment regimen if discormfort continues since the angina is often due to a decrease in the supply end of the myocardial oxygen supply-demand system. A beta blocker such as propanolol may also be needed if symptoms continue.

4.2 Coronary artery bypass surgery should be recommended for patients with unstable angina who have left main coronary artery obstruction, tripple vessel coronary artery obstruction, or double-vessel coronary artery obstruction.

4.3 Percutaneous transluminal coronary angioplasty may be recommended for patients with unstable angina who have reachable single-vessel coronary disease.

4.4 Medical management after coronary bypass surgery may include a beta blocker and perhaps an antiplatelet drug. Postangioplasty medical treatment should include antiplatelet drugs and a calcium antagnist.

4.5 Patients with unstable angina who do not have coronary bypass surgery or coronary angioplasty should be treated as if they have a small myocardial infarction. Drug therapy may include long-acting nitrates,

a beta blocker, and diltiazem or nifedipine with a beta blocker.

4.6 Patients with unstable angina pectoris should be encouraged to stop smoking, attain a normal body weight, and achieve a normal blood pressure. Exercise is prohibited for patients with unstable angina pectoris until definitive treatment such as angioplasty or bypass surgery has been achieved.