

# The Continuum of Myocardial Ischemia and Infarction

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**C**oronary artery disease remains a major cause of death and disability in the US despite major advances in diagnosis and treatment.<sup>1</sup> Although the death rate from stroke and myocardial infarction (MI) has decreased consistently and significantly during the last three decades, death from complications of ischemic heart disease, such as ventricular arrhythmias and heart failure, has increased. Coronary artery disease prevalence increases with age and is a major public health problem in the elderly. As many as 25% of patients aged 75–84 years have angina pectoris; about 80% of all deaths from MI occur after age 65; and 60% of all MI deaths occur after age 75.<sup>2,3</sup> The pathologic process of atherosclerosis in coronary arteries leads to development of ischemic heart disease and is often associated with the signs and symptoms of peripheral vascular disease.

## Myocardial Ischemia

Therapeutic decisions regarding patients with ischemic heart disease are based on an understanding of the pathophysiology of ischemic syndromes, and precision in diagnosis must be coupled with precision in choosing and monitoring the drug therapy. Angina occurs when oxygen requirements of the myocardium exceed the myocardial oxygen supply for a significant period. This condition can occur from either a significant decrease in oxygen supply or an increase in demand. The most common pathology in elderly patients is that atherosclerosis limits the coronary artery blood flow to a critical point, where modest increases in the myocar-

dial oxygen demand from exertion are not accompanied by a corresponding increase in the oxygen supply. The results are often anginal chest pain and typical ischemic changes on the electrocardiogram. Traditionally, the determinants of myocardial oxygen demand have been defined in terms of heart rate, myocardial contractility, and left-ventricular (LV) wall stress, but the latter two are rarely measured in routine clinical practice. From a clinical perspective, the readily measured determinants of myocardial oxygen demand are heart rate and systolic blood pressure. Therapeutic maneuvers to reduce either of these determinants will decrease myocardial oxygen demand and reduce the likelihood of ischemia.

Treatment of anginal syndromes with nitrates,  $\beta$ -blockers, and calcium-channel antagonists is primarily directed at decreasing the myocardial oxygen demand and preventing angina. Each of these drug classes has effects that also may increase myocardial oxygen supply. Nitrates prevent the collapse of stenosed epicardial coronary arteries during exercise or mental stress;  $\beta$ -blockers increase the diastolic filling time by decreasing the heart rate; and calcium-channel blockers decrease resting coronary tone. Concomitant conditions that decrease myocardial oxygen supply must also be treated; for example, pulmonary function and hemoglobin concentration should be optimized.

Ischemic syndromes include chronic stable angina pectoris, unstable angina, and acute MI. A patient will likely cycle through several ischemic syndromes during the course of care. Chronic stable angina is associated with a chronic stable atheroma; unstable angina involves a ruptured atheroma that is associated with spasm, as well as platelet and thrombin deposition. In chronic stable angina, symptoms occur at about the same exercise duration that has not changed for at least two months. MI represents a total thrombotic occlusion in addition to a ruptured atheroma. Specific therapy is directed at each condition.

Various reversible ischemic syndromes and their classic distinguishing features, along with characteristic signs in the elderly, are presented in Table 1.<sup>4</sup> Acute reversible (subtotal) coronary occlusion produces an unstable anginal pattern that is associated with a ruptured atherosclerotic plaque.<sup>5-7</sup> Determining when a patient's condition represents unstable angina requires a clear definition of the patient's usual exercise capacity. Unstable angina diagnosis and management guidelines are available from the Agency for Health Care Policy and Research (AHCPR) and provide a good definition of unstable angina, with treatment algorithms based on the risk of acute MI.<sup>8</sup> Unstable angina can rapidly progress to a total thrombotic occlusion of a coronary artery, resulting in acute MI.

## Chronic Stable Angina

Not all chest pain represents myocardial ischemia. Typical angina has classic features, including chest tightness or chest pressure associated with exertion. The pain or pressure is usually deep and visceral in character, lasts a few minutes, and may radiate to the lower jaw, shoulder, or inside of the left arm. Obtaining a good medical history enables the patient's symptoms to be classified into one of three categories: typical angina, atypical angina, or nonanginal chest pain. Patients with a history typical of angina should be evaluated and treated to eliminate or markedly limit the occurrence of myocardial ischemia. Patients with other causes of chest pain (nonanginal pain) need treatment of their primary condition with no further cardiovascular workup. Patients with atypical angina have symptoms of typical angina and symptoms that are not usually associated with angina, including chest wall pain lasting for hours. Since patients can have two concurrent pain syndromes, patients with atypical angina should be assumed to have angina until the diagnosis becomes clear. A definitive diagnosis can be made after further cardiovascular testing.

Chest pain or pressure is a frequent complaint in the elderly with a history of ischemic heart disease, and these patients are not a major diagnostic

**Table 1.** Stable reversible ischemic syndromes: classic and geriatric presentations<sup>4</sup>

Syndrome	Common Features
Stable angina	effort-induced at stable and reproducible workload; pain duration <20 min; symptoms unchanged $\geq 2$ mo; prompt relief with rest or nitroglycerin
Variant angina (Prinzmetal's angina)	anginal pain unrelated to exertion or rest; pain duration <20 min; ST-segment elevation; documented coronary spasm
Syndrome X	anginal symptoms; documented ischemia; normal coronary arteries on angiogram
Unstable angina	new-onset chest pain at rest lasting >20 min; a significant decrease in exercise duration to where chest pain occurs while walking <2 blocks or while climbing a flight of stairs
Silent ischemia	spontaneous asymptomatic ischemia at rest or exercise; may be in addition to known symptomatic angina
Geriatric MI presentation	women present often; at-rest symptoms; mental stress-induced symptoms; multiple comorbid conditions: confusion, dyspnea, excessive sweating, excessive fatigue, palpitations, syncope

MI = myocardial infarction.

dilemma. However, variations in the presentation of coronary disease in the elderly can make the diagnosis difficult.<sup>9</sup> Some elderly patients with preserved (LV) systolic function present with silent ischemia late in the course of ischemic heart disease. One report found a 15% incidence of silent ischemia, and one-third of all patients with ischemic heart disease developed MI, yet more than 90% of all patients late in their course of ischemic heart disease had an ejection fraction greater than 35%.<sup>10</sup> In several studies, the primary presentation for elderly patients was dyspnea. These patients (70–80 y) had a history of hypertension, but cardiac catheterization revealed multivessel disease with only mild to moderate LV systolic dysfunction.<sup>11–13</sup> Others report a 30–40% incidence of silent ischemia in the elderly.<sup>14,15</sup> Any acute illness may present as confusion in patients with dementia or cognitive impairment. In the elderly, however, symptoms of neurologic deficits, stroke, or vertigo are associated with new or worsening coronary disease. Patients with the combination of ischemia and arrhythmias may benefit from revascularization and deserve noninvasive testing.

Patients with suspected angina should keep sublingual nitroglycerin available and be instructed in its proper storage and use. Sublingual nitroglycerin is effective, safe, and inexpensive and can be taken before activities known to precipitate symptoms.<sup>16</sup> Nitroglycerin spray also is effective and may be preferred by some patients. The spray has a more rapid onset of action for patients with a dry mouth, in whom the sublingual tablet takes a minute to dissolve. The spray is more expensive but, if used infrequently, may be cost-effective, since the spray is stable for three years. Unused sublingual tablets are stable until the manufacture expiration date when stored under reasonable conditions, such as in a medication cart in a long-term care facility. Sublingual nitroglycerin relieves exercise-induced anginal pain in three to 15 minutes in approximately 90% of patients. In an attempt to avoid a hospital visit, patients often remain at home, taking nitroglycerin repeatedly, with only partial or temporary relief of chest pain. All healthcare professionals should instruct angina patients to seek emergency medical evaluation for chest pain that is not completely relieved or recurs after taking three sublingual nitroglycerin tablets. This is especially important in the elderly population, where thrombolytic therapy provides the greatest relative risk reduction in mortality and is highly cost-effective.<sup>17</sup> Nitroglycerin should relieve effort angina, but nitrates may not completely relieve the chest pain of MI. Therefore, patients should be instructed to cease the precipitating activity at the onset of angina, sit down, and use sublingual nitroglycerin. The dose may be repeated every five minutes until pain is relieved or three doses are taken. If chest pain persists or recurs, then the pa-