perfusion defects and transient wall motion abnormalities on echocardiography. More sophisticated invasive testing may demonstrated the presence of stress-induced metabolic abnormalities characteristic of ischemia and endothelial dysfunction.

Exercise-related ischemic symptoms may respond to β-blocker therapy. Microvascular angina also tends to respond well to nitrates, both short-acting sublingual nitroglycerin and long-acting oral nitrates. Calcium channel antagonists are sometimes used together with nitrates to control angina related to microvascular ischemia.

Silent Myocardial Ischemia

Not all episodes of myocardial ischemia are associated with angina. Some patients may only experience episodes of silent myocardial ischemia as evidenced by transient ST depression with ECG monitoring. Such patients can also have silent MI. It is also possible, and probably not uncommon, for patients to have both silent myocardial ischemia episodes and typical angina; this is termed *mixed angina*. Episodes of silent myocardial ischemia can be observed in all settings of CAD: chronic stable angina, unstable angina, and coronary vasospasm. Silent ischemia is more common in diabetic patients. Medical therapy directed at controlling symptomatic angina also reduces the number of episodes of silent ischemia.

Prognosis

Contemporary therapies for stable ischemic heart disease have significantly reduced the risks of cardiac events and mortality. The annual rate of major ischemic events such as MI is in the range of 1% to 2%, and the yearly mortality rate is 1% to 3%. CAD is frequently associated with systemic vascular disease, making these patients prone to a host of other events. Patients with stable ischemic heart disease have a yearly combined outcome risk for cardiovascular death, MI, or stroke in the range of 4.5%.

Despite advances in medical and revascularization therapies, up to 30% of patients face some limiting symptoms of recurrent angina. Revascularization does not abolish the need for ongoing antianginal medical therapy in 80% of patients.

Patients with stable ischemic heart disease should first be treated with medical therapy appropriate to reduce the risk of ischemic events (aspirin, statins) and to control symptoms of angina (nitrates, β-blockers, calcium channel antagonists). Revascularization therapy with either PCI or CABG is an option for patients who continue to have lifestyle-limiting symptoms despite the use of medical therapy and risk factor modification. The goal of all therapies for patients with stable ischemic heart disease should be individualized, taking advantage of information from controlled trials and directed at improving overall lifestyle and reducing the risk of death and disability due to progressive CAD or systemic vascular disease.

Acute Coronary Syndrome: Unstable Angina and NSTEMI

Definition

Asymptomatic CAD or chronic stable angina may undergo transition to a more aggressive stage of disease called acute coronary syndrome (ACS). ACS comprises a spectrum of clinical presentations, ranging from unstable angina to NSTEMI or STEMI. Unstable angina represents the new onset of angina at rest or on exertion, or an increase in frequency of previously stable anginal symptoms, particularly at rest. ACS manifesting as MI, either NSTEMI or STEMI, is differentiated from unstable angina on the basis of prolonged symptoms, characteristic ECG changes, and the presence of biomarkers in blood. Unstable angina may be a harbinger of either NSTEMI or STEMI, and the diagnosis of unstable angina identifies a patient who requires careful assessment and treatment.

Epidemiology

The occurrence of ACS represents a significant clinical event in up to 1.4 million Americans annually. One third of those categorized as having ACS are diagnosed with NSTEMI. More than half of patients with NSTEMI are 65 years of age or older, and approximately one-half are women. NSTEMI is more common in patients with diabetes, peripheral vascular disease, or chronic inflammatory disease (e.g., rheumatoid arthritis).

Primary ACS is the most common form of the disease and reflects underlying plaque rupture leading to intracoronary thrombus formation and limitation of blood flow. Secondary ACS reflects imbalances in myocardial oxygen supply and demand leading to myocardial ischemia. Examples of decreased oxygen supply include profound anemia, systemic hypotension, and hypoxemia. Increased demand occurs in the face of severe systemic hypertension, fever, tachycardia, and thyrotoxicosis. Secondary ACS not uncommonly unmasks previously asymptomatic obstructive CAD, but it may also occur in the absence of CAD. Treatment of secondary ACS is directed at correcting the underlying medical condition.

Pathology

Most patients who experience NSTEMI do so as a result of plaque rupture with subsequent thrombosis causing subtotal occlusion of the coronary artery. The limitation of coronary blood flow in this situation leads to subendocardial ischemia in the distribution of the affected coronary artery. The same pathology underlies STEMI, although in that case complete vessel occlusion occurs, leading to more extensive MI. It is possible for patients with obstructive CAD to develop collateral support of the affected artery, and in that case plaque rupture with complete vessel occlusion may lead to NSTEMI as opposed to STEMI.

A smaller percentage of patients have ACS due to coronary vasospasm, which, if severe and prolonged, can lead to myocardial necrosis. Vasospasm may occur in regions of endothelial dysfunction induced by atherosclerotic plaque, or it may be triggered by exogenous vasoconstrictors such as cocaine ingestion, the use of serotonin agonists (for migraine therapy), or chemotherapeutic agents (e.g., 5-fluorouracil). Less common causes of ACS include coronary vasculitis and spontaneous coronary dissection (peripartum coronary dissection).

Atherosclerotic plaques rich in LDL are prone to develop inflammation, which in turn degrades the collagen-rich fibrous cap, leading to rupture and thrombosis. Oxidized LDL within the plaque leads to accumulation of macrophages and T lymphocytes, causing inflammation within the plaque. Cytokines