for underlying CAD as a cause of symptoms. The echocardiogram may also show evidence of other abnormalities as causes of chest discomfort, such as pericarditis, pulmonary embolism, or aortic dissection.

Patients with a high risk for future coronary events should be directed toward coronary angiography. In the absence of contraindications, coronary angiography is indicated for patients with clear evidence of NSTEMI based on clinical presentation of symptoms, ECG changes, and positive biomarkers. Patients undergoing evaluation for unstable angina who have significant stress test abnormalities are also candidates for coronary angiography. Some patients who have ambiguous stress test findings or ongoing symptoms in the absence of other findings of NSTEMI require coronary angiography to resolve the issue as to whether underlying CAD is present.

Up to 15% of patients undergoing coronary angiography for NSTEMI have no significant obstructive CAD. In a number of patients, there will be a clear "culprit" lesion showing the earmarks of plaque rupture with ulceration, associated thrombus, or reduced coronary flow. Lesions that may have played a role in symptoms, ECG findings, or biomarker release that are not clearly stenotic may be assessed for physiologic significance with the use of a fractional flow reserve (FFR) study using a pressure wire device.

Patients who have new-onset chest pain require careful monitoring in an appropriate care setting that allows for rhythm monitoring as well as repeat evaluations of ECG findings and biomarker measurements. Risk assessment is aided by the use of risk scores calculated with either the Thrombolysis in Myocardial Infarction (TIMI) or the Global Registry of Acute Coronary Events (GRACE) algorithms (see Chapter 72, "Acute Coronary Syndrome: Unstable Angina and Non-ST Elevation Myocardial Infarction," in *Goldman-Cecil Medicine,* 25th Edition). The overall assessment in cases of new symptoms of chest discomfort aims to triage patients based on risk for coronary events. Low-risk patients can be spared aggressive anticoagulation protocols and coronary angiography, whereas high-risk patients are likely to benefit from these approaches. The use of appropriate therapies in high-risk patients (medical therapy or revascularization or both) leads to a 20% to 40% decrease in recurrent ischemic events and a 10% reduction in mortality.

Differential Diagnosis

The initial assessment of patients with possible ACS should include consideration of other potentially life-threatening conditions such as pulmonary embolism and aortic dissection. These considerations are particularly important if the patient's presentation does not entirely fit that of ACS. Pulmonary embolism can be associated with ECG changes and troponin elevation, and such findings lead to early use of coronary angiography. If there is no CAD-related explanation of the patient's presentation, prompt investigation for pulmonary embolism is warranted. If the patient has findings suggestive of aortic dissection, that diagnosis should be aggressively pursued with appropriate imaging techniques, given the high risk of mortality associated with that disease. Valvular heart diseases such as aortic stenosis or regurgitation and hypertrophic cardiomyopathy can manifest with symptoms and ECG findings suggestive of ACS. Physical examination should aid in consideration of these conditions. Pericarditis and myopericarditis can also present diagnostic dilemmas related to chest pain, ECG abnormalities (ST and T-wave changes mimicking ischemia), and positive biomarkers. Stress cardiomyopathy (Takotsubo's syndrome) also manifests with chest pain, T-wave inversion, and positive biomarkers. Patients with this diagnosis frequently undergo urgent catheterization to assess for CAD. The absence of a culprit lesion and findings of characteristic wall motion abnormalities establish the diagnosis.

Treatment

Patients with chest pain suggestive of ACS need urgent evaluation for evidence of ischemia (serial ECGs) and myocardial necrosis (serial biomarkers). Serial biomarker measurements, in the current era usually troponin, establish the diagnosis of MI. Continuous ECG monitoring is important given the risk of ischemia-mediated arrhythmias, and serial ECGs establish a pattern of ST changes consistent with ischemia. Patients are also prescribed bedrest and supplemental oxygen. Those with a high index of suspicion for ACS require hospital admission for observation and appropriate diagnostic testing. Chest pain lends itself well to diagnosis and treatment algorithms that guide the clinician through decision trees based on expert opinion and evidence-based medicine (see Chapter 72, "Acute Coronary Syndrome: Unstable Angina and Non-ST Elevation Myocardial Infarction," in *Goldman-Cecil Medicine,* 25th Edition). STEMI is typically diagnosed at the time of initial presentation. Those without evidence of ST elevation can be risk stratified, as discussed earlier, using the guidance of recurrent symptoms, ECG changes, or abnormal biomarker levels. Treatment of patients who are categorized as having unstable angina or NSTEMI is directed by their allocation to either low- or high-risk status.

Once recognized as having ACS, patients require antiplatelet therapy with aspirin (75 to 162 mg per day) and clopidogrel, because plaque rupture and thrombosis is a frequent underlying pathology. Prasugrel, another thienopyridine, is an option in place of clopidogrel for those going to coronary angiography. Antiplatelet therapy significantly reduces mortality risk in patients with NSTEMI. The aspirin/clopidogrel combination is indicated as ongoing therapy in the year following diagnosis of NSTEMI. Symptoms of chest discomfort can be treated with nitrates (sublingual, topical, or intravenous drip) and β-blockers. The latter therapy slows heart rate and reduces blood pressure, effects that translate into reduced myocardial oxygen demand in the face of limited supply. It is important not to give nitrates to patients who have taken phosphodiesterase-5 inhibitors (sildenafil, tadalafil, or vardenafil) within the previous 24 to 48 hours. Attention to this detail minimizes the risk for nitrate-induced hypotension. Calcium channel antagonists may be used in lieu of β-blockers, particularly if there is a need for blood pressure control, but they should be avoided in patients with reduced EF or overt heart failure. The dihydropyridine calcium channel blocker nifedipine can be effective in controlling blood pressure and promoting coronary vasodilation, but it should be given in conjunction with a β-blocker because of the potential for the drug to induce reflex tachycardia and thereby increase myocardial oxygen demand.