The following represent additions to UpToDate since the last version that were considered by the authors and editors to be of particular interest. The new material described below represents a small subset of the updating that has been performed since approximately 40 percent of the topic reviews are updated during each four month cycle.

ARRHYTHMIAS

A large randomized placebo-controlled trial (GISSI-AF) involving patients with prior atrial fibrillation (AF) found that the angiotensin receptor blocker valsartan did not reduce the incidence of recurrent AF [1]. The low prevalence of heart failure or left ventricular dysfunction may have contributed to the lack of effect since secondary analyses of randomized trials performed for other reasons found that the benefit of angiotensin inhibition was greatest in patients with these conditions. (See "ACE inhibitors, angiotensin II receptor blockers, and atrial fibrillation", section on GISSI-AF trial).

Catecholaminergic polymorphic ventricular tachycardia (CPVT), a recognized cause of stress-induced syncope and sudden cardiac arrest, is due to mutation in either the cardiac ryanodine receptor (RyR2) or calsequestrin 2 (CASQ2) gene. Patients typically present at a young age, and are often symptomatic despite treatment with a beta blocker, calcium channel blocker, and an implantable cardioverter-defibrillator. The recent discovery that the sodium channel blocker flecainide also inhibits current through RyR2 channels makes this a promising new agent for the treatment of CPVT. In a mouse model and in two patients with this disorder, flecainide markedly reduced the incidence of catecholamine- or exercise-induced arrhythmia [2]. (See "Catecholaminergic polymorphic ventricular tachycardia and other polymorphic ventricular tachycardias with a normal QT interval", section on Flecainide).

The ACTIVE A trial examined the efficacy and safety of dual antiplatelet therapy in patients with atrial fibrillation (AF) who were not candidates for therapy with a vitamin K
antagonist \[3\]. Compared with aspirin alone, treatment with clopidogrel plus aspirin resulted in a significantly lower annual rate of stroke, systemic embolization, MI, or vascular death, but this was offset significantly by an increased incidence of major bleeding that was similar to that of warfarin therapy. Thus, dual antiplatelet therapy may be a reasonable alternative to therapy with aspirin alone in high risk patients with AF who cannot be treated with oral anticoagulation because of lack of access to adequate INR monitoring, widely fluctuating and difficult to control INR, or because of patient preference following careful consideration of the advantages of oral anticoagulation. (See "Antithrombotic therapy to prevent embolization in nonvalvular atrial fibrillation", section on Aspirin plus clopidogrel).

Dronedarone is an antiarrhythmic drug that is similar to amiodarone but has fewer side effects. The efficacy and safety of dronedarone in patients with persistent or paroxysmal AF was evaluated in the ATHENA trial \[4\]. Compared with placebo, dronedarone significantly reduced death or cardiovascular hospitalization and had a favorable safety profile. Notably, patients with decompensated or NYHA class IV heart failure were excluded in ATHENA; the earlier ANDROMEDA trial, which examined the safety and efficacy of dronedarone in patients with NYHA class II to IV heart failure and depressed left ventricular function, was terminated early because of increased mortality in patients receiving dronedarone. Dronedarone is not currently available in the United States, however, in March, 2009 the Cardiovascular and Renal Drugs Advisory Committee of the USFDA voted in favor of approval of dronedarone for the treatment of atrial fibrillation (AF) in patients without severe heart failure. (See "Antiarrhythmic drugs to maintain sinus rhythm in patients with atrial fibrillation: Clinical trials", section on Dronedarone).

**CORONARY HEART DISEASE**

Coronary artery bypass graft surgery and percutaneous coronary intervention are therapeutic options for patients who require revascularization. The SYNTAX trial randomly assigned 1800 patients with three-vessel or left main coronary artery disease to either CABG or PCI with drug-eluting stents \[5\]. The composite primary endpoint (death from any cause, stroke, MI or repeat revascularization) was significantly higher in the PCI group (17.8 versus 12.4 percent), driven primarily by a need for more frequent revascularization. However, the results of the SYNTAX trial need to be interpreted in the context of its limitations, including its short duration of follow-up, male predominance (78 percent), and suboptimal use of medical therapy in the CABG cohort. (See "Bypass surgery versus percutaneous intervention in the management of stable angina pectoris: Clinical trials", section on stenting versus CABG for multivessel disease and see "Management of left main coronary artery disease", section on Stents versus CABG).

Women of child bearing age with familial hypercholesterolemia present special challenges, including the potential for pregnancy while on statin therapy, the risks of pregnancy in the presence of advanced coronary artery disease or aortic stenosis, and the use of lipid lowering therapy during breast feeding. The 2008 United Kingdom National Institute for Health and Clinical Excellence (NICE) Clinical Guidelines and Evidence Review for Familial
Hypercholesterolemia attempted to address these difficult issues with recommendations such as [6]: FH women who are on statin therapy and anticipate becoming pregnant should stop statins three months prior to attempting to conceive; contraceptive options should be explored with fertile FH patients; for those women who choose to use an oral contraceptive, the potential for an increased risk of a cardiovascular event needs to be discussed; an assessment of coronary artery disease and aortic stenosis risk should be made prior to conception, particularly in homozygotes; and cholesterol measurements should not be performed during pregnancy as no therapy is indicated.

(See "Primary disorders of LDL-cholesterol metabolism", section on Management).

Autosomal dominant hypercholesterolemia (ADH) is a disorder characterized by elevated plasma LDL-cholesterol and premature atherosclerosis. At least three unrelated genetic mutations with an autosomal dominant mode of inheritance, including familial hypercholesterolemia, lead to ADH. Mutations in the gene that codes for proprotein convertase subtilisin kexin 9 (PCSK9) are the most recently studied of the three types [7]. (See "Primary disorders of LDL-cholesterol metabolism", section on Mutations in the PCSK9 gene).

Long term dual antiplatelet therapy with aspirin and a thienopyridine is standard care for patients with ST-elevation myocardial infarction who undergo primary percutaneous intervention with stenting. The efficacy of prasugrel, a newer thienopyridine, was compared to clopidogrel in the randomized TRITON-TIMI 38 trial [8]. At a 15 month follow-up, the primary efficacy end point of cardiovascular death, nonfatal MI, or nonfatal stroke occurred significantly less often in patients treated with prasugrel, driven primarily by a significant reduction in nonfatal MI. The incidence of major bleeding was not significantly different between the two agents. (See "Antiplatelet agents in acute ST elevation myocardial infarction", section on Primary PCI).

HEART FAILURE AND CARDIOMYOPATHY

Data are inconclusive on the utility of anticoagulation to reduce thromboembolic events in patients with heart failure (HF) who are in sinus rhythm. The WATCH trial compared aspirin, clopidogrel and warfarin in adults in sinus rhythm with symptomatic heart failure and left ventricular ejection fraction ≤35 percent [9]. There were no significant differences among the three treatment arms for the primary end point of time to first occurrence of death, nonfatal myocardial infarction, or nonfatal stroke. Warfarin was associated with significantly fewer nonfatal strokes than clopidogrel or aspirin (0.2 versus 2.1 and 1.7 percent). However, this effect was no longer significant when central nervous system bleeds and fatal strokes were included. (See "Indications for anticoagulation in heart failure" section on Efficacy of anticoagulation).

The impact of exercise training in patients with heart failure was evaluated in the HF ACTION trial [10]. Patients with NYHA class II to IV HF (99 percent with class II or III symptoms) were randomly assigned to either a supervised exercise training program or usual care including recommendation of regular exercise [10]. There was a significant
decrease in all-cause mortality and hospitalization for the exercise training program group after adjustment for major prognostic baseline factors, although there was no difference in the unadjusted analysis. (See "Cardiac rehabilitation in patients with heart failure").

Limited data are available on the incidence of and risk factors for heart failure (HF) in young adults. A report from the CARDIA study of 5115 subjects aged 18 to 30 years who were prospectively followed for 20 years found that incident heart failure before 50 years of age is substantially more common among blacks than whites (1.1, 0.9, 0.08, and 0 percent in black women, black men, white women, and white men, respectively) [11]. Among blacks, independent predictors before age 30 years of subsequent early HF included higher diastolic blood pressure, high body-mass index, lower HDL cholesterol, kidney disease and left ventricular systolic dysfunction on echocardiogram at age ≤35 years. (See "Epidemiology and causes of heart failure" section on Incidence in younger adults).

Surgical anterior ventricular endocardial restoration (SAVER) excludes noncontracting segments of the dilated remodeled left ventricle after anterior myocardial infarction. The efficacy of this technique was evaluated in 1000 patients with ischemic cardiomyopathy who were randomly assigned to either CABG alone or CABG with SAVER [12]. Entry criteria included coronary artery disease amenable to CABG, a left ventricular ejection fraction ≤35 percent, and an anterior akinetic or dyskinetic region of myocardium amenable to ventricular reconstruction. Most patients had symptomatic heart failure. Despite a significantly greater reduction in end-systolic volume index with CABG plus ventricular reconstruction compared to CABG alone, there was no significant difference at two-year follow-up in the rate of the primary outcome (death from any cause and hospitalization for cardiac causes). (See "Surgical management of heart failure" section on SAVER procedure).

Tissue changes in arrhythmogenic right ventricular cardiomyopathy (ARVC) are heterogeneous and patchy so biopsy results have limited accuracy. A preliminary report suggests that identification of reduction in plakoglobin signal (in the presence of preservation of N-cadherin signal) on immunohistochemical analysis of myocardial biopsy specimens is a sensitive and specific test for ARVC [13]. Further data are needed to determine the clinical utility of this technique. (See "Clinical manifestations and diagnosis of arrhythmogenic right ventricular cardiomyopathy").

INTERVENTIONAL CARDIOLOGY

Glycoprotein IIb/IIIa inhibitor therapy is recommended for many patients with non-ST segment elevation acute coronary syndrome (ACS), but the optimal time for initiating such therapy is uncertain. In EARLY ACS trial high risk non-ST elevation ACS patients who were scheduled to undergo an invasive strategy were randomly assigned to either early (after randomization) eptifibatide or placebo with provisional use of eptifibatide after angiography (delayed) [14]. The study found no significant reduction in the rate of the primary composite outcome of death from any cause, myocardial infarction, recurrent ischemia requiring urgent revascularization, or thrombotic bailout at 96 hours with early compared to delayed therapy. (See "Antiplatelet agents in unstable angina and acute non-ST elevation myocardial infarction", section on Glycoprotein IIb/IIIa inhibitors).
Bleeding complications resulting from the combined use of potent antiplatelet and anticoagulant agents are a major risk of percutaneous coronary intervention (PCI). The issue of whether heparin is necessary in patients at very low risk of ischemic complications after PCI was addressed in the CIAO trial of 700 patients already taking aspirin and clopidogrel and undergoing elective PCI for an uncomplicated lesion [15]. The primary end point of death, MI, or urgent target vessel revascularization at thirty days occurred more frequently in the heparin group (3.7 versus 2.0 percent), but this difference was not statistically significant. Despite the results of this small study, we believe that anticoagulant therapy should be used in all low risk patients. (See "Antithrombotic therapy for intracoronary stent implantation: Clinical trials", section on Heparin).

The issue of whether the rate of death and MI when stenting is performed for off-label (ie, higher risk) indications differs between drug-eluting and bare metal stents has been addressed in large observational studies of real world (higher risk) patients. In three recent reports, two found lower rates of death or MI with drug-eluting stents [16,17] and one found equivalent rates [18]. (See "Use of drug-eluting intracoronary stents", section on Long term safety concerns).

Three cases of acute interstitial pneumonitis, a type of hypersensitivity reaction which lead to death within 20 days after placement a paclitaxel eluting stent have been reported [19,20]. While (paclitaxel) causality cannot be proven with certainty in these cases, it is plausible given reports of cases in patients who have received the drug to treat cancer. (See "Use of drug-eluting intracoronary stents", section on Long term safety concerns).

The management of distal left main coronary artery disease using percutaneous coronary intervention is technically challenging due to the frequent presence of significant disease in either the proximal left anterior descending or circumflex branches. The Left Main Taxus registry evaluated outcomes after paclitaxel eluting stent placement in 291 patients, 78 percent of whom had distal disease [21]. Provisional side branch T stenting was used in 92 percent of the patients with distal disease and the side branch was stented in 43 percent. At two year follow-up the was an 8.9 percent cumulative need for target lesion revascularization and a cardiac mortality rate of 5.4 percent. (See "Management of left main coronary artery disease", section on Distal lesions).

The list of risk factors for early stent thrombosis with either drug-eluting or bare metal stents continues to grow. The best available data on the risk factors for early (≤30 days) stent thrombosis in real world populations comes from an analysis of the 21,009 patients in the Dutch Stent Thrombosis Registry [21]. After matching cases to controls the most important risk factors for early stent thrombosis were undersizing, dissection, TIMI flow grade <3 post-PCI, CAD ≥50 percent proximal of the culprit lesion, malignancy, no aspirin at the time of the procedure, and left ventricular ejection fraction <30 percent. (See "Coronary artery stent thrombosis: General issues", section on Other risk factors).

Intravascular ultrasound (IVUS) allows the operator to visualize how well a stent is deployed. However, it is uncertain if IVUS is necessary for optimal stent deployment when
high pressure techniques are used. The AVID trial, which randomly assigned 800 patients to either angiography directed or IVUS directed therapy after elective bare metal stent placement, addressed this issue [22]. At 12 months the overall rate of target lesion revascularization was not significantly lower in the IVUS group. (See "General principles of the use of intracoronary stents", section on IVUS).

**VALVULAR DISEASE**

Timing of mitral valve repair in asymptomatic patients with severe mitral regurgitation (MR) is controversial. A prospective observational study followed 447 asymptomatic patients with severe degenerative MR and preserved left ventricular systolic function. Patients who underwent early surgery had fewer subsequent admissions for HF, and lower mortality compared to those managed by watchful waiting. These findings favoring early surgery may be applicable to settings where there is a high success rate of mitral valve repair with low operative mortality. (See "Indications for corrective surgery in severe chronic mitral regurgitation" section on Outcomes with watchful waiting).

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