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Cardiac Current Awareness Newsletter

February 2015

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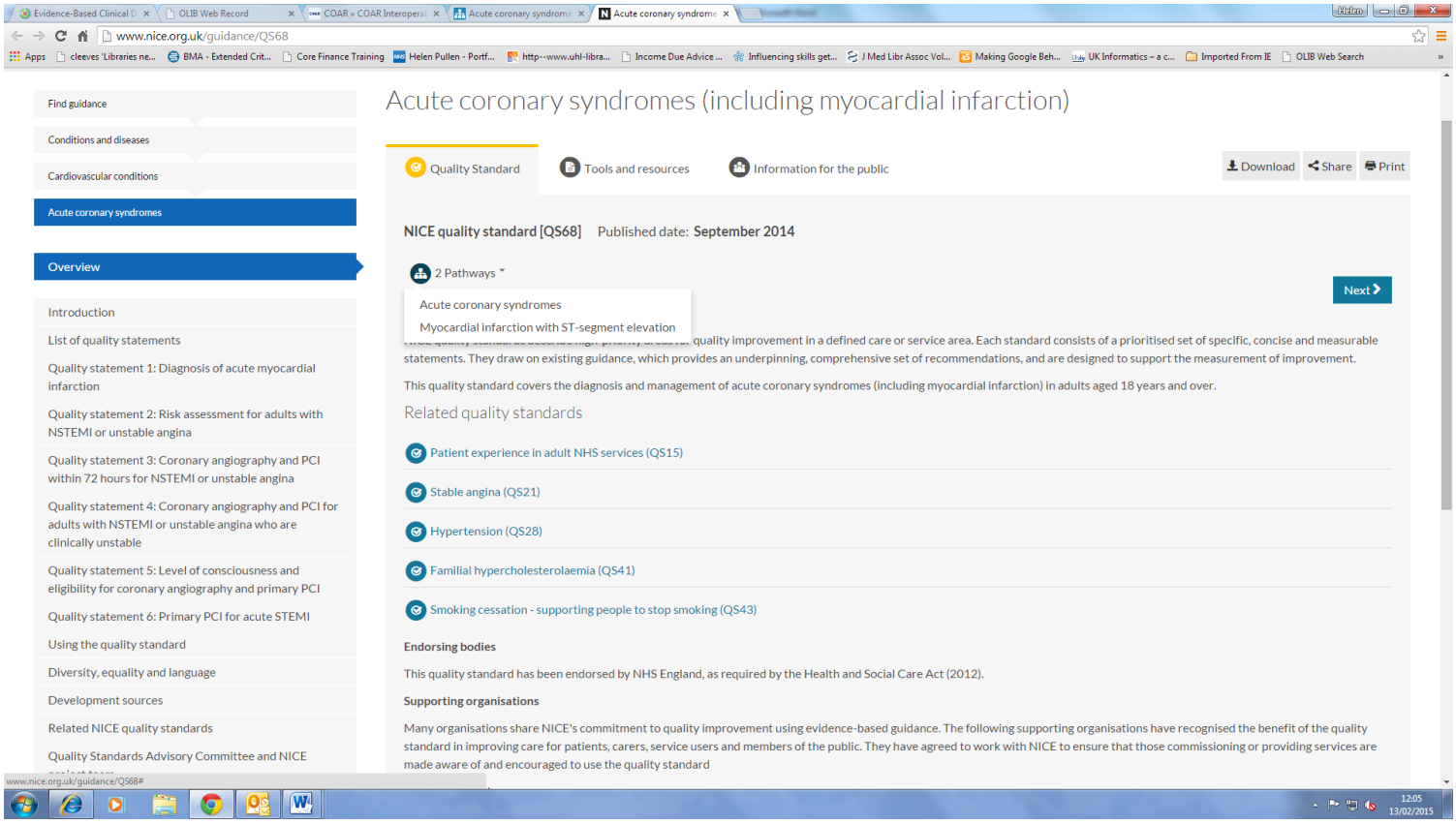
New NICE Guidance

Acute coronary syndromes (including myocardial infarction)

http://www.nice.org.uk/guidance/QS68

NICE quality standard [QS68] Published date: September 2014
2 Pathways



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Philip RA Baker, Daniel P Francis, Jesus Soares, Alison L Weightman, Charles Foster
Online Publication Date: January 2015

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New activity in UpToDate

What's new in cardiovascular medicine
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Literature review current through: Jan 2015. | **This topic last updated:** Feb 10, 2015.

The following represent additions to UpToDate from the past six months that were considered by the editors and authors to be of particular interest. The most recent What's New entries are at the top of each subsection.

ARRHYTHMIAS

Approval of the direct factor Xa inhibitor edoxaban (January 2015)

The US Food and Drug Administration has approved the oral direct factor Xa inhibitor edoxaban (Savaysa; Lixiana in Japan) for the prevention of stroke in nonvalvular atrial fibrillation and the treatment of venous thromboembolism, based upon earlier randomized trials demonstrating non-inferiority to warfarin [1-3]. Dosing is once daily at a fixed dose without monitoring. There are Boxed Warnings regarding avoidance of edoxaban in patients with atrial fibrillation who have a creatinine clearance >95 mL/minute, spinal/epidural hematoma in patients undergoing neuraxial procedures, and ischemic events following premature discontinuation. (See "Atrial fibrillation: Anticoagulant therapy to prevent embolization" and "Lower extremity deep venous thrombosis: Long-term anticoagulation (10 days to three months)" and "Anticoagulation in acute pulmonary embolism" and "Anticoagulation with direct thrombin inhibitors and direct factor Xa inhibitors", section on 'Edoxaban'.)

Lower risk of fatal bleeding with target specific oral anticoagulants versus warfarin (November 2014)

All anticoagulants carry a risk of bleeding, and the lack of an antidote for direct factor Xa inhibitors (rivaroxaban, apixaban, edoxaban) and the direct thrombin inhibitor dabigatran increases concerns about this risk. Reassuringly, a meta-analysis of 12 randomized trials in patients with atrial fibrillation or venous thromboembolism that compared bleeding risk with these agents versus vitamin K antagonists found lower rates of fatal bleeding, major bleeding, and intracranial bleeding with the direct factor Xa and direct thrombin inhibitors [4]. Individual patient factors continue to play a role in anticoagulant choice and the development of reversal agents for the factor Xa and thrombin inhibitors is underway. (See "Management of bleeding in patients receiving target-specific oral anticoagulants", section on 'Risk of bleeding'.)

The role of digoxin in rate control for patients with AF (August 2014)

The role of digoxin in ventricular rate control in patients with atrial fibrillation (AF) has been limited due to relative poor efficacy and the possibility of an increase in mortality in patients without heart failure. The observational TREAT-AF study evaluated mortality in over 120,000 patients with a recent diagnosis of nonvalvular atrial fibrillation [5]. In this new study, digoxin use was associated with a nearly 25 percent increase in all-cause mortality across all subgroups, including those with and without heart failure. Important limitations of this study include its retrospective design and the absence of a detailed evaluation of the potential impact of digoxin levels. We limit the use of digoxin in AF patients without heart failure to those in whom beta blockers and calcium channel blockers have not achieved adequate rate control and who are not considered candidates for non-pharmacologic therapy to control rate. (See "Control of ventricular rate in atrial fibrillation: Pharmacologic therapy", section on 'Digoxin'.)

Prophylactic ICD implantation for patients with LVEF 30 to 35 percent (July 2014)

Although most studies of prophylactic implantable cardioverter-defibrillator (ICD) implantation have included patients with a left ventricular ejection fraction (LVEF) ≤35 percent, most study patients had LVEF <30 percent, resulting in uncertainty regarding benefit in patients with LVEF between 30 and 35 percent. In a retrospective cohort study using data from two large registries of patients with and without ischemic disease (National Cardiovascular Data Registry of patients who underwent ICD implantation and Get With The Guidelines-Heart Failure patients without an ICD) in which the benefits of ICD implantation were separately evaluated for patients with LVEF <30 percent and those with LVEF 30-35 percent, all-cause mortality was significantly lower in patients with an ICD and any level of LVEF, compared with those without an ICD [6]. These data, although not from a randomized trial, support our recommendation to implant an ICD in patients with heart failure and an LVEF of 35 percent or lower. (See "Primary prevention of sudden cardiac death in heart failure and cardiomyopathy", section on 'LVEF and risk'.)

CONGENITAL HEART DISEASE, ADULT

Angiotensin II receptor blocker versus beta blocker for Marfan syndrome (November 2014)

Studies in patients with Marfan syndrome (MFS) and aortic root dilation have suggested that angiotensin II receptor blocker therapy may be more effective than beta blocker therapy for prevention of further dilation. A randomized trial comparing losartan with atenolol in 608 children and adults with MFS and aortic root dilation found no significant difference in the rate of dilation between the two treatment groups over a three-year period [7]. We recommend beta blocker therapy for patients with MFS with aortic root dilation and suggest addition of an angiotensin II receptor blocker as tolerated. (See "Management of Marfan syndrome and related disorders", section on 'Therapy targeting the renin-angiotensin system'.)

CORONARY ARTERY BYPASS GRAFT SURGERY

Colchicine for prevention of post-cardiac injury syndrome (September 2014)

Colchicine is effective for the prevention and treatment of acute and recurrent pericarditis as well as post-cardiac injury syndrome, but its effectiveness is limited in many patients due to side effects. In the COPPS-2 trial, a randomized trial of colchicine or placebo beginning 48 to 72 hours prior to cardiac surgery, colchicine significantly reduced the occurrence of the post-cardiac injury syndrome at three months but was associated with significantly more adverse effects, primarily gastrointestinal [8]. Based on the collective results of this trial and the first COPPS trial, in which colchicine was begun postoperatively and showed similar reductions in post-cardiac injury syndrome with significantly less GI toxicity, for most patients undergoing cardiac surgery, we suggest a course of colchicine beginning one to three days following surgery to reduce the risk of developing post-cardiac injury syndrome. (See "Post-cardiac injury syndromes", section on 'Prevention'.)

CORONARY HEART DISEASE, ACUTE

Culprit-only or multivessel PCI in patients with STEMI (October 2014)

The optimal revascularization strategy with percutaneous coronary intervention (PCI) is not known for the 40 to 50 percent of patients with acute ST-elevation myocardial infarction (STEMI) found to have significant lesions (≥50 percent luminal narrowing) in addition to the lesion responsible for the

acute MI. A 2014 meta-analysis of three randomized trials found that the risks of subsequent revascularization and nonfatal MI were lower with multivessel compared to culprit only PCI [9]. For many patients with non-culprit lesions, we now proceed with multivessel revascularization at the time of primary PCI. We do **not** perform immediate non-culprit PCI when patients meet the following criteria: chronic kidney disease; administration of a large contrast volume; less than TIMI III flow in the culprit vessel after optimal PCI; complex non-culprit stenosis; patient, operator, or health care team fatigue; anticipated need for coronary artery bypass graft surgery or valve surgery in the near future; severe comorbidities. (See "Primary percutaneous coronary intervention in acute ST elevation myocardial infarction: Periprocedural management", section on 'Non-culprit PCI'.)

2014 ACC/AHA guideline on NSTE-ACS (October 2014)

The American College of Cardiology/American Heart Association (ACC/AHA) has updated its guideline for the management of patients with non-ST elevation acute coronary syndromes (NSTE-ACS) [10]. We agree with recommendations made in this guideline, which covers multiple aspects of care of patients with NSTE-ACS. Changes from the 2011 version of this guideline include no longer recommending platelet function testing to determine platelet inhibitory response, or genotyping for a CYP2C19 loss of function variant, in patients with NSTE-ACS. (See "Clopidogrel resistance and clopidogrel treatment failure", section on 'Recommendations of others'.)

Routine thrombus aspiration in STEMI not helpful (September 2014)

Intracoronary thrombus is found in the majority of patients with ST-elevation myocardial infarction (STEMI), and higher burdens of thrombus are associated with worse outcomes. Thrombus aspiration prior to percutaneous intervention (PCI) can reduce the thrombus burden; however, there has been conflicting evidence on whether this improves outcomes. A prior meta-analysis of randomized trials indicated a reduced risk of all-cause mortality with aspiration thrombectomy, although there were some concerns about the analysis and generalizability of the underlying trials. The TASTE trial, not included in the meta-analysis, randomly assigned 7244 patients to routine thrombus aspiration followed by PCI or to PCI only. Previously reported 30-day results found no difference in the primary end point of death from any cause. In a newly published report of outcomes at one year from the TASTE trial, there was similarly no difference in mortality for patients treated with and without thrombectomy (5.3 versus 5.6 percent) [11]. Based on these results, we no longer suggest the routine use of thrombus aspiration prior to PCI in STEMI patients. It is reasonable to continue to use aspiration thrombectomy in patients with a large thrombus burden. (See "Suboptimal reperfusion after primary percutaneous coronary intervention in acute ST elevation myocardial infarction", section on 'Thrombectomy'.)

Heparin preferred to bivalirudin for primary PCI (August 2014)

The recommended anticoagulant strategy in patients with ST-elevation myocardial infarction (STEMI) who are treated with primary percutaneous coronary intervention (PCI) continues to evolve. In recent years bivalirudin has been the preferred agent. In the HEAT-PPCI single center trial, unfractionated heparin (UFH) was directly compared to bivalirudin in 1829 such patients [12]. The use of glycoprotein IIb/IIIa inhibitors was about 15 percent in both groups and all patients received a potent oral $P2Y_{12}$ platelet receptor blocker (ticagrelor or prasugrel). The primary efficacy outcome, a

composite of all-cause mortality, cerebrovascular accident, reinfarction, or additional unplanned target lesion revascularization, occurred significantly more often in the bivalirudin group (8.7 versus 5.7 percent), while the rate of bleeding did not differ significantly. For STEMI patients undergoing primary PCI who receive a potent $P2Y_{12}$ receptor blocker, we now prefer UFH rather bivaliruidin. Furthermore, glycoprotein IIb/IIIa inhibitors do not appear to be routinely indicated with UFH. (See "Anticoagulant therapy in acute ST elevation myocardial infarction", section on 'UFH compared to bivalirudin'.)

CORONARY HEART DISEASE, STABLE

Optimal duration of dual antiplatelet therapy after coronary stenting (December 2014)

All patients who undergo percutaneous coronary intervention with stenting receive dual antiplatelet therapy (DAPT), which is the combination of aspirin and a $P2Y_{12}$ receptor blocker. However, the optimal duration of DAPT is not known; 12 months has been the commonly recommended duration. The DAPT trial randomly assigned 9961 such patients, who had been successfully treated with 12 months of aspirin and a $P2Y_{12}$ receptor blocker (either clopidogrel or prasugrel), to continue receiving the $P2Y_{12}$ receptor blocker or placebo for another 18 months; all patients continued aspirin [13]. The rates for each of the co-primary end points of stent thrombosis and major adverse cardiovascular and cerebrovascular events (a composite of death from any cause, MI, or stroke) were lower with continued $P2Y_{12}$ therapy (0.4 versus 1.4 percent and 4.3 versus 5.9 percent). However, the rate of moderate or severe bleeding was increased (2.5 versus 1.6 percent). Based on available evidence, including the DAPT trial, we recommend DAPT for 12 months in patients not at high risk of bleeding, which is the major complication of this therapy. After 12 months of uncomplicated DAPT therapy, we suggest an additional 18 months of treatment. (See "Antiplatelet therapy after coronary artery stenting", section on 'Drug-eluting stents'.)

Risk of myocardial infarction and nonobstructive coronary heart disease (November 2014)

Given the slow progression of atherosclerosis, patients with coronary heart disease (CHD) may be asymptomatic for years, and the prognosis related to nonobstructive coronary lesions is uncertain. Nonobstructive CHD refers to stenosis ≥20 percent but <70 percent, while obstructive CHD is identified when at least one stenosis is ≥70 percent. In a retrospective cohort study of over 37,000 patients (96 percent male) without prior CHD events who underwent elective coronary angiography and were followed for one year, the risk of myocardial infarction (MI) increased with the extent of both nonobstructive and obstructive lesions [14]. Compared to patients without CHD, the risk of MI trended higher for patients with one vessel nonobstructive CHD and was significantly greater for two and three vessel nonobstructive CHD. Patients found to have nonobstructive CHD should be treated with usual secondary prevention measures. (See "Epidemiology of coronary heart disease", section on 'Non-obstructive CHD'.)

Ivabradine not effective for stable angina (September 2014)

Over the past two decades there have been no important additions to options for medical therapy of angina pectoris aside from ranolazine. In early trials, the chronotropic drug ivabradine appeared to improve symptoms of angina. However, the SIGNIFY trial, which randomly assigned over 19,000 patients with stable coronary artery disease without clinical heart failure and a heart rate of 70 beats per minute or more to ivabradine or placebo, found no difference in the composite end point of

cardiovascular death or nonfatal myocardial infarction [15]. Additionally, among patients with Canadian Cardiovascular Society class II angina or higher, the composite outcome occurred significantly more often in the group treated with ivabradine. Based on these results, we do not recommend the use of ivabradine in patients with stable angina who do not have clinical heart failure. (See "New therapies for angina pectoris", section on 'Ivabradine'.)

Beta blockers in stable coronary heart disease (August 2014)

Although beta blocker therapy improves survival in patients who have sustained an acute myocardial infarction (MI), there is no convincing evidence for this benefit in patients with stable disease. In an observational study of over 26,000 patients discharged after a first coronary heart disease event (an acute coronary syndrome or coronary artery revascularization) and followed for nearly four years, there was no difference in the risk of death in the subgroup without recent MI between those who did or did not receive beta blocker [16]. In patients with stable coronary heart disease who have not had a recent acute MI, beta blockers are indicated to treat angina but not to improve survival. (See "Secondary prevention of cardiovascular disease", section on 'Beta blockers'.)

HEART FAILURE

Beta-blocker therapy in patients with atrial fibrillation and heart failure (September 2014)

An individual patient data meta-analysis of patients with heart failure (predominantly due to systolic dysfunction) found that beta blocker therapy did not reduce mortality in patients with atrial fibrillation, though it reduced mortality in patients in sinus rhythm [17]. This meta-analysis raises questions about the role of beta blockers as standard therapy to improve prognosis in patients with atrial fibrillation and systolic heart failure, though these results are not sufficient to change our treatment recommendations at this time. (See "Use of beta blockers in heart failure due to systolic dysfunction", section on 'General approach'.)

Neprilysin inhibitor plus angiotensin II receptor blocker in systolic heart failure (September 2014)

A randomized double-blind trial in patients with systolic heart failure found that sacubitril-valsartan (LCZ696) reduced the primary outcome of cardiovascular mortality and hospitalization for heart failure and also reduced all-cause mortality compared to a proven dose of the ACE inhibitor enalapril [18]. Sacubitril-valsartan is an investigational drug combining the neprilysin inhibitor sacubitril (which raises natriuretic peptide levels) and the angiotensin II receptor blocker valsartan. The sacubitril-valsartan group had higher rates of hypotension and nonserious angioedema but lower rates of renal impairment, hyperkalemia, and cough compared to the enalapril group. (See "Angiotensin II receptor blocker and neprilysin inhibitor therapy in heart failure due to systolic dysfunction", section on 'Rationale'.)

LIPID DISORDERS

Lower HMG CoA reductase activity increases risk of diabetes (January 2015)

A Mendelian randomization study found that decreased genetic HMG CoA reductase activity is associated with a higher risk of type 2 diabetes, such that at least some of the risk of diabetes seen

with statin therapy appears to be due to its inhibition of HMG CoA reductase [19]. Since this inhibition is thought responsible for the primary efficacy of statin therapy, this finding means that any effective statin will probably increase the risk of diabetes [20]. (See "Statins: Actions, side effects, and administration", section on 'Diabetes mellitus'.)

Evolocumab for drug-resistant hypercholesterolemia (November 2014)

In the past two years, multiple randomized trials have found that monoclonal antibodies to PCSK9 (a protease produced in the liver that degrades hepatocyte low density lipoprotein receptors) significantly lower low density lipoprotein-cholesterol (LDL-C) levels in patients with drug-resistant hypercholesterolemia. Two placebo-controlled studies in patients on stable lipid lowering therapy, TESLA Part B and RUTHERFORD-2, provide additional evidence for the efficacy and safety of evolocumab, one such drug in this class. TESLA Part B randomly randomized 50 patients with homozygous familial hypercholesterolemia (FH) [21] and RUTHERFORD-2 randomized 331 patients with heterozygous FH [22]. In these studies, evolocumab lowered LDL-C by 31 and 60 percent, respectively; no new safety concerns were identified. Evolocumab is currently an investigational drug. (See "Inherited disorders of LDL-cholesterol metabolism" and "Treatment of drug-resistant hypercholesterolemia".)

Statin-associated adverse muscle events (October 2014)

Terminology around statin-associated adverse muscle events is variable and has changed over time. The 2014 National Lipid Association Statin Muscle Safety Task Force has proposed new definitions for these adverse events [23], which are reflected in our discussion of statin myopathy. Additionally, we no longer suggest a trial of Coenzyme Q10 (CoQ10) for patients experiencing such statin-associated adverse muscle events. (See "Statin myopathy", section on 'Coenzyme Q10' and "Statin myopathy", section on 'Definitions'.)

MYOPERICARDIAL DISEASE

Hereditary transthyretin amyloid cardiomyopathy in older African-Americans (January 2015)

One of the most common hereditary transthyretin amyloid cardiomyopathies is caused by the Val122Ile mutation. This mutation is present in 3 to 4 percent of the African-American population but the penetrance of disease caused by this mutation is uncertain. A prospective community-based observational study of 124 carriers and 3732 noncarriers suggested that the penetrance of disease caused by the Val122Ile mutation is low [24]. After over two decades of follow-up starting at a median age of 53 years, there was no significant difference in mortality between carriers and noncarriers although the risk of incident heart failure was increased in carriers. (See "Clinical manifestations and diagnosis of amyloid cardiomyopathy", section on 'TTR mutation'.)

Corticosteroids of limited benefit in tuberculous pericarditis (September 2014)

Whether corticosteroids are beneficial for patients with tuberculous pericarditis has been controversial. A randomized trial including 1400 adults initiating antimicrobial treatment for definite or probable tuberculous pericarditis in South Africa (approximately two-thirds of patients had concomitant HIV infection) demonstrated no effect of adjunctive corticosteroids on the primary composite efficacy outcome of death, cardiac tamponade requiring pericardiocentesis, or

development of constrictive pericarditis [25]. Corticosteroid use did reduce the incidence of constrictive pericarditis alone (4.4 versus 7.8 percent). The overall lack of benefit may have reflected harm from corticosteroid treatment in patients with HIV, and it remains possible that patients without HIV could benefit from corticosteroids. Based on the totality of the evidence, we do not routinely use adjunctive corticosteroids in the absence of constrictive disease or high risk for constrictive disease. This approach is in disagreement with prior guidelines favoring routine use of corticosteroids for all patients with tuberculous pericarditis.

We continue to suggest administration of corticosteroids for patients with constrictive tuberculous pericarditis and for those felt to be at high risk of developing the condition (ie, large effusion, high level of pericardial fluid inflammatory cells, or early signs of constriction). (See "Tuberculous pericarditis", section on 'Role of corticosteroids'.)

PREVENTIVE CARDIOLOGY

Running and cardiovascular risk (August 2014)

Several professional society guidelines recommend at least 30 minutes of moderate-intensity exercise five to seven days per week, but this is not achievable for all patients. In a prospective cohort study with a mean follow-up of over 15 years, over 55,000 adults (mean age 44 years) reported duration, distance, frequency, and speed of any running or jogging [26]. Runners had significantly lower risks of all-cause and cardiovascular mortality compared to non-runners. Additionally, the derived mortality benefit was similar for all runners regardless of the total running time, including for those who ran less than 51 minutes per week. These findings from a non-randomized study may represent unidentified confounding factors, and do not prove causation. However, these data support the concept that even small amounts of exercise are better than no exercise while at least 30 minutes of moderate-intensity exercise five to seven days per week remains a reasonable goal for most patients. (See "Exercise and fitness in the prevention of cardiovascular disease", section on 'Type, intensity, and duration of exercise'.)

REVASCULARIZATION

Optimal duration of dual antiplatelet therapy after coronary stenting (December 2014)

All patients who undergo percutaneous coronary intervention with stenting receive dual antiplatelet therapy (DAPT), which is the combination of aspirin and a $P2Y_{12}$ receptor blocker. However, the optimal duration of DAPT is not known; 12 months has been the commonly recommended duration. The DAPT trial randomly assigned 9961 such patients, who had been successfully treated with 12 months of aspirin and a $P2Y_{12}$ receptor blocker (either clopidogrel or prasugrel), to continue receiving the $P2Y_{12}$ receptor blocker or placebo for another 18 months; all patients continued aspirin [13]. The rates for each of the co-primary end points of stent thrombosis and major adverse cardiovascular and cerebrovascular events (a composite of death from any cause, MI, or stroke) were lower with continued $P2Y_{12}$ therapy (0.4 versus 1.4 percent and 4.3 versus 5.9 percent). However, the rate of moderate or severe bleeding was increased (2.5 versus 1.6 percent). Based on available evidence, including the DAPT trial, we recommend DAPT for 12 months in patients not at high risk of bleeding, which is the major complication of this therapy. After 12 months of uncomplicated DAPT

therapy, we suggest an additional 18 months of treatment. (See "Antiplatelet therapy after coronary artery stenting", section on 'Drug-eluting stents'.)

VALVULAR HEART DISEASE

Surgery for moderate ischemic mitral regurgitation (December 2014)

Ischemic mitral regurgitation (MR) is associated with increased risk of heart failure and mortality. However, the benefit of performing mitral valve repair at the time of coronary artery bypass grafting (CABG) is uncertain. In a multicenter trial, 301 patients with moderate ischemic MR were randomly assigned to CABG alone or CABG plus mitral valve repair [27]. At one year follow-up, the degree of reverse remodeling, functional status, and mortality rates were the same in the two groups. The combined procedure group had a lower prevalence of moderate or severe MR but a longer bypass time, a longer hospital stay after surgery, and more neurologic events. Longer follow-up is needed to determine whether the reduction in MR leads to long-term clinical benefit. (See "Ischemic mitral regurgitation", section on 'Moderate to severe MR'.)

Genetic predisposition to hyperlipidemia associated with aortic valve disease (December 2014)

Plasma low-density lipoprotein cholesterol (LDL-C) is associated with risk of calcific aortic valve disease but the genetic contribution to this risk is uncertain. A Mendelian randomization study found an association between the weighted genetic risk score (GRS, a measure of the genetic predisposition to elevation in plasma lipids) for low-density lipoprotein cholesterol (LDL-C) and aortic valve calcium in 6942 participants in community-based studies [28]. The LDL-C GRS was also associated with incident aortic stenosis in a separate community-based population. Trials of lipid lowering therapies in patients with aortic stenosis have not shown convincing benefit but the potential effect of lipid lowering therapy initiated earlier is uncertain. (See "Aortic valve sclerosis and pathogenesis of calcific aortic stenosis", section on 'Genetic factors'.)

OTHER CARDIOLOGY

Icatibant for ACE-inhibitor associated angioedema (February 2015)

Angiotensin-converting enzyme (ACE) inhibitors cause episodic, bradykinin-mediated angioedema in less than 1 percent of recipients, but this accounts for approximately one-third of angioedema cases presenting to emergency departments in countries where these medicines are widely used. The most common approach to management of severe episodes affecting the airway has been discontinuation of the ACE inhibitors and supportive care, which may involve intubation and even tracheotomy. Icatibant, a bradykinin receptor antagonist approved for use in hereditary angioedema, has now been shown to be effective for ACE inhibitor-associated angioedema [29]. In a randomized trial of 27 adults presenting to the emergency department with angioedema of the upper aerodigestive tract while taking an ACE inhibitor, patients received one dose of icatibant or standard therapy (an intravenous glucocorticoid plus an antihistamine). Symptoms in the icatibant group resolved in a median of 8 hours, compared with 27 hours in the glucocorticoid/antihistamine group, and icatibant was well tolerated. Icatibant is most likely to be effective if given in the first few hours of an angioedema attack when the swelling is still increasing. (See "ACE inhibitor-induced angioedema", section on 'Icatibant'.)

Increased serum digoxin in patients taking dronedarone (November 2014)

Digoxin, because of its pharmacologic properties, is subject to numerous drug-drug interactions which alter its availability and potentially lead to toxicity. The PALLAS trial randomized patients with permanent atrial fibrillation to dronedarone or placebo in addition to usual care, and found an increase in cardiovascular death with dronedarone. A subgroup analysis was done to determine if adverse events correlated with use of digoxin [30]. Among patients who had been taking digoxin at baseline, digoxin levels during the trial were higher in patients taking dronedarone than placebo. Additionally, there were more cardiovascular deaths in patients co-administered dronedarone and digoxin compared to placebo and digoxin. When dronedarone and digoxin are co-administered, the digoxin dose should be reduced by 50 percent, and digoxin levels should be monitored closely to maintain serum concentrations of 0.5-0.8 ng/mL. (See "Clinical uses of dronedarone", section on 'Metabolism and drug interactions'.)

Investigational agent for reversal of multiple anticoagulants (November 2014)

Reversal agents for the target specific oral anticoagulants are lacking. In a study of 80 healthy volunteers given a therapeutic dose of the direct factor Xa inhibitor edoxaban, a reversal agent under development (PER977) normalized the whole blood clotting time within 10 minutes; in contrast, normalization of the clotting time took 12 to 15 hours in individuals given edoxaban followed by placebo [31]. In addition to binding direct factor Xa inhibitors, PER977 also binds the direct thrombin inhibitor dabigatran, as well as unfractionated and low molecular weight heparins. (See "Management of bleeding in patients receiving target-specific oral anticoagulants", section on 'Antidotes under development'.)

REFERENCES

1. http://www.accessdata.fda.gov/drugsatfda_docs/label/2015/206316lbl.pdf (Accessed on January 09, 2015).
2. Giugliano RP, Ruff CT, Braunwald E, et al. Edoxaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2013; 369:2093.
3. Hokusai-VTE Investigators, Büller HR, Décousus H, et al. Edoxaban versus warfarin for the treatment of symptomatic venous thromboembolism. N Engl J Med 2013; 369:1406.
4. Chai-Adisaksopha C, Crowther M, Isayama T, Lim W. The impact of bleeding complications in patients receiving target-specific oral anticoagulants: a systematic review and meta-analysis. Blood 2014; 124:2450.
5. Turakhia MP, Santangeli P, Winkelmayer WC, et al. Increased mortality associated with digoxin in contemporary patients with atrial fibrillation: findings from the TREAT-AF study. J Am Coll Cardiol 2014; 64:660.
6. Al-Khatib SM, Hellkamp AS, Fonarow GC, et al. Association between prophylactic implantable cardioverter-defibrillators and survival in patients with left ventricular ejection fraction between 30% and 35%. JAMA 2014; 311:2209.
7. Lacro RV, Dietz HC, Sleeper LA, et al. Atenolol versus losartan in children and young adults with Marfan's syndrome. N Engl J Med 2014; 371:2061.
8. Imazio M, Brucato A, Ferrazzi P, et al. Colchicine for prevention of postpericardiotomy syndrome and postoperative atrial fibrillation: the COPPS-2 randomized clinical trial. JAMA 2014; 312:1016.
9. Sekercioglu N, Spencer FA, Cruz Lopes L, Guyatt GH. Culprit Vessel Only vs Immediate Complete Revascularization in Patients With Acute ST-Segment Elevation Myocardial Infarction: Systematic Review and Meta-Analysis. Clin Cardiol 2014; 37:765.
10. Amsterdam EA, Wenger NK, Brindis RG, et al. 2014 AHA/ACC Guideline for the Management of Patients With Non-ST-Elevation Acute Coronary Syndromes: Executive Summary: A Report of

the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014; 64:2645.
11. Lagerqvist B, Fröbert O, Olivecrona GK, et al. Outcomes 1 year after thrombus aspiration for myocardial infarction. N Engl J Med 2014; 371:1111.
12. Shahzad A, Kemp I, Mars C, et al. Unfractionated heparin versus bivalirudin in primary percutaneous coronary intervention (HEAT-PPCI): an open-label, single centre, randomised controlled trial. Lancet 2014; 384:1849.
13. Mauri L, Kereiakes DJ, Yeh RW, et al. Twelve or 30 months of dual antiplatelet therapy after drug-eluting stents. N Engl J Med 2014; 371:2155.
14. Maddox TM, Stanislawski MA, Grunwald GK, et al. Nonobstructive coronary artery disease and risk of myocardial infarction. JAMA 2014; 312:1754.
15. Fox K, Ford I, Steg PG, et al. Ivabradine in stable coronary artery disease without clinical heart failure. N Engl J Med 2014; 371:1091.
16. Andersson C, Shilane D, Go AS, et al. β-blocker therapy and cardiac events among patients with newly diagnosed coronary heart disease. J Am Coll Cardiol 2014; 64:247.
17. Kotecha D, Holmes J, Krum H, et al. Efficacy of β blockers in patients with heart failure plus atrial fibrillation: an individual-patient data meta-analysis. Lancet 2014.
18. McMurray JJ, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med 2014; 371:993.
19. Swerdlow DI, Preiss D, Kuchenbaecker KB, et al. HMG-coenzyme A reductase inhibition, type 2 diabetes, and bodyweight: evidence from genetic analysis and randomised trials. Lancet 2014.
20. Frayling TM. Statins and type 2 diabetes: genetic studies on target. Lancet 2014.
21. Raal FJ, Honarpour N, Blom DJ, et al. Inhibition of PCSK9 with evolocumab in homozygous familial hypercholesterolaemia (TESLA Part B): a randomised, double-blind, placebo-controlled trial. Lancet 2014.
22. Raal FJ, Stein EA, Dufour R, et al. PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolaemia (RUTHERFORD-2): a randomised, double-blind, placebo-controlled trial. Lancet 2014.
23. Rosenson RS, Baker SK, Jacobson TA, et al. An assessment by the Statin Muscle Safety Task Force: 2014 update. J Clin Lipidol 2014; 8:S58.
24. Quarta CC, Buxbaum JN, Shah AM, et al. The amyloidogenic V122I transthyretin variant in elderly black Americans. N Engl J Med 2015; 372:21.
25. Mayosi BM, Ntsekhe M, Bosch J, et al. Prednisolone and Mycobacterium indicus pranii in tuberculous pericarditis. N Engl J Med 2014; 371:1121.
26. Lee DC, Pate RR, Lavie CJ, et al. Leisure-time running reduces all-cause and cardiovascular mortality risk. J Am Coll Cardiol 2014; 64:472.
27. Smith PK, Puskas JD, Ascheim DD, et al. Surgical treatment of moderate ischemic mitral regurgitation. N Engl J Med 2014; 371:2178.
28. Smith JG, Luk K, Schulz CA, et al. Association of low-density lipoprotein cholesterol-related genetic variants with aortic valve calcium and incident aortic stenosis. JAMA 2014; 312:1764.
29. Baş M, Greve J, Stelter K, et al. A randomized trial of icatibant in ACE-inhibitor-induced angioedema. N Engl J Med 2015; 372:418.
30. Hohnloser SH, Halperin JL, Camm AJ, et al. Interaction Between Digoxin and Dronedarone in the PALLAS Trial. Circ Arrhythm Electrophysiol 2014; 7:1019.
31. Ansell JE, Bakhru SH, Laulicht BE, et al. Use of PER977 to reverse the anticoagulant effect of edoxaban. N Engl J Med 2014; 371:2141.

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