Observer extra:

Post-Myocardial Infarction

The latest evaluation, management and treatment strategies
Medical management following myocardial infarction:
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Myocardial infarction (MI) is the leading cause of death in the U.S. According to the American College of Cardiology/American Heart Association's most recent guidelines for managing acute MI, 250,000 of the approximately 800,000 people in the country affected by MI annually die before reaching the hospital.

The survival rate for patients who receive timely medical care—consisting of therapies to restore coronary blood flow—is 90% to 95%. But patients who survive MI still may face a difficult recovery. Medical management of post-MI patients often requires unwelcome lifestyle changes, compliance with new medication regimens, and coping with significant psychological after-effects. These changes are important in order to prevent subsequent events including death, reinfarction, and rehospitalization as well as minimize left ventricular (LV) remodeling and prevent arrhythmias and progression to heart failure. Patients also may need assistance with the transition back to regular life after MI.

The evaluation and follow-up of patients who have experienced MI begins before hospital discharge and consists of establishing a stable medical regimen and deciding on further noninvasive or invasive evaluation of the underlying coronary artery disease (CAD) and its potential complications.

For post-MI care to be effective, open and supportive communication between the patient and physician is perhaps more important than anything because it reinforces the message that targeted prescription regimens and lifestyle changes can greatly reduce the risk for reinfarction. This supplement to the ACP Observer provides clinicians updated information on the best evaluation, management and treatment strategies for the post-MI patient.

**Drug Therapy**

Drug therapy is an important component to long-term care following an MI and should begin in the hospital with aspirin, heparin, beta-adrenoceptor blocking agents and possibly nitrates, as well as with appropriate analgesia to reduce pain and anxiety. An ACE inhibitor or ARB and a statin are also often prescribed shortly after MI, as are other drugs to reduce clotting and minimize blockages. Further drug therapy is based on the type of MI and other factors.

**Antiplatelet agents**

Give aspirin therapy promptly and continue indefinitely. If aspirin is contraindicated due to hypersensitivity or gastrointestinal complications, use clopidogrel—a thienopyridine derivative that exerts an irreversible antiplatelet effect by antagonizing adenosine phosphate—as an alternative. Antiplatelet agents prevent clotting in patients who have had a heart attack. They reduce the incidence of MI in patients with unstable angina and mortality in patients with acute unstable angina or acute MI. The anti-inflammatory properties of aspirin may also contribute to its beneficial effects.

Clopidogrel provides additional antiplatelet activity when added to aspirin. Administer clopidogrel in addition to aspirin as soon as possible to patients for whom a noninterventional approach is planned and continue for at least one month and up to nine months; for patients for whom PCI is planned and who are not at high-risk for bleeding, continue clopidogrel for at least one month and for up to 12 months. Routine administration of clopidogrel to all patients may not be cost-effective.

Many clinicians withhold clopidogrel until it is clear that patients are not likely to undergo early coronary bypass surgery due to the increased risk of perioperative bleeding with its use. Discontinue clopidogrel for five to seven days before elective coronary bypass surgery to eliminate the risk of major bleeding.

**Anticoagulants**

**Unfractionated Heparin:** There are no randomized trials demonstrating improved clinical outcomes with the addition of unfractionated heparin to fibrin-specific or non-fibrin specific fibrinolytic agents. However, three small angiographic studies (two of which did not give aspirin) demonstrated improved infarct-related artery patency with use of heparin in addition to TPA. Based on this, it is recommended by the ACC/AHA guidelines that UFH be administered with fibrin-specific thrombolytic agents.
UFH is not recommended for use with a non-fibrin specific thrombolytic (such as streptokinase) unless the patient is a high risk for systemic embolism.

**Low molecular weight heparin:** The CREATE trial demonstrated that the addition of reviparin to aspirin improves mortality, recurrence of MI and stroke but at an increased cost of bleeding compared with placebo in STEMI. Reviparin is not widely available in North America. The ASSENT 3 study demonstrated a reduction in death or MI with administration of enoxaparin for about one week over UFH for 48 hours in STEMI, but at a higher risk of bleeding. In addition, data from the ASSENT 3 and the ASSENT 3 Plus trial have shown that bleeding and intracranial hemorrhage are increased with the use of enoxaparin in the elderly. The recent EXTRACT trial of over 20,000 patients demonstrated a reduction in death or MI with enoxaparin given for seven days compared with 48 hours of UFH. However, mortality was not significantly reduced and there was a significant increase in major bleeding of approximately 40%. In addition, enoxaparin was associated with a significant increase in fatal bleeding compared with UFH. Therefore, caution is recommended with use of enoxaparin, especially in the elderly or those at increased risk of bleeding (eg. renal insufficiency). The appropriate management of anticoagulation for a rescue PCI procedure is also not clear when enoxaparin is administered. This needs to be studied further.

**Fondaparinux:** Fondaparinux was evaluated in the OASIS 6 trial of over 12,000 patients with STEMI. There was a significant benefit of fondaparinux in reducing death or MI over control therapy. Importantly, there was a significant reduction in mortality. The effects of fondaparinux in reducing death or MI was similar when the comparator agent was UFH or when the comparator agent was placebo. Unlike enoxaparin, there was no increase in the risk of bleeding with fondaparinux compared with UFH. There was a significant reduction in the risk of cardiac tamponade with fondaparinux compared with UFH. Fondaparinux did not differ from UFH in those undergoing primary PCI in the study, and therefore in this group UFH is recommended. However in those patients receiving fibrinolytic therapy or in those ineligible for reperfusion therapy, fondaparinux resulted in a marked efficacy benefit with no increase in bleeding. If a patient requires a rescue PCI procedure, standard UFH is recommended and this strategy proved safe and effective in the OASIS 6 trial.

**Glycoprotein IIb/IIIa antagonists**

The glycoprotein IIb/IIIa receptor is present on the platelet surface; glycoprotein IIb/IIIa antagonists bind these receptors and do not allow platelet aggregation to take place. Administer glycoprotein IIb/IIIa in addition to aspirin and heparin in patients with non-ST-elevation MI and an adjunctive therapy in patients with ST-elevation MI undergoing primary PCI. In particular, administer eptifibatide or tirofiban in patients with continuing ischemia, an elevated troponin level, or with other high-risk features including angina at rest with ST-segment changes, congestive heart failure, diabetes or recent MI, as well as to patients in whom catheterization and PCI are planned. It can be administered just before PCI.

**Thrombolysis**

Thrombolytics, such as streptokinase and tissue-type plasminogen activator, restore perfusion to the ischemic area by lysing the clot, thereby reducing infarct size and improving survival. Consider a thrombolytic agent as an alternative to primary PCI in suitable candidates with:

- ST-elevation MI, including those with new left bundle branch block (LBBB)
- patients who present more than 12 hours after onset of chest pain that persists

Recognize, however, that primary PCI is an alternative to thrombolytic therapy and may be associated with improved outcomes in selected patients.
**Beta Blockers**

Beta-blockers may initially diminish myocardial oxygen demand by reducing heart rate, systemic arterial pressure, and myocardial contractility; in addition, prolongation of diastole may augment perfusion to injured myocardium. Clinical trials show that beta-blocker therapy reduces infarct size and the frequency of recurrent myocardial ischemia, and improves short- and long-term survival.

One trial showed that treatment within five hours of symptom onset reduced mortality in the first week by about 15%. Another trial showed that treatment of patients with evolving MI reduced 15-day mortality from 4.9% to 4.3% compared with controls. In both trials, the mortality difference was evident by day one and sustained afterwards.

Administer beta-blockers early, unless there are significant contraindications, and continue indefinitely. In particular, consider initiation of the beta blocker carvedilol in patients with LV dysfunction within three to 21 days after MI because it reduces heart rate and systemic arterial pressure and potentially attenuates adverse LV modeling.

**Nitrates**

The vasodilation action of nitroglycerin has been shown to result in combined preload and afterload reduction, decreased cardiac work, and lower myocardial oxygen requirements. The direct vasodilator effect on the coronary bed also improves myocardial blood flow.

Administer intravenous nitrates for the first 24 to 48 hours to patients with unstable angina, acute uncomplicated MI with ongoing chest discomfort, or MI complicated by congestive heart failure, large anterior infarction, persistent ischemia, or hypertension. Use with extreme caution, if at all, in patients with suspected right ventricular infarction. Avoid use in patients with marked bradycardia, tachycardia or hypotension. Once a patient with MI has stabilized and the acute phase has passed, oral nitrates can prevent recurrent chest pain.

**Ace Inhibitors**

Angiotensin-converting enzyme (ACE) inhibitors expand blood vessels and decrease resistance by lowering levels of angiotensin II, allowing blood to flow more easily. Clinical trials show that ACE inhibitors significantly reduce the risk of recurrent MI and other vascular events.

**ARBs**

Rather than lowering levels of angiotensin II (as ACE inhibitors do), angiotensin II receptor blockers (ARBs) prevent this chemical from having any effect on the heart and blood vessels, and this keeps blood pressure from rising. Like ACE inhibitors, ARBs can improve clinical outcomes in patients with acute MI complicated by heart failure, LV systolic dysfunction, or both.

Because clinical trials involving more than 100,000 patients have documented the benefits of ACE inhibitors following acute MI, ACE inhibitors are the first-choice agents in this population. An ARB is an acceptable alternative to an ACE inhibitor in patients with clinical heart failure or LV dysfunction (ejection fraction ≤35%) within 10 days after MI, based on the results of two large trials.

**Statins**

Statins are used to lower LDL cholesterol, raise high-density lipoprotein (HDL) cholesterol and lower triglyceride levels. In post-MI patients, statin therapy appears to improve endothelial function and reduce the risk for future coronary events. Recent research suggests that statin therapy may have an emerging benefit beyond lowering LDL, including plaque stabilization and improvement in endothelial
function. Consider initiating therapy early in the setting of ACS.

**Selective Aldosterone Blockers**

Eplerenone, a selective aldosterone blocker, limits collagen formation and ventricular remodeling after acute MI and also has a favorable effect on the neurohormonal profile. Despite treatment with ACE inhibitors and beta-blockers, patients with impaired LV systolic function after MI are at an increased risk for heart failure and death, in part due to progressive deterioration in LV performance resulting from ventricular structural remodeling. A large trial found that eplerenone administered within three to 14 days and continued for 16 months reduced total mortality from 16.7% in the placebo group to 14.4% in the eplerenone group (RR, 0.85, P = 0.008). Consider early initiation of eplerenone in patients with LV ejection fraction ≤40% after MI.

Another aldosterone antagonist, spironolactone has previously been shown to reduce mortality and hospitalization in patients with severe LV systolic dysfunction and heart failure, but its efficacy in patients with recent MI is unknown. Note that aldosterone antagonists should be used with great caution or not at all in patients with renal insufficiency or preexisting hyperkalemia.

**Controlling Glycemia, Blood Pressure, and Cholesterol**

For patients who have experienced MI, gaining control of high glycemic, blood pressure, and cholesterol levels is important to aiding recovery and reducing CAD. Along with lifestyle changes, the medications listed above plus specific diabetes medications may be useful for achieving this goal.

In patients with diabetes, aim for tight glycemic control consisting of HbA1c <7.0%. Hyperglycemia contributes to microvascular disease is a known risk factor for MI. Consider referring patients to a diabetic teaching program and providing them counseling on diet and weight reduction.

Aim for a goal blood pressure of <135/85 mm Hg (<130/80 mm Hg in patients with diabetes, renal insufficiency, or heart failure). High blood pressure is a known modifiable risk factor for MI. Discuss with patients the importance of good control.

Control serum cholesterol levels, particularly low-density lipoprotein (LDL) levels. Current NCEP guidelines recommend a goal LDL <100 mg/dL. Cholesterol-lowering therapy after MI or unstable angina reduces vascular events and death. Inform patients about the importance of good control.

Note that many post-MI patients fail to receive all appropriate prescriptions prior to leaving the hospital. Strategies that can improve drug prescribing and the delivery of preventive services while reducing medication errors include reminder systems and structured order forms and checklists.

**Non-drug Therapy**

Besides supplemental oxygen for at least six hours post MI and bed rest, and continuous electrocardiography monitoring for at least 12 hours post-MI, consider the role of primary percutaneous revascularization and intra-aortic balloon pump support for some patients.

**Cardiac Catheterization**

Cardiac catheterization provides an effective way to check blood flow in the coronary arteries. Consider early cardiac catheterization during hospitalization for patients with recurrent symptoms, serious complications, or other serious high-risk features (i.e. hypotension, congestive heart failure, recurrent chest pain).

Consider prompt transfer to a referral center for primary percutaneous coronary intervention (PCI) as an alternative to thrombolytic therapy in experienced centers, particularly in patients with ST-segment elevation, new LBBB, or true posterior acute MI. PCI is associated with a lower 30-day mortality rate and lower risk of hemorrhagic stroke compared with thrombolytic therapy. Note that the beneficial effects of transfer for PCI are contingent upon transfer within two to three hours of initial hospital arrival.

If any coronary arteries are blocked, PCI using a catheter, guide wire, and balloon opens them and improves blood flow. The three most common types of PCI are:

- Angioplasty - uses bal-
loons to widen and increase blood flow in blocked arteries, resulting in decreased angina and heart attack risk and increased ability for physical activity.

**Stenting** - a wire tube often inserted during angioplasty to hold open the artery improve blood flow. Reclosure of the artery is less likely when a stent is used.

**Atherectomy** - similar to angioplasty, using a rotating, shaver-tipped catheter or laser beam to remove plaque and open the blocked artery.

The American Heart Association’s practice guidelines advise that cardiac catheterization with subsequent percutaneous or surgical revascularization is appropriate in patients with recurrent ischemic-type chest discomfort. Numerous studies support the use of cardiac catheterization to aid post-MI recovery. For example, recent studies showed that an early invasive approach (i.e., cardiac catheterization within four to 48 hours after presentation) vs. a conservative approach in combination with a GP IIb/IIIa inhibitor in patients with non-ST-segment elevation MI or unstable angina significantly reduces major cardiac events.

Furthermore, consider placement of an intra-aortic balloon pump (IABP) during cardiac catheterization in specific subsets of patients, such as those with refractory post-MI angina, for stabilization before angioplasty and revascularization or cardiogenic shock. The IABP reduces afterload during systole and increases coronary perfusion during diastole. Studies have shown that in selected patient populations, IABP significantly improves survival rates.

**Exercise Stress Testing**

Use exercise stress testing for prognostic assessment in stable patients post MI without high-risk features, such as hypotension, CHF, recurrent chest pain or inability to exercise. By doing stress testing early post-MI, the clinician can assess functional capacity, evaluate efficacy of the patient’s current medical regimen, and risk of future events.

### Risk Stratification and Management of Patients with Acute Coronary Syndrome

<table>
<thead>
<tr>
<th>Extremely high-risk features</th>
<th>High-risk features</th>
<th>Moderate risk features</th>
<th>Low-risk features</th>
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<tbody>
<tr>
<td><strong>Historical features</strong></td>
<td>Recurrent pain despite aspirin, heparin, and medical treatment</td>
<td>Presenting history of recurrent rest pain plus history of CAD/MI</td>
<td>Recurrent ischemic rest pain plus history of CAD/MI</td>
</tr>
<tr>
<td><strong>Lab and ECG features</strong></td>
<td>Elevated troponin with acutely ischemic ECG, including ST elevations with chest pain or persistent new ST depressions &gt;0.5 mm</td>
<td>Elevated troponin I plus acutely ischemic-appearing ECG</td>
<td>Negative serial troponins with ECG showing nonspecific ST/T wave changes</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Urgent referral for acute coronary angiography with therapeutic PTCA in a high volume center with door-to-needle time &lt;75 minutes vs. thrombolitics (only if ST-cluster or new LBBB) plus GP IIb/IIIa, heparin, ASA, and medical treatment</td>
<td>Admission to the hospital plus GP IIb/IIIa, heparin, ASA, medical treatment followed by early inpatient investigation (e.g., coronary angiography vs. stress test)</td>
<td>Admission to the hospital plus LMWH, ASA followed by possible inpatient investigation (e.g., inpatient stress test)</td>
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**Source:** PIER module on Acute Coronary Syndrome

ACS = acute coronary syndrome; ASA = acetylsalicylic acid; CAD = coronary artery disease; ECG = electrocardiography; LBBB = left bundle branch block; LMWH = low-molecular-weight heparin; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angiography.
stratify the patient according to likelihood of future cardiac events.

- Consider an exercise treadmill test with or without radionuclide imaging if the patient can exercise, and a pharmacologic stress test if the patient cannot exercise.
- Obtain a submaximal stress test four to seven days post MI or a symptom-limited exercise test at 14 to 21 days post-MI. A submaximal protocol has a predetermined endpoint of a heart rate of either 120 bpm, 70% of predicted maximum heart rate, or a peak MET level of 5. A symptom-limited test continues until the patient shows signs or symptoms that require the test to be terminated (i.e. angina, fatigue, ST-segment depression ≥ 2 mm, ventricular arrhythmias, or ≥10 mm Hg drop in systolic BP from baseline).
- Consider the addition of imaging (myocardial perfusion or echocardiography) to improve the sensitivity and specificity of the test.
- Predictors of future adverse events in post-MI patients include inability to exercise, exercise induced ST-segment depression, failure to achieve five METs during treadmill testing, and failure to increase systolic blood pressure by 10 to 30 mm Hg during exercise.

Note that the AHA guidelines recommend concomitant nuclear imaging when baseline abnormalities of the ECG limit interpretation, and there is some evidence that nuclear imaging can also aid in further risk stratification. In one study, stable post-MI patients underwent assessment of LV function and had adenosine tomography done early (5±3 days) after infarction. Cardiac events occurred in 30 (33%) of 92 patients over 15.7 ± 4.9 months. Independent predictors of all events were quantified perfusion defect size (<0.0001), absolute extent of LV ischemia (<0.000001) and ejection fraction (<0.0001). The results suggested that risk stratification of individual patients early after infarction is possible based on the extent of ischemia and severity of LV dysfunction.

**Cardiac Rehabilitation**

Strongly encourage patients to participate in a cardiac rehabilitation program to prevent recurrent heart attacks. Cardiac rehabilitation programs should include:

- Exercise training
- Strategies for reducing modifiable risk factors for cardiovascular disease, including managing lipid levels, diabetes, blood pressure and weight
- Nutritional and smoking cessation counseling
- Encouragement to adhere to prescribed drug therapy
- Psychosocial and vocational or occupational counseling
- Baseline and follow-up patient assessments

**Patient Education**

**Exercise training**

Exercise training alone can improve blood vessel function, cardiovascular risk factors, improved coronary blood flow, and electrical stability of the heart muscle while also reducing the risk of blood clots and cardiac work and oxygen requirements. Research has shown that average cardiac death was 26% lower in rehabilitation patients who were exercise-trained compared with those who received usual care, and there were also 21% fewer nonfatal heart attacks, 13% fewer bypass surgeries and 19% fewer angioplasties in the exercise-trained people, according to an updated scientific statement in 2005 from the American Heart Association.

**Smoking Cessation**

Counsel all patients who smoke to quit. Studies have shown that smoking triggers coronary vasospasm, reduces the anti-ischemic effects of beta-blockers, and doubles the risk of death after MI. Consider referring patients to a smoking cessation program and prescribing nicotine replacement therapy. Combining pharmacotherapy with behavioral therapy increases cessation success rates.

**Diet modifications**

A heart healthy diet is recommended to reduce LDL and blood pressure. Heart healthy diet guidelines include:

- limiting total calories from fat to ≤30% or less of the day’s total calories.
- limiting total calories from saturated fat to 8-10% of the day’s total calories.
- limiting cholesterol intake to <300 milligrams per day.

Research has shown that average cardiac death was 26% in rehabilitation patients who were exercise-trained compared with those who received usual care.
History and physical exam

- Ask about recurrent chest pain, dyspnea, palpitations, and syncope. Focus on early recognition of anginal symptoms and further evaluation as needed.
- Measure blood pressure at each follow-up visit and maintain at 135/85 mm Hg (lower in selected patients).
- Perform a cardiac exam including auscultation looking for new arrhythmias at every visit.
- Look for new murmurs or gallops and signs of congestive heart failure at every visit.

Laboratory testing

- Measure total cholesterol, LDL, HDL, and triglyceride levels at six to 12 weeks after discharge and at subsequent visits until goal LDL cholesterol <100 mg/dL is reached. HDL should be >40 mg/dL and triglycerides <150 mg/dL. Once goal is reached, measure annually. Keep in mind that if a statin drug is prescribed, liver function tests should be drawn before starting therapy and at 12 weeks, then annually thereafter. A creatinine kinase level should be obtained before starting therapy and if muscle soreness or tenderness develops during treatment.
- Measure C-reactive protein (serum value, normal <2.0 mg/L) to identify other potential risk factors for atherosclerotic disease on initial visit after discharge. Elevated levels may indicate a higher risk for a second event.

Follow-up

Patients should be followed regularly following MI, approximately every two to three months for the first year and then twice yearly.

Drug therapy

- Review medications begun in the hospital, including beta-blockers, ACE inhibitors, aspirin, statins, nitrates, and anticoagulants, and continue as appropriate. Review dose and adherent to regimen at each visit. Measure international normalized ratio (INR) every two to four weeks once levels are stable; long-term anticoagulation is only recommended in patients who are in persistent atrial fibrillation post-MI or in patients with LV thrombus by ECHO.
- Consider prescribing folic acid (1 mg/d), which has been shown to reduce serum levels of homocysteine. Evidence for the benefit of lowering homocysteine is lacking but preliminary data suggests that folic acid therapy may be beneficial in some high-risk patients.
- Review D12-2367CK 23302 hormone therapy (HT) in women. Initiation of HT in post-menopausal women with CAD is contraindicated. Whether HT should be stopped in women who are already receiving it is unknown.

Depression Screening

Talk with patients about the fact that heart attack patients feel a wide range of emotions including depression, fear, and anger, for about two to six months post-MI. The emotional aftermath of MI can be disruptive to returning to normal life, and may require counseling or other intervention. Consider screening for depression in all patients post-MI. Studies indicate that about 20% of patients experience depression after acute MI and that the presence of depression is associated with increased risk for recurrent hospitalization and death.

Patient education

- Urge exercise either by referral to a formal cardiac rehabilitation program or by establishing a home exercise program.
- Counsel regarding a heart healthy diet and consider providing a referral to dietician.
- Counsel patients who smoke about smoking cessation.
- Review symptoms requiring physician notification or need for emergency room visit.

Activity

- Provide patients with specific instruction on the type and level of activity that is permissible. Activity may be beneficial to patients’ cardiovascular and emotional health.
- Encourage daily walking immediately after hospital discharge.
- Follow driving regulations depending on applicable state laws.
- Counsel that sexual activity can be resumed in stable patients within seven to 10 days.
- Individualize instructions regarding strenuous activity, such as heavy lifting, climbing stairs and yard work, to each patient based on results of exercise testing.
- Note that no randomized clinical trials have assessed when to resume normal activity, however the ACC/AHA guidelines are in accordance with the above recommendations.

Limiting sodium intake to 2,400 milligrams a day. Consuming just enough calories to achieve or maintain a healthy weight and reduce blood cholesterol level.

Among patients who drink alcohol, moderate consumption is advised.

To assist with dietary changes, consider referring patients for consultation with a registered dietitian.