Treatment of the Post–Myocardial Infarction Patient: A Concise Review

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Abstract

- **Objective:** To review secondary prevention strategies for patients with acute coronary syndrome.
- **Methods:** Review of the literature.
- **Results:** Patients with acute myocardial infarction represent an important high-risk cohort in which secondary vascular disease prevention is likely to be particularly effective and cost-effective. Lifestyle modification such as regular exercise, weight management, and smoking cessation should be encouraged. Tight glucose control in diabetics and optimal blood pressure control are important goals. Effective pharmacologic therapies include statins, antiplatelet agents, β-blockers, and angiotensin-converting enzyme inhibitors. Attention to disease management opportunities may improve quality of care for acute myocardial infarction patients.
- **Conclusion:** Aggressive risk factor and lifestyle modification and pharmacologic therapies improve patient survival, reduce recurrent events, and improve quality of life in post–myocardial infarction patients.

Acutecoronary syndrome represents a major medical problem, accounting for 2.5 million hospitalizations and 500,000 deaths annually in the United States. Of the 2.5 million hospitalized, 1.5 million will have a final diagnosis of unstable angina and the remaining will be diagnosed with non-ST or ST segment elevation myocardial infarction. The long-term management of patients after acute myocardial infarction (AMI) presents a challenge to the clinician as treatment strategies continue to evolve. This review focuses on the optimal treatment of the post–myocardial infarction patient.

**Lifestyle Modification**

Several lifestyle modifications may improve clinical outcome in the post–myocardial infarction patient (Table). Daily walking should be encouraged immediately after discharge followed by regular structured exercise. Optimal blood pressure control is an important goal, and hypertensive patients should be appropriately educated. Systolic and diastolic blood pressures should be in the normal range (systolic < 140 mm Hg, diastolic < 90 mm Hg). Attention should be paid to complete smoking cessation in this individual. Referral to a smoking cessation program and the use of nicotine patches or gum is recommended and should be considered at discharge after an acute coronary event [1]. However, patients should be advised and warned that the high nicotine levels produced when smoking is combined with nicotine patch use may be hazardous. Bupropion, an anxiolytic agent, has been effective when added to brief regular counseling sessions in helping patients to quit smoking. Family members who live in the same household should be encouraged to quit smoking to help reinforce the patient’s effort and to decrease the risk of secondhand smoke for everyone.

Tight glucose control (HbA1c < 7.0%) in diabetics during and after AMI (DIGAMI study) has been shown to lower acute and 1-year mortality rates and microvascular disease [2]. The UK Prospective Diabetes Study (UKPDS) demonstrated that the control of glycemia reduces diabetes-related events, including AMI (16% reduction; P = 0.052), in newly detected type 2 diabetics [3–5]. Overweight patients should be recommended a structured weight loss program, with emphasis on the importance of regular exercise and a lifelong prudent diet to maintain ideal weight. If appropriate, patients need to be reassured that sexual activity is possible. The resumption of sexual activity typically can occur within 7 to 10 days in stable patients. A word of caution: nitrates and sildenafil or similar drugs such as vardenafil or tadalafil should not be used within 24 hours of each other to avoid severe hypotension.

The Vestfold Heartcare Study Group demonstrated that a comprehensive lifestyle intervention on top of a modern secondary prophylaxis regimen in a heterogeneous population resulted in a significant improvement in dietary, exercise, and smoking habits when compared with usual care. The authors further demonstrated a 22% reduction in the calculated relative 5-year risk of developing nonfatal AMI or coronary
**Table. Secondary Prevention After a Myocardial Infarction (MI)**

<table>
<thead>
<tr>
<th>Goals</th>
<th>Recommendations</th>
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<tbody>
<tr>
<td><strong>Smoking</strong></td>
<td>Assess tobacco use. Strongly encourage patient and family to stop smoking and to avoid secondhand smoke. Provide counseling, pharmacologic therapy, including nicotine replacement and bupropion, and formal smoking cessation programs as appropriate.</td>
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<td><strong>Blood pressure control</strong></td>
<td>Initiate lifestyle modification (weight control, physical activity, alcohol moderation, moderate sodium restriction, and emphasis on fruits, vegetables, and low-fat dairy products) in all patients with blood pressure &gt; 130 mm Hg systolic or 80 mm Hg diastolic. Add blood pressure medication, individualized to other patient requirements and characteristics (ie, age, race, need for drugs with specific benefits) if blood pressure is not &lt; 140 mm Hg systolic or 90 mm Hg diastolic or if blood pressure is not &lt; 130 mm Hg systolic or 85 mm Hg diastolic for individuals with heart failure or renal insufficiency (&lt; 80 mm Hg diastolic for individuals with diabetes).</td>
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<tr>
<td><strong>Lipid management</strong></td>
<td>Start dietary therapy in all patients (&lt; 7% saturated fat and &lt; 200 mg/d cholesterol) and promote physical activity and weight management. Encourage increased consumption of omega-3 fatty acids. Assess fasting lipid profile in all patients and within 24 hr of hospitalization for those with an acute event. If patients are hospitalized, consider adding drug therapy on discharge. Add drug therapy according to the following guide:</td>
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<tr>
<td><strong>Physical activity</strong></td>
<td>Assess risk, preferably with exercise test, to guide prescription. Encourage minimum of 30 to 60 minutes of activity, preferably daily or at least 3 or 4 times weekly (walking, jogging, cycling, or other aerobic activity) supplemented by an increase in daily lifestyle activities (eg, walking breaks at work, gardening, household work). Advise medically supervised programs for moderate- to high-risk patients.</td>
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<td><strong>Weight management</strong></td>
<td>Calculate BMI and measure waist circumference as part of evaluation. Monitor response of BMI and waist circumference to therapy. Start weight management and physical activity as appropriate. Desirable BMI range is 18.5–24.9 kg/m². When BMI &gt; 25 kg/m², goal for waist circumference is &lt; 40 inches in men and &lt; 35 inches in women.</td>
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<tr>
<td><strong>Diabetes management</strong></td>
<td>Appropriate hypoglycemic therapy to achieve near-normal fasting plasma glucose, as indicated by HbA₁c. Treat other risks (eg, physical activity, weight management, blood pressure, and cholesterol management).</td>
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<td><strong>Antiplatelet agents/anticoagulants</strong></td>
<td>Start and continue indefinitely aspirin 75 to 325 mg/d if not contraindicated. Consider clopidogrel 75 mg/d if aspirin contraindicated. Manage warfarin to international normalized ratio of 2.0 to 3.0 in post–MI patients when clinically indicated or for those not able to take aspirin or clopidogrel.</td>
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<tr>
<td><strong>ACE inhibitors</strong></td>
<td>Treat all patients indefinitely post–MI; start early in stable high-risk patients (anterior MI, previous MI, Killip class II [S₃ gallop, rales, radiographic CHF]). Consider chronic therapy for all other patients with coronary or other vascular disease unless contraindicated.</td>
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<tr>
<td><strong>β Blockers</strong></td>
<td>Start in all post–MI and acute ischemic syndrome patients. Continue indefinitely. Observe usual contraindications. Use as needed to manage angina, rhythm, or blood pressure in all other patients.</td>
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</table>

ACE = angiotensin-converting enzyme; BMI = body mass index; CHF = congestive heart failure; HDL = high-density lipoprotein; LDL = low-density lipoprotein; TG = triglycerides. (Adapted with permission from reference 53.)

*The use of resin is relatively contraindicated when TG > 200 mg/dL.

†Non-HDL cholesterol = total cholesterol minus HDL cholesterol.
death in this cohort with aggressive lifestyle modification, which included a low-fat diet, regular exercise, smoking cessation, psychosocial support, and education [6]. Data suggest that patients who have suffered an AMI benefit from exercise-related risk stratification and a comprehensive cardiovascular rehabilitation program [7].

**Pharmacologic Therapies**

The last decade has seen a significant increase in pharmacologic therapies with proven efficacy in reducing morbidity and mortality in patients with vascular diseases. These agents, affectionately called the “Fab Four,” include statins, antiplatelet agents, β blockers, and angiotensin-converting enzyme (ACE) inhibitors. They are individually very effective in reducing secondary cardiovascular events [8].

**Statins**

Multiple studies have demonstrated effectiveness of statin therapy in patients presenting with AMI [9–13]. Statins not only lower lipids but also have salutary effects on platelet adhesion, thrombosis, endothelial function, inflammation, and plaque stability. The Heart Protection Study (HPS) has provided further evidence of the clinical benefits of statins for a wide range of high-risk patients with coronary and vascular diseases [14]. The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT) [15] randomly assigned 10,305 patients who were not on cholesterol-lowering therapy and who had high cholesterol to placebo or atorvastatin. There were 32 fewer strokes on atorvastatin therapy (1 fewer for every 1000 treated per year) in this study [15]. The Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE-IT) trial demonstrated that among patients who have recently had an acute coronary syndrome, an intensive lipid-lowering statin regimen with atorvastatin 80 mg provided greater protection against death or major cardiovascular events than a standard regimen using pravastatin 40 mg [16]. These findings indicate that such patients benefit from early and continued lowering of low-density lipoprotein (LDL) cholesterol to levels substantially below current target levels of 100 mg/dL.

Patients should be educated regarding cholesterol reduction and their current and target cholesterol levels. Patients who have undergone revascularization derive particular benefit from cholesterol lowering [17]. The National Cholesterol Education Program expert panel III recommends a target LDL cholesterol level less than 100 mg/dL for the post-myocardial infarction patient [18]. If baseline LDL cholesterol is 130 mg/dL or greater, therapeutic lifestyle changes (TLC) with physical activity, weight loss, and maximal control of other risk factors should be started. Moreover, for most patients, an LDL-lowering drug will be required to achieve an LDL cholesterol level of less than 100 mg/dL; thus, an LDL cholesterol-lowering drug can be started simultaneously with TLC to attain the goal of therapy. If LDL cholesterol levels are between 100 and 129 mg/dL, either at baseline or on LDL-lowering therapy, several therapeutic approaches are available, including initiation or intensification of lifestyle and/or drug therapies specifically to lower LDL [18]. The treatment of hypertriglyceridemia and low high-density lipoprotein cholesterol (< 40 mg/dL) with gemfibrozil has resulted in reduced cardiovascular events in men with coronary heart disease [19]. If the patient has significantly elevated triglyceride levels (> 500 mg/dL), LDL-lowering therapies can be delayed and fibrates or niacin should be considered as initial therapy.

Patients in whom lipid-lowering therapy is begun in the hospital are much more likely to be on such therapy at a later time. The Cardiovascular Hospitalization Atherosclerosis Management Program (CHAMP) study demonstrated the advantages of early initiation of statin therapy. In this study, in-hospital initiation of lipid-lowering therapy increased the percentage of patients treated with statins 1 year later from 10% to 91% and among those with an LDL cholesterol less than 100 mg/dL from 6% to 58% [20].

**Antiplatelet Agents**

Antiplatelet therapy has been demonstrated to be significantly beneficial in patients with AMI, with a survival advantage demonstrated with aspirin by the Antithrombotic Trialists Collaboration meta-analysis [21]. Antiplatelet therapy should be initiated promptly on presentation and continued indefinitely. In patients with non–ST elevation MI in whom an early noninterventional approach is planned, it is now recommended that clopidogrel should be added to aspirin as soon as possible on admission and administered for at least 1 month and for up to 9 months [22]. In patients for whom a percutaneous coronary intervention is planned, clopidogrel should be started and continued for at least 1 month and up to 12 months in patients who are not at high risk for bleeding [23]. The Clopidogrel for the Reduction of Events During Observation (CREDO) trial demonstrated that 12 months of dual antiplatelet therapy with aspirin and clopidogrel significantly reduces the risk of adverse ischemic events in patients undergoing percutaneous coronary intervention [24]. In patients taking clopidogrel in whom elective coronary artery bypass grafting is planned, the drug should ideally be withheld for 5 to 7 days before surgery. The recommendation for dual antiplatelet therapy with clopidogrel is derived from the results of the Clopidogrel in Unstable Angina to Prevent Recurrent Events (CURE) trial [25], which randomly assigned unstable angina/non–ST elevation myocardial infarction patients to aspirin alone or aspirin plus clopidogrel.

There was a 20% reduction in the composite endpoint of cardiovascular death, myocardial infarction, or stroke with only
a slight increase in the risk of bleeding with combination antiplatelet therapy. The factors that limit more widespread use of clopidogrel in this setting are cost and increased bleeding complications in patients who undergo bypass surgery. Two ongoing trials, COMMIT/CCS-2 (Clopidogrel and Metoprolol Myocardial Infarction Trial/Second Chinese Cardiac Study) and CLARITY-TIMI 28 (Clopidogrel as Adjunctive Reperfusion Therapy/Thrombolysis In Myocardial Infarction Study 28) will further evaluate the role of dual antiplatelet therapy in patients presenting with AMI.

ACE Inhibitors
The Heart Outcomes Prevention Evaluation study demonstrated that ramipril, an ACE inhibitor, significantly reduced the rate of cardiovascular death, myocardial infarction, and stroke in patients at high risk of cardiovascular events [26]. One study has demonstrated that ACE inhibition reduces troponin release in non–ST elevation AMI, an effect that is perhaps mediated by the beneficial effects of ACE on vascular reactivity and the coagulation system [27]. The European Trial on Reduction of Cardiac Events with Perindopril in Stable Coronary Artery Disease (EUROPA) demonstrated that among patients with stable coronary heart disease without apparent heart failure, perindopril can significantly improve outcome [28]. About 50 patients need to be treated for a period of 4 years to prevent 1 major cardiovascular event [28]. Current American College of Cardiology/American Heart Association (ACC/AHA) guidelines suggest that ACE inhibitors should be considered for secondary prevention for all patients with known coronary disease [29] and strongly recommended for patients with clinical heart failure, left ventricular dysfunction, or AMI accompanied by hypertension.

β Blockers
β Blockers have been shown in many clinical trials to improve the survival rate of patients with recent AMI. These agents have been shown in several large randomized trials to improve the survival rate and prevent stroke and heart failure in patients with coronary artery disease [30]. In the Atenolol Silent Ischemia Trial (ASIST), patients with documented coronary disease and angina were treated with 100 mg of atenolol daily [31]. After 1 year, fewer patients in the atenolol group experienced the combined endpoint of death, ventricular tachycardia and fibrillation, myocardial infarction, hospitalization, aggravation of angina, or revascularization [31]. The atenolol-treated patients also had a longer time until their first adverse event. β Blockers are currently indicated in all patients after AMI in the absence of contraindications [22]. The absolute cardiac contraindications for the use of β blockers are severe bradycardia, preexisting high-grade atrioventricular block, sick sinus syndrome, and severe unstable heart failure (mild to moderate heart failure is actually an indication for β blockers). Asthma and active bronchospasm are relative contraindications.

Thus, medications such as statins, antiplatelet agents, β blockers, and ACE inhibitors have been associated with significantly improved outcomes in patients presenting with AMI. We recently demonstrated significant synergistic effects of the combination of antiplatelet therapy, statins, ACE inhibitors and β blockers in patients presenting with acute coronary syndromes. Combined treatment correlated with a striking survival advantage at just 6 months of follow-up (Figure) [8]. Patients should optimally be discharged on the “Fab Four.” aspirin, a β blocker, a statin, and an ACE inhibitor (Table).

Disease Management
Antiplatelet agents, statins, β blockers, and ACE inhibitors are very effective in reducing secondary cardiovascular events. Despite strong and unequivocal benefits of these agents, secondary preventive therapies continue to be underutilized [32,33]. Quality improvement projects that promote use of systems that embed guideline knowledge into the care process itself may significantly increase the utilization rate of these effective therapies. In one such improvement initiative, the Guidelines Applied in Practice (GAP) project in the state of Michigan, 1 physician and 1 nurse leader from outside the hospital system from the Southeast Michigan Quality Forum were assigned to serve as opinion leaders [34]. They assisted in the development of quality improvement plans, tool kit customization, and project implementation. The project was initiated at each hospital with grand rounds that introduced the project protocol and presented the hospital’s baseline quality indicator performance as compared with the state average and the aggregate of other GAP hospitals. The project demonstrated quality improvement among a variety of institutions, patients, and caregivers [34]. An important component of the GAP tools included providing more patients with education and empowerment to help them better understand their disease and the long-term goals of its treatment, including lifestyle strategies. Even more important was the emphasis on standard orders and discharge tools that reminded caregivers to consider evidence-based therapies in every patient. Creation of a system and inclusion of the patient, nurse, and physician in a review of care priorities are methods that promote quality [34].

A similar initiative, the Get With The Guidelines program, was developed and piloted by the AHA to reduce the gap in the application of secondary prevention guidelines in hospitalized cardiovascular disease patients [35]. The Get With The Guidelines program, a template of learning sessions with didactic presentations, best practices sharing, and collaborative
multidisciplinary team meetings supported by an internet-based data collection and reporting system, has now been adopted as a national program.

Cardiac Rehabilitation

Cardiac rehabilitation programs combine structured exercise training with education about coronary risk factor modification techniques. Formal rehabilitation programs have been shown to improve functional capacity, promote compliance, decrease emotional distress, improve quality of life, reduce cardiovascular mortality, and reduce risk of subsequent coronary events [36–39]. Despite these benefits, only 15% to 20% of qualified patients participate in cardiac rehabilitation due to lack of physician referral, poor motivation, logistic or financial constraints, or a combination of these factors [40]. Home exercise training programs have been shown to be beneficial in certain low-risk patient groups and offer the advantages of convenience and low cost but may lack the elements of education and group interaction that structured cardiac rehabilitation programs have.

Antidepressants

The prevalence of major depression in individuals with coronary artery disease ranges from 15% to 23% [41–43]. Many large studies have identified depression as a potent and independent risk factor for adverse cardiovascular outcomes in patients with coronary artery disease [44–47]. There is, however, considerable evidence that tricyclic antidepressants are potentially dangerous in patients with coronary artery disease [48]. The Sertraline Antidepressant Heart Attack randomized Trial (SADHART) suggested that sertraline, a selective serotonin reuptake inhibitor, is a safe and effective treatment for recurrent depression in patients with recent myocardial infarction or unstable angina [49]. The larger Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) randomized trial demonstrated that cognitive behavioral therapy improved depression and social isolation after AMI but did not increase event-free survival [50]. Post hoc analysis of the subgroup that was treated with a selective serotonin reuptake inhibitor antidepressant revealed significantly lower risk of death or nonfatal myocardial infarction [50].

Summary

AMI remains a major public health issue and is the leading cause of death in the United States [51]. Evidence from clinical studies suggests that aggressive risk factor and lifestyle modifications and pharmacologic therapies improve patient survival, reduce recurrent events, and improve quality of life. Patients with an AMI represent an important high-risk cohort in which secondary vascular disease prevention is likely to be particularly effective and cost-effective. Clinicians have an opportunity to provide high-quality and appropriate evidence-based care to this high-risk cohort and to seize this opportunity to aggressively treating the underlying atherosclerotic process through lifestyle modifications and effective pharmacologic therapies. However, despite strong and unequivocal benefits of these agents, secondary preventive therapies continue to be underutilized as demonstrated in
previous studies [32,52]. Attention to these disease management opportunities results in a significant survival advantage in this high-risk cohort and underscores the importance of ACC- and AHA-initiated projects such as the GAP [34] and the Get With The Guidelines programs [35] to improve utilization of appropriate therapies.

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