Medical management after myocardial infarction

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“Control of coronary risk factors for secondary prevention is a cornerstone in post-MI patients to limit the progression of coronary heart disease”

First draft submitted: 23 March 2019; Accepted for publication: 28 March 2019; Published online: 31 May 2019

Keywords: angiotensin-converting enzyme inhibitors • antiplatelet drugs • β blockers • coronary risk factors • myocardial infarction • statins

It is well known that patients that have suffered from a myocardial infarction (MI) are at a significantly increased risk of another infarction in the future, making it imperative that appropriate secondary preventative measures are taken in the attempt to reduce this risk. This article aims to offer a brief summary of current recommendations for the medical management of patients' post-MI, based on the current available evidence.

Management of major coronary risk factors

Control of coronary risk factors for secondary prevention is a cornerstone in post-MI patients to limit the progression of coronary heart disease (CHD) and reduce cardiovascular events and mortality.

The American College of Cardiology (ACC)/American Heart Association (AHA) 2013 guidelines recommend that patients should be counseled on smoking cessation during and after hospitalization for MI [1]. A smoking cessation program should be recommended to smokers [1,2]. Patients should be advised at every physician office visit to avoid passive exposure to tobacco smoke at work, at home and in public places [2].

The patients with hypertension should have their blood pressure lowered to less than 130/80 mmHg by lifestyle measures plus antihypertensive drugs [3]. The patients with hypertension after MI should be treated with a β blocker plus an angiotensin-converting enzyme (ACE) inhibitor [3–5]. If a third antihypertensive drug is indicated, it should be a dihydropyridine calcium channel blocker (CCB), aldosterone antagonist or thiazide diuretic (preferably chlorthalidone) depending on the comorbidities [3–5]. If the left ventricular ejection fraction (LVEF) is reduced, the β blocker used should be either carvedilol, metoprolol succinate or bisoprolol [3–5].

The patients with hypercholesterolemia after MI should be treated with lifestyle measures plus high-dose statins (40–80 mg of atorvastatin or 20–40 mg of rosuvastatin) or maximum tolerated statin therapy [6]. The patients after MI with either a recent acute coronary syndrome or history of ischemic stroke, or symptomatic peripheral arterial disease or if they have multiple high-risk conditions (age 65 years and older, heterozygous familial hypercholesterolemia, history of prior coronary revascularization, diabetes mellitus, hypertension, chronic kidney disease, current smoking, history of heart failure) who have on maximally tolerated statin therapy a serum LDL-cholesterol of ≥ 70 mg/dl, should have ezetimibe added to statin therapy [6]. If the LDL-cholesterol is still ≥ 70 mg/dl on maximally tolerated statin therapy plus ezetimibe, consider the addition of alirocumab or evolocumab to the therapeutic regimen [6].

Type 2 diabetes mellitus should be treated with lifestyle measures, an appropriate diet, weight reduction if indicated and exercise. Metformin is generally the initial drug to treat hyperglycemia [7]. A hemoglobin A1c target of $<7.0\%$ is reasonable [2]. However, for elderly frail patients with multiple comorbidities, a target of 7.0–7.9% is recommended.

Obesity should be treated with lifestyle modification. Guidelines from the AHA/ACC/Obesity Society recommend that patients with a BMI ≥ 35 kg/m² with an obesity-related comorbid condition who have not responded to lifestyle modification with or without pharmacotherapy to achieve sufficient weight loss should be referred to an experienced bariatric surgeon for consideration of bariatric surgery [8].

General treatment recommendations post-MI

The 2014 ACC/AHA guidelines recommend that patients after MI should be referred to a comprehensive cardiac rehabilitation program [9]. A symptom-limited exercise test is recommended before beginning an exercise program to know the safety of an exercise program and to guide the initial exercise program.

Aspirin 75–162 mg daily is recommended in all patients with CHD unless contraindicated [2,10]. Clopidogrel 75 mg daily is recommended as an alternative for patients who are intolerant of or allergic to aspirin [2,10]. The addition of a thienopyridine (clopidogrel 75 mg daily, prasugrel 10 mg daily or ticagrelor 90 mg twice daily) in patients after an acute coronary syndrome, especially in those who have received a stent during percutaneous coronary intervention, causes a greater reduction in cardiovascular events than aspirin alone with an increased risk of bleeding [2,10]. Clopidogrel is generally used in elderly patients after MI. Prasugrel is not recommended for use in patients older than 75 years, for those with a prior stroke or transient ischemic attack or those with low body weight [9]. Proton pump inhibitors reduce the risk of gastrointestinal bleeding in patients being treated with dual antiplatelet therapy.

The AHA/ACC guidelines recommend as indications for long-term use of anticoagulants after MI: secondary prevention of MI in post-MI patients unable to tolerate daily aspirin or clopidogrel; in post-MI patients with atrial fibrillation; in post-MI patients with a LV thrombus, and; in post-MI patients with a mechanical heart valve [2]. Routine use of an anticoagulant with dual antiplatelet therapy is associated with an unacceptable bleeding risk, especially in elderly patients [11].

β blockers are very effective antianginal and anti-ischemic agents that should be administered to all patients with angina pectoris or silent myocardial ischemia due to CHD unless there are specific contraindications to their use [12]. Teo *et al.* [13] analyzed 55 randomized controlled trials comprising 53,268 patients that investigated the use of β blockers after MI. β blockers significantly reduced all-cause mortality by 19% in this study [13]. A meta-analysis of trials also demonstrated that the use of β blockers after non-Q-wave MI is likely to reduce all-cause mortality and recurrent MI by 25% [14]. The AHA/ACC guidelines recommend that patients without a clear contraindication to β blocker therapy should receive β blockers within a few days of MI if not initiated acutely [2]. If the LVEF is reduced, carvedilol, metoprolol succinate or bisoprolol should be administered indefinitely. If the LVEF is normal, β blockers should be used for at least 3 years. It is reasonable to continue β blockers indefinitely in these patients [2]. β blockers with intrinsic sympathomimetic activity should not be used.

Long-acting nitrates are effective antianginal and anti-ischemic drugs and should be administered alongside β blockers following MI in patients that also have angina pectoris [12,15]. The prescribed dosage of oral isosorbide dinitrate should be gradually increased to a dose of 30–40 mg three-times daily, if tolerated. A 60 mg dose of isosorbide-5-mononitrate may be given once daily. There should be a nitrate-free interval of 12 h each day in order to avoid nitrate tolerance. During the nitrate-free interval, β blockers should be used to prevent angina pectoris and rebound myocardial ischemia.

In the European trial on reduction of cardiac events with perindopril in stable coronary artery disease (EUROPA trial), at 4.2-year follow-up of 13,655 patients with prior MI and stable CHD compared with placebo, patients randomized to the ACE inhibitor perindopril had a 20% significant reduction in cardiovascular death, recurrent MI or cardiac arrest [16]. The AHA/ACC guidelines recommend administration of an ACE inhibitor indefinitely after MI, especially if the LVEF is $\leq 40\%$ and in patients who have hypertension, diabetes mellitus or chronic kidney disease, unless there are contraindications to their use [2]. It is reasonable to use an angiotensin receptor blocker after MI in patients who are ACE inhibitor tolerant [2].

At 16-month follow-up of 6632 patients after MI with a LVEF of $\leq 40\%$ and either congestive heart failure or diabetes mellitus treated with an ACE inhibitor or angiotensin receptor blocker and 75% treated with β blockers, compared with placebo treatment, patients randomized to the aldosterone antagonist eplerenone 50 mg daily had a 15% significant reduction in all-cause mortality and a 13% significant reduction in cardiovascular death or hospitalization for cardiovascular events [17]. The AHA/ACC guidelines recommend use of an aldosterone antagonist after MI in patients receiving therapeutic doses of an ACE inhibitor plus a β blocker who have a LVEF of $\leq 40\%$ and either diabetes mellitus or heart failure without significant renal dysfunction or hyperkalemia [2].

A CCB should not be used after MI unless it is indicated for the treatment of hypertension in patients already receiving a β blocker plus an ACE inhibitor or in patients with persistent angina pectoris despite treatment with a β blocker plus a long-acting nitrate [12]. A nondihydropyridine CCB such as verapamil or diltiazem should be added to the therapeutic regimen if the LVEF is normal. If the LVEF is abnormal, a dihydropyridine CCB such as amlodipine or felodipine should be added to the therapeutic regimen.

At 6.8-year follow-up of 2763 women with documented CHD in the Heart Estrogen/Progestin Replacement Study (HERS), compared with placebo, hormone replacement did not reduce cardiovascular events and insignificantly increased all-cause mortality by 10% [18]. Hormone replacement therapy significantly increased venous thromboembolism by 208% and biliary tract surgery by 48%. Hormone replacement therapy also insignificantly increased the incidence of any cancer by 19% and of any fracture by 4%. The investigators concluded that hormone replacement therapy should not be used to reduce cardiovascular events in women with CHD [18]. On the basis of the available data, current AHA/ACC guidelines give the following class III recommendation (harmful, should not be performed) for the secondary prevention of coronary events in postmenopausal women after MI [9].

A meta-analysis of 59 randomized controlled trials comprising 23,229 patients that investigated the use of class I antiarrhythmic drugs after MI showed that these drugs significantly increased mortality by 14% [13]. β blockers are the only antiarrhythmic drugs that have been demonstrated to reduce mortality in patients with nonsustained ventricular tachycardia or complex ventricular arrhythmias after MI in patients with abnormal [19] or normal LVEF [20]. The ACC/AHA/Heart Rhythm Society guidelines recommend implantation of an automatic implantable cardioverter-defibrillator to reduce all-cause mortality in New York Heart Association class II or III patients with a LVEF <35% due to a prior MI at least 40 days previously and in New York Heart Association class I patients with a LVEF <30% due to a prior MI at least 40 days previously [21].

Evidence from cohort studies and a randomized clinical trial indicate that annual vaccination against seasonal influenza reduces cardiovascular events and mortality in patients with cardiovascular disease [22]. The AHA/ACC guidelines recommend an annual influenza vaccination in the patients with CHD [2,22].

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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