Secondary prevention after acute coronary syndromes

The GP's role

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In patients who have survived an acute coronary syndrome (ACS), optimal secondary prevention is crucial to minimise morbidity and mortality. Although secondary prevention starts during the index hospital admission, GPs have a key role in ensuring it is instituted and maintained, and in supporting patients so that they have the best chance of long-term survival.

KEY POINTS

- Although survival after acute coronary syndrome (ACS) has improved, ACS is still associated with significant morbidity and mortality.
- Secondary prevention is crucial to minimising the risk of future cardiovascular events after ACS.
- Secondary prevention measures extend beyond pharmacological therapy alone and patients may benefit from the input of a multidisciplinary team.
- Support of a GP is crucial to achieving long-term success in secondary prevention therapy.

Coronary artery disease (CAD) and its consequences (including myocardial infarction, cardiac arrest and heart failure) are the leading causes of death in Australia.[1] Acute coronary syndrome (ACS) is a spectrum of disorders all caused by CAD, ranging from unstable angina to acute myocardial infarction and sudden cardiac death. Treatment options for ACS have improved significantly. Although a significant proportion of patients are managed with medical therapy alone, many undergo revascularisation with percutaneous coronary intervention (PCI) or coronary artery bypass graft surgery and can achieve good long-term survival.

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As short-term survival after an ACS has improved, the importance of secondary prevention therapy to prevent long-term morbidity, hospital readmissions and mortality has increased significantly. There is good evidence to show that patients who engage in secondary prevention therapies (both pharmacological and lifestyle based) have significantly lower rates of cardiovascular events in the first year after an ACS.[2] Morbidity and repeat cardiovascular events after an ACS also place a significant economic and resource burden on the healthcare system. Secondary prevention therapy must be instituted before patients

are discharged from hospital after presentation with an ACS. However, GPs have a key role in ensuring ongoing adherence to prescribed cardioprotective medications, risk factor optimisation and adoption of healthy lifestyle behaviours.[3]

This article outlines the key components of secondary prevention therapy that can help patients after an ACS achieve a favourable long-term outcome. The components are summarised in the Box.

Pharmacological therapy

National and international guidelines recommend five main classes of medications that all patients should be on after an ACS.[4,5] There may be some variations to this in clinical practice, such as in patients requiring oral anticoagulation (e.g. for atrial fibrillation or prosthetic heart valves), which should be discussed with the patient's cardiologist. Some medications should be continued lifelong whereas others may be discontinued after 12 months if certain conditions are met. Frequent review to ensure appropriateness of drug therapy as well as to reinforce to patients the importance of medication adherence is essential.

Aspirin

All patients who have experienced an ACS should take low-dose aspirin (100 to 150 mg daily) indefinitely, regardless of whether they were treated with revascularisation or with medical therapy alone. Aspirin has well-proven benefits in preventing repeat cardiovascular events in patients with CAD. Those who experience gastrointestinal side effects from aspirin may benefit from switching to enteric-coated aspirin or taking a proton pump inhibitor as well.

Second antiplatelet agent

Guidelines state that patients should receive dual antiplatelet therapy with aspirin and a second antiplatelet agent (a P2Y12 inhibitor) for 12 months after an ACS.[4] Dual antiplatelet therapy may be discontinued earlier or continued for beyond 12 months depending on the extent of CAD, type of stent implanted (bare metal or drug eluting), risk of bleeding, need for major surgery and need for anticoagulation. These decisions should be made in conjunction with the patient's cardiologist.

Until a few years ago, clopidogrel (75 mg daily) was the most widely used second antiplatelet agent. It can be used both in patients after an ACS who are medically managed and in those who have been revascularised with PCI.[6] In the past few years, two newer antiplatelet agents have emerged – prasugrel and ticagrelor. These have both been shown to be associated with fewer recurrent ischaemic events than clopidogrel but are associated with an increased risk of bleeding.[7,8] Prasugrel (10 mg daily) is indicated only for patients post ACS treated with PCI and not for those who are medically managed. Also, prasugrel should not be used in elderly patients (over 75 years of age), those who weigh less than 60 kg and those with previous stroke or transient ischaemic attack because of an increased risk of bleeding in these subgroups.

Ticagrelor (90 mg twice daily) can be used in all patients after an ACS regardless of treatment strategy (class I indication).[5] Up to 20% of patients taking ticagrelor may experience dyspnoea, necessitating a change of antiplatelet agent, although this usually happens early after starting treatment.

RECOMMENDED COMPONENTS OF SECONDARY PREVENTION AFTER AN ACS

- Prescribe pharmacological therapy
  - aspirin
  - second antiplatelet agent (e.g. clopidogrel, prasugrel, ticagrelor)
  - cholesterol-lowering therapy (statin +/– ezetimibe, fenofibrate, evolocumab)
  - beta blocker: consider a cardioselective beta blocker if there is left ventricular systolic dysfunction
  - ACE inhibitor or angiotensin receptor blocker
- Optimise cardiovascular risk factors
  - control blood pressure
  - optimise lipid profile
  - screen for and manage diabetes
- Encourage lifestyle modifications
  - smoking cessation
  - regular moderate-intensity physical activity
  - healthy diet
  - healthy weight
- Recommend cardiac rehabilitation
- Screen for and treat depression
- Ensure patient has chest pain management plan

Cholesterol-lowering therapy

All patients who have survived ACS should take high-dose statin therapy irrespective of their cholesterol levels. This guideline recommendation is based on a robust body of evidence, making statins a key element of secondary prevention therapy. Statins should be continued indefinitely, although lowering the dose may be considered in the longer term if LDL cholesterol (LDL-C) levels can be maintained below the target level.

If LDL-C levels continue to exceed the target level despite high-dose statin therapy then ezetimibe 10 mg daily can be added, as it has been shown to reduce LDL-C levels

TABLE. GUIDELINE-RECOMMENDED TARGETS FOR CARDIOVASCULAR RISK FACTORS IN PATIENTS AFTER AN ACS[10]

Risk factor	Target
Blood pressure	<130/80 mmHg
Cholesterol	LDL-cholesterol <1.8 mmol/L HDL-cholesterol >1.0 mmol/L Triglycerides <2.0 mmol/L
Diabetes	HbA_{1c} <53 mmol/mol (<7%)
Body mass index	<25 kg/m^2
Waist circumference	<94 cm for men, <80 cm for women

Abbreviation: ACS = acute coronary syndrome.

and recurrent cardiovascular events when used in addition to statins.[9] Although statins should be considered first-line therapy, the addition of fibrates (e.g. fenofibrate 145 mg daily) may be considered in patients with high triglyceride and low HDL cholesterol (HDL-C) levels.[10]

In patients with CAD who are unable to achieve LDL-C targets on oral therapy, there is an emerging role for proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors such as evolocumab, which is given as a single, monthly, subcutaneous injection. The recently published FOURIER trial showed that evolocumab added to statins in patients with known CAD can significantly reduce cardiovascular morbidity and mortality.[11] Evolocumab is currently available under the PBS only for patients with familial hypercholesterolaemia (requiring an authority prescription).

Beta blockers

All patients who have experienced an ACS should take a beta blocker for at least 12 months unless there are well-documented contraindications, such as severe asthma with bronchodilator reversibility, significant cardiac conduction disease or severe peripheral vascular disease. Patients who have left ventricular systolic dysfunction, as evidenced by a reduced left ventricular ejection fraction, should be commenced on a cardioselective beta blocker (e.g. metoprolol, bisoprolol, carvedilol or nebivolol). Beta blocker doses should be uptitrated to the maximum tolerated dose, which may need to be done slowly and therefore in the outpatient setting by the GP. If left ventricular systolic function is normal after 12 months then cessation of beta blockers should be considered, because there is limited evidence supporting their use in patients with stable CAD and preserved left ventricular function. However, if there is persistent left ventricular systolic dysfunction then lifelong beta blocker therapy is recommended.[12]

ACE inhibitors and angiotensin receptor blockers

After a myocardial infarction, all patients should take an ACE inhibitor or angiotensin receptor blocker (ARB) unless contraindicated at the maximum tolerated dose. The evidence supporting the use of these drugs is strong in those with left ventricular systolic dysfunction after ACS and they should continue using them lifelong.[13] ARBs are supported by a less extensive evidence base than ACE inhibitors and therefore should be used only in patients with severe side effects of ACE inhibitors, such as persistent dry cough or angioedema.

Optimisation of cardiovascular risk factors

Management of cardiovascular risk factors and adjustment of treatments to achieve set targets are an important element of outpatient secondary prevention therapy that are facilitated by a lifelong commitment between the patient and healthcare provider (Table). Risk factor management has been undisputedly shown to reduce the risk of recurrent cardiovascular events. This task often falls to the GP, who is well placed to set targets and ensure they are met through regular reviews and adjustments to therapy. Chronic disease management plans may also help.

Blood pressure control

Current national guidelines recommend a blood pressure target of 130/80 mmHg or below for all patients after an ACS.[10] ACE inhibitors, ARBs and beta blockers should be uptitrated to maximal tolerated doses for all patients post ACS. If blood pressure targets are still not met then other antihypertensive agents, including spironolactone, thiazide diuretics and calcium channel blockers, can be used depending on patient characteristics. In patients who have left ventricular systolic dysfunction and blood pressure above the target level, spironolactone may be of particular benefit and should be considered.

Improve lipid profile

Current national guidelines recommend a target LDL-C level of less than 1.8 mmol/L, HDL-C level of more than 1.0 mmol/L and a triglyceride level of less than 2.0 mmol/L.[10] The LDL-C level is the most important predictor of future cardiovascular events and, in general, the lower the LDL-C level, the better. In addition to cholesterol-lowering pharmacotherapy mentioned previously, dietary modification is crucial to the optimal management of hypercholesterolaemia. All patients should be advised on dietary modification to lower the consumption of saturated fats and simple sugars, while aiming for regular consumption of fruits and vegetables. Some patients may benefit from referral to a dietitian.

Diabetes screening and management

Patients with ACS are usually screened for diabetes during their hospital admission because up to 20% of patients who experience an ACS have previously undiagnosed type 2 diabetes.[14] Nondiabetic patients with CAD need regular review in the long term to screen for the development of diabetes because these patients often have or develop the metabolic syndrome.

Patients should be screened with measurement of fasting plasma glucose

level, with diabetes diagnosed if fasting plasma glucose is 7 mmol/L or higher. If fasting plasma glucose is in the range 5.5 to 6.9 mmol/L then an oral glucose tolerance test should be performed to confirm the presence or absence of diabetes. Patients with impaired glucose tolerance or diabetes should be referred to a diabetes educator and dietitian as well as, potentially, an endocrinologist if glycaemic control is poor. Patients with diabetes should aim for a target glycated haemoglobin (HbA_{1c}) level of less than 7%. Care should be taken to avoid hypoglycaemia (particularly in elderly patients), because it is known to be associated with worse cardiovascular outcomes.[15]

Lifestyle modifications

Lifestyle modifications incorporating a healthy diet, smoking cessation, increased physical activity and maintenance of a healthy body weight are crucial to favourable outcomes in the long term for all patients after an ACS. Cardiologists and GPs have a key role to emphasise regularly the importance of making longstanding and sustainable lifestyle modifications. Referral to other members of a multidisciplinary team, including dietitians, diabetic educators and clinical psychologists, should be considered if appropriate.

Smoking cessation

It is imperative that all patients with CAD who smoke aim to achieve complete abstinence from smoking. Patients with CAD who continue to smoke are more likely to have unfavourable outcomes than those who quit smoking. Smoking status should be assessed at each visit, and patients who continue to smoke need to be counselled and supported to achieve abstinence. Several pharmacological and nonpharmacological resources are available to help patients achieve smoking cessation, and best results are obtained when both types of treatment are combined.

Nonpharmacological resources include Quitline (13 78 48), which can provide psychosocial support by phone and advise on strategies to improve smoking cessation rates. Pharmacological therapeutic options include nicotine replacement therapy, varenicline and bupropion. Nicotine replacement therapy can be used safely in patients with stable CAD. There is also growing evidence that it can be used safely under close medical supervision in patients within two weeks of an ACS, cerebrovascular event or a significant cardiac arrhythmia. Varenicline or bupropion can be used as monotherapy or combined with nicotine replacement therapy if necessary. All pharmacotherapies should be combined with resources for psychosocial support to achieve best results. Participation in a comprehensive support and counselling program for smoking cessation is

a requirement to access subsidised treatment with varenicline under the PBS.

Physical activity

All patients with CAD should undertake at least 30 minutes of moderate-intensity activity on at least five days of the week. Most patients who have had an ACS should be encouraged to start some physical activity from the time of hospital discharge, and to build up their activities level gradually. Aerobic activities such as walking or swimming are preferred over weight-training activities.

Healthy diet

The National Heart Foundation of Australia provides clear guidelines on what constitutes a healthy diet, which includes mainly plant-based foods, moderate amounts of reduced-fat dairy products and lean meats, and a reduced salt intake.[10] There is good evidence to show that Mediterranean-type diets including regular consumption of vegetables, monounsaturated fats (such as found in olive oil), nuts and lean meats or fish can reduce the risk of sudden cardiac death and myocardial infarction.[16] Patients and their families should be educated on these dietary guidelines to make lifelong dietary changes.

Maintenance of a healthy weight

Body mass index (BMI) and waist circumference should both be monitored in patients after an ACS as high BMI and central obesity are both risk factors for CAD. Waist circumference should be less than 94 cm for men and less than 80 cm for women, and BMI should be less than 25 kg/m^2. Patients may need to be encouraged and supported to increase physical activity and reduce caloric intake. Meal replacement therapy and bariatric surgery could be considered for patients with morbid obesity (BMI more than 35 kg/m^2), although the latter has not yet been well studied in patients post ACS.

Cardiac rehabilitation

After ACS, all patients should be actively referred to a cardiac rehabilitation program during their index hospital admission. There is good evidence showing that cardiac rehabilitation is associated with better quality of life in patients after an ACS. Cardiac rehabilitation assists patients in improving physical activity and incorporating healthy lifestyle changes into their daily life. However, participation in cardiac rehabilitation continues to remain low, perhaps because many patients perceive their revascularisation procedures as a one-stop cure for their condition. It has been shown that a patient's decision to attend cardiac rehabilitation is heavily influenced by whether their doctor directly recommends they attend the program.[17]

Management of depression

It is increasingly being recognised that depression is three times more common in patients who have had an ACS compared with the general population. One in three survivors of an acute myocardial infarction experience symptoms of depression within 12 months.[18] Among patients post ACS, those with depression tend to have poorer outcomes compared with those without depression, largely because depression is associated with poor adherence to secondary prevention therapy.[19] Depression is often undiagnosed during the hospital admission, particularly as patients spend less and less time in hospital after an ACS. Depressive symptoms may also manifest weeks to months after the ACS event. All patients who have experienced an ACS should be screened for depression, which is more likely to be diagnosed by GPs who have an established relationship with the patient. Pharmacotherapy is indicated in patients with major depressive illness, and selective serotonin reuptake inhibitors (SSRIs) are the preferred agents because of their minimal cardiac side effects. There is, however, limited evidence supporting SSRI use in patients post ACS with milder features of depression.

Chest pain management plan

All patients who have experienced an ACS should have a chest pain management plan to assist them in the safe long-term self-management of CAD. Patients need to be educated about recognising angina, the importance of having access to sublingual glyceryl trinitrate at all times (in tablet or spray form) and a plan to call an ambulance if they have severe symptoms of angina or angina equivalents that last more than 10 minutes despite the use of glyceryl trinitrate. It is imperative that patients and their immediate family members are familiar with this emergency plan.

Conclusion

GPs have a key role in the management of patients who survive an ACS by ensuring that optimal secondary prevention therapy is instituted and maintained. Adherence to evidence-based pharmacological and nonpharmacological therapies can help to give these patients the best chance of long-term health and survival. MT

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A list of references is included in the online version of this article (www.medicinetoday.com.au).

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