PEER REVIEWED FEATURE

Acute coronary syndromes

The importance of secondary prevention

MATIAS B. YUDI MB BS, FRACP
ANDREW E. AJANI MB BS, MD, FRACP

Managing patients with acute coronary syndromes extends well beyond hospitalisation with the index event. It is essential to recognise the importance of secondary prevention as patients with acute coronary syndromes experience higher mortality and morbidity and are at high risk of future cardiovascular events. GPs play a crucial role in optimising secondary prevention to ensure these patients receive the best possible cardiac care.

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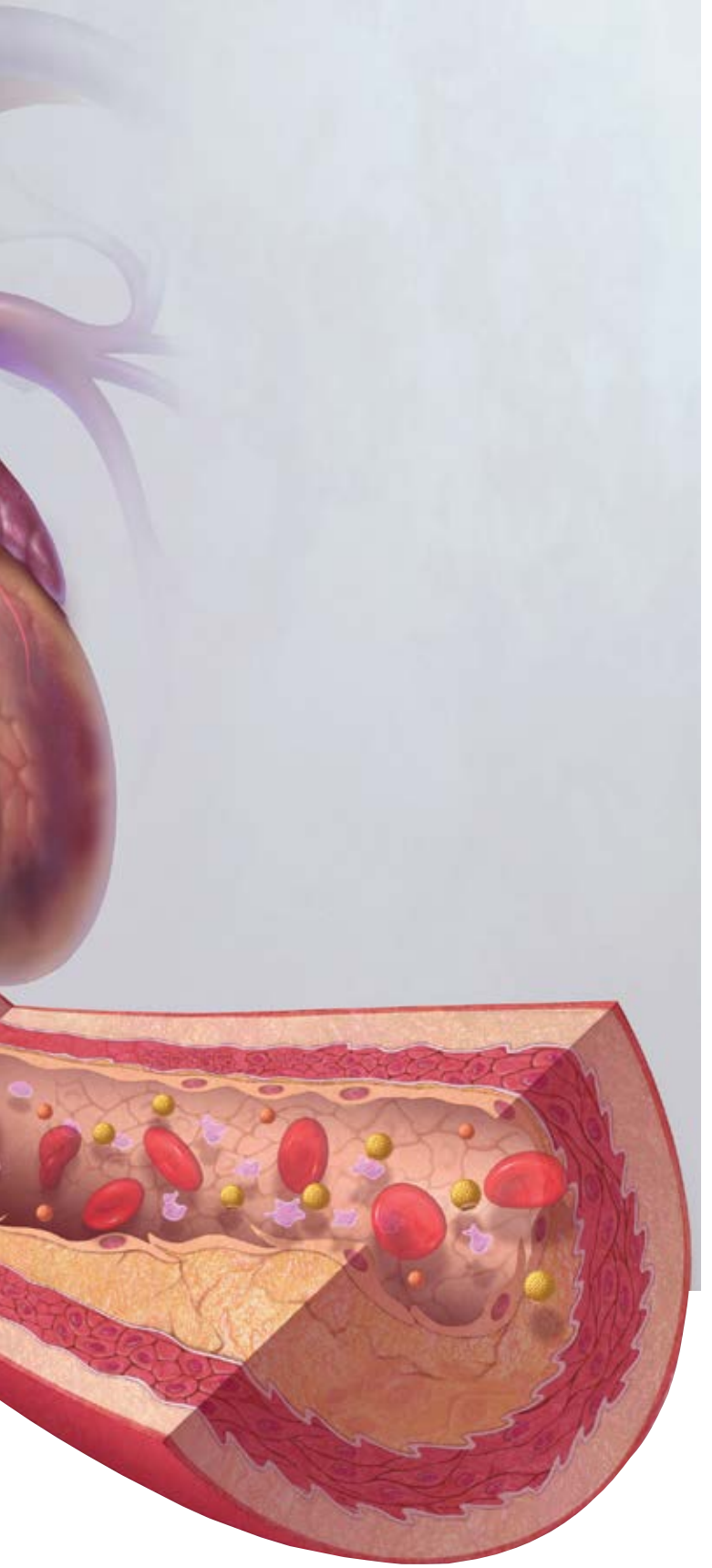
Dr Yudi is an Interventional Cardiology and Research Fellow at Austin Health, Melbourne. Associate Professor Ajani is an Interventional Cardiologist and Director of the Coronary Care Unit at Royal Melbourne Hospital, Melbourne. He also holds academic positions at the Centre of Cardiovascular Research & Education in Therapeutics, Department of Epidemiology and Preventive Medicine, Monash University, and at Melbourne University, Melbourne, Vic.

Coronary heart disease (CHD) is Australia's biggest killer. It is responsible for about 20% of deaths in Australia every year and it accounts for significant long-term morbidity.[1] Acute coronary syndrome (ACS) is a clinical spectrum of CHD that ranges from unstable angina to acute myocardial infarction and sudden cardiac death. ACS represents an atherosclerotic plaque rupture with superimposed thrombosis. Subsequent ischaemia and infarction are markers of worse outcomes. Treatment options include revascularisation, either percutaneous coronary intervention or cardiac bypass surgery, although a significant proportion of patients are managed with medical therapy alone.[2]

It is essential to recognise the importance of secondary prevention because patients who suffer from an ACS are likely to have further cardiovascular events. In fact, repeat heart attacks are associated



with a twofold increased risk of death. Economically, repeat events have a higher burden of disease cost than initial events, and account for $8.4 billion in costs per year.[3]

GPs have a crucial role in the secondary prevention of CHD. This article highlights six key areas that have to be optimised to ensure ACS patients receive optimal cardiac care.

Key points

- **Acute coronary syndromes (ACS) are associated with increased mortality and morbidity.**
- **It is essential to continue optimal ACS care after patients have been discharged from hospital.**
- **Secondary prevention strategies focus on six key themes.**
- **Optimising secondary prevention measures ensure the risk of future cardiovascular events is decreased.**
- **GPs play an integral role in patient care after ACS.**

Six key areas to ensure optimal cardiac care in patients post ACS

1. Adherence to proven drug therapy

National and international guidelines are clear in their recommendation of medications for secondary prevention after an ACS (Table 1).[4,5] It is essential that patients have their medications reviewed frequently to ensure optimal medical management and compliance. It is also important that patients are educated about the importance of drug therapy in ACS.

Aspirin

Low-dose aspirin (100 to 150 mg daily) is recommended for all patients post ACS indefinitely, regardless of whether they were treated with or without revascularisation. The benefit of aspirin in preventing repeat cardiovascular events far outweighs the small but definite risk of gastrointestinal bleeding.

Dual antiplatelet therapy

A second antiplatelet drug (a P2Y12 inhibitor) is recommended for all patients post ACS, along with aspirin. This is associated with a reduction in cardiac events, again at the expense of a higher risk of bleeding. The recommended duration of dual antiplatelet therapy is 12 months, although some variation is seen in clinical practice depending on factors such as risk of bleeding, type of stent used (drug eluting versus bare metal) and need for oral anticoagulation (e.g. atrial fibrillation, mechanical heart valve).

Clopidogrel (75 mg once daily) is the oldest drug with the most clinical experience and is indicated in patients who have had percutaneous coronary intervention and those who are medically managed.[6] Ticagrelor (90 mg twice daily) has been shown to be more efficacious than clopidogrel in all patients who have had an ACS, and has a class I indication for this use.[7] Prasugrel (10 mg once daily) is only indicated in those patients treated with percutaneous coronary intervention, as it has better outcomes than clopidogrel in these patients. Prasugrel is not indicated in medically managed patients.[8]

Statin therapy

The role of statin therapy in the secondary prevention of CHD is based on robust data. Statins should be prescribed at high doses, if tolerated, in all patients post ACS.[9] It is important to emphasise that

all patients with coronary artery disease should take statins irrespective of their cholesterol levels.

Beta blockers

Beta blockers are recommended in all patients post ACS for at least 12 months, unless they have true contraindications such as severe bronchial asthma, significant conduction abnormalities or advanced peripheral vascular disease. The evidence is particularly compelling in patients with reduced left ventricular ejection fraction, and in these patients a cardioselective beta blocker (bisoprolol, carvedilol, metoprolol extended release, nebivolol) should be continued indefinitely.[10] The benefit of beta blockers in patients with stable coronary artery disease with preserved left ventricular ejection fraction beyond 12 months is limited.

Angiotensin converting enzyme inhibitors and angiotensin receptor blockers

All patients who have had an ACS should take an angiotensin converting enzyme inhibitor, unless contraindicated. The cardiovascular benefit is particularly strong if there is a reduced left ventricular ejection fraction.[11] Angiotensin receptor blockers should only be used if angiotensin converting enzyme inhibitors are not tolerated, as their evidence base is not as extensive.

2. Optimisation of cardiovascular risk factors

There is undisputed evidence that comprehensive risk-factor management reduces the risk of premature death and recurrent cardiovascular events while improving quality of life. Thus it is of paramount importance that patients are reviewed regularly and management is proactive to ensure risk factors are at target (Table 2).

Blood pressure

Patients post ACS should aim for a blood pressure target of 130/80 mmHg or below, as per national recommendations.[12] Angiotensin converting enzyme inhibitors (or angiotensin receptor blockers) and beta blockers are used routinely in patients post ACS. If after appropriate titration the blood pressure target is not met, other agents such as thiazide diuretics, calcium channel blockers, spironolactone and centrally acting antihypertensive medications can be added. The optimal agent of choice will depend on patient-specific characteristics.

Cholesterol level

The LDL-cholesterol (LDL-C) level is the most important predictor of cardiovascular events. In general, a lower LDL-C level is associated with fewer future cardiovascular events. All patients post ACS should be taking high-intensity statin therapy, if tolerated, irrespective of their cholesterol level. If the LDL-C target (<1.8 mmol/L) is not reached, ezetimibe 10 mg can be incorporated as it decreases LDL-C levels by a further 23% when used with statin therapy.[13]

Pharmacological management of patients with low HDL-cholesterol and high triglyceride levels, aside from statin therapy, is not uniformly recommended due to conflicting clinical trial results. In a subset of patients with metabolic syndrome, fenofibrate 145 mg daily may be considered.[12]

Diet is integral in the management of hypercholesterolaemia, with low consumption of saturated and trans fatty acids recommended.

Diabetes screening and management

Screening for diabetes should have been carried out during the hospital admission. Blood glucose levels can be transiently elevated during an ACS and thus repeat screening as an outpatient is recommended. If the fasting glucose level is 5.5 to 6.9 mmol/L, an oral glucose tolerance test should be performed to confirm the presence or absence of diabetes mellitus. Patients with confirmed impaired glucose tolerance should be followed up closely and referred to a dietician and diabetes educator due to their high risk of progression to diabetes mellitus. Patients with confirmed diabetes mellitus should

Table 1. Recommended medications for secondary prevention of acute coronary syndromes

Medication	Maintenance dose	Recommended duration of treatment
Aspirin	100 to 150 mg daily	Lifelong
P2Y12 inhibitor – Clopidogrel – Prasugrel – Ticagrelor	 75 mg daily 10 mg daily* 90 mg twice daily	12 months
High-intensity statin – Atorvastatin – Rosuvastatin	 40 to 80 mg daily 20 to 40 mg daily	Lifelong
Angiotensin converting enzyme inhibitors/angiotensin receptor blocker	Uptitrated to maximum tolerated dose	If left ventricular dysfunction, lifelong therapy recommended
Beta blocker – Use cardioselective beta blocker (bisoprolol, carvedilol, metoprolol extended release, nebivolol) if left ventricular dysfunction is present	Uptitrated to maximum tolerated dose	If left ventricular function normal, consider ceasing beta blocker after 12 months If left ventricular dysfunction, lifelong therapy recommended

* 5 mg in the elderly or patients with low body weight. Contraindicated if there is a history of stroke (see product information).

Table 2. Recommended targets for cardiovascular risk factors

Risk factor	Target
Blood pressure	130/80 mmHg or below
Cholesterol levels	LDL-cholesterol <1.8 mmol/L HDL-cholesterol >1.0 mmol/L Triglycerides <2.0 mmol/L
Diabetes mellitus	HbA_{1c} <7% (53 mmol/mol)
Body weight	BMI <25 kg/m^2
Waist measurements	Men <94 cm Women <80 cm
Physical activity	30 minutes of moderate intensity physical activity at least 5 days a week

generally aim for a target HbA_{1c} of less than 7% with appropriate lifestyle and pharmacological interventions. The intensity of blood glucose lowering interventions should however be based on the patient's individual risk of hypoglycaemia. Special care should be taken with elderly patients and those taking multiple hypoglycaemic agents.

3. Motivation to make positive lifelong changes

Lifestyle changes, particularly smoking cessation, a healthy diet, appropriate alcohol intake, weight loss and increased physical activity, have been shown to alter the natural history of CHD. Inducing and maintaining lifelong behavioural changes should be emphasised at every visit. A multidisciplinary team approach involving dieticians, physiotherapists, exercise physiologists, diabetic educators and, if needed, clinical psychologists, is crucial in making longlasting behavioural changes.

Cigarette smoking

Smokers with CHD should aim to stop smoking completely. During every consultation, patients should be asked about their smoking status and every smoker should be advised to quit. Quitline (phone: 13 QUIT) provides phone support and gives the smoker proven strategies to increase smoking cessation success rates.

Nicotine replacement therapy is generally safe in smokers with CHD, but caution needs to be exercised in patients with recent (≤2 weeks) myocardial infarction or cerebrovascular event, unstable angina or significant arrhythmias. Pharmacotherapy can be considered and combined with nicotine replacement therapy, if necessary. Varenicline and bupropion are commonly used antismoking agents and should be used in combination with psychosocial support.

Healthy diet

The aim is to encourage patients to adopt a healthy eating pattern that will persist for the rest of their lives. Dietitian support should be strongly considered to help the patient achieve appropriate dietary goals.

Healthy diet guidelines[12]

- Consume mainly plant-based foods (fruit, vegetables, wholegrain)
- Consume moderate amounts of reduced, low or no fat dairy products
- Consume moderate amounts of lean unprocessed meats, poultry and fish
- Consume moderate amounts of polyunsaturated and monosaturated fats (olive oil, canola oil)
- Consume 2 to 3 g per day of phytosterols (margarine, cereal, reduced fat yoghurt/milk)
- Consume 1 g daily of combined eicosapentaenoic acid plus docosahexaenoic acid. This can be achieved by eating two to three serves of 150 g of oily fish per week and/or other foods enriched with n-3 PUFA and/or fish oil capsules or liquid
- Consume more than 2 g alpha linolenic acid (canola or soybean based oils, linseeds, walnuts, legumes, eggs and green leafy vegetables)
- Reduce salt intake by avoiding processed foods, takeaway foods, salty snacks and adding salt to foods

Dietary interventions have a strong evidence base in secondary prevention. The Mediterranean diet, in particular, has a striking protective effect in ACS patients by reducing cardiac death and recurrent myocardial infarction.[14] Furthermore, omega-3 fatty acids derived from fish oil have been shown to decrease sudden cardiac death.[15] The clear dietary guidelines from the National Heart Foundation of Australia are summarised in the Box.[12]

Physical activity

It is recommended that patients with coronary artery disease undertake a minimum of 30 minutes of moderate intensity activity at least five times per week, but preferably every day. The activity should cause a definite and noticeable increase in the work of breathing and the respiratory rate but the patient should still be able to talk. Most patients who have had an ACS should be encouraged to increase their physical activity as soon as they are discharged from hospital. Physical activity restraints should only be put in place in the small subset of patients with decompensated heart failure, unstable angina, uncontrolled arrhythmias, malignant hypertension or severe aortic stenosis.

Healthy weight

It is important to monitor the waist circumference, as well as the body mass index (BMI), in patients post ACS because it is a good predictor of cardiac disease. Ideal waist circumference for men is less than 94 cm and for women is less than 80 cm. Weight loss strategies should concentrate initially on reducing caloric intake as well as increasing physical activity. Some patients, particularly those in the morbidly obese range (BMI more than 35 kg/m^2) may benefit from supervised very low calorie diets, meal replacement therapy or bariatric surgery.

4. Referral and encouragement of cardiac rehabilitation participation

Cardiac rehabilitation is associated with improved survival and better quality of life. The problem is the underwhelming level of referral, participation and completion of such programs. As cardiac rehabilitation is an integral component of ACS management, it should be non-negotiable.

Every patient who has had an ACS should be actively referred (and re-referred) to a program that is most likely to meet the individual patient's need. New models of care, such as web-based and smartphone-based programs, are emerging and this may help with poor participation.

5. Assessment for depression

It is becoming increasingly recognised that depression is three times more common in patients who have had an ACS than in the general population. In addition, prognosis in patients with depression and ACS is worse than in those with CHD alone.[16]

After an ACS, patients should be screened for depression and treatment initiated if appropriate. Counselling strategies are very effective although referral of the patient to a psychologist may be warranted for intensive cognitive behavioural therapy. Selective serotonin reuptake inhibitors are the drugs of choice in patients post ACS with depression. Tricyclic antidepressants should be avoided due to their associated arrhythmic potential.

6. Action plan

Education and planning are vital in ensuring symptoms of a heart attack or progressive angina are recognised early and acted upon appropriately. An action plan should include:

- recognition of symptoms
- availability of glyceryl trinitrate at all times
- a call to the emergency services if symptoms are severe and last more than 10 minutes despite use of glyceryl trinitrate.

There is no substitute for a clear action plan that the patient understands and will use in an emergency.

Conclusion

The management of patients with acute coronary syndromes extends well beyond hospitalisation with the index event. GPs have a key role to play in ensuring secondary prevention measures are optimised in these patients. **CT**

References

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

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