

Eight challenges faced by general practitioners caring for patients after an acute coronary syndrome

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General practitioners have an essential role in the management of patients who have recently been discharged from hospital after an acute coronary syndrome (ACS). As the duration of hospital stay has shortened over recent decades, this role has become even more important. There are many challenges facing the GP in fulfilling this demanding role. This article deals with eight common challenges faced by the GP caring for patients after an ACS.

Not enough information from the hospital

Insufficient documentation ranks as one of the major gripes of GPs dealing with hospitals. It is a worldwide problem, and not limited to ACS, although arguably of greater consequence in this potentially unpredictable and life-threatening condition. The discharge summary is the most important and often the only form of communication from hospitals to primary care. An Australian study in 2001 showed that only 37% of hospital discharge summaries reached the GP.¹ Audits of discharge summaries in Victorian hospitals found high completion rates within hospital records (88%–100%) but significant delays in sending them to GPs (only 4%–32% within 14 days), with fewer than a third available to GPs at the first post-discharge visit.² Quality improvement initiatives can improve these rates — a recent national audit as part of quality improvement showed that 77% of GPs reported receiving a discharge summary for patients with ACS at a median time of 3 days (range, 0–41 days) after discharge.³ The addition of electronic discharge summaries from hospitals in Australia has improved timeliness, with 83% of GPs receiving them within 2 weeks from hospitals with such a service.⁴

It is essential that the discharge summary from the hospital conveys the information necessary for the GP to manage the patient's condition after hospital. The list of medications with proof of benefit is quite large, and the ACS patient may be taking an additional four or five new medications at discharge from hospital. The antithrombotic regimen varies according to whether the patient received conservative management, insertion of a bare-metal stent, or insertion of a drug-eluting stent in hospital.

The patient may be confused about the purpose of their medications or be unconvinced of their benefit, a setting ripe for non-adherence. There is clear evidence that non-adherence to evidence-based medications can have highly adverse effects on outcome after an ACS.⁵ A clear-cut management plan has been shown to improve adherence and to improve outcomes.⁶ This is recommended by the National Heart Foundation of Australia⁷ and should be considered as part of an overall effort to improve risk factor reduction, adherence to medications and improvement of outcomes.⁸ A timely hospital

Summary

- The general practitioner is essential in the management of the patient who has recently been discharged from hospital following an acute coronary syndrome (ACS), particularly as duration of hospital stay is shorter than in previous decades.
- GPs caring for patients after an ACS face numerous challenges. Often, the first of these is insufficient or delayed documentation from the discharging hospital, although electronic discharge summaries are alleviating this problem.
- Post-ACS patients often have comorbidities, and GPs play a key role in managing these. Patients taking dual antiplatelet therapy who need surgery, and post-ACS patients with atrial fibrillation, require particular care from GPs.
- Patients will often approach their GP for advice on the safety of other drugs, such as smoking cessation medication, and phosphodiesterase type 5 inhibitors for erectile dysfunction.
- For patients complaining of persistent lethargy after an ACS, GPs must consider several differential diagnoses, including depression, hypotension, hypovolaemia, and side effects of β -blockers.
- GPs play an important ongoing role in ensuring that target cholesterol levels are reached with statin therapy; this includes ensuring long-term adherence. They may also need to advise patients who want to stop statin therapy, usually due to perceived side effects.
- Many of these challenges can be met with improved and respectful communication between the hospital, the treating cardiologist and the GP.
- The patient needs to be closely involved in the decision-making process, particularly when balancing the risks of bleeding versus thrombosis.

summary that includes this basic information avoids the patient and the GP wasting valuable time obtaining the information.

The patient is taking dual antiplatelet therapy and needs surgery

The patient who needs surgery during the 12 months after an ACS or insertion of a drug-eluting stent presents a particular challenge. In the stented patient, there is concern about the risk of stent thrombosis, and this is reduced with dual antiplatelet therapy (DAPT; ie, aspirin with a P2Y₁₂ inhibitor such as clopidogrel, ticagrelor or prasugrel).⁹ Drug-eluting stents significantly reduce the risk of restenosis at the site of the stent, but require a longer period of DAPT than bare-metal stents to allow for re-endothelialisation of the coronary artery lesion.¹⁰ As a result, international guidelines recommend 1–3 months of DAPT for patients who have received a bare-metal stent and 12 months of DAPT for patients who have received a

drug-eluting stent, with strict adherence to these guidelines recommended.¹¹ Some cardiologists prefer a longer course of DAPT if there has been a complex percutaneous coronary intervention or if there is evidence of previous stent thrombosis. There are recent challenges to the recommendations, which have now been in place for more than 5 years and were based on data from older stents.¹² A recent meta-analysis of more modern drug-eluting stent technology shows that 6 months of treatment compared with 12 months reduces the risk of bleeding without any adverse effect on stent thrombosis.¹³

For the patient requiring surgery while taking DAPT, close communication between the surgeon, cardiologist and GP is essential. The risk of thrombosis versus the risk of bleeding needs to be carefully assessed for each case.¹⁴ Some types of minor surgery (eg, removal of superficial skin lesions) can be undertaken while maintaining DAPT. Most surgical procedures can be conducted safely with the patient maintained on aspirin alone. For higher risk procedures, such as neurosurgical or neurovascular procedures, bridging with an alternative rapidly acting antiplatelet regimen using a glycoprotein IIb/IIIa inhibitor may be recommended.¹⁵

For those who have been managed conservatively, the relatively high risk of recurrence and the proven efficacy of DAPT¹⁶ has led to the current recommendation that DAPT remain for 12 months.¹⁷ As these patients have not received a coronary stent, their risk of coronary thrombosis may be lower, particularly after the first few months. The patient needs to be apprised of the risks and engaged in the decision-making process.

The post-ACS patient with atrial fibrillation

Atrial fibrillation (AF) commonly coexists with coronary heart disease, or may occur after ACS.¹⁸ The antithrombotic regimen for the post-ACS patient targets atherothrombosis, and DAPT is mandated for 12 months after ACS for most patients (see above). The risk of stroke is a concern in patients with AF, with an annual risk of 5%, two to seven times that of people without AF.¹⁹ Aspirin, clopidogrel or DAPT have not been shown to be protective against the risk of stroke in AF,²⁰ and anticoagulation with warfarin or a novel oral anticoagulant is recommended in all AF guidelines for patients at risk of stroke, as determined by their CHA₂DS₂-VASc (congestive heart failure, hypertension, age \geq 75 years, diabetes mellitus, stroke, vascular disease, age 65 to 74 years, sex) score.^{21,22} Therefore, most post-ACS patients with AF require triple antithrombotic therapy with a combination of an oral anticoagulant and DAPT. This nearly doubles the risk of bleeding compared with warfarin monotherapy, so the patient requires careful monitoring.²³

Recent studies have looked at shortening the duration of DAPT with newer stents,¹³ or withdrawing one of the antiplatelet agents. A trial in post-stented patients with AF that compared the effect of triple antithrombotic therapy (aspirin, clopidogrel and warfarin) with that of double antithrombotic therapy (clopidogrel and warfarin) showed no adverse effects with stroke or coronary thrombosis and a substantial reduction in bleeding.²⁴ Similar results were seen in the “real world” of a large Danish

registry study.²⁵ While this is not definitive evidence, it suggests that it may be possible to withdraw aspirin after a few weeks of triple antithrombotic therapy and continue with warfarin and clopidogrel. There are no clinical trials or observational studies to guide therapy in patients taking the new oral anticoagulants or with newer antiplatelet agents such as ticagrelor, and such studies are urgently needed.

The patient wants to consider smoking cessation medication

Smoking cessation is essential after an ACS. Although it is true that there have not been controlled clinical trials to confirm the benefits of cessation of smoking after an ACS, there are ample observational studies to show that continuation of smoking leads to greatly increased risk of death and recurrence of myocardial infarction,²⁶ and cessation can reduce the risk by about a third.²⁷ While unassisted cessation is the most effective method,²⁸ the reality of clinical practice is that many patients feel they need assistance. A Cochrane review of nicotine replacement therapies (NRTs) in trials involving more than 50 000 patients has shown that all the methods of delivery (chewing gum, transdermal patches, oral and nasal sprays, inhalers and tablets/lozenges) are effective, at least in the short term, in assisting quitting, with 50%–70% of patients achieving abstinence.²⁹

The Cochrane review confirmed that NRTs did not increase the risk of coronary events. Despite this, there are widespread apprehensions among patients³⁰ and stop-smoking practitioners³¹ about the safety of NRTs, and this limits their use, effectiveness and adherence. GPs have an important role in reassuring post-ACS patients that these safety concerns are misplaced.³²

Bupropion is an antidepressant with partial nicotine antagonist properties, and has been extensively evaluated as adjunctive therapy for smoking cessation. It is effective in the short term, and a Cochrane review showed no adverse cardiovascular effects.³³ Varenicline has similarly been extensively evaluated in clinical trials, and formal analysis shows no adverse cardiovascular or serious psychiatric adverse effects.³⁴ A summary of the evidence for NRTs, bupropion and varenicline concluded that combination NRTs and varenicline had the highest rate of cessation and the lowest risk of long-term relapse.³⁵ Both varenicline and bupropion have United States Food and Drug Administration (FDA) warnings about the risk of unusual changes in behaviour, with thoughts of suicide or dying in some patients,³⁶ but the warning does not refer specifically to cardiovascular risks for either drug. The GP can discuss the use of these smoking cessation drugs with their patients, and can reassure in general terms about the cardiovascular risks, but may conclude that counselling and support may be more appropriate.

The patient complains of persistent lethargy after ACS

With modern management, the patient who has recovered from an ACS without suffering extensive myocardial damage can usually be expected to return to normal

activities a week or two after the event. Unusual lethargy continuing after a coronary event can be a major clinical challenge. Depression is a common comorbidity and an important factor indicating a poor prognosis,³⁷ and should be actively considered in the patient with post-ACS lethargy. The American Heart Association has recently recommended that depression should be elevated to the status of a risk factor for adverse medical outcomes in patients with ACS. However, there is currently no evidence to link causality of depression to ACS, nor that treating depression improves survival from ACS.³⁷

Tricyclic antidepressants have well recognised adverse cardiac effects³⁸ and should be avoided except in low doses. A multicentre study showed that the selective serotonin reuptake inhibitor (SSRI) sertraline was safe and effective among post-ACS patients³⁹ and, subsequently, meta-analysis of the SSRI trials have shown no adverse effect on cardiovascular outcomes.⁴⁰

Drug-induced causes of lethargy should also be considered. With increasing use of potent antiplatelet regimens after ACS, the risk of gastrointestinal bleeding has increased, and this may lead to lethargy from iron-deficiency anaemia. The negative chronotropic effect of β -blockers may also contribute. There is ongoing debate about the ideal duration of β -blockers after ACS, but in the patient who has recovered well with no left ventricular dysfunction or angina, it may be possible to taper off the β -blocker without adverse effect.⁴¹

Hypotension and hypovolaemia are also common in the early post-hospital phase of ACS management. This may be due to unnecessary continuation of diuretics or over-enthusiastic dosing with angiotensin-converting enzyme (ACE) inhibitors. This is easily recognised and its early management can lead to a dramatic improvement in wellbeing. If the patient is free of symptoms of cardiac failure and there is no left ventricular dysfunction on echocardiography, there is no benefit in continuing diuretic therapy. Reduction of the dose of ACE inhibitor may be very helpful for the patient with lethargy from persistent hypotension. Of course, the patient may be lethargic because of cardiac failure, and it is important to check left ventricular function with an echocardiogram or by measuring B-type natriuretic peptide to rule out this possibility.

The patient wants to stop statin therapy

Statins have been extensively studied, and a detailed meta-analysis of 170 000 participants in 26 statin trials has shown them to be very effective and safe in most patients, with a 21%–22% relative risk reduction in cardiovascular disease events per 1 mmol/L reduction in low-density lipoprotein cholesterol (LDL-C) levels over 5 years.⁴² The evidence is so persuasive that most authoritative bodies now recommend that statins of moderate to high intensity be prescribed after ACS irrespective of the cholesterol level.⁴³

However, there has been a lot of publicity in Australia about the side effects of statins. Some of the reporting has been alarmist and irresponsible,⁴⁴ and many patients are confused about this issue. The highlighting in 2012 by the US FDA of possible cognitive dysfunction was a

major concern for many patients.⁴⁵ The FDA's advice was widely promulgated despite meta-analysis of all studies from 1986 to 2012 showing no evidence of increase in dementia or Alzheimer disease.^{46,47} The meta-analysis cited above showed no sign of an increase in cancer.⁴⁶

An increase in the risk of rhabdomyolysis is the main serious side effect that has been shown with statins in controlled trials. This is exceedingly rare, occurring in about one patient per million prescriptions.⁴⁸ It is dependent on the type of statin, with a higher rate from high-dose simvastatin than atorvastatin among post-ACS patients.^{49,50} On the other hand, myalgia, with or without marginal elevation of creatine kinase, is common and may occur in about 10% of patients.⁵¹ Recent reports of an increase in diabetes⁵² are further cause for concern with some patients, but it is important to point out that a statin is one of the most effective treatments for lipid management in established diabetes.⁵³

For the patient who is unconvinced by the overwhelming scientific data, a trial of a lower dose or a change in statin may be helpful. If the patient insists on a trial of alternative "natural" cholesterol-lowering drugs, this should be monitored with cholesterol levels if possible. A dramatic increase in total cholesterol or LDL-C level with alternative therapies may be sufficient to persuade the patient to continue with statin therapy. An agreement with the patient that a period of several weeks off the statin to assess the effect on muscle soreness or mental agility may demonstrate that the "side effects" are related to either normal sensations or other causes, rather than a drug side effect.

Among patients who have proven side effects, the use of an alternative LDL-C-lowering agent, such as ezetimibe, cholestyramine or newer experimental agents, may need to be considered. Ezetimibe can effectively lower LDL-C levels, but the benefit of this on outcomes is yet to be established.⁵⁴ Nicotinic acid has not been shown to be effective.⁵⁵

Dietary management has shown reductions in LDL-C levels. About 2 g/day of plant stanols and sterols has been shown to reduce LDL-C levels by about 10%,⁵⁶ and the addition of fish oils in those who cannot take statins may show statistically significant reductions in adverse outcomes, despite conflicting recent meta-analyses.⁵⁷ This dietary management for reduction in LDL-C levels can be additive to a low-fat diet and cholesterol-lowering medication.

The patient has not reached the target level with statin therapy

The target LDL-C level for post-ACS patients was set at <1.8 mmol/L after the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE IT – TIMI 22) study.⁴⁹ This demonstrated that a high-intensity statin was more effective than a moderate-intensity statin. The median LDL-C level achieved during treatment in the high-intensity (atorvastatin 80 mg) group was 62 mg/dL (1.60 mmol/L) and in the moderate-intensity (pravastatin 40 mg) group was 95 mg/dL (2.46 mmol/L). The outcome was to set the US target level for post-ACS patients to

below 70 mg/dL (1.8 mmol/L),⁵⁸ and Australia followed suit on this.⁵⁹

A recent revision of the US guidelines has recognised that the target levels were never tested in clinical trials and are based on an extrapolation of the clinical trial evidence.⁴⁵ These new revised guidelines recommend high-intensity statin therapy (defined as a daily dose that lowers LDL-C by $\geq 50\%$) rather than moderate-intensity statin therapy (lowering LDL-C by 30% to <50%). High-intensity statins available on the Australian Pharmaceutical Benefits Scheme are atorvastatin 40–80 mg and rosuvastatin 20–40 mg.

The GP's role is to check that the patient is taking one of these drugs at the correct dose. If there is persistent elevation of the LDL-C level, a careful check on adherence may be needed. Statin adherence rates overall in Australia are low, with a community-wide study in 2011 showing 43% of patients discontinued statin within 6 months, 23% failed to collect their first repeat prescription at 1 month, and a median persistence of 11 months.⁶⁰ If adherence has been confirmed, a higher dose of statin could be considered (eg, an increase of atorvastatin from 40 to 80 mg/day, or rosuvastatin from 20 to 40 mg/day). The addition of ezetimibe or another lipid-lowering agent to a statin has been shown to further lower LDL-C levels, but there is no current evidence of a benefit on cardiovascular outcomes.⁶¹

The patient seeks advice on erectile dysfunction and the safety of PDE5 inhibitors

People with coronary heart disease have a risk of erectile dysfunction because of the associated endothelial dysfunction,⁶² and possibly the effect of some cardiovascular drugs.⁶³ While men are notoriously reluctant to seek advice on erectile dysfunction, it may be an indicator of worsened cardiovascular risk and the GP needs to be alert to subtle clues to indicate evidence of erectile dysfunction and encourage discussion.⁶⁴ Adjustment of medications (such as reduction of β -blockers and diuretics)⁶⁵ and reduction of cardiovascular risk factors may be helpful.⁶⁶

Usually, however, use of phosphodiesterase type 5 (PDE5) inhibitors may need to be considered.⁶⁷ There are multiple studies to confirm the overall safety of PDE5 inhibitors in patients with cardiovascular disease,⁶⁸ although the longstanding caution that they must not be used in conjunction with nitrates remains valid.⁶⁹ The GP must check the post-hospital medications to ensure that nitrates in any form (isosorbide mononitrate, nitrate patches, nicorandil) are not being taken by the patient, and that glyceryl trinitrate spray is not used within 24 hours of sildenafil or vardenafil administration or within 48 hours of tadalafil administration.⁶⁴ Choice of PDE5 inhibitor is a matter of preference. A recent meta-analysis concluded the safety profile of each of the agents was similar.⁷⁰ The use of low-dose daily tadalafil has been explored as an alternative to intermittent use, with some success and a good safety profile.⁷¹ The patient's partner may express concern about "strain on the heart" of enhanced sexual activity with successful use of a PDE5 inhibitor, but the information that the absolute risk

increase for myocardial infarction associated with 1 hour of sexual activity per week is estimated to be only 2 to 3 per 10000 person-years may be of some reassurance.⁷²

Conclusion

Of these eight challenges, most can be managed with improved communication between the hospital, the treating cardiologist and the GP. A team approach is essential to deliver effective evidence-based care. When balancing risks (for instance, bleeding versus thrombotic risk), the patient needs to be fully engaged in the decision making.

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