Lifelong Learning

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Patients Post Myocardial Infarction:

Tailored Management Improves Outcomes

Patients who have had a myocardial infarction need aspirin and statin therapy and careful evaluation to identify those who will benefit from revascularisation or implantable device therapy and appropriate additional pharmacological treatment.

The management of the patient post myocardial infarction (MI) is a team effort between the hospital, cardiologist and GP to ensure that he or she receives the benefit of the substantial advances in treatment shown over the past 20 years to improve outcomes. The hospital has a responsibility to provide sufficient details on whether the patient had an ST elevation or non-ST elevation MI (STEMI or NSTEMI), the extent and location of myocardial damage, the procedures undertaken in hospital, his or her discharge medications and plans for follow-up investigations. The cardiologist needs to communicate the management plan clearly to the patient and GP. The GP needs to understand the rationale for treatment, ensure that the post-MI management plan is followed and ensure any treatment side effects are addressed appropriately. Fortunately, there is a large evidence base and detailed guidelines to help tailor post-coronary care management to the individual patient who has suffered a STEMI[1-3] or NSTEMI.[4-6]

About the authors

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Evaluation of the patient

In the evaluation of the patient post MI, three questions should be addressed:

- Is coronary angiography indicated and will this patient benefit from coronary revascularisation?
- What is the ideal pharmacological management and how long should it continue?
- Should this patient be considered for device therapy?

The following tests are available to help answer these questions, in addition to consideration of the detailed review of the in-hospital course and clinical assessment of the patient.

Coronary angiography

Coronary angiography is often performed in the early stages of hospital treatment and the coronary anatomy guides decisions about post-MI management. If the patient has not had angiography and it is not readily available, non-invasive testing such as exercise testing/stress imaging can be used to stratify risk and decide on referral for angiography. Despite advances in the technique of coronary CT angiography, it still has significant limitations[7] and coronary angiography by cardiac catheterisation remains the usual method of assessing coronary anatomy in the patient who has had a coronary event. Coronary CT angiography is not recommended for routine evaluation of the patient post MI at this time.[8] Although coronary angiography is now performed in most patients who have had a STEMI or NSTEMI, when it is not available or contraindications exist alternative modalities such as stress imaging may be considered.

Exercise electrocardiography

Exercise electrocardiography remains a very useful investigation to detect

Key points

- A large evidence base and detailed guidelines are available to help tailor post-coronary care management to the individual patient.
- Definite indications for coronary revascularisation include patients who have had a myocardial infarction (MI) with on-going symptoms and the presence of a critical coronary stenosis, left main disease or triple vessel coronary artery disease with extensive ischaemia.
- Although all patients post MI should be given aspirin and statins, the choice and duration of other pharmaceutical therapy is determined by the patient's symptoms and presence of left ventricular dysfunction.
- Early implantation of an implantable cardioverter defibrillator does not benefit patients immediately post MI. However, device therapy is indicated in those who had an MI more than 40 days previously and whose ejection fraction is persistently below 35%.

Indications for revascularisation

Definite indications

- **Ongoing symptoms with a critical coronary stenosis**
  The usual treatment is PCI. The choice of stent will depend on the clinical situation.
- **Ongoing symptoms with left main or triple vessel coronary artery disease**
  CABG is the usual recommended approach; however, the role of multivessel PCI is being evaluated.[14]

Possible indications

- **Triple vessel disease and LV dysfunction**
  CABG surgery is less effective when the LV dysfunction is due to extensive post-infarction scarring. Myocardial viability needs to be established with radionuclide myocardial perfusion scanning, MRI or PET scanning.
- **Asymptomatic with tight residual stenosis**
  It is important to clarify the functional significance of a tight residual stenosis. If the stenosed vessel supplies an akinetic scar, there is little to be gained from percutaneous intervention.
- **Totally occluded infarct related artery**
  PCI or CABG are usually considered only if the patient is symptomatic or has a large area of residual ischaemia. There is less enthusiasm for treating the asymptomatic patient since the 'open artery' hypothesis was tested in a randomised clinical trial and no benefit of late opening of the occluded artery was demonstrated.[15]

ABBREVIATIONS: CABG = coronary artery bypass grafting; LV = left ventricular; MRI = magnetic resonance imaging; PCI = percutaneous coronary intervention; PET = positron emission tomography.

myocardial ischaemia. It is of particular value for stable patients at low risk of further coronary events where ready access to coronary angiography or other imaging modalities is not available.

Echocardiography

Assessment of left ventricular (LV) function in the patient who has had a coronary event is best achieved with an echocardiogram. Serial echocardiographic assessment of LV function can assist not only in overall risk stratification[9] but in making decisions regarding implantation of an implantable cardioverter defibrillator (ICD).

Stress imaging studies

Stress imaging studies with radionuclide myocardial perfusion scanning or stress echocardiography may be required to localise and assess the extent of myocardial ischaemia. The choice between the two modalities may depend on local experience and expertise.[10, 11]

Specialised investigations

Specialised investigations with cardiac magnetic resonance imaging or positron emission tomography scanning can assess cardiac viability with a high specificity and sensitivity. They may be needed in specialised situations to establish whether an extensive area of ischaemic myocardium will benefit from revascularisation.

Will this patient benefit from coronary revascularisation?

By the time patients who have had a myocardial infarction visit their GP for follow up, many will have already had revascularisation - percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) - in hospital. The trend for the patient at high risk of further coronary events managed in a tertiary hospital is to try to deliver early revascularisation on arrival or before hospital discharge. For patients at lower risk or those managed in a secondary or regional hospital who have not had revascularisation, the question of whether to refer for revascularisation is one of the most complex decisions. Surprisingly little evidence exists to guide decision-making and it been the subject of much debate.[12, 13]

The definite and possible indications for revascularisation are listed in the box on this page.[14, 15]

What is the ideal pharmacological management and its duration?

Beta blockers

Guidelines recommend indefinite beta blocker treatment in all patients who have had STEMI[16] but the role of beta blockers in the patient who has had STEMI and a successful coronary reperfusion with restoration of LV function to normal and no evidence of residual myocardial ischaemia remains doubtful.[17] The recommendations for the patient who has suffered a small NSTEMI treated with PCI are based on even less strong evidence.

It would be acceptable practice to consider cessation of beta blockers several months after hospital discharge in a patient who has minimal residual coronary stenoses, no evidence of residual myocardial ischemia and no LV dysfunction, particularly if beta blockade has been associated with side effects. The recommendations for beta blocker treatment are shown in Table 1.

Aspirin

Aspirin in a dose of 75mg to 325mg is recommended in all post-coronary management guidelines for patients who have had STEMI or NSTEMI. It is a low-cost and effective treatment, associated with a significant 25% reduction in major vascular events, or an absolute risk reduction of 35 vascular events per 1000 patients treated over two years.[18] Observational studies suggest that bleeding complications are fewer with the lower dose but randomised allocation to low dose (100mg or less) versus standard dose (101mg to 325mg) showed no differences in bleeding.[19] Enteric coated formulations may be associated with fewer adverse gastric effects than buffered aspirin, but the data remain unclear.[20]

Thienopyridines

Clopidogrel in combination with aspirin is the usual dual antiplatelet therapy

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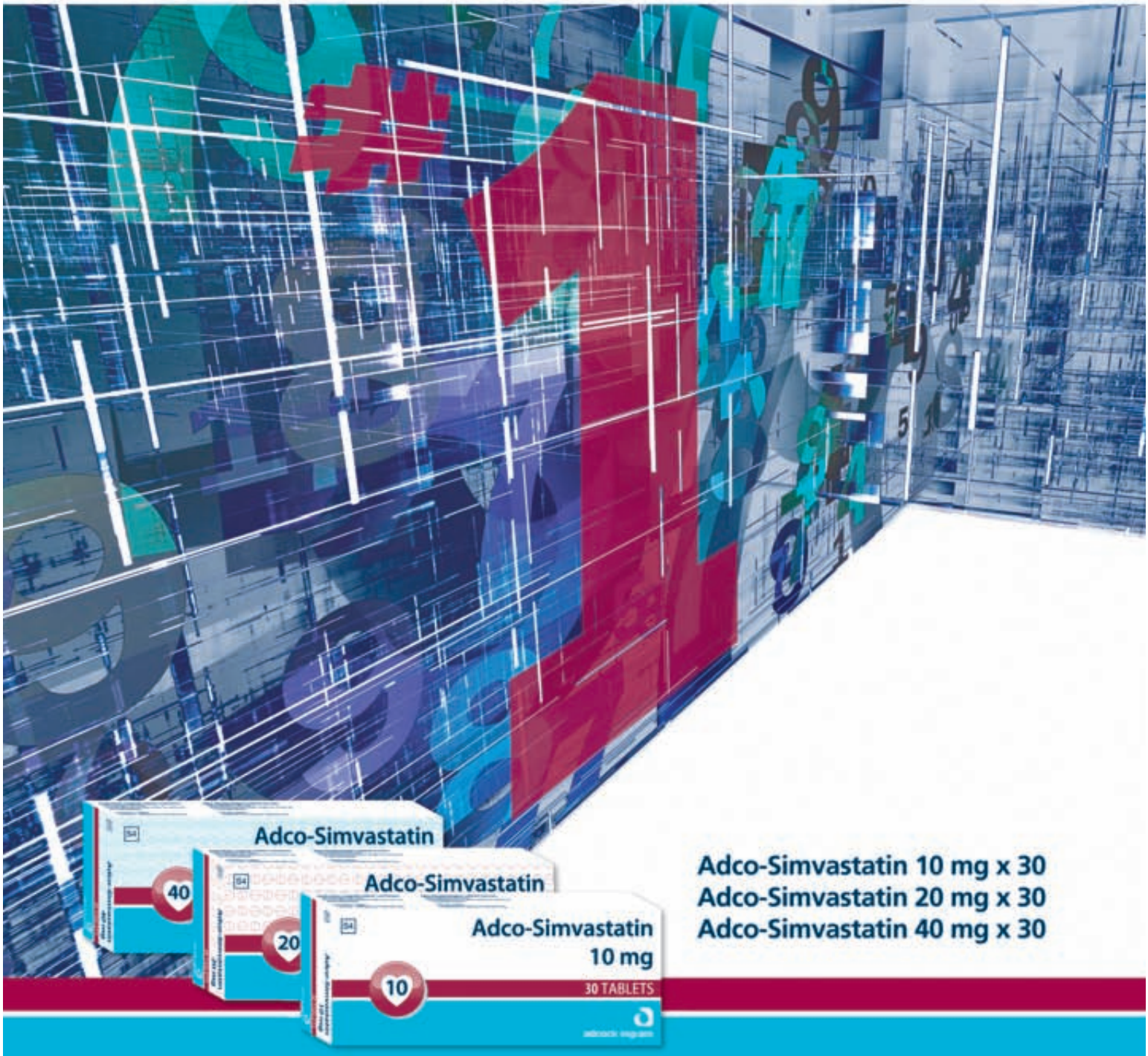

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TABLE 1

Drugs and other management in patients post MI

Patient category	Drug	Other management
Asymptomatic patient without LV dysfunction	• Aspirin 100–150mg/day • Beta blockers (eg, metoprolol 25mg–50mg twice daily or atenolol 25mg–50mg/day) • Statin (atorvastatin 80mg/day or equivalent)	Consider referral for cardiac rehabilitation
Asymptomatic patient with LV dysfunction	• Aspirin • Statin • Beta blockers of proven benefit in LV dysfunction (eg, bisoprolol, carvedilol, nebivolol or extended release metoprolol) • ACE inhibitor or angiotensin receptor blocker • Aldosterone antagonist (spironolactone or eplerenone)	If LV dysfunction is persistent and severe (LVEF<35%), consider referral for implantation of ICD
Symptomatic patient	• As above • If angina: standard antianginal therapy • If dyspnoea: diuretics	Refer for detailed evaluation including coronary angiography and consideration of PCI and CABG

ABBREVIATIONS: ACE = angiotensin converting enzyme; CABG = coronary artery bypass grafting; ICD = implantable cardioverter defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

(DAPT) for the patient who has received PCI.[21,22] The duration of DAPT depends on the complexity of the coronary anatomy and the type of PCI. The recommendations are summarised in Table 2. Patients need to be made aware that there is a risk of stent thrombosis if the DAPT is stopped for any reason (including elective surgery) during these recommended periods. When DAPT needs to be stopped during these periods, the issue should be discussed with the treating cardiologist.

The role of DAPT in patients who have recovered from conservative management of MI and have not received an intracoronary stent is moot. There is a risk of bleeding with long-term treatment[23] and, although 12 months of treatment may be justified, the benefit after six weeks is minimal.[24] In patients who have not received a stent, the long-term use of clopidogrel may be best limited to those who are at high risk of a thrombotic event and those who demonstrated a heavy thrombus burden at coronary angiography.

Prasugrel, a recently available alternative to clopidogrel, is more effective than clopidogrel in reducing coronary events. However, the early phase of treatment is complicated by a higher bleeding rate, particularly in patients going to bypass surgery.[25] Its role in long-term treatment of patients after a coronary event remains to be established.[26,27] but it may have a role in patients who have a history of stent thrombosis when taking aspirin and clopidogrel.

Statins

Statin therapy is an essential part of the post-MI regimen. It is associated with an average reduction in post-coronary events of 25% to 30%[30] and an absolute reduction for each 1.0mmol/L reduction in LDL cholesterol of 48 major vascular events per 1000 patients treated.[31] The statin should be commenced in hospital and continued after discharge.[32] The usual post-coronary statin used, based on the PROVE-IT trial (Pravastatin or Atorvastatin Evaluation and Infection Therapy trial), is 80mg of atorvastatin.[33]

The target LDL cholesterol level for patients after a coronary event is less than 2.0mmol/L.[34] The safety of high dose atorvastatin has been confirmed.[35] It remains unclear whether a patient who achieves a reduction of LDL cholesterol to target levels with 80mg of atorvastatin should be changed to a lower dose of statin, but it may be reasonable to do this to limit side effects. A trial of high dose (80mg) of simvastatin was associated with a higher than acceptable incidence of myopathy.[36]

Although rosuvastatin has been shown to be effective in high-risk cohorts, there is no specific trial to support its use in patients post infarction. Ezetimibe, either alone or in conjunction with statins, has the potential to lower LDL cholesterol levels[37] but, to date, there is no data to demonstrate any clinical benefit.

Other lipid modulations

Lowering triglycerides

There is no clear-cut benefit for lowering triglyceride levels in patients post myocardial infarction. Trials of gemfibrozil[38] and bezafibrate[39] have not been sufficiently persuasive to establish fibrate therapy in the patient who has had a coronary event, and a large trial with fenofibrate did not achieve its primary end point in patients with type 2

TABLE 2

Duration of dual antiplatelet therapy (DAPT) Post-MI

Intervention or patient category	DAPT duration
Balloon angioplasty*	1–3 months
Bare metal stent*	12 months recommended, 1 month mandatory
Drug eluting stent	12 months†
Complex stenting or high risk complex coronary anatomy	Indefinite
Patient who has not had PCI	3–12 months (longer for patients at high risk of further events)

* Patients with planned surgery may have balloon angioplasty or bare metal stent to limit the duration of DAPT and allow early surgery.

† Newer drug-eluting stents may require shorter duration of DAPT, but this remains unclear.

Abbreviations: DAPT = dual antiplatelet therapy; MI = myocardial infarction; PCI = percutaneous coronary intervention.

diabetes at relatively high risk of further coronary events.[40]

Raising HDL cholesterol

To date there is no effective HDL cholesterol raising drug available. A trial of torcetrapib demonstrated an increased mortality in patients at high cardiovascular risk.[41] On-going trials with dalcetrapib may demonstrate a role for HDL cholesterol raising in the patient after a coronary event.[42]

Omega-3 fatty acids

Fish oil-derived omega-3 fatty acids have been shown to moderately reduce total and sudden post-coronary deaths, but it is not clear if this is by a triglyceride lowering effect or other mechanisms.[43]

ACE inhibitors and angiotensin

ACE inhibitors have a clear-cut role in patients with cardiac failure and

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significant LV dysfunction.[44] However, their use in the absence of post-coronary LV dysfunction remains moot. Angiotensin receptor blockers as an alternative to ACE inhibitors have been trialled in patients who have had coronary events; however, the evidence base for this is not as extensive as it is for use of ACE inhibitors post infarction.[45]

Aldosterone blockade

Spironolactone and eplerenone have shown clear-cut benefit in patients with cardiac failure and LV dysfunction.[46] Meticulous monitoring of renal function and potassium levels is required, particularly in patients taking concomitant ACE inhibitors.[47]

Calcium channel blockers

Verapamil and diltiazem are contraindicated in patients who have had an MI and who have LV dysfunction.[48,49] Amlodipine use has been shown to be safe in the presence of LV dysfunction.[50] The calcium channel blockers have not been shown to have a clear-cut benefit on prognosis and are not recommended for routine use for the patient post infarction.

Antiarrhythmic drugs

Antiarrhythmic drugs have not been shown to improve prognosis for the patient post MI and their use in this setting is not recommended.[51]

Nitrate therapy

Nitrates are indicated for the patient with symptomatic angina but do not have a role in the management of the patient post infarction who does not have angina.[52]

Diuretics and digoxin

Diuretics are useful for the symptomatic relief of cardiac failure but they have not been convincingly shown to improve prognosis.[53] It is important to review a patient's need for ongoing diuretic therapy at the time of hospital discharge. Digoxin does not have any clear-cut role in the patient post infarction, except in those who require it in addition, or as an alternative, to beta blockers for rate control of atrial fibrillation.[54]

Coumadins and oral antithrombins

Coumadins do not have a clear-cut role in preventing recurrence in the patient post MI. If a patient has had a large infarction, he or she may benefit from a period of warfarin anticoagulation to prevent stroke.[55] This is particularly the case in the presence of severe LV dysfunction and/or large apicoanterior infarct and definitely if there is intra-cardiac thrombus demonstrated on echocardiography.[56] New oral antithrombins such as rivaroxaban have been tested in patients who have had coronary events and shown to reduce recurrences but at an increased risk

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Clearing the way to lower cholesterol

- Fluvastatin achieves significant improvement in lipid parameters in patients with and without metabolic syndrome compared with placebo ($p < 0,001$ from baseline for all parameters)[1]
- Fluvastatin significantly reduces the relative risk of cardiovascular morbidity and mortality in patients with metabolic syndrome[1]

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Monoamine oxidase B inhibitors

Monoamine oxidase B deactivates dopamine in the brain. Inhibitors of monoamine oxidase B therefore increase dopamine levels in the brain and are an additional therapeutic option for the treatment of Parkinson's disease. Two monoamine oxidase B inhibitors are indicated for the treatment of Parkinson's disease: selegiline and rasagiline.

Selegiline

Selegiline should be used in low doses (5mg twice daily) as higher doses may also inhibit monoamine oxidase A and result in side effects such as hypertension. Selegiline was commonly used in early-onset disease and in combination with levodopa for maintenance. However, concerns over cardiac side effects have been raised, and there is a potential risk of adverse effects when it is used in combination with selective serotonin re-uptake inhibitors and tricyclic anti-depressants. Selegiline is generally well tolerated as monotherapy, although side effects such as nausea, dizziness, headaches and dry mouth may occur.

Rasagiline

Rasagiline is indicated for the symptomatic treatment of idiopathic Parkinson's disease as monotherapy (without concomitant levodopa/DDCI therapy) or as adjunct therapy (with concomitant levodopa/DDCI therapy). In patients with Parkinson's disease receiving monotherapy with a monoamine oxidase B inhibitor, the effects on motor symptoms are modest.[3] In patients with Parkinson's disease receiving treatment with levodopa/DDCI therapy, the addition of a monoamine oxidase B inhibitor has similar effects as the addition of entacapone in reducing daily OFF time.[4]

Future directions

Pharmacological dopamine replacement is generally very effective in early disease but it is only a symptomatic therapy. Future therapeutic strategies should focus not only on ameliorating the symptoms of Parkinson's disease but on neuroprotective or neurorescue therapies that can favourably modify the natural course of the disease and slow the progression of both motor and non-motor manifestations.

Strategies pursuing restorative approaches to Parkinson's disease therapy involve attempts to replace the degenerating nigrostriatal dopaminergic network with cells. Fetal ventral mesencephalic tissue transplants are under continuing investigation and the stem cell field is advancing rapidly. However, further development and optimisation of the safety and efficacy of techniques involved in generating and manipulating these stem cells, and other cell sources, will be essential before any further clinical trials are done. Other experimental strategies currently under investigation include anti-apoptotic strategies and implantation of genetically engineered cells.

Future advances will include novel medication delivery systems such as transdermal or inhaled therapies (eg, VR040); novel levodopa/carbidopa formulations with prolonged action (eg, IPX066); enzyme inhibitors that can prolong the duration of action of levodopa (eg, safinamide); anti-Parkinson medication with novel receptor targeting (eg, preladenant); safinamide, and medications that improve non-motor symptoms (eg, L-dihydroxyphenylserine); or levodopa-induced dyskinesias (eg, AFQ056).

A list of references is available on request.

Patients Post Myocardial Infarction

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of bleeding.[57] The modern DAPT era has complicated the management of patients with concurrent acute coronary syndrome and/or recent stenting and atrial fibrillation – in these patients, the use of triple therapy (DAPT plus anticoagulation) significantly increases the risk of adverse bleeding events.[58]

Should this patient be considered for device therapy?

The early implantation of an ICD in patients who have had an MI has been shown not to deliver any additional benefit.[59] Patients who have had ventricular fibrillation during the early hours of their MI do not need an ICD. Those who had an infarction more than 40 days previously and whose ejection fraction is persistently below 35% should have an ICD implanted, although there are healthcare access and economic limitations to this recommendation. Patients should be on maximal tolerated medical therapy prior to re-evaluation of LV function to prevent unnecessary device implantation and potential morbidity from the device.

Conclusion

Contemporary post-MI management should be tailored according to patient characteristics and local access to coronary angiography or noninvasive imaging modalities. Aggressive medical management has a proven benefit for secondary prevention. Coronary revascularisation is indicated for persisting symptoms and high-risk, extensive ischaemia. Implantable defibrillators should be considered in those patients who have persisting severe LV dysfunction (ejection fraction less than 35%).

References are available on request.