POSTINFARCTION PATIENT MANAGEMENT

Ph Meurin, MD and JY Tabet, MD
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Figure 1. Risk of infarction as a function of exposure to various risk factors (after INTERHEART). Smk: smoking, DM: diabetes mellitus, HTN: hypertension, ApoB/A1: dyslipidemia, Obes: obesity, PS: psychological and social factors, All RFs: all risk factors.
Summary

Cardiovascular diseases, particularly ischemic heart diseases, remain the leading cause of death for men and women in developed countries. However, over the last 30 years, a decrease in the mortality related to ischemic heart disease has occurred. The improvement is two-thirds due to primary prevention (Figures 1 and 2) and one-third due to the improvement in management of the acute phases of infarction and secondary prevention. The 5-year mortality postinfarction remains 25% to 30%.

Individual risk stratification is designed to enable adaptation of pharmacologic treatment and a decision as to revascularization or defibrillator implantation after the patient’s discharge from the intensive care unit (ICU).

Numerous multicenter, randomized, prospective studies of postinfarction patients, including thousands of patients, have demonstrated the benefit of the following therapies which are to be systematically combined:

- β-blockers: metoprolol, acebutolol, timolol, propranolol
- Angiotensin-converting enzyme (ACE) inhibitors: perindopril, ramipril
- Platelet-aggregation inhibitors: aspirin + clopidogrel (for a variable duration generally estimated to be between 9 and 12 months)
- Statins
- Mediterranean diet
- Smoking cessation
- Exercise reconditioning

![Figure 2. Smoking and dyslipidemia are two major risk factors.](image-url)
Introduction

In the year following myocardial infarction (MI), 10% of patients die, half of them experiencing sudden death (1%). The deaths mainly occur in the first 3 to 6 months, but, in reality, the risk may vary from less than 1% to more than 50%, depending on the seriousness of the myocardial infarction. The 5-year mortality among hospital-phase survivors remains about 25%. The management of postinfarction patients thus involves risk stratification, which begins on discharge from the intensive care unit and is to be regularly updated throughout the coronary artery disease (CAD) patient’s life. The results of the assessment orient medium- and long-term management.

1. Clinical factors (Figure 3)

In all the trials, age >65 years is a pejorative prognostic factor, even after adjustment for parameters frequently related to age (diabetes mellitus, congestive heart failure, less frequent reperfusion attempts, etc.). The same applies to female gender, although it is difficult to determine whether the gender-related excess risk cannot be simply explained by the later age of infarction onset in women and by management, which is frequently less energetic.

Continuing smoking is an independent pejorative prognostic factor postinfarction, as is diabetes mellitus (even if treated) and untreated hypercholesterolemia. The occurrence of an episode of congestive heart failure and the absence of revascularization during the acute phase are also pejorative criteria. The existence of residual angina pectoris postinfarction is considered a poor prognostic factor in the absence of revascularization. This concerns about 30% of patients.

2. Resting EKG electrocardiogram (ECG) (Figure 4)

An anterior infarct site frequently reflects more extensive necrosis and is associated with excess mortality at time point 1 year. The prognostic value of the absence of a Q wave is controversial: in a review of 18 trials conducted before the era of acute-phase revascularization, the long-term survivals were comparable, Q wave vs no Q wave, but certain more recent trials appear to show that the presence of a Q wave exacerbates the medium-term prognosis. In addition, the extent of ST-segment elevation, the broadening of the QRS interval, and the presence of permanent ST-segment depression are factors related to medium-term excess mortality. Lastly, the persistence of ST-segment elevation in the infarct territory more than 10 days after the acute episode frequently reflects the constitution of a ventricular aneurysm. In contrast, the presence of ventricular rhythm disorders during the acute phase is frequently related to ischemia or reperfusion phenomena and is not related to excess mortality after discharge from the ICU.

### Table: Factors determining prognosis post infarction

<table>
<thead>
<tr>
<th>Factors determining prognosis post infarction</th>
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<tbody>
<tr>
<td><strong>General factors</strong></td>
</tr>
<tr>
<td>Advanced age</td>
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<tr>
<td>Female gender</td>
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<tr>
<td>Diabetes mellitus</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Continued smoking</td>
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<tr>
<td>Elevated cholesterol</td>
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<tr>
<td><strong>Mechanical factors</strong></td>
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<tr>
<td>Large infarct size</td>
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<tr>
<td>Decreased left ventricular ejection fraction (&lt; 40%)</td>
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<tr>
<td>Increased left ventricular end-systolic and end-diastolic volume</td>
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<tr>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Anterior myocardial infarction</td>
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<tr>
<td><strong>Electrophysiological factors</strong></td>
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<tr>
<td>Atrial fibrillation and other supraventricular arrhythmias.</td>
</tr>
<tr>
<td>New bundle branch block (including fascicular blocks).</td>
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<tr>
<td>Mobitz type II second degree block or complete heart block.</td>
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<td>Ventricular tachycardia or fibrillation.</td>
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<tr>
<td>Complex or frequent ventricular ectopy.</td>
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<tr>
<td>Abnormal signal-averaged electrocardiogram.</td>
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<td>Inducible sustained monomorphic ventricular tachycardia during electrophysiological study.</td>
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<tr>
<td><strong>Ischemic factors</strong></td>
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<tr>
<td>Non-Q wave infarction</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
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<tr>
<td>Reinfarction or infarct extension.</td>
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<tr>
<td>Severe coronary artery disease.</td>
</tr>
<tr>
<td>Persistent occlusion of the infarct related artery.</td>
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<tr>
<td>Postinfarction angina.</td>
</tr>
<tr>
<td>Abnormal exercise test (manifested by symptomatic or silent ischemia, ventricular ectopy, or hypotension).</td>
</tr>
</tbody>
</table>

Figure 3. Factors determining prognosis post infarction.

Figure 4. Anterior myocardial infarction becoming established.
3. Investigation for myocardial ischemia

The investigation is conventionally based on the exercise test and stress scintigraphy or exercise echocardiography (Figure 5). Magnetic resonance imaging (MRI) remains of limited importance at the present time due to a lack of accessibility.

**Exercise testing (Figures 6 and 7)**

The role of the exercise test in the assessment of postinfarction patients has been clearly established. Depending on the team, the exercise test may be implemented as of day 6 postinfarction (when it will always be symptom-limited by β-blocker treatment and low level) and/or after day 21 (when the test will be high level and may or may not be β-blocker symptom-limited).

The aims of the test are to:
- investigate for residual ischemia, (Figure 8)
- assess the patient’s functional capacities and the scope for social and professional reintegration,
- assess the efficacy of medical treatment,
- screen for rhythm or conduction disorders during exercise and recovery,
- prescribe an exercise-reconditioning program.

The group of patients at the highest risk consists of patients who cannot undergo an exercise test, irrespective of the reason. Low intensity (<5 MET) and an absence of blood pressure elevation during exercise are poor prognostic factors.

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**Physical exercise** | **Dipyridamole** | **Dobutamine**
---|---|---
**Mechanism** | Physiological stimulation | Vasodilatation | β1-receptor stimulation
**Hemodynamics** | ↑ MVO₂ | ↑ O₂ supply | ↑ MVO₂
**Contraindications** | Peripheral arterial disease of the legs | COAD, asthma | arrhythmias
**Diagnostic sensitivity** | + | ++ | +++
**Diagnostic specificity** | ++ | ++ | +++
**Prognostic value** | ++ | ++ | ++

MVO₂: myocardial oxygen consumption, AOL: arteritis of the legs, COAD: chronic obstructive airways disease.

**Figure 5.** Ischemia Ischemia-triggering mechanisms under various stresses.

<table>
<thead>
<tr>
<th>ST-segment depression amplitude (mm)</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>84%</td>
<td>57%</td>
</tr>
<tr>
<td>1</td>
<td>62%</td>
<td>89%</td>
</tr>
<tr>
<td>1.5</td>
<td>48%</td>
<td>100%</td>
</tr>
<tr>
<td>Overall &gt;1</td>
<td>68%</td>
<td>77%</td>
</tr>
</tbody>
</table>

(meta-analysis)

**Figure 6.** Early positive exercise test: major ST-segment depression at a heart rate of 100 bpm. Ischemia Ischemia-triggering mechanisms under various stresses. MVO₂: myocardial oxygen consumption, AOL: arteritis of the legs, COAD: chronic obstructive airways disease.

**Figure 7.** Exercise-induced ST-segment depression that is rapidly corrected then reappears during the recovery period after exercise, which generally means the lesions are severe, narrow, and/or extensive.

**Figure 8.** Sensitivity and specificity of the exercise test as a function of ST-segment depression amplitude in the screening for coronary artery disease.
**Scintigraphy**
The principle consists in studying regional myocardial perfusion by comparing the distribution of a marker (most frequently radiolabeled thallium 201 Tl) injected during exercise testing and following a period of rest, enabling study of the redistribution at hour 4 (Figure 9). The value of exertional scintigraphy, vs. a simple exercise test, resides in the fact that it affords enhanced sensitivity and specificity. Exertional scintigraphy also supplies information on the topography of the myocardial ischemia (unlike the exertional electrocardiogram). The information is pertinent to deciding whether or not coronary revascularization is indicated. The procedure also supplies information on the functional value of the myocardium. Lastly, when exercise is impossible for purely mechanical reasons (osteoarthritis, etc.), it may be replaced by dipyridamole injection. The limitations with respect to interpretation of septal defects, particularly in the event of left bundle-branch block, should not be overlooked.

**Exercise echocardiography**
The efficacy of exercise echocardiography with respect to evaluation of myocardial ischemia in CAD patients is good (sensitivity and specificity: 80%), and comparable to that of scintigraphy. After an acute event, the procedure enables superior risk stratification compared to a standard exercise test. In early postinfarction, dobutamine echocardiography is less used by certain teams (due to its arrhythmogenic potential) than exercise echocardiography. In the medium term, both procedures may be used, and yield similar results.

**Cardiac MRI magnetic resonance imaging**
(Magnetic resonance imaging)
(Magnetic resonance imaging)
(Figures 12, 13, 14, 15, 16) MRI enables early quantification quantification of the size of the infarct and, in combination with pharmacologic stimulation (dobutamine), detection of residual ischemia. The main limitation on MRI use today remains the lack of machine accessibility.

**Ambulatory electrocardiogram recording (Holter recording)**
(Figure 17)
The value of Holter recording with respect to investigating for myocardial ischemia remains highly controversial. Overall, with regard to screening for myocardial ischemia, there is currently not sufficient evidence of the contribution of 24-hour Holter recording, vs. the exercise EKG, to enable recommendation of Holter recording to screen for myocardial ischemia in postinfarction patients.

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**Figure 9.** Exercise thallium scintigraphy: indication for revascularization. A: exertional anteroseptal and apical hypoperfusion.

**Figure 10.** Normal dobutamine echocardiography: normal thickening of all the left ventricle walls at a heart rate of 144 bpm.

**Figure 11.** Dobutamine echocardiography post-inferior infarction: indication for right coronary angioplasty. A: baseline state, B: increased thickening of the basal part of the inferior wall on low-dose dobutamine reflecting the existence of myocardial viability, C: secondarily, decreased systolic thickening of the same zone reflecting residual ischemia.
Figure 12. Myocardial MRI. A: Transmural anteroapical MI without viability except at neck level. B: Limited non-transmural inferior myocardial infarction, residual inferior ischemia on persantine at the right.

Figure 13. Noninvasive coronary angiography using MRI. Images from a three-dimensional sequence taken with the patient breathing freely and without injection of contrast medium (slice thickness 1.3 mm, resolution 0.7 × 0.7 mm) (Siemens Symphony, 1.5T). The right coronary artery (on the left) can be seen as far as the origin of the third segment in a normal subject (above) and in a patient (below) with stenosis of the inferior part of the second segment (arrow). The proximal and middle parts of the anterior interventricular artery and the circumflex artery with their branches (right) are visualized in a subject without coronary artery disease (above) and in a patient (below) with diffuse coronary atheroma and two focal lesions of the proximal and middle part of the interventricular artery (arrows).

Figure 14. Corresponding views on conventional angiography (left) and MRI (right) in a patient with stenosis of the proximal interventricular artery (above, arrows) and in a patient with stenosis of the circumflex artery (below, arrows) before the origin of the marginal branch.
Figure 15. Noninvasive coronary angiography using MRI (clinical magnet, 1.5 T). High-resolution images taken from a three-dimensional sequence during free breathing (navigator echo) in a patient who had a stent implanted in the initial part of segment 2 of the right coronary artery (left) and in the proximal interventricular artery (right). The magnetic susceptibility artifact due to the presence of stents is seen as an area without any signal (arrows). The presence of stents is not a contraindication to performing cardiac MRI.

Figure 16. MRI after two apical intramyocardial injection of stem cells labeled with iron oxide particles in a pig free of myocardial infarction. The iron-labeled cells emit a hyposignal of magnetic susceptibility (arrows). B. MRI with inversion-recovery 15 minutes after intravenous injection of gadolinium in a pig with an experimental septo-apical infarct (hypersignal) that had 3 intramyocardial injections of stem cells labeled with iron oxide (hyposignal within the infarcted area, arrows).

Figure 17.
Evaluation of infarct size and left ventricular function

Post-infarction left ventricular function is one of the key components of the prognosis. Numerous methods enable assessment of left ventricular function:

- Two-dimensional echocardiography is the method most widely used to evaluate left ventricular ejection fraction (LVEF). Echocardiography is to be conducted very early in order to determine the size and repercussions of the infarction (determination of the LVEF, evaluation of systolic pulmonary artery pressure and filling pressures) and to enable screening for certain complications (ischemic mitral incompetence, left intraventricular thrombus, pericardial effusion, septal defect, etc). (Figures 18, 19, 20)

- However, other methods enable direct or indirect evaluation of left ventricular function:
  - clinical signs (presence or absence of peripheral signs of heart failure)
  - radionuclide ventriculography with scintigraphy, iodine ventriculography with coronary angiography
  - myocardial CT scan and MRI
  - electrocardiogram (sites and number of leads bearing a Q wave) remains an indirect indicator of average performance
  - lastly, the duration of exercise and the peak oxygen consumption are correlated with left ventricular ejection fraction. However, the correlations are modest since exercise tolerance also depends on muscle and peripheral vascular status. The latter parameters are independent of left ventricular function.

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**Figure 18 A and 18 B.** Anteroseptal infarction with septal sequela (thin and hyperdense wall). 18A: diastole, 18B: systole, L: lateral wall, S: interventricular septum.

**Figure 19.** Left intraventricular apical thrombus in a context of sequelae of anterior infarction.

**Figure 20.** Mechanical complication of myocardial infarction: rupture of the interventricular septum.
The arrhythmia risk (Figure 21)

It is important to clearly distinguish between patients who have presented with episodes of serious arrhythmia (sustained ventricular tachycardia or ventricular fibrillation) after the acute phase. Those patients are to undergo a rhythm assessment, most frequently invasive, and the implantation of a defibrillator is to be considered (cf. see corresponding section).

In contrast, most patients, i.e., patients having presented with a ventricular rhythm disorder in the acute phase (which is not, as previously noted, particularly predictive of a distant event) and the patients who have not presented with a severe episode of arrhythmia are to undergo a non-invasive assessment enabling evaluation of the medium-term risk of sudden death.

The most important parameter for distinguishing between patients at a high and at a low risk of arrhythmia is left ventricular function. The risk is low when LVEF >40%. In such patients, no prophylactic therapy has shown any benefit with respect to preventing sudden death.

Twenty-four-hour Holter recording enables screening for patients presenting with very frequent ventricular extrasystoles or unsustained ventricular tachycardia. Those phenomena are associated with a higher risk of sudden death.

The “late-potential” high-amplification electrocardiogram (Figure 22) enables investigation for an anatomical substrate predisposing to reentry ventricular tachycardia. The presence of late potentials appears to be associated with an increase in the incidence of sudden death in postinfarction patients but the positive predictive value of the investigation is too low (<30%). The therapeutic implications of a positive result are therefore unclear. The investigation is not conducted systematically. Similarly, the sinus variability of heart rate is not systematically investigated.

The presence of complex ventricular arrhythmia during exercise is associated with excess mortality due to sudden death.

In conclusion, the basic rhythm assessment is simple. It is based on evaluating left ventricular ejection fraction, Holter recording and exercise testing.

Investigating for myocardial viability

Certain anomalies of left ventricular kinetics may be corrected if myocardial perfusion is restored. This potentially reversible disorder of contractility is referred to as myocardial viability. The investigation for myocardial viability is fundamental since, first, the absence of revascularization of viable myocardium is associated with excess mortality, and, secondly, revascularization of viable myocardium is associated with a reduction in that mortality.

Depending on the equipment available, the first-line investigation may be either thallium 201 nuclear imaging or low-dose dobutamine echocardiography. The limitation of both methods is their relative lack of sensitivity. They are thus frequently combined.

Cardiac MRI also enables detection of viable myocardium. The very good spatial resolution and excellent tissue characterization achieved with this method enable very good differentiation of viable and nonviable tissue.

Positron-emission tomography (PET) is the reference procedure (Figure 23). Hibernating myocardium is characterized by the mismatch between the relative or absolute decrease in regional myocardial blood flow rate and the preservation of metabolic activity, particularly glucose metabolism (determined by F-fluorodeoxyglucose uptake). The characteristic image of the mismatch between metabolism and perfusion demonstrates myocardial viability.

Figure 21

Criteria for the presence of late potentials (in the absence of bundle branch block)

1. QRS >120 ms; 2. RMS <40 ± 20 µV shaded area; 3. LAS >40 ms arrow.

Figure 22. Investigating for late potentials. 1. Duration of the QRS complex; 2. Amplitude of the last 40 ms of the signal-averaged QRS (RMS 40 = root mean square); 3. Duration of potentials of less than 40 µV (LAS = low amplitude signal)
Figure 23. Positron emission scanning. A: evaluation of blood flow using 13N: reduction in apical perfusion. B: glucose (18FDG) uptake: high level of absorption reflecting good viability.

Figure 24. Coronary angiography: single-vessel occlusion of the IVA, right arteries free from lesions.

Figure 25. Coronary angiography post-inferior infarction: tight stenoses of the proximal and intermediate right coronary artery.

Figure 26. Intermediate lesion of the interventricular coronary artery on coronary angiography.

Figure 27. Intermediate lesion of the interventricular coronary artery on coronary angiography seen on a CT scan.
Figure 28. Baseline phase contrast magnetic resonance imaging (below) of the interventricular coronary artery (IVA) and with adenosine, four months after insertion of a stent in the proximal IVA. The plane of the MRI section (red line) is downstream of the stent. Absence of restenosis (left): the ratio of the adenosine/baseline blood flow rate gives a coronary reserve reading of 3. Restenosis of the IVA (right): the ratio of the coronary blood flow rates gives a coronary flow reserve of 1.2. This method is an extremely effective diagnostic method for detecting restenosis in a noninvasive manner after stent implantation.

Figure 29. Coronary angiography during the acute phase of an infarction: multiple areas of stenosis of the right coronary artery, which is occluded at the end of the second segment. Note the presence of a temporary pacing wire inserted at the tip of the right ventricle because of atrioventricular conduction disturbances at the same time as the infarction.

Figure 30. Imaging the anterior interventricular artery (IVA) using 2D-mode multi-detector-array CT scanning. A: using multiprojection volume reconstruction (MPVR) with automatic effacing of the heart chambers, B: image of the IVA in its long axis.
During the acute phase of MI, patients increasingly frequently undergo emergency coronary angiography for primary angioplasty and/or on suspicion of thrombolysis failure. In those patients, the initial coronary angiography indication is thus not an issue.

In other patients, coronary angiography is considered indispensable if:

- spontaneous myocardial ischemia or ischemia induced by minimal exertion persists,
- a mechanical complication requires treatment (mitral incompetence, interventricular septal defect, etc),
- there is persistent hemodynamic instability,
- the initial infarction presented without ST-segment elevation.

Coronary angiography is also strongly recommended for patients presenting with the following:

- postinfarction heart failure
- ventricular arrhythmia
- LVEF < 40%
- suspected unusual mechanism (coronary embolism, metabolic disease, etc)
- occupation at risk (truck driver, shift work, etc).

Lastly, coronary angiography is indicated for almost all patients at high or intermediate risk, other than patients not considered candidates for revascularization for non-cardiologic medical or personal reasons. The multi slice scanner is a promising technique which is currently evaluating.

In practice: postinfarction risk stratification

In the first section, all the investigations of potential value postinfarction were addressed. They are obviously not all to be used systematically, and the investigations are to be appropriate to the specific situation. It is to be noted that echocardiography, exercise testing, and Holter recording are to be systematic. As previously noted, if coronary angiography is not conducted during the acute phase, it is to be almost systematic. Lastly, if left ventricular sequelae persist on echocardiography, investigation for viability is indispensable.

Figure 32. 3D-imaging of the left coronary arteries (multi-detector-array CT scanner) with automatic effacement of the heart chambers. A: frontal B: lateral C: spider view D: Left anterior oblique and craniocaudal views.
Figure 33. Evaluation of left ventricular systolic function using multi-detector-array CT scanning: normal thickening of the systolic left ventricular myocardium. A: large axis, diastole. B: large axis, systole. C: small axis, diastole. D: small axis, systole.

Figure 34. Normal coronary CT scan: circumflex artery.

Figure 35. Normal coronary CT scan: right coronary artery.

Figure 36. Normal coronary CT scan: interventricular artery.
Pharmacologic treatments

Platelet-aggregation inhibitors

Aspirin decreases the risk of infarction recurrence in a very significant manner at moderate doses (between 75 and 300 mg/day). The treatment is to be taken indefinitely. Thienopyridines (ticlopidine and clopidogrel) are to be systematically associated with aspirin, in particular for patients having undergone coronary stenting. The duration of the aspirin + clopidogrel combination is most frequently 9 to 12 months. Aspirin is subsequently pursued indefinitely. On the basis of the results of the CAPRIE study, clopidogrel may replace aspirin in patients at risk of ischemic events. The indications for long-term oral anticoagulant treatment are more debatable. Treatment is obviously indicated for patients with arrhythmia due to chronic atrial fibrillation, patients having undergone valve replacement and patients with a postinfarction left intraventricular thrombus. The indication is more controversial in patients presenting with a large left ventricular sequela, particularly an apical sequela. In certain situations (post-stenting and left intraventricular thrombus; post-stenting and valve replacement; etc.), triple therapy with aspirin, clopidogrel, and an oral anticoagulant is sometimes necessary transiently, despite the hemorrhagic risk.

Outside of post-stenting settings, aspirin is currently preferred to oral anticoagulants due to its greater simplicity of use and superior cost effectiveness. If, however, only the efficacy of treatment is considered, it is to be noted that the ASPECT 2 study compared 3 three strategies in 993 patients having experienced an acute coronary syndrome (of which, 87% infarctions). The treatments consisted in 80 mg of aspirin vs. 80 mg of aspirin + Coumadin (mean INR = 2.4) and vs. vs Coumadin alone (mean INR = 3.2). At time point 1 year, the frequency of the primary criterion (composite criterion: death, infarction, and stroke) was significantly lower in the patients receiving an oral anticoagulant alone (5.2%) or an oral anticoagulant combined with aspirin (5.1%), compared toocompared with the patients on aspirin alone (9.2%).

ß-blockers

The international recommendations are clear: all patients (including heart failure patients) not presenting with a contra-indication to ß-blockers are to receive long-term ß-blocker therapy post-myocardial infarction (MI).

The drugs have a dual value in that indication: their method of anti-ischemic action and their antiarrhythmic action. Thus, ß-blockers significantly reduce cardiac mortality postinfarction and have an even more marked effect on sudden death. The results are greater if treatment is initiated early.

The most recently published meta-analysis (1999) addressing the subject is by Freemantle and included over 50 000 patients. The long-term mortality was 11% in the placebo groups and 8.4% in the treated groups (relative risk reduction: 23%). It is to be noted that a significant reduction in mortality has only been demonstrated with four ß-blockers: acebutolol, metoprolol, propranolol, and timolol. It is also to be noted that, even though it is the subject of consensus, the utility of very long-term ß-blockade (more than 5 years) has not been evaluated.

Angiotensin-converting enzyme (ACE) inhibitors

ACE inhibitors have clearly demonstrated their efficacy postinfarction. All ACE inhibitors decrease the loading conditions of the left ventricle and thus enable a decrease in left ventricular remodeling (Figure 37). In the short term, ACE inhibitors thus limit the expansion of the infarct zone by decreasing the intracardiac forces. In the long term, they decrease the dilatation and hypertrophy of the infarct-free left ventricular zone.

Five major trials have confirmed the value of ACE inhibitors postinfarction: AIRÉ, SAVE, SMILE, Trace, PREAMI. The first 4 trials included patients presenting with left ventricular dysfunction and not having undergone thrombolysis. The patients were therefore at high risk. The reduction in medium-term mortality (1 year to 50 months) was marked (relative risk reduction from 19% to 29% and absolute risk reduction from 4.1% to 7.6%). It is thus very clear that ACE inhibitors are to be prescribed for all postinfarction patients pre-

Hemodynamic effects
- Improved subendocardial perfusion (A,B)
- Substained effects of blood pressure reduction (A,B)

Vascular effects
- Prevention of smooth muscle cell migration and proliferation (A,B)
- Enhanced endothelial production of EDRF (B)
- Antithrombotic effects (A,B)
- Reduced incidence of plaque rupture (A)

Antithrombotic effects
- Platelet inhibition (A)
- Increased endothelial t-PA production (B)
- Reduced endothelial production of PAI-1 (A)

Figure 37. Anti-ischemic action mechanisms of ACE inhibitors.
senting with left ventricular dysfunction. The PREAMI study was designed to evaluate the effect of perindopril 8 mg (the EUROPA study dosage) on left ventricular remodeling. The composite primary endpoint/end point of the study consisted in mortality, hospitalization for heart failure, and left ventricular remodeling >8%.

Only elderly patients with preserved left ventricular function post-recent MI (mean <11 days) were included. Perindopril was administered at a dosage of 4 mg then, 8 mg, as a function of blood pressure safety. As of month 6, left ventricular remodeling was significantly reduced by perindopril (Figure 38). The number of clinical events during the study was low. Two findings have emerged from the study:

> post-MI patients, including those with preserved left ventricular function, undergo remodeling of the left ventricle; the remodeling can be prevented with perindopril 8 mg.
> patient age is not a restriction to post-MI ACE-inhibitor prescription.

The clinical and blood pressure safety of perindopril was good and almost all the patients received the dosage of 8 mg daily.

Thus, the PREAMI study demonstrated that administration of high-dose perindopril (8 mg/day) was well tolerated in postinfarction elderly subjects with no initial left ventricular dysfunction. Treatment enabled a reduction in left ventricular remodeling even after a small infarction. More recently, on the basis of the results of the HOPE,32 EUROPA,33 PREAMI and PEACE34 studies (Figure 39), the indications for ACE inhibitors were expanded to include long-term treatment of all non-hypertensive postinfarction patients (SBP ≥110 mm Hg).

It is necessary to analyze the results of the EUROPA and PEACE studies since they may, at first sight, appear contradictory.

The results of the PEACE study conducted on CAD patients without left ventricular dysfunction (Figure 40) showed no long-term improvement in the composite end point (death, infarction, and revascularization) ontrandolapril. However, the results are difficult to interpret since the composite end point (death, infarction, and revascularization) on perindopril (8 mg/day) was well tolerated in postinfarction elderly subjects with no initial left ventricular dysfunction. Treatment enabled a reduction in left ventricular remodeling even after a small infarction. More recently, on the basis of the results of the HOPE,32 EUROPA,33 PREAMI and PEACE34 studies (Figure 39), the indications for ACE inhibitors were expanded to include long-term treatment of all non-hypertensive postinfarction patients (SBP ≥110 mm Hg).

Aspirin 75% 92% 90%

Beta-blockers 39% 62% 60%

Statins 28% 58% 70%

PTCA 18% 29% 42%

CABG 26% 29% 38%

Diabetes 39% 12% 18%

Table: Inclusion criteria for the HOPE, EUROPA, and PEACE studies

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Age</th>
<th>Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOPE</td>
<td>&gt;65</td>
<td>CAD/CVA/peripheral arterial disease of the legs or Diabetes + (high cholesterol, low HDL, smoking, hypertension, microalbuminuria)</td>
</tr>
<tr>
<td>EUROPA</td>
<td>&gt;18</td>
<td>CAD</td>
</tr>
<tr>
<td>PEACE</td>
<td>&gt;50</td>
<td>CAD, coronary artery disease; CVA, cerebrovascular accident; HDL, high-density lipoprotein.</td>
</tr>
</tbody>
</table>

Figure 39. Inclusion criteria for the HOPE, PEACE and EUROPA studies; the inclusion criteria for PEACE and EUROPA are similar. CAD: coronary artery disease, Stroke: history of stroke, A DL: arteritis of the legs.

Table: Exclusion criterion

<table>
<thead>
<tr>
<th>Exclusion criterion</th>
<th>HOPE</th>
<th>EUROPA</th>
<th>PEACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of patients with an LVEF result</td>
<td>51%</td>
<td>82%</td>
<td>100%</td>
</tr>
<tr>
<td>% of patients with an LVEF &lt;40%</td>
<td>8.1%</td>
<td>3%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Figure 40. The small proportion of patients presenting with left ventricular dysfunction in the HOPE and EUROPA studies proves that the positive results were not due to enhanced benefit in patients with heart failure.

Table: Inclusion criteria for the HOPE, EUOPA, and PEACE studies; the inclusion criteria for PEACE and EUROPA are similar. CAD: coronary artery disease, Stroke: history of stroke, A DL: arteritis of the legs.

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>CAD/CVA/peripheral arterial disease of the legs or Diabetes + (high cholesterol, low HDL, smoking, hypertension, microalbuminuria)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HOPE</td>
<td>&gt;65</td>
</tr>
<tr>
<td>EUROPA</td>
<td>&gt;18</td>
</tr>
<tr>
<td>PEACE</td>
<td>&gt;50</td>
</tr>
</tbody>
</table>

Figure 41. The patients included in the EUROPA and PEACE studies were similar. The difference between the results of the two studies therefore cannot be explained by a between-population difference in disease seriousness.

<table>
<thead>
<tr>
<th>Disease</th>
<th>HOPE</th>
<th>EUROPA</th>
<th>PEACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66</td>
<td>60</td>
<td>64</td>
</tr>
<tr>
<td>Diabetes</td>
<td>39%</td>
<td>12%</td>
<td>18%</td>
</tr>
<tr>
<td>MI</td>
<td>52%</td>
<td>65%</td>
<td>54%</td>
</tr>
<tr>
<td>CABG</td>
<td>26%</td>
<td>29%</td>
<td>38%</td>
</tr>
<tr>
<td>PTCA</td>
<td>18%</td>
<td>29%</td>
<td>42%</td>
</tr>
<tr>
<td>Statins</td>
<td>28%</td>
<td>58%</td>
<td>70%</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>39%</td>
<td>62%</td>
<td>60%</td>
</tr>
<tr>
<td>Aspirin</td>
<td>75%</td>
<td>92%</td>
<td>90%</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>139/79</td>
<td>137/82</td>
<td>134/78</td>
</tr>
</tbody>
</table>

Figure 42. Statistical results: blood pressure.

<table>
<thead>
<tr>
<th>Blood pressure</th>
<th>HOPE</th>
<th>EUROPA</th>
<th>PEACE</th>
</tr>
</thead>
<tbody>
<tr>
<td>139/79</td>
<td></td>
<td>137/82</td>
<td>134/78</td>
</tr>
</tbody>
</table>

Figure 43. Statistical results: blood pressure.
POSTINFARCTION PATIENT MANAGEMENT

Many CAD patients have already experienced MI. Preventive therapy used as of the onset of ischemia saves many lives and conserves LV function. In the EUROPA study, 7910 patients had a history of MI: 3962 in the treated group and 3948 in the placebo group. Perindopril induced a significant 22.5% reduction in cardiovascular death, MI, and cardiac arrest in the post-MI population. Moreover, the 28% reduction in the risk of MI was also significant (P <0.01). The reduction in MI incidence in the non-revascularized post-MI population was 35%.

In conclusion, it would appear that ACE inhibitors are indicated postinfarction even in the absence of left ventricular dysfunction or diabetes mellitus. The indication has been clearly demonstrated for ramipril and perindopril.

The negative results of the PEACE study may be due to the poor end-point point and/or may call into question the “class effect” of ACE inhibitors. The PERTINENT study has demonstrated the vascular action of perindopril. The drug was anti-inflammatory (reduction in TNF-α), inhibited platelet aggregation (reduction in Von Willebrand factor), and acted on vascular tone (reduction in apoptosis and improvement in the bradykinin/angiotensin ratio).

Lipid-lowering agents

Outside of the very rare patients whose LDL cholesterol level is spontaneously <0.7 g/L, all patients are to receive HMG coA reductase inhibitor treatment over the long term post-MI. The therapeutic target is LDL cholesterol <1 g/L (or 0.7 g/L for certain patients). Lipid-lowering agents procure a very marked reduction in cardiovascular morbidity and mortality due to their cholesterol-lowering effect and their pleiotropic effect on atheromatous plaque. Lipid-lowering agents also have ancillary effects (perhaps antiarrhythmic and/or anti-osteoporotic effects and/or effects on left ventricular function) that are currently under investigation. It is probable that treatments enabling elevation of HDL cholesterol are effective but nicotinic acid, the drug whose development is most advanced in that context, is undergoing assessment with respect to morbidity and mortality.

The role of fibrates is small. Fibrates are perhaps of use in patients presenting with both diabetes mellitus and hypertriglyceridemia (FIELD study).

Aldosterone blockers

Left ventricular dysfunction is correlated with elevated aldosterone. The EPHESUS study clearly showed that eplerenone treatment is of value in patients whose postinfarction LVEF is <40%. There was a significant reduction in the number of cardiovascular deaths due to the anti-remodeling and antiarrhythmic effect. However, combination therapy with an aldosterone blocker and ACE inhibitor necessitates monitoring serum creatinine and potassium.
Antiarrhythmics

The basic systematic antiarrhythmic treatment consists in $\beta$-blockers. As the CAST study\textsuperscript{37} showed, class I antiarrhythmics are harmful postinfarction. This applies to subclasses IA, IB, and IC. The role of amiodarone is debatable since the two main studies on its utility postinfarction (CAMIAT\textsuperscript{38} and EMIAT\textsuperscript{39}) did not demonstrate a reduction in overall mortality, although there was a decrease in arrhythmia-related deaths. The frequency of adverse reactions and the mixed results of those studies are not conducive to systemic prescription. Amiodarone may be combined with $\beta$-blockers for certain groups of patients at high risk of arrhythmia, but use of that drug postinfarction is likely to fall due to the development of implantable defibrillators.

\[\omega\]-3 fatty acids and diet

Except for patients presenting with type IV hypertriglyceridemia and obese patients, it has to be admitted that a lipid-lowering diet is not very effective. HMG CoA reductase inhibitors have largely replaced dieting. In contrast, the Mediterranean diet has been clearly shown to enable a decrease in postinfarction mortality. In particular, a study conducted in Lyon\textsuperscript{41} compared the effects of a Mediterranean diet with a high $\omega$-linoleic acid content with the lipid-lowering diet conventionally prescribed postinfarction. The subjects had experienced MI more than 6 months previously. The Mediterranean diet had a high bread, fruit, vegetable and fish content and, except for poultry, a low meat content. Butter and cream were replaced by olive oil. The 605 patients included were followed up for 27 months. The study had to be prematurely discontinued because of an interim analysis demonstrating the clear superiority of the Mediterranean diet. At time point 27 months, the composite primary endpoint (cardiovascular mortality + non-fatal infarction) was 5\% for the treatment group vs. vs 21\% (P <0.001) for the control group. Overall mortality was also significantly decreased. The Mediterranean diet is thus to be systematically prescribed postinfarction.

Dietary supplementation with $\omega$-3 fatty acids is also probably necessary, as demonstrated by the GISSI-PREVENZIONE trial.\textsuperscript{42}

Current state of the management and what to improve

A recent Danish national hospital registry recording 55 135 survivors of AMI found concerning initiation, dosages, and long-term compliance in acute MI that:

- post-MI patients who did not start therapy shortly after discharge had a low probability of starting treatment later, specially for the use of beta-blockers and ACE-inhibitors.

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure43.png}
\caption{Meta-analysis of EUROPA, HOPE, PEACE and QIET.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure44.png}
\caption{ACE-inhibitor efficacy as a function of baseline risk.}
\end{figure}

\begin{figure}
\centering
\includegraphics[width=\textwidth]{figure45.png}
\caption{Cumulative frequency ...}
\end{figure}
thirty days after discharge, 58.3% patients received β-blockers, 29.1% ACE-inhibitors, and 33.5% statins. On the contrary, if treatment started early post-MI, patients adhered to it for many years and multiple drug therapy did not reduce compliance.

The dosages prescribed are generally 50% or less the dosages used in clinical trials, and dosages did not increase during the observation period. For instance, ACEis dosages were 50% or less that proved to be effective in clinical trials.

Though, the main problem with underuse of recommended treatment after AMI is that treatment is not initiated at an appropriate dosage shortly after AMI. A focused effort in the immediate post-infarction period would appear to provide long-term benefit.

**Coronary revascularization**

The improvement in prognosis associated with coronary revascularization is derived from the protection of non-necrotic territories, the improvement in hibernating myocardial zones, and the limitation of the remodeling process.

After the acute phase, revascularization is probably indispensable in certain situations:

- **left main vessel lesion**
- **triple main vessel lesion with poor left ventricular function**
- **myocardial ischemia recalcitrant to medical treatment.**

In other cases, the role of surgery, medical treatment, and coronary angioplasty are to be discussed on a case-by-case basis. The discussion is to incorporate local practices, the patient’s physiological age, and the individual risk assessment. (Figure 46)

**Coversyl in revascularized patients**

Revascularization of CAD patients by percutaneous transluminal coronary angiography (PTCA) or coronary artery bypass grafting (CABG) is now common, and may be implemented very early after discovery of CAD progression. Coversyl is the first ACE inhibitor to be indicated for the reduction of cardiac events in patients who have already undergone effective, invasive therapy.

Out of the 12,218 patients in the EUROPA trial, 6709 had undergone prior revascularization (54.9%): 3122, PTCA; and 3136, CABG. The baseline characteristics of those subgroups were similar to those of the EUROPA population.

For the revascularized patients, the reduction in the EUROPA primary end point: cardiovascular death, MI, and cardiac arrest, was significant with a RRR of 17.3% ($P=0.036$) (Figure 46A). This explains why Coversyl is now indicated for all patients having undergone coronary revascularization to reduce cardiac events, irrespective of whether PTCA or CABG is used. Moreover, in that low-risk population, Coversyl reduces the MI risk by 23% ($P=0.015$) (Figure 46B).

With regard to the revascularized patients with no history of MI, the reduction in MI was even greater: 32% ($P=0.026$) (Figure 46C). Thus, Coversyl 8 mg is highly beneficial in all revascularized patients, including those not having experienced MI, ie, in primary prevention.

Following the EUROPA results, the EMEA granted a new indication for perindopril in the reduction of cardiac events in revascularized CAD patients and post-MI patients.
The implantable defibrillator markedly reduces sudden death in patients at high risk. The numerous studies conducted (in particular the MADIT-2 study) have gradually enabled the selection of patients for whom the procedure is effective to be refined. Unfortunately, in many countries, defibrillators remain underused due to their cost. Moreover, the learned societies’ recommendations differ depending on the country. In certain settings, the defibrillator is indispensable:

- cardiac arrest due to ventricular fibrillation or ventricular tachycardia with no acute or reversible cause
- sustained ventricular tachycardia or ventricular fibrillation triggered on medical treatment
- symptomatic, spontaneous, sustained ventricular tachycardia in a context of heart disease with impairment of contractile function.

On the basis of the MADIT 2 study publication, a defibrillator should also be implanted for all patients having presented with MI and with LVEF <30% even in the absence of ventricular arrhythmia. A classification of the indications has been proposed.

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>Mean LVEF%</th>
<th>Reduction in mortality with defibrillator (%)</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MADIT</td>
<td>196</td>
<td>26</td>
<td>54</td>
<td>27</td>
</tr>
<tr>
<td>CABG-Patch</td>
<td>900</td>
<td>27</td>
<td>negative study</td>
<td>32</td>
</tr>
<tr>
<td>MUSTT</td>
<td>704</td>
<td>29</td>
<td>51</td>
<td>39</td>
</tr>
<tr>
<td>MADIT II</td>
<td>1232</td>
<td>23</td>
<td>31</td>
<td>20</td>
</tr>
<tr>
<td>DYNAMIT</td>
<td>674</td>
<td>28</td>
<td>negative study</td>
<td>30</td>
</tr>
</tbody>
</table>

French recommendations (the most recent international recommendations) for implantable defibrillator indications.

- Ventricular fibrillation without a reversible acute cause:
  - class I, level A
- Spontaneous, sustained symptomatic ventricular tachycardia:
  - class I, level B
- Coronary artery disease patients with or without symptoms of mild or moderate heart failure (New York Heart Association class II or III), a left ventricular ejection fraction (LVEF) 30%, measured at least 1 month after a myocardial infarction (MI) and 3 months after a revascularization procedure:
  - class I, level of evidence B
- Coronary artery disease patients with left ventricular dysfunction (LVEF 31% to 35%) measured at least 1 month after MI and 3 months after a revascularization procedure, with a triggered ventricular arrhythmia (VT, VF):
  - class IIa, level B
- Coronary artery disease patients with a previous MI with left ventricular dysfunction (LVEF 31% to 35%):
  - class IIb, level C
Diabetes mellitus, hypertension

Optimization of blood glucose control is obviously advisable. The preferred treatments are biguanides (in the absence of left ventricular dysfunction) and insulin. The UKPDS trial\(^4\) has shown the benefit of metformin in overweight, non-insulin-dependent diabetics (but the study addressed primary prevention and not prevention postinfarction). The DIGAMI study\(^5\) has shown that pursuit of insulin treatment for at least 3 months post-institution in the acute phase of infarction reduced the total mortality at time point 1 year by almost 30%. However, those results were not confirmed by the DIGAMI 2 study\(^6\), which simply confirmed that blood glucose control (using insulin or a sulfonylurea) was beneficial.

The PROACTIVE study\(^7\) seems to show the value of pioglitazone in heart disease patients but this requires confirmation, in particular in patients presenting with left ventricular dysfunction. Similarly, the increased risk of heart failure observed with rosiglitazone in the DREAM trial raises some questions to answers.

In the EUROPA population, 12% of the population had diabetes. In this population at higher risk, the primary end-point, death, MI, and cardiac arrest, was reduced by 18.9%, the risk of MI was reduced by 33.7%, and hospitalization for heart failure was reduced by 46.3%.

To prevent one cardiovascular death or nonfatal MI, 27 diabetic patients would need to be treated for 4 years. Moreover, 57% of the EUROPA population (n=7064 patients) were hypertensive. Among this subgroup of CAD patients with hypertension, Coversyl 8 mg significantly reduces the primary end point by 18.6% (P=0.05).

In short, it would appear that blood glucose control is more important than the type of drug used. The value of ACE inhibitors for diabetic patients and the absence of a contra-indication to β-blocker treatment are to be noted. Blood pressure control is obviously indispensable in hypertensive patients. Once again, drugs having demonstrated their value in terms of morbidity and mortality postinfarction (ie, β-blockers and ACE inhibitors) are to be preferred.

![Figure 52. Reduction of MI and HF in the PERSUADE population.](image1)

![Figure 53. Reduction in cardiac events in hypertensives with Coronary artery disease: 18.6% RRR of cardiovascular death-MI-cardiac arrest in hypertensive patients with CAD (SBP>140 mmHg at baseline).](image2)
Epidemiological studies have shown that only one CAD smoker out of two quits smoking within 6 months of MI. While the smoker cannot smoke during hospitalization, he/she frequently relapses on returning home or going back to work.

Even in the absence of randomized studies, which would not be ethically feasible, there is indisputable evidence for the benefits to be expected when patients stop smoking. Several studies have shown that smokers experiencing MI and quitting have a mortality over the years following the infarction that may be 50% lower than that for patients having continued to smoke. The excess risk for the persistent smoker is related to the increase in the risk of reinfarction (pro-thrombotic and pro-atheromatous effect) and to an increase in the arrhythmia risk. It is of fundamental importance to stress the fact that few medical or surgical procedures can rapidly procure such an important benefit as quitting smoking. Moreover, the cost is negligible and there is no risk of adverse effects. While the benefit may be great, it is difficult to quit definitively given the dual physical and psychological dependence. Management must therefore be multidisciplinary and, in particular, consist in:

1) evaluating smoker status
The following are to be evaluated: nicotine dependence (Fagerström’s test), the history (and duration) of previous attempts to quit, the patient’s motivation for quitting, and the patient’s social and professional environment.

2) awareness of quitting aids
Nicotine replacement products are extremely effective for quitting smoking if used at high doses. Five different dosage forms are available (chewing-gum, spray, inhaler, patch, and lozenge). They may be safely administered to CAD smokers as of discharge from the cardiologic ICU. The products are not endowed with cardiac toxicity since, first, their kinetics are very different from those of inhaled nicotine, and, secondly, the principal toxic constituent of cigarette smoke at cardiovascular level, i.e., carbon monoxide, is not present in the replacement products. It has been clearly shown that long-term administration of nicotine in patch or gum form (5 years) is not associated with cardiac excess risk in ex-smokers vs. vs ex-smokers not using a nicotine-replacement product.

Bupropion
Initially used as an antidepressant, bupropion has been clearly shown to be effective in quitting smoking. The usual dosage is 150 mg/day for 1 week, then 300 mg/day for 9 weeks. The contra-indications are to be clearly understood. The main risks are related to a reduction in the seizure threshold, decompensation of a dietary disorder, anxiety/depression, sleep disorders, and skin allergies. The safety of bupropion has been demonstrated in heart disease patients providing that it is administered more than 3 months after an acute event.

3) Psychological and behavioral management
The psychological and behavioral management of quitting smoking is fundamental. It is based on:

- motivational interviews: these enable positive “manipulation” of the patient and are similar to “coaching” in the business world. The objective is to obtain, through attentiveness to, and reorientation of, the patient’s discourse, patient self-conviction and hence self-motivation with regard to the importance of quitting smoking.
- cognitive and behavioral therapy: the objective is to make the patient aware of the events and situations which promote the craving to smoke. Acute cravings are to be prevented by, for example, avoiding certain risk situations or modifying and/or managing them (drinking a glass of water, chewing nicotine gum, eating fruit, physical exercise, etc.)
Exercise reconditioning

The beneficial effects of physical exercise are exerted on both the risk factors and the cardiovascular system itself:

- aerobic physical exercise plays an important role in the autonomic nervous system: reduction of sympathetic activity and increase in parasympathetic activity. The latter activity is involved in the fall of peripheral resistances, achieving an antithrombotic effect and decreasing ventricular arrhythmia.
- long-term exercise is accompanied by a 10-mm Hg reduction in systolic blood pressure and a 5-mm Hg reduction in diastolic blood pressure through lowered peripheral resistances due, in part, to restitution of endothelium-dependent vascular relaxation and a lowering of the sympathetic tone of the arteries supplying the muscles.
- weight loss, enhanced blood glucose control in diabetics and improvement of the lipid profile are consistently observed and reflect a decrease in insulin resistance.
- in addition to the peripheral vasodilatation due to endothelial secretion of nitric oxide (NO) and action on the autonomic nervous system, physical exercise probably accelerates angiogenesis, stimulating the formation of collateral coronary arteries. Exercise also promotes myocardial preconditioning.

In CAD patients, the duration of exertion has been clearly shown to predict survival. For example, in the APSIS study, the patients whose exercise test lasted more than 13 minutes had an infarction recurrence-free survival at time point 40 months that was markedly higher than those whose exercise duration was <9 minutes. The CORPUS CHRISTI study was conducted on postinfarction patients: 406 patients were followed up for 7 years. The patients were divided into 4 groups: patients who remained sedentary postinfarction, those who remained active, those who increased their physical exercise, and those who reduced it. The results were clear: the patients who remained active or increased their physical exercise had a total mortality that was 79% (relative risk: 0.21) and 89% (relative risk: 0.11) lower than that of sedentary patients. A benefit was also observed with respect to infarction recurrence.

The NEHDP study published in 1999 enables quantification of the life expectancy gain as a function of the exertional capability gain: postinfarction, each 1 MET increase in exertion capability was associated with a decrease in mortality of 8% to 14%, depending on follow-up duration (from 3.5 to 19 years).

These recent studies, published in prestigious journals, confirm the data from the meta-analyses by Oldrige and O’Connor. At the end of the 1980s, the latter authors showed that a correctly implemented reconditioning program resulted in a 20% reduction in total and cardiovascular mortality at time points 3 and 5 years. It is noteworthy that those benefits exist even independently of the correction of other risk factors and the treatments administered.

In conclusion, patient survival postinfarction is clearly related to the quality of the management of the acute phase (prevention of irreversible myocardial lesions) and in the long term. The many published studies now enable long-term follow-up truly in compliance with evidence-based medicine.
References


POSTINFARCTION PATIENT MANAGEMENT

Coversyl is a long-acting ACE inhibitor. International nonproprietary name: Perindopril.

Indications:
- Essential hypertension.
- Stable coronary artery disease: reduction of risk of cardiac events in patients with a history of myocardial infarction and/or revascularization.
- Treatment of symptomatic heart failure.

Dosage and administration:
Coversyl should be taken in the morning before food.

Hypertension:
- A starting dose of 4 mg for 2 weeks is recommended, then titration to 8 mg once daily, depending on acceptability.

Stable coronary artery disease:
- A starting dose of 4 mg for 2 weeks is recommended, then titration to 8 mg once daily, depending on acceptability.

Congestive heart failure:
- Coversyl should be started under close medical supervision at a starting dose of 2 mg. This may be increased to 4 mg once blood pressure acceptability has been demonstrated. Elderly patients: start treatment at 2 mg daily.

Contraindications:
- Children.
- Pregnancy.
- Lactation.
- Patients with a history of hypersensitivity to Coversyl.

Precautions:
- Assess renal function before and during treatment where appropriate.
- Renovascular hypertension.
- Surgery/anesthesia.
- Renal failure: the dose should be cautiously adjusted in accordance with the creatinine clearance (refer to complete data sheet).
- Symptomatic hypotension is rarely seen, but is more likely in volume depleted patients, those receiving diuretics, or with the first two doses. In diuretic treated patients, stop the diuretic 3 days before starting Coversyl. A diuretic may later be given in combination if necessary. Potassium-sparing diuretics are not recommended. Combination with nonsteroidal anti-inflammatory drugs may increase the hypotensive effect. Serum lithium concentrations may rise during Coversyl therapy.
- Side effects: Rare and mild, usually at the start of treatment. Cough, fatigue, headache, disturbances of mood and/or sleep have been reported. Loss of appetite, nausea, abdominal pain, and rash have been reported. Proteinuria has occurred in some patients. Rarely, angioneurotic edema and decreases in hemoglobin, red cells, and platelets have been reported.

Recommended starting dose* for 2 weeks

Maintenance dose

Stable coronary artery disease:
Coversyl 8 mg once daily

Also available under the brand names:
- Aceon®, Acretil®, Armix®, Coverene®, Coverex®, Coversum®, Prestarium®, Prexanil®, Prexum®, Procaptan®

Coversyl 4 mg 8 mg

Composition:
- Each tablet contains 4 mg or 8 mg of the tert-butylamine salt of perindopril.

Presentation:
Packs of 30 tablets of Coversyl 4 mg (scored). Packs of 30 tablets of Coversyl 8 mg (scored).

*Converting information may vary from country to country; please refer to the complete data sheet supplied in your country. Les Laboratoires Servier - France. Correspondent: Servier International, 22, rue Garnier 92578 Neuilly-sur-Seine Cedex, France. www.servier.com