Prophylaxis for patients who have experience a myocardial infarction

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YOU KNOW CPR — GREAT! BUT DO YOU KNOW EHAC — EARLY HEART ATTACK CARE?

DELAY AND DENIAL
MILD CHEST DISCOMFORT
SEVERE CHEST PAIN
HEART ATTACK

ALL HEART ATTACKS ARE NOT CREATED EQUAL!
Heart attacks come in different sizes and shapes. In most cases, they begin with a warning sign that tells us something — this is, heart damage and/or death is impending. The road to destruction and the "crash" of your life has stop-off points that can save you if you recognize the signs.
Aim of the guideline

- To provide evidence-base recommendation to guide health care professionals in the appropriate primary care management of secondary prophylaxis for patients who have previously experienced a myocardial infarction.

- Decision to adopt any particular recommendation must be made by the practitioner in the light of circumstances presented by individual patients and available resources.
The scope of this first edition of the guideline is necessarily limited to address key areas of current uncertainty.

Given the range of treatments available, it is increasingly important to examine the value of each and the extent to which treatments might be complementary. Thus the aim of the guideline is to provide evidence-based guidance on the value of different treatments options and their prioritisation.
The objective

- To examine and present the evidence concerning the appropriate sequencing of drugs and other intervention for secondary prophylaxis in patients with a prior MI
- And to identify whether this differs according to prognostic risk factor (principally heart failure).
categories of evidence

- Ia: evidence from meta-analysis of randomised controlled trials.
- Ib: evidence from at least one randomised controlled trial.
- IIa: evidence from at least one control study without randomisation
- IIb: evidence from at least one other type of quasi-experimental study
- IIIa: evidence from non-experimental descriptive studies, such as comparative studies, correlation and case control studies
- IV: evidence from expert committee report or opinions and/or clinical experience of respected authorities
Strength of recommendation

- A directly based on category I evidence
- B directly based on category II evidence or extrapolated recommendation from category I evidence
- C directly based on category III evidence or extrapolated recommendation from category I or II evidence
- D directly based on category IV evidence or extrapolated from category I, II, III evidence
Statins

- Based on data from randomised controlled trials in 1000 patients who have experience an MI, treatment with statins for a year will avoid about 4 deaths, six non-fatal MIs and 2 strokes. These benefits appear similar regardless of initial cholesterol level (Ia).

- Most of evidence comes from trials of pravastatin and simvastatin (Ib).

- Most trials started statins 12 weeks after myocardial infarction (Ia).

- The effectiveness of statin in patients who develop heart failure in addition to MI has not been adequately assessed (Ia).

- None of the studies considered included patients with an initial cholesterol < 4 mmol/l (Ia).
Beta-blocker for unselected patient

- In 1000 unselected patients who have experienced prior MI, treatment with a beta-blocker for a year will avoid about 13 deaths 8 non-fatal MIs (Ia)

- Potential benefits from beta-blockers may be achieved through early initiation of therapy. However, these will continue to accrue over long term use (Ia).

- In 1000 patients treated for a year, in about twelve of those who discontinue therapy, the discontinuation is attributable to the drug (1a)

- Beta-blockers with intrinsic sympathomimetic activity are associated with a near significant reduction in therapeutic effect compared with agents without this characteristic (Ia)

- Most evidence for long beta-blocker use comes from trials propranolol, timolol and metoprolol
ACE inhibitors in unselected patients

- ACE inhibitors are associated with a small reduction in short term use immediately after acute MI. In 1000 patients who have experienced MI, treatment with an ACE inhibitor for a year will avoid about two deaths (Ia).

- In longer term use in patients at raised cardiovascular risk, ACE inhibitors are associated with a moderate reduction in mortality. If 1000 patients are treated for one year, 4 deaths will be avoided (Ib).
ACE inhibitors in selected patients

- Long term treatment with ACE inhibitors is associated with a substantial reduction in all causes mortality in selected patients with sign of heart failure who have recently experience an MI. Treating 1000 patients with heart failure with ACE inhibitors for a year, commencing soon after an index MI, will avoid 18 deaths (Ia).

- ACE inhibitors may also reduce the incidence of non-fatal MI (Ia).

- The tolerability of ACE inhibitors in the trials was very similar to that achieved with placebo (Ia).
ACE inhibitors and beta-blockers

Beta-blockers are associated with substantial reduction in all cause mortality in patients with symptoms of heart failure being treated with an ACE inhibitors, who may or may not have experience an MI. Treating 1000 patients with hear failure for a year with beta-blockers will avoid 35 deaths (Ia).
Figure 10: Annual reduction in the rate of death in patients with heart failure treated with an ACE inhibitor, a beta-blocker, or combination.
Spironolactone in patients with severe heart failure

- Spironolactone is associated with a decrease in all-cause mortality among patients with moderate to severe heart failure treated optimally with ACE inhibitors (Ib).
Antiplatlet therapy with aspirin or alternative agents in patients with prior MI

- Antiplatlet therapy is associated with a reduction in all cause mortality and non-fatal MI in patients who experience a previous MI (Ia).

- There is no evidence that any alternative antiplatlet agent is more effective than aspirin in this patient group; the majority of evidence comes from trials of aspirin (Ia).

- There is some evidence from subgroup analysis of major trials that the benefits of aspirin and ACE inhibitors are not completely additive in patient with heart failure (Ia).
Insulin glucose infusion followed by subcutaneous insulin in patients with diabetes with prior MI

- There is evidence that rigorous control of diabetes post myocardial infarction lowers mortality (Ib).
- Insulin-glucose infusion for at least 24 hours followed by subcutaneous insulin 4 times a day for at least 3 months.
Calcium channel blockers (patient with prior MI)

- Calcium channel blockers are not associated with a reduction in mortality in patients with MI, with the exception of verapamil. However, even for verapamil the observe effect may simply be due to the play of chance (Ia).

- Several calcium channel blockers are associated with a reduction in non-fatal MI, though this effect is hard to interpret in the absence of an effect upon mortality.
Calcium channel blockers in patients with heart failure

- Calcium channel blockers do not lead to a statistically significant reduction in mortality in trials in patients with heart failure. Further data are required to provide greater certainty on the effect of calcium channel blockers in this patient group (Ia).
Potassium channel activators and nitrates in patients with prior MI

- There is no evidence to support the use of nicorandil in patients with prior MI, to prevent mortality or major morbidity (Ib).

- Two very large trials post MI found no evidence for the routine use of nitrate in patients who have experienced an MI if the aim is to prevent mortality or major morbidity (Ib).
Shall I read that back to you, sir? Help! Help! Help! I'm having a heart attack! Help!
There is good evidence that cardiac rehabilitation programs that include an exercise component are associated with a reduction in mortality and morbidity in patients post myocardial infarction. If 1000 patients were treated with cardiac rehabilitation commencing soon after MI and followed up between 3 months and 5 years, 24 deaths will be avoided (Ia).
Cardiac rehabilitation

- The importance of different component of cardiac rehabilitation is poorly understood, although the trials included in the overview provided consistent result (Ia).
Dietary changes in line with a mediterranean type diet (in particular the avoidance of meat and dairy product and an increase in the consumption of fatty fish) appear to reduce mortality. Implementing dietary advice on mediterranean diet for 1000 people for one year would lead to the avoidance of 18 deaths (Ia).
The modelling approach

- In patients with previous myocardial infarction, beta-blockers and aspirin are effective. Statins or ACE inhibitors when used in addition to these treatment are also effective. (I)

- In patients with previous myocardial infarction and heart failure ACE inhibitors are effective. In addition, spirinolactone (in moderate or severe patients) or a beta-blocker are also effective. (I)

- All available treatment are estimated to be cost-effective. (III)
Figure 20: Survival curves extrapolated from trials of patients receiving an ACE inhibitor or placebo.

Curves shown are for male patients aged 60 at the start of treatment.
Post Myocardial Infarction

**ACE inhibitors** (Ramipril, 5mg bd)

**Antiplaletes** (Aspirin, 75mg od)

**Beta-blockers** (Propranolol, 80mg tds)
(Metoprolol, 100mg bd)

**Cardiac Rehabilitation**

**Statins** (Pravastatin, 40mg od)
(Simvastatin 20-40mg od)

Post Myocardial Infarction and Heart Failure

**ACE Inhibitors** (Captopril, 25-50mg tds)
(Ramipril, 2.5-5mg bd)

**Beta-blockers** (Propranolol, 40mg tds)
(Bisoprolol, 5-10mg od)

Sapacitabine (generic, 25mg cap)
Figure 23: Estimated survival gains and 95% confidence intervals assuming common underlying risk for all treatments underlying risk reported in trials (common underlying risk assumes initial 5% annual all cause mortality in all patients). Results shown are for male patients aged 65 at the start of treatment.
## INHERITED Clinical Guideline A: Summary Table

**Prophylaxis for patients who have experienced a myocardial infarction**

**Drug treatment, cardiac rehabilitation and dietary manipulation**

**National Institute for Clinical Excellence**

<table>
<thead>
<tr>
<th>Drug treatment</th>
<th>Monitoring</th>
<th>Notes</th>
<th>Non drug treatment</th>
<th>Rehabilitation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRIOR MI NO HEART FAILURE</strong></td>
<td>Early initiation (in hospital) of beta-blocker + anti-plalet agent &gt; ACE-inhibitor.</td>
<td>ACE-inhibitors: check renal function prior to initiation &amp; at each significant dose increase.</td>
<td>Continue treatment long term.</td>
<td>Be guided by functional ability and patient preference.</td>
</tr>
<tr>
<td></td>
<td>Those initiated in hospital, Primary Care should initiate ASAP.</td>
<td></td>
<td>Be beta-blockers &amp; ACE inhibitors also considered for management of symptoms (e.g. unstable angina) or risk factors (e.g. hypertension)</td>
<td>No need to refer.</td>
</tr>
<tr>
<td></td>
<td>Patients not taking a statin should be Restarted &amp; have treatment initiated 12 weeks after index MI.</td>
<td>Statins: measure initial serum or creatinine to exclude renal or lipid disorder &amp; identify comorbidities.</td>
<td>Calcium channel blockers, nitrates, and potassium channel blockers can be used in patients intolerant of beta-blockers or ACE-inhibitors.</td>
<td>Be referred if treatment with calcium channel blockers, nitrates or potassium channel blockers is not appropriate.</td>
</tr>
<tr>
<td><strong>PRIOR MI WITH HEART FAILURE</strong></td>
<td>Early initiation (in hospital) of an anti-plalet agent (aspirin) plus an ACE-inhibitor.</td>
<td>ACE-inhibitors: check renal function prior to initiation &amp; at each significant dose increase.</td>
<td>Particular care is required when initiating drug treatments in this group of patients.</td>
<td>Be referred if treatment with calcium channel blockers, nitrates or potassium channel blockers is not appropriate.</td>
</tr>
<tr>
<td></td>
<td>Those initiated in hospital, Primary Care should initiate ASAP.</td>
<td></td>
<td>Confirm blood loss.</td>
<td>Be referred if treatment with calcium channel blockers, nitrates or potassium channel blockers is not appropriate.</td>
</tr>
<tr>
<td></td>
<td>Early initiation at any point in patients with moderate or severe heart failure (NYHA 3 or 4).</td>
<td></td>
<td>Patients are likely to continue to have symptomatic treatment with anti-plalet agents.</td>
<td>Be referred if treatment with calcium channel blockers, nitrates or potassium channel blockers is not appropriate.</td>
</tr>
<tr>
<td><strong>PRIOR MI WITH DIABETES</strong></td>
<td>Early initiation at any point in patients with diabetes or severe heart failure (NYHA 3 or 4).</td>
<td></td>
<td>Diabetes patients who require hospitalization for initiation. There may be a group of patients with heart failure for whom effect is based on knowledge of the patients' clinical condition &amp; not on the knowledge of the healthcare person.</td>
<td>Be referred if treatment with calcium channel blockers, nitrates or potassium channel blockers is not appropriate.</td>
</tr>
<tr>
<td></td>
<td>Early initiation at any point.</td>
<td></td>
<td>Diabetes patients who require hospitalization for initiation.</td>
<td>Be referred if treatment with calcium channel blockers, nitrates or potassium channel blockers is not appropriate.</td>
</tr>
</tbody>
</table>

To achieve the beneficial outcomes in the single trial in this area within a study that had implications for others 2 months.
Which drug?
MI without heart failure

- Long term treatment firstly with a beta-blocker and an antiplatelet (aspirin), and then with a statins and an ACE inhibitors (A).
- Licence indications currently suggest a lower limit of 4.8 mmol/l or 5.5 mmol/l depending on the drug used (D).
- Beta-blockers and ACE inhibitors will also be considered for the management of symptoms or risk factors (e.g. hypertension) (D).
- Calcium channel blockers, nitrates, and potassium channel activators have no effect on premature mortality making their role the management of symptoms and risk factors (A).
Continuation of treatment

- Based on the evidence from the trial, treatment should continue long term (D).
- 3 and ½ years for antiplatelet (aspirin) (D)
- 4 years for beta-blockers and ACE inhibitors (D)
- Six years for statins (D)
- In the absence of a clear reason to stop treatment, it seems reasonable to continue treatment indefinitely (D).
MI and heart failure

- Long term treatment (A)
- ACE inhibitor and then a beta-blocker (A)
- In addition antiplatelet drug (aspirin) (A)
- Spironolactone in patients with moderate or severe heart failure (A)
- Patients are likely to need symptomatic treatment with a loop diuretic (D)
- Statins use will be influenced by clinical and practical considerations (D).
Continuation of treatment

- Treatment should continue long term (D).
- 3 and half years for ACE inhibitors (D)
- 2 and half years for beta-blockers (D)
- 2 years for spirinolactone (D)
- In the absence of a clear reason to stop treatment it seems reasonable to continue treatment indefinitely (D)
Rehabilitation

- Patient should be offered enrolment in a rehabilitation programme that has a prominent exercise component in it (A).

- Functional mobility and patient preference should be considered instead of upper age limit for recruitment (D)
Diet

- Given the nature of the available evidence of the effectiveness of the dietary manipulation as a strategy for secondary prevention it is not possible to recommend specific dietary manipulation (B).
Thank you

Any feedback and comments?