Q/ Which drugs should post-MI patients routinely receive?

Evidence-based answer

A patients should be placed on the following medications (Table):

- antiplatelet agents: aspirin (75-325 mg) started soon after the onset of acute MI significantly reduced mortality, reinfarction, and stroke at 1 month compared with placebo (absolute risk reduction [ARR]=3.8%; number needed to treat [NNT]=26; 95% confidence interval [CI], 23-30).

- a statin: atorvastatin has the best evidence (SOR: B, a single RCT)
- a beta-blocker: meta-analysis
- renin-angiotensin-aldosterone system blockers, whether or not the ejection fraction is diminished after myocardial infarction (MI) (SOR: A, meta-analysis for angiotensin-converting enzyme [ACE] inhibitor; B, single RCT for ACE inhibitor plus aldosterone blocker).

Evidence summary

A systematic review of 9 RCTs demonstrated that aspirin (75-325 mg) started soon after the onset of acute MI significantly reduced mortality, reinfarction, and stroke at 1 month compared with placebo (absolute risk reduction [ARR]=3.8%; number needed to treat [NNT]=26; 95% confidence interval [CI], 23-30).

One large RCT involving 17,187 patients with suspected acute MI showed that 162 mg aspirin given on the day of the MI resulted in a 2.6% ARR (NNT=38; 95% CI, 29-63) in vascular deaths at 35 days compared with placebo. The survival benefit persisted for as long as 10 years. The RCT also found no significant difference between aspirin and placebo in rates of cerebral hemorrhage or bleeding requiring transfusions.

Patients who have had an MI without ST segment elevation should take clopidogrel (75 mg/d) and aspirin (81 mg/d) for 12 months. The combination has been shown to result in a 2.1% ARR (NNT=48) in deaths, recurrent MI, and stroke compared with aspirin alone.

Intensive atorvastatin therapy lowers risk of death

The PROVE IT-TIMI 22 trial showed the benefit of early intensive therapy with the hydroxymethyl glutaryl coenzyme A reductase inhibitor atorvastatin to lower low-density lipoprotein <70 mg/dL post-MI. At 30 days after the event, atorvastatin 80 mg daily resulted in a 1.2% ARR in death and recurrent acute coronary syndrome (NNT=83; hazard ratio [HR]=0.72; 95% CI, 0.52-0.99). From 6 months to 24 months after the event, the ARR was 2.6% (NNT=38; HR=0.82; 95% CI, 0.69-0.99).

Beta-blockers significantly decrease late mortality

One systematic review of 63 RCTs showed that, in long-term trials, use of a beta-blocker significantly reduced the late mortality rate (NNT=48; odds ratio [OR]=0.77; 95% CI, 0.70-0.85). In another review of 82 RCTs, the mortality rate between 6 months and 4 years after MI decreased markedly in patients receiving a beta-blocker (OR=0.77; 95% CI, 0.69-0.85).

ACE inhibitors decrease overall mortality, sudden cardiac death

An ACE inhibitor should be started regard-
Patients who have had an MI without ST segment elevation should take clopidogrel and aspirin for 12 months.

less of the ejection fraction or the presence or absence of left ventricular systolic dysfunction. One systematic review that compared long-term mortality rates of patients started on an ACE inhibitor within 14 days of acute MI versus placebo found that ACE inhibitors significantly decreased overall mortality and sudden cardiac deaths between 2 and 42 months after the MI (NNT=42; OR=0.83; 95% CI, 0.71-0.97).8

Eplerenone + ACE inhibitor benefit patients with post-MI heart failure
The selective aldosterone blocker eplerenone appears to benefit patients with a decreased ejection fraction post-MI. The EPHESUS study demonstrated that eplerenone, when added to an ACE inhibitor, reduced all-cause mortality (ARR=1.4%; NNT=71; 95% CI, 47-200; RR=0.69; 95% CI, 0.54-0.89) and sudden cardiac death (ARR=0.5%; NNT=200; 95% CI, 125-∞; RR=0.63; 95% CI, 0.40-1.00) up to 30 days in patients with post-MI heart failure. Benefits were also seen after 16 months of treatment.9

Recommendations
The American College of Cardiology (ACC) and American Heart Association (AHA) provide the following recommendations in their joint 2006 Guidelines for Secondary Prevention for Patients with Coronary and Other Atherosclerotic Vascular Disease:10
- Low-dose aspirin should be used, as well as clopidogrel in combination with aspirin for up to 12 months after a non-ST elevation MI
- ACE inhibitors or angiotensin receptor blockers should be considered in all patients, and an aldosterone antagonist should be prescribed for patients with a diminished ejection fraction post-MI
- Beta-blockers should be used in all post-MI patients without contraindications.

The ACC/AHA 2007 Guidelines for the Management of Patients with Unstable Angina/Non-ST-Elevation Myocardial Infarction recommend the same medication combinations.11 So does the 2007 Focused Update of the ACC/AHA 2004 Guidelines for the Man-

### TABLE

**Recommended drugs for post-MI patients**

<table>
<thead>
<tr>
<th>Drug type</th>
<th>Examples</th>
<th>Precautions</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet agents</td>
<td>Aspirin 81 mg/d; clopidogrel 75 mg/d</td>
<td>Risk for bleeding; use caution in patients taking warfarin</td>
<td>Active bleeding; hypersensitivity</td>
</tr>
<tr>
<td>RAAS blockers</td>
<td>Lisinopril 20 mg/d; losartan 50 mg/d; eplerenone 50 mg/d</td>
<td>Hypotension, hyperkalemia, renal failure Use eplerenone only with decreased ejection fraction</td>
<td>Hypersensitivity; systolic blood pressure &lt;90 mm Hg</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>Metoprolol 100 mg bid</td>
<td>Hypotension, bradycardia, reactive airways</td>
<td>Systolic blood pressure &lt;90 mm Hg; pulse rate &lt;50 bpm</td>
</tr>
<tr>
<td>Statins</td>
<td>Atorvastatin 80 mg/d</td>
<td>Elevated AST/ALT, myositis</td>
<td>Active liver disease; pregnancy/nursing</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BPM, beats per minute; RAAS, renin-angiotensin-aldosterone system.
agreement of Patients with ST-Elevation Myocardial Infarction, with the exception that clopidogrel in combination with aspirin is recommended for at least 14 days.12

Similarly, the British National Institute for Clinical Excellence Clinical Guideline 48 recommends that all post-MI patients be offered a combination of an ACE inhibitor, aspirin with clopidogrel, a beta-blocker, and a statin.13

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References


Atorvastatin has been found to decrease the risk of death and recurrent acute coronary syndrome.

Late-onset male hypogonadism and testosterone replacement therapy in primary care

This CME supplement and supporting webcast discuss:

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