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

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EVIDENCE-BASED ANSWER

A/ PATIENTS SHOULD BE PLACED ON THE FOLLOWING MEDICATIONS (TABLE):

- antiplatelet agents (strength of recommendation [SOR]: **A,** meta-analysis for aspirin; **A,** multiple randomized controlled trials [RCTs] for aspirin plus clopidogrel)
- a statin; atorvastatin has the best evidence (SOR: **B,** a single RCT)
- a beta-blocker (SOR: **A,** 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).

Starting aspirin soon after an acute MI reduces mortality, reinfarction, and stroke at 1 month.

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).[1]

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.[2] 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.[3] Patients who have had an ST segment elevation MI should take clopidogrel in combination with aspirin for at least 2 weeks.[4]

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.[5] 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).[6] 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).[7]

ACE inhibitors decrease overall mortality, sudden cardiac death

An ACE inhibitor should be started regard-

TABLE
Recommended drugs for post-MI patients

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

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BPM, beats per minute; RAAS, renin-angiotensin-aldosterone system.

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-

agement 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] JFP

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