

Adding ACEIs and/or ARBs to Standard Therapy for Stable Ischemic Heart Disease: Benefits and Harms

Key Clinical Issue

Should standard medical therapy in patients with stable ischemic heart disease be augmented with an ACEI (angiotensin-converting enzyme inhibitor) or an ARB (angiotensin II receptor blocker)?

Background Information

Patients who have chronic stable angina, or stable ischemic heart disease (IHD) with preserved left ventricular systolic function (LVSF), can remain symptomatic and at risk for fatal and nonfatal cardiovascular events, even though they may be optimally treated with standard medical therapy or revascularization.

- Standard medical treatment may include aspirin, statins, β-blockers, dual antiplatelet therapy, or combinations of these agents. Nitrates and calcium channel blockers may also be used to achieve symptomatic relief.
- Revascularization procedures can include balloon angioplasty with or without stenting to open up the affected vessels of the heart or coronary artery bypass grafting that attempts to bypass a diseased vessel.

ACEIs and ARBs have been shown to reduce morbidity and mortality in patients with left ventricular systolic dysfunction (LVSD) in the settings of chronic heart failure and myocardial infarction and also in patients with diabetes mellitus that is accompanied by proteinuria or chronic kidney disease.

This summary does not discuss ACEI or ARB therapy for patients with currently accepted indications for these drugs, including LVSD, evidence or diagnosis of heart failure, or a diagnosis of cardiomyopathy. This summary presents the benefits and risks of supplementing standard medical therapy with ACEIs or ARBs to patients with stable IHD and preserved LVSF. It is based on a systematic review of the research conducted for this population, which included 12 trials (n=41,672).

Clinical Bottom Line

Treatment modality	Possible benefits	Possible harms*
Adding an ACEI to standard treatment	REDUCES total mortality, nonfatal myocardial infarction, heart failure-related hospitalization, and the need for revascularizations. <i>Level of Confidence:</i> ●●●	INCREASES the risk for syncope, cough, and hyperkalemia. <i>Level of Confidence:</i> ●○○
Adding an ARB to standard treatment	For patients who are intolerant to ACEIs, REDUCES the combined end points of cardiovascular mortality, nonfatal myocardial infarction, and stroke. <i>Level of Confidence:</i> ●●○	INCREASES the risk of hyperkalemia. <i>Level of Confidence:</i> ●○○
Adding both an ACEI and an ARB to standard treatment	Provides no additional clinical benefit when compared to an ACEI alone. <i>Level of Confidence:</i> ●●○	INCREASES the risk of hypotension, sudden fainting, and renal impairment. <i>Level of Confidence:</i> ●●○
Adding an ACEI or ARB close to a revascularization procedure	Provides no additional clinical benefit over standard therapy. <i>Level of Confidence:</i> ●●○	INCREASES the risk for needing subsequent revascularizations (●●●) and for hypotension(●●○).

* For additional information about possible harms see *Note Regarding Possible Harms* on the back page.

Confidence Scale

- High:** ●●● There are consistent results from good-quality studies. Further research is very unlikely to change the conclusions.
- Moderate:** ●●○ Findings are supported, but further research could change the conclusions.
- Low:** ●○○ There are very few studies, or existing studies are flawed.

Outcomes Table

ACEI outcomes	Event rate per 100 patients, over 4 years		Absolute difference in event rates	RRR ¹	NNT ²
	Without ACEI	With ACEI			
Total mortality	8.5	7.4	1.1	13%	91
Nonfatal myocardial infarction	6.1	5.0	1.1	17%	91
Heart failure–related hospitalization	2.6	2.0	0.6	22%	167
Need for revascularization ³	13.6	12.3	1.3	10%	77
ARB outcomes					
Combined end points of cardiovascular mortality, nonfatal myocardial infarction, or stroke. ⁴	14.8	13.0	1.8	12%	56

¹ RRR is relative risk reduction (difference between the two event rates, divided by the event rate for patients not treated with an ACEI or an ARB).
² NNT is number of patients who would need to be treated with an ACEI (or an ARB) to prevent one additional adverse outcome.
³ Event rate is over 3.7 years.
⁴ Data only relevant to patients who are intolerant to ACEIs.

Note Regarding Possible Harms

Adverse event reporting was not consistent across trials. Additionally, candidates who were intolerant to the study drug were excluded in several trials. This may limit the applicability of the harms data for the overall IHD population. Please refer to the full comparative effectiveness review for details.

A 2007 AHRQ review of ACEIs and ARBs states that angioedema, a rare but potentially serious reaction, had been reported in several studies. Patients who are or may become pregnant while taking ACEIs or ARBs should also be made aware of the risk of birth defects caused by these drugs.

Source

The information in this summary is based on *Comparative Effectiveness of Angiotensin Converting Enzyme Inhibitors or Angiotensin II Receptor Blockers Added to Standard Medical Therapy for Treating Stable Ischemic Heart Disease*, Comparative Effectiveness Review No. 18, prepared by the University of Connecticut/Hartford Hospital Evidence-based Practice Center under Contract No. 290-2007-10067-I for the Agency for Healthcare Research and Quality, October 2009. Available at: www.effectivehealthcare.ahrq.gov. This summary was prepared by the John M. Eisenberg Center for Clinical Decisions and Communications Science at Baylor College of Medicine, Houston, Texas.

Ordering Information

For electronic copies of *ACE Inhibitors and ARBs To Protect Your Heart, A Guide for Patients* (AHRQ Pub. No. 10-EHC002-A), this clinician guide, and the full systematic review, visit www.effectivehealthcare.ahrq.gov. To order free print copies, call the AHRQ Publications Clearinghouse at 800-358-9295.

Gaps in Knowledge

Additional research and meta-analyses are needed regarding both benefits and harms in studies analyzing patient characteristics such as age, gender, race, and ethnicity; subpopulations such as African-Americans and Latinos; comorbidities such as hypertension and diabetes mellitus; use of concomitant therapies such as antiplatelet regimens; and the presence of single or multivessel disease, among others.

What To Discuss With Your Patients

- If an ACEI or an ARB will reduce your patients' risk of death, heart attack, or stroke.
- Whether or not the possible adverse effects outweigh the benefits for your individual patients.
- How your patients' need for revascularization impacts your decision to add ACEIs or ARBs to their other therapies.
- How an ACEI or an ARB may interact with your patients' concomitant therapies.

Resources for Patients

ACE Inhibitors and ARBs To Protect Your Heart, A Guide for Patients is a free companion to this clinician guide. It can help people talk with their health care professional about:

- The possible problems caused by coronary heart disease.
- The benefits of adding an ACEI or an ARB.
- The possible risks of adding these medicines.

