Losartan did not differ from captopril for reducing all-cause mortality after acute myocardial infarction

Dickstein K, Kjekshus J. **Effects of losartan and captopril on mortality and morbidity in high-risk patients after acute myocardial infarction: the OPTIMAAL randomised trial. Optimal Trial in Myocardial Infarction with Angiotensin II Antagonist Losartan.** Lancet. 2002;360:752-60.

QUESTION

In patients with acute myocardial infarction and heart failure or left ventricular dysfunction, is losartan more effective than captopril for reducing all-cause mortality?

DESIGN

Randomized (allocation concealed*), blinded (patients, outcome assessors, and monitoring committee),* controlled trial with mean follow-up of 2.7 years.

SETTING

329 centers in 7 European countries.

PATIENTS

5477 patients ≥ 50 years of age (mean age 67 y, 71% women) who had objectively documented acute myocardial infarction and heart failure during the acute phase or a new Q-wave anterior infarction or reinfarction. Exclusion criteria included supine systolic arterial blood pressure < 100 mm Hg at the time of randomization, current receipt of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin II antagonist, and unstable angina. Follow-up was 100%.

INTERVENTION

Patients were allocated and titrated to a target dose of losartan, 50 mg once daily (n = 2744), or captopril, 50 mg 3 times daily (n = 2733).

MAIN OUTCOME MEASURES

All-cause mortality. Secondary outcomes included a composite endpoint of sudden cardiac death or resuscitated cardiac arrest, and adverse effects.

MAIN RESULTS

Analysis was by intention to treat. The groups did not differ for all-cause mortality or the composite endpoint of sudden death or resuscitated cardiac arrest (Table). The rates of adverse effects, including cough, hypotension, skin rash, and taste disturbance, were lower in the losartan group than in the captopril group (Table). Fewer patients in the losartan group than in the captopril group discontinued the allocated study medication because of adverse effects (17% vs 23%, $P < 0.001$).

CONCLUSION

In patients with acute myocardial infarction and heart failure or left ventricular dysfunction, losartan did not differ from captopril for reducing all-cause mortality.

Source of funding: Merck, Sharp and Dohme Research Laboratories.

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*See Glossary.

Losartan vs captopril in acute myocardial infarction at a mean follow-up of 2.7 years†

Outcomes	Losartan	Captopril	RRI (95% CI)	NNH
All-cause mortality	18.2%	16.4%	13% (–1 to 28)	Not significant
Composite endpoint	8.7%	7.4%	19% (–1 to 43)	Not significant
			RRR (CI)	NNT (CI)
Cough	9.3%	18.7%	50% (43 to 57)	11 (9 to 14)
Hypotension	13.3%	16.3%	18% (7 to 28)	34 (21 to 91)
Skin rash	3.1%	4.6%	32% (11 to 48)	68 (40 to 219)
Taste disturbance	0.6%	2.7%	78% (63 to 87)	48 (36 to 69)

†Composite endpoint = sudden cardiac death or resuscitated cardiac arrest. Abbreviations defined in Glossary; RRI, RRR, NNH, NNT, and CI calculated from data in article.

COMMENTARY

In patients with left ventricular dysfunction (symptomatic or asymptomatic), myocardial infarction, or high cardiovascular risk, ACE inhibitors prolong life, improve or prevent symptoms of heart failure, and reduce hospitalizations. When added to ACE inhibitors, angiotensin-receptor blockers (ARBs) sometimes improve symptoms and reduce hospitalizations but do not prolong life in patients with symptomatic heart failure (1). ARBs also do not reduce mortality or hospitalizations in patients with heart failure more than ACE inhibitors (2).

Dickstein and colleagues now show that losartan does not differ from captopril for reducing all-cause mortality, cardiovascular events, or hospitalizations in high-risk patients after acute myocardial infarction. They also confirm that hypotension after the first dose as well as cough, taste disturbance, and rash are more common in patients treated with ACE inhibitors than in those treated with ARBs. However, the data suggested a possibility that losartan (50 mg/d) might actually increase the risk for death in some patients compared with captopril. A similar trend was found in another industry-funded trial (3), in which mortality was increased when valsartan was given to a subgroup of patients with heart failure already receiving ACE inhibitors and β-blockers.

Dickstein and colleagues excluded 43% of otherwise-eligible patients because of previous treatment with either an ACE inhibitor or an ARB, and most patients received aspirin, β-blockers, and diuretics during the trial. Although multiple- rather than single-drug therapy is common fare, clinicians should not yet routinely include ARBs in their pantry of proven effective therapies for patients with heart disease.

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