

Losartan did not improve survival more than did captopril but was better tolerated in symptomatic heart failure

Pitt B, Poole-Wilson PA, Segal R, et al., on behalf of the ELITE II investigators. Effect of losartan compared with captopril on mortality in patients with symptomatic heart failure: randomised trial—the Losartan Heart Failure Survival Study ELITE II. *Lancet*. 2000 May 6;355:1582-7.

QUESTION

Is losartan more effective and better tolerated than captopril in older adults with symptomatic heart failure?

DESIGN

Randomized {allocation concealed*}†, blinded (patients and outcome assessors),* controlled trial with median follow-up of 1.5 years.

SETTING

289 centers in 46 countries (Evaluation of Losartan in the Elderly [ELITE] II Losartan Heart Failure Survival Study).

PATIENTS

3152 patients \geq 60 years of age (mean age 71 y, 69% men, 82% white) who had New York Heart Association class II to IV heart failure and left ventricular ejection fraction \leq 40% and who received angiotensin-converting enzyme (ACE) inhibitor therapy \leq 7 days in the previous 3 months. Exclusion criteria were intolerance to ACE inhibitors, systolic blood pressure $<$ 90 mm Hg or diastolic blood pressure $>$ 95 mm Hg, heart fail-

ure with potentially reversible causes, recent cardiac or cerebrovascular events, or creatinine level $>$ 220 μ mol/L. Follow-up was 99.9%.

INTERVENTION

After stratification for β -blocker use, patients were allocated to losartan, 12.5 mg once daily titrated to 50 mg once daily ($n = 1578$), or captopril, 12.5 mg 3 times/d titrated to 50 mg 3 times/d ($n = 1574$).

MAIN OUTCOME MEASURES

All-cause mortality, sudden death, resuscitated cardiac arrest, hospital admission, and adverse effects.

MAIN RESULTS

Analysis was by intention to treat. The losartan and captopril groups did not differ for rates of all-cause mortality (17.7% vs 15.9%, $P = 0.16$), the combined end point of sudden death or resuscitated cardiac arrest (9.0% vs 7.3%, $P = 0.08$), all-cause hospital admission (41.8% vs 40.5%, $P = 0.45$), hospital admission for heart failure (17.1% vs 18.6%, $P = 0.32$), or the

combined end point of all-cause mortality or all-cause hospital admission (47.7% vs 44.9%, $P = 0.18$). After excluding those patients who died (280 [17.7%] in the losartan group and 250 [15.9%] in the captopril group), fewer patients who received losartan discontinued treatment because of adverse effects (9.7% vs 14.7%, $P < 0.001$) or cough (0.3% vs 2.7%, $P < 0.001$) than did those who received captopril.

CONCLUSION

In older adults with symptomatic heart failure, losartan did not improve survival more than did captopril but was better tolerated.

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*See Glossary.

†Information provided by author.

COMMENTARY

Angiotensin-receptor blockers (ARBs) inhibit angiotensin II more completely and raise local levels of bradykinin less than do ACE inhibitors. As a result, ARBs may reduce mortality in heart failure more than do ACE inhibitors, with a lower incidence of side effects. In the ELITE study (1), the precursor study to ELITE II, mortality was lower with losartan, but the results were not definitive. ELITE II, a larger study designed with all-cause mortality as the primary end point, failed to confirm the mortality findings of ELITE.

The confidence interval around the mortality estimate is too wide to conclude that losartan and captopril have equivalent effects on mortality. Thus, ACE inhibitors remain the first-line treatment for heart failure. Therapy with ACE inhibitors in heart failure may be limited by severe cough in 15% of patients or by the occurrence of angioedema. An ARB is probably the best second-line agent for such patients. No evidence shows that ARBs cause less-severe declines in renal function or less-symptomatic hypotension.

ELITE II is not the final word on ARBs in heart failure. The sample size for ELITE II was chosen with the expectation of a relatively large effect in mortality reduction (25%); the possibility of a statistically significant but smaller effect cannot be excluded. Combination

therapy with both an ACE inhibitor and an ARB may be superior to either agent alone (2). An ARB with a longer duration of action may be more effective than losartan. 2 ongoing studies of ARBs in heart failure test these hypotheses (3, 4).

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