

Review: Effectiveness of ACE inhibitors is similar across various baseline risks for disease progression in nondiabetic nephropathy

Kent DM, Jafar TH, Hayward RA, et al. Progression risk, urinary protein excretion, and treatment effects of angiotensin-converting enzyme inhibitors in nondiabetic kidney disease. *J Am Soc Nephrol.* 2007;18:1959-65.

Clinical impact ratings: Nephrology ★★★★★☆

QUESTION

In patients with nondiabetic nephropathy at various baseline risks for disease progression, what is the relative effectiveness of angiotensin-converting enzyme (ACE) inhibitors?

METHODS

Data sources: {MEDLINE (May 1977 to September 1997), abstracts in the proceedings of U.S. and international conferences, bibliographies of relevant studies and reviews, and investigators for unpublished studies}.*

Study selection and assessment: English-language, randomized, controlled trials (RCTs) comparing the effectiveness of antihypertensive regimens containing ACE inhibitors (captopril, enalapril, cilazapril, benazepril, and ramipril) with antihypertensive regimens not containing ACE inhibitors (control) in patients with nondiabetic nephropathy followed for ≥ 1 year. All patients had to have hypertension or decreased renal function and received antihypertensive drugs to achieve a target blood pressure (BP) < 140/90 mm Hg. {Exclusion criteria were acute renal failure, receipt of immunosuppressive drugs, congestive heart failure, obstructive uropathy, renal artery stenosis, active systemic disease, type 1 diabetes, history of transplantation or allergy to ACE inhibitors, and pregnancy.}† 11 RCTs (n = 1860, mean age 52 y, 65% men,

94% white) met the selection criteria. Patients were categorized into different risk quartiles for kidney disease progression based on age, sex, serum creatinine, urinary protein excretion, and systolic BP.

Outcomes: Treatment effect of ACE inhibitors across the lowest- to highest-risk groups for kidney disease progression on the composite endpoint of a 2-fold increase from baseline in serum creatinine level or kidney failure (need for long-term dialysis).

MAIN RESULTS

The ACE inhibitor and control groups had heterogeneous risks for the composite endpoint across lowest- to highest-risk quartiles (Table). Multivariate analysis showed that risk quartiles did not differ for the treatment effect of ACE inhibitors (P = 0.8).

CONCLUSION

The effectiveness of angiotensin-converting enzyme inhibitors does not differ across various baseline risks for disease progression in patients with nondiabetic nephropathy.

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*Jafar TH, Schmid CH, Landa M, et al. *Ann Intern Med.* 2001;135:73-87.

Antihypertensive medication with vs without angiotensin-converting enzyme (ACE) inhibitors for the composite endpoint of a 2-fold increase from baseline in serum creatinine level or kidney failure (onset of long-term dialysis) in nondiabetic nephropathy at 1 year†

Risk quartile	ACE inhibitors	No ACE inhibitors	RRR (95% CI)	NNT (CI)
1 (lowest)	0.2%	0.4%	51% (–436 to 96)	Not significant
2	1.7%	2.8%	37% (–38 to 71)	Not significant
3	5.9%	10.7%	46% (18 to 65)	21 (15 to 52)
4 (highest)	19.7%	28.7%	28% (7.3 to 44)	13 (8 to 48)

†Abbreviations defined in Glossary. RRR, NNT, and CI calculated from control event rates and hazard ratios provided by author.

COMMENTARY

Slowing the progression of chronic kidney disease (CKD) is a major goal for renal physicians and health systems. Since the early 1990s, studies showed that ACE inhibitors reduce decline of glomerular filtration rate through both BP-dependent and -independent effects. The benefits of ACE inhibitors on renal function are strongly associated with initial and sustained decrease in urinary protein excretion. Heavy proteinuria is an important factor in CKD progression and a target of renoprotective treatment, but less evidence exists to show that ACE inhibitor-based therapy provides the same benefit to patients with non-proteinuric nephropathies. In patients with CKD and variable rates of progressive renal disease, individual data meta-analysis is a powerful tool to measure the treatment effect according to individual risk profiles, similar to the method used in cardiovascular prevention trials (1).

The study by Kent and colleagues showed that a proportional-effects model appropriately described the effect of ACE inhibitors on the pro-

gression of nondiabetic kidney disease. The relative risk reduction was remarkably consistent across the lowest- to highest-risk groups. The analysis also confirmed that patients with higher amounts of proteinuria have higher risk for progressive renal disease and patients with proteinuria levels < 500 mg/d do not have any measurable benefit from ACE inhibitor-based treatment. The results are essential for physicians to assess benefit-risk ratios of their prescriptions in individual patients, especially those with advanced CKD.

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Reference

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