

Hospitalizations for New Heart Failure Among Subjects With Diabetes Mellitus in the RENAAL and LIFE Studies

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We sought to study the risk factors for heart failure (HF) and the relation between antihypertensive treatment with losartan and the first hospitalization for HF in patients with diabetes mellitus in the Losartan Intervention For Endpoint reduction in hypertension (LIFE) and Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) studies. We evaluated 1,195 patients with hypertension, left ventricular hypertrophy, and diabetes from the LIFE study and 1,513 patients with type 2 diabetes and nephropathy from the RENAAL study. The comparative treatments were atenolol in the LIFE study and placebo in the RENAAL study. Patients with a history of HF were excluded from this analysis. Losartan significantly reduced the incidence of first hospitalizations for HF versus placebo in the RENAAL study (hazard ratio 0.74, $p = 0.037$) and versus atenolol in the LIFE study (hazard ratio 0.57, $p = 0.019$). Patients enrolled in the RENAAL study were at

HF in the RENAAL study were urinary albumin/creatinine ratio, age, peripheral vascular disease, the Cornell product, body mass index, and previous angina; in the LIFE study they were the Cornell product, previous myocardial infarction, peripheral vascular disease, baseline atrial fibrillation, alcohol use (inverse relation), and urinary albumin/creatinine ratio. The beneficial effect of losartan on the reduction of risk for hospitalization for new HF was demonstrated in patients who were at high renal and/or high cardiovascular risk. © 2005 Elsevier Inc. All rights reserved. (Am J Cardiol 2005;96:1530–1536)

Two randomized, double-blind outcome trials enrolling substantial numbers of patients with diabetes mellitus without a history of heart failure (HF) and using the angiotensin II receptor antagonist losartan have been conducted. In this analysis, we report the occurrence of, and risk predictors for, the first hospitalization for HF in these trials, which encompassed patients with a wide range of renal and/or cardiovascular risk of the development of HF.

Methods

Study design and patients: The Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan (RENAAL) study evaluated the renoprotective effects of losartan versus placebo in 1,513 patients with type 2 diabetes mellitus and nephropathy.¹ Antihypertensive therapy was maintained during the baseline phase and administered as needed during the double-blind period, except for angiotensin-converting enzyme inhibitors and other angiotensin II receptor antagonists, for which there was a 6-week placebo run-in phase. Randomized patients were treated with losartan 50 mg, titrated to 100 mg if the goal blood pressure (BP) of <140 mm Hg systolic and <90 mm Hg diastolic was not met. Nephropathy was defined as a urinary albumin/creatinine ratio >300 mg/g or a 24-hour urine protein >500 mg and baseline serum creatinine >1.5 mg/dl in men (1.3 mg/dl in women or men <60 kg in weight) to 3.0 mg/dl. The primary efficacy measure was the time to the first event of the composite end point of a doubling of serum creatinine and macroalbuminuria (one term diabetic renal trans-

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