

**BACKGROUND:** The role of cardiac glycosides in treating patients with chronic heart failure and normal sinus rhythm remains controversial. We studied the effect of digoxin on mortality and hospitalization in a randomized, double-blind clinical trial.

**METHODS:** In the main trial, patients with a left ventricular ejection fraction of 0.45 or less were randomly assigned to digoxin (3397 patients) or placebo (3403 patients) in addition to diuretics and angiotensin-converting-enzyme inhibitors (median dose of digoxin, 0.25 mg per day; average follow-up, 37 months). In an ancillary trial of patients with ejection fractions greater than 0.45, 492 patients were randomly assigned to digoxin and 496 to placebo.

**RESULTS:** In the main trial, mortality was unaffected. There were 1181 deaths (34.8 percent) with digoxin and 1194 deaths (35.1 percent) with placebo (risk ratio when digoxin was compared with placebo, 0.99; 95 percent confidence interval, 0.91 to 1.07; P=0.80). In the digoxin group, there was a trend toward a decrease in the risk of death attributed to worsening heart failure (risk ratio, 0.88; 95 percent confidence interval, 0.77 to 1.01; P=0.06). There were 6 percent fewer hospitalizations overall in that group than in the placebo group, and fewer patients were hospitalized for worsening heart failure (26.8 percent vs. 34.7 percent; risk ratio, 0.72; 95 percent confidence interval, 0.66 to 0.79; P<0.001). In the ancillary trial, the findings regarding the primary combined outcome of death or hospitalization due to worsening heart failure were consistent with the results of the main trial.

**CONCLUSIONS:** Digoxin did not reduce overall mortality, but it reduced the rate of hospitalization both overall and for worsening heart failure. These findings define more precisely the role of digoxin in the management of chronic heart failure.