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Spironolactone for Heart Failure with Preserved Ejection Fraction

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ABSTRACT

BACKGROUND

Mineralocorticoid-receptor antagonists improve the prognosis for patients with heart failure and a reduced left ventricular ejection fraction. We evaluated the effects of spironolactone in patients with heart failure and a preserved left ventricular ejection fraction.

METHODS

In this randomized, double-blind trial, we assigned 3445 patients with symptomatic heart failure and a left ventricular ejection fraction of 45% or more to receive either spironolactone (15 to 45 mg daily) or placebo. The primary outcome was a composite of death from cardiovascular causes, aborted cardiac arrest, or hospitalization for the management of heart failure.

RESULTS

With a mean follow-up of 3.3 years, the primary outcome occurred in 320 of 1722 patients in the spironolactone group (18.6%) and 351 of 1723 patients in the placebo group (20.4%) (hazard ratio, 0.89; 95% confidence interval [CI], 0.77 to 1.04; P=0.14). Of the components of the primary outcome, only hospitalization for heart failure had a significantly lower incidence in the spironolactone group than in the placebo group (206 patients [12.0%] vs. 245 patients [14.2%]; hazard ratio, 0.83; 95% CI, 0.69 to 0.99, P=0.04). Neither total deaths nor hospitalizations for any reason were significantly reduced by spironolactone. Treatment with spironolactone was associated with increased serum creatinine levels and a doubling of the rate of hyperkalemia (18.7%, vs. 9.1% in the placebo group) but reduced hypokalemia. With frequent monitoring, there were no significant differences in the incidence of serious adverse events, a serum creatinine level of 3.0 mg per deciliter (265 μmol per liter) or higher, or dialysis.

CONCLUSIONS

In patients with heart failure and a preserved ejection fraction, treatment with spironolactone did not significantly reduce the incidence of the primary composite outcome of death from cardiovascular causes, aborted cardiac arrest, or hospitalization for the management of heart failure. (Funded by the National Heart, Lung, and Blood Institute; TOPCAT ClinicalTrials.gov number, NCT00094302.)

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*A complete list of investigators and committees in the Treatment of Preserved Cardiac Function Heart Failure with an Aldosterone Antagonist (TOPCAT) trial is provided in the Supplementary Appendix, available at NEJM.org.

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