Effect of oral digoxin in high-risk heart failure patients: a pre-specified subgroup analysis of the DIG trial.

AIMS: In the Digitalis Investigation Group (DIG) trial, digoxin reduced mortality or hospitalization due to heart failure (HF) in several pre-specified high-risk subgroups of HF patients, but data on protocol-specified 2-year outcomes were not presented. In the current study, we examined the effect of digoxin on HF death or HF hospitalization and all-cause death or all-cause hospitalization in high-risk subgroups during the protocol-specified 2 years of post-randomization follow-up.

METHODS AND RESULTS: In the DIG trial, 6800 ambulatory patients with chronic HF, normal sinus rhythm, and LVEF ≤45% (mean age 64 years, 26% women, 17% non-whites) were randomized to receive digoxin or placebo. The three high-risk groups were defined as NYHA class III-IV symptoms (n = 2223), LVEF <25% (n = 2256), and cardiothoracic ratio (CTR) >55% (n = 2345). In all three high-risk subgroups, compared with patients in the placebo group, those in the digoxin group had a significant reduction in the risk of the 2-year composite endpoint of HF mortality or HF hospitalization: NYHA III-IV [hazard ratio (HR) 0.65; 95% confidence interval (CI) 0.57-0.75; P < 0.001], LVEF <25% (HR 0.61; 95% CI 0.53-0.71; P < 0.001), and CTR >55% (HR 0.65; 95% CI 0.57-0.75; P < 0.001). Digoxin-associated HRs (95% CI) for 2-year all-cause mortality or all-cause hospitalization for subgroups with NYHA III-IV, LVEF <25%, and CTR >55% were 0.88
(0.80-0.97; P = 0.012), 0.84 (0.76-0.93; P = 0.001), and 0.85 (0.77-0.94; P = 0.002), respectively.

**CONCLUSIONS:** Digoxin improves outcomes in chronic HF patients with NYHA class III-IV, LVEF <25%, or CTR >55%, and should be considered in these patients.

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