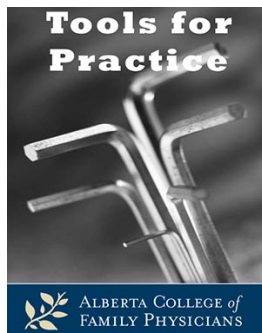


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Digoxin: Old friend or best left on the shelf?

Clinical Question: Does digoxin change clinical outcomes for patients with congestive heart failure or atrial fibrillation?

Bottom-line: For systolic congestive heart failure (CHF), a randomized controlled trial (RCT) demonstrated that digoxin decreases CHF related hospitalizations (for one in 13 patients) without altering mortality. Stopping digoxin in stable CHF patients may worsen symptoms. Post-hoc analysis suggests low serum digoxin levels may actually decrease mortality. Cohort data for atrial fibrillation (AF) or CHF suggests digoxin increases mortality, although cause and effect is not established.

Evidence:

- Systolic CHF:
 - High quality RCT of 6,800 patients (NYHA class II-III, mean age 63) on digoxin (median 0.25 mg/day) or placebo¹ which contributed 98% of outcomes to subsequent systematic review² found at three years:
 - Overall mortality or hospitalizations: No difference.
 - CHF hospitalizations: 27% Digoxin versus 35% placebo, Number Needed to Treat (NNT)=13.
 - Limitation: Study occurred before routine beta blocker (BB) use.
 - Post-hoc analysis:³
 - Digoxin levels:
 - <0.9 ng/ml: 6% absolute lower mortality and overall hospitalizations rate compared to placebo.
 - >1.2 ng/ml: 12% absolute higher mortality.
 - 12 week RCTs of Digoxin withdrawal in stable CHF resulted in:^{4,5}
 - Clinical deterioration (necessitating study withdrawal)⁴ or treatment failure (adding/increasing CHF meds, emergency department visit/admission)⁵ Number Needed to Harm~5.^{4,5}
 - Deterioration more likely in patients older, not on angiotensin converting enzyme inhibitors (ACEI) or more cardiomegaly/CHF symptoms.⁶
- AF:

- A systematic review of 12 cohort studies (235,047 patients)⁷ including three largest studies from US,⁸ Sweden,⁹ and Canada¹⁰ using digoxin post hospital discharge^{8,9} or outpatient visit^{9,10} demonstrated a 29% increased mortality associated with digoxin (HR 1.29; 95% CI, 1.21-1.39).
 - Limitations: Unsure if possible residual confounding (patients receiving digoxin are sicker).

Context:

- Current guidelines recommend digoxin after:
 - Diuretics, ACEI, BBs, and aldosterone antagonists in CHF.¹¹
 - Calcium channel blockers or BBs in AF.¹²
- Clinical symptoms, age, and renal function should guide digoxin dosing, digoxin levels being ordered if questioning toxicity.
- Digoxin toxicity typically presents with cardiac arrhythmias, visual, or gastrointestinal symptoms¹³ and remains a relatively common reason for hospitalizations in the elderly.¹⁴

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Disclosure:

Authors do not have any conflicts to disclose.

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