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BRIEF QUESTIONS AND ANSWERS ON CURRENT CLINICAL CONTROVERSIES

# Q: When should digoxin be used in patients with diastolic dysfunction?

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**A:** DIGOXIN STILL HAS A ROLE in the management of heart failure, but most of the evidence is from patients with systolic dysfunction, not diastolic dysfunction. Digoxin's potential impact on symptoms is less than that of angiotensin-converting enzyme (ACE) inhibitors; thus, treatment with digoxin should be individualized.

Current drug therapies for diastolic dysfunction include beta-blockers, calcium channel blockers, and ACE inhibitors. Additional studies are needed before digoxin is used routinely in patients with diastolic dysfunction.

## DIGOXIN HELPS MANAGE SYMPTOMS OF SYSTOLIC HEART FAILURE

Several small trials, as well as two large withdrawal studies published in 1993—PROVED (Prospective Randomized Study of Ventricular Function and Efficacy of Digoxin)[1] and RADIANCE (Randomized Assessment of Digoxin and Inhibitors of Angiotensin-Converting Enzyme)[2]—showed that digoxin is effective in treating the symptoms of systolic heart failure.

In light of these findings, the 1994 guidelines from the Agency for Health Care Policy and Research[3] and the 1995 guidelines from the American College of Cardiology and the American Heart Association[4] recommended digoxin for patients who continue to have symptoms despite adequate treatment with an ACE inhibitor and a diuretic.

These guidelines, however, focus on patients with left ventricular systolic dysfunction and do not tell us what to do for patients with diastolic dysfunction (relatively preserved systolic function with a left ventricular ejection fraction > 45%), who account for almost 40% of the heart failure population.

## DIGITALIS TRIAL SHOWS BENEFIT IN DIASTOLIC DYSFUNCTION

In 1997, the DIG (Digitalis Investigation Group) trial[5] effectively ended the 200-year-old controversy regarding whether digoxin reduces morbidity and mortality in heart failure.

The DIG investigators conducted two parallel trials: a main trial with 6,800 patients with left ventricular systolic dysfunction, and an ancillary trial with 988 patients with diastolic dysfunction. The primary end point measured in the main trial was death; in the ancillary trial the primary end point was death or hospitalization due to worsening heart failure. Patients in both groups were randomized to receive digoxin or placebo and were followed for an average of 37 months.

Patients with diastolic dysfunction who received digoxin experienced an 18% risk reduction in the combined end point of death or hospitalization due to worsening heart failure (95% confidence interval 0.63–1.07). For the diastolic dysfunction group, the reduction in the combined end point was mainly because of a reduction in hospitalizations. Still, the DIG trial was the only randomized controlled trial to date to find that digoxin has any beneficial effects in patients with diastolic dysfunction. Overall, digoxin did not increase the survival rate in either group.

## DIGOXIN FOR DIASTOLIC DYSFUNCTION AND ATRIAL FIBRILLATION?

The next logical question is whether digoxin has a role in the management of patients with both diastolic dysfunction and atrial fibrillation. Indeed, the electrophysiologic effects of

**Treatment with digoxin should be individualized**

digoxin and the resulting decrease in atrioventricular node conduction make it an attractive therapeutic strategy for controlling the ventricular rate in patients with atrial fibrillation. However, the clinical efficacy of digoxin in this group of patients is controversial.

This controversy was fueled recently by the finding that digoxin potentiates the shortening of the atrial effective refractory period. Hence, its use may, in fact, facilitate short-term recurrences of atrial fibrillation and increase a patient's risk for future episodes.[6] Therefore, digoxin is not an ideal first-line agent in this group of patients. Other agents such as beta-blockers constitute a better therapeutic strategy to control the ventricular rate in patients with atrial fibrillation and diastolic dysfunction.

## REFERENCES


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