Digoxin tied to increased risk of death in patients with atrial fibrillation

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In An Account of the Foxglove and Some of its Medical Uses, published in 1785, Sir William Withering cautioned readers that extracts from the plant foxglove, also called digitalis, was not a perfect drug. "Time will fix the real value upon this discovery," he wrote.

Now, more than 200 years later, researchers at the Stanford University School of Medicine have validated Withering's warning with the discovery that patients with atrial fibrillation—a rapid and irregular heart rhythm—who are treated with the digitalis-derivative digoxin are more likely to die than similar patients who received different treatments.

"The take-home point is to question whether people should really be on this drug," said the study's lead author, Mintu Turakhia, MD, assistant professor of cardiology at Stanford and director of cardiac electrophysiology at the Veterans Affairs Palo Alto Health Care System. "These data challenge the current guidelines."

The study will be published online Aug. 11 in the *Journal of the American College of Cardiology*, and will appear in the Aug. 19 print issue of the journal.

Turakhia and his team analyzed records from 122,465 patients who received a new diagnosis of atrial fibrillation from the U.S. Department of Veterans Affairs health-care system between 2003 and 2008. Doctors prescribed digoxin to 23 percent of the patients, and 70 percent of those patients were still on the drug one year later. Patients treated with

digoxin were 1.2 times more likely to die than comparable patients prescribed other therapies. Patients receiving digoxin were more likely to die regardless of age; use of other drugs such as beta-blockers, amiodarone or warfarin; or the presence of other factors such as kidney disease, heart attack or heart failure, the study found.

"This is going to be as close to proof positive as we get because we may never have a randomized trial of this drug," Turakhia said. Pharmaceutical companies lack the incentive to finance studies on a long-accepted, generic drug.

Although recent studies showed mixed results, doctors and patients trusted digoxin because of its historic status, Turakhia said.

"There's an evidence gap," he said, adding that he launched the investigation because digoxin hasn't been rigorously tested like the many other atrial fibrillation treatment options.

The VA patient pool was predominantly male—only 1,980, or 1.6 percent, were female—and Turakhia has called for additional studies to establish whether the results are applicable to women as well.

Turakhia said many other drugs with better safety results are available to treat atrial fibrillation. Digoxin slows the heart rate but does not correct it to a normal rhythm. "We are not asserting this drug should never be used," he said. "However, in light of the many other drugs that can be used to slow down the heart rate in atrial fibrillation, patients and providers need to ask whether digoxin should be the treatment of choice when there are other, safer drugs. "

Provided by Stanford University Medical Center