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## Blood-Thinning Treatment Standards Changing for Heart Patients, New Research Shows

***Researchers at the University of Cincinnati and Massachusetts General Hospital have found that warfarin, a known anticoagulation (blood-thinning) drug, may not be as beneficial to some patients with atrial fibrillation as previously thought.***

These findings were published online this week ahead of print in the journal *Circulation: Cardiovascular Quality and Outcomes*.

Warfarin is commonly prescribed to prevent blood clotting, particularly for patients with atrial fibrillation -- a type of abnormal heart rhythm.

Mark Eckman, MD, a UC Health physician, Professor of Medicine and Lead Investigator of the study, says that this finding could change the way patients with the heart condition manage stroke risk.

"When considering patient-specific decision making for patients with atrial fibrillation, patients at lower risk of stroke and at high risk of bleeding should not receive oral anticoagulant therapy; patients at higher risk of stroke and at low risk of bleeding should receive anticoagulant therapy," he says. "The more difficult decisions lie in the middle where the risks of stroke and bleeding are more closely balanced. Here lies the so-called 'tipping point'."

"Our goal was to revisit the tipping point in light of more contemporary data suggesting a declining stroke risk for any of the typically defined risk factors. We also wished to explore, how the future availability of a new, safer anticoagulant, such as the direct thrombin inhibitor dabigatran, in the United States would impact anticoagulant therapy?"

Eckman and researchers used a Markov state transition decision model -- a mathematical framework for modeling decision-making in situations where outcomes are partly due to chance and partly under the control of a decision maker -- to analyze the CHADS2 score above which anticoagulation is preferred.

The CHADS2 model is used to estimate stroke risk in patients with atrial fibrillation.

"CHADS2 takes into account the patient's age as well as other medical conditions, including congestive heart failure, hypertension, diabetes and prior stroke and is used by many guidelines to help make treatment recommendations for anticoagulant or blood-thinning therapy," Eckman says, adding that researchers also used outcomes from the Anticoagulation and Risk Factors in Atrial Fibrillation (ATRIA) study to define a more contemporary risk of stroke among patients with atrial fibrillation.

The ATRIA study has followed outcomes in a large group of more than 13,500 patients with atrial fibrillation and has found that the risk of stroke has declined over the past two decades.

Researchers explored outcomes of four strategies: anticoagulate with warfarin; anticoagulate with a new, "safer" agent, using dabigatran (another anticoagulant) as the prototype; treat with aspirin; and no antithrombotic therapy.

"We used a standard computer program to build the model, analyze results and perform sensitivity analyses," Eckman says. "Our base case involved a hypothetical 69-year-old man with non-valvular atrial fibrillation who had no contraindications to warfarin therapy."

Researchers found that warfarin is preferred above a stroke rate of 1.7 percent per year, corresponding to a CHADS2 score of 0 using the historically higher rates of stroke of the older CHADS2 derivation cohort.

Eckman continues, "Using more contemporary and lower estimates of stroke risk raises the threshold for use of

warfarin to a CHADS2 score of greater than or equal to 2 (moderate to high risk). However, anticoagulation with a new, 'safer' agent leads to a lowering of the threshold for anticoagulation to a stroke rate of 0.9 percent per year.

"Our analysis suggests that the 'tipping point,' the threshold of ischemic stroke risk below which anticoagulant therapy should be withheld and above which anticoagulant therapy should be prescribed, has changed," he says. "The risk of ischemic stroke in non-valvular atrial fibrillation appears to have declined, perhaps as a result of more aggressive control of blood pressure and lipid levels. Our analysis, using a more contemporary group of patients with atrial fibrillation from the ATRIA study, suggests that the threshold has shifted such that the balance of risk and benefit of anticoagulation tips in favor of warfarin at a higher CHADS2 score than in the past."

However, he says that as safer anticoagulants become available, the tipping point will shift again.

"With the advent of new anticoagulants and antithrombotic therapies, along with non-pharmacological interventions for atrial fibrillation, and the improbability of clinical trials performing head-to-head comparisons of these treatments, a decision-analytical framework may be one of the few ways to compare new treatments as they become available," he says. "These data have implications for future guidelines as well as real-world bedside decision-making."

The investigators were supported by the National Center for Research Resources, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Heart, Lung, and Blood Institute, and the National Library of Medicine.

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