

New assessment quantifies risks and benefits of warfarin treatment for atrial fibrillation

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Warfarin therapy for patients with atrial fibrillation - the most common type of significant heart rhythm disorder - appears to be most beneficial for the oldest patients, those who have had a prior stroke and for patients with multiple risk factors for stroke, according to a new study by Kaiser Permanente and Massachusetts General Hospital researchers. This comparative effectiveness research study - among the first and largest to quantify warfarin's net clinical benefit, how much a treatment's potential benefits outweigh its risks, in the usual clinical care of patients with atrial fibrillation - appears in the September 1 *Annals of Internal Medicine*.

As part of the ongoing ATRIA (AnTicoagulation and Risk Factors In Atrial Fribrillation) study, researchers followed 13,559 adults with atrial fibrillation treated within Kaiser Permanente of Northern California from 1996 to 2003. To evaluate the risks and benefits of warfarin treatment and give patients and physicians quantitative guidance in making therapeutic decisions, the researchers analyzed rates of the two most significant adverse events associated with warfarin therapy ischemic stroke, the type produced by arterial blockage, and intracranial hemorrhage, bleeding within and around the brain. For patients who did and did not take warfarin, the investigators balanced the reduction in ischemic stroke attributable to treatment against the increase in intracranial bleeding associated with warfarin. Since intracranial hemorrhages usually have worse outcomes than ischemic strokes, bleeding events were given greater weight in the comparison.



While warfarin therapy benefited most atrial fibrillation patients, the balance of benefits over risks was greatest in those at highest risk of stroke - those with multiple risk factors, those with a history of stroke and the oldest patients. The benefits of treatment increased strikingly with age, with no clear benefit in the average patient younger than 65 but a reduction of more than two strokes per 100 patients in those 85 and older.

Occurring when the upper chambers of the heart quiver instead of smoothly contracting, atrial fibrillation affects more than 2.3 million Americans. Because the heart rhythm disturbance promotes the formation of blood clots that can travel to the brain and block an artery, atrial fibrillation increases the risk of stroke fivefold. The condition is highly age-dependent and affects 10 percent of those over age 80. Researchers have long known that warfarin is effective in preventing such strokes, but the treatment can be difficult to control and often leads to hemorrhage. In fact, warfarin is associated with the most emergency admissions for drug-related adverse reactions. Balancing the benefits of warfarin against its most severe risks is critical to making the best therapeutic decisions for individual atrial fibrillation patients, explains the study's senior author Alan S. Go, MD, director of the Comprehensive Clinical Research Unit at the Kaiser Permanente Division of Research.

Daniel Singer, MD, of the Massachusetts General Hospital (MGH) Clinical Epidemiology Unit, the report's lead author, adds, "This comparative effectiveness study gives us more information about which atrial fibrillation patients are most likely to benefit from carefully administered warfarin therapy." He explains that, by assessing warfarin within a "real world" practice setting, the study provides a more contemporary assessment of the therapy's overall effects than do older clinical studies.



Go explains that Kaiser Permanente physicians partner with pharmacistrun anticoagulation clinics to provide thorough and nimble administration and careful monitoring of warfarin therapy for atrial fibrillation patients. This allows for delivery of high-quality anticoagulation therapy through frequent testing and appropriate dose adjustment to account for changes in diet, medications and clinical status that may impact the therapy's narrow therapeutic window.

Singer adds, "One of our distinctive findings is that stroke risk continues to increase in patients age 85 and older and that warfarin provides substantial net protection for these elderly patients. A caution is that all these patients were presumably judged by their physicians to be reasonable candidates for warfarin therapy, so these results do not automatically apply to all elderly <u>atrial fibrillation</u> patients."

Source: Massachusetts General Hospital (<u>news</u>: <u>web</u>)

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