
Lack of Evidence for Aspirin in Heart Failure



The WARCEF (Warfarin Versus Aspirin in Reduced Ejection Fraction) trial indicates that, compared to warfarin, aspirin does not increase the risk of hospitalisation for heart failure. The study findings contrast with those of two previous trials that showed an increase in such risk, notes an editorial published in JACC: Heart Failure.

The randomised trial, which involved 2,305 patients with heart failure in sinus rhythm and with a left ventricular ejection fraction $\leq 35\%$, was both the largest and most methodologically robust trial comparing warfarin and aspirin for heart failure.

While the results "allay some of the fears" raised by previous trials that aspirin could increase the risk of congestion, the editorial states that these results "provide no evidence that either warfarin or aspirin should be given routinely to patients with heart failure in sinus rhythm.

Aspirin is a nonspecific cyclo-oxygenase inhibitor that blocks the production of a range of prostaglandins. Many prostaglandins are thought to have beneficial actions, including vasorelaxation, maintenance of glomerular filtration, and reductions in platelet adhesion to vessel walls; whereas others, such as thromboxane, increase platelet aggregation, providing a theory to support the supposed benefits of aspirin in patients with coronary artery disease.

"The balance of beneficial and harmful effects of aspirin is likely to vary according to the clinical setting," writes John G.F. Cleland, MD, Robertson Centre for Biostatistics & Clinical Trials, University of Glasgow (UK) in the editorial. In the presence of ulcerated plaque, benefit may greatly outweigh risk, the doctor explains. In heart failure, prostacyclin may be an important counter-regulatory mechanism that causes vasorelaxation, protects renal function, and reduces sodium retention, thereby reducing the risk of worsening heart failure. "This may be a mechanism by which angiotensin-converting enzyme (ACE) inhibitors exert benefit," he points out.

In addition, there is a great deal of evidence that the benefits of ACE inhibitors are diminished in the presence of antiplatelet therapy, predominantly aspirin, according to Dr. Cleland. One possible explanation is that aspirin may interfere with the beneficial effects of ACE inhibitors, which is biologically plausible. Or it could be that ACE inhibitors and aspirin exert benefit through a common pathway but the effects are not additive (statistically plausible).

Meanwhile, randomised trials of aspirin compared to warfarin show that warfarin reduces the risk of stroke but increases major bleeding; overall mortality was similar on aspirin and warfarin. Further, the importance of occult or incident atrial fibrillation to strokes in patients with heart failure is uncertain. "So why do we use antithrombotic agents in heart failure?" Dr. Cleland asks. Cardiologists will generally respond that they are not treating the heart failure; they are treating the associated coronary artery disease, he says.

The doctor continues: "So what evidence is there that patients with coronary artery disease benefit from long-term aspirin? Surprisingly, at least to most cardiologists, no trial of long-term aspirin administration to patients with proven coronary disease has shown a reduction in mortality."

He says that if we are going to use aspirin for generations to come, it's important to know which doses are effective and safe. "Unfortunately, dose-comparison studies are not very helpful because if no dose of aspirin is known to be effective, then there is no reference-dose!" adds the author.

Source: [JACC: Heart Failure](#)
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