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Aspirin, Yes, for at-risk elderly— but what about the healthy elderly?

This study paints a decidedly different picture as to what role—if any—aspirin can play in the primary prevention of CVD for older adults.

PRACTICE CHANGER

Do not prescribe aspirin for primary prevention of cardiovascular disease in your elderly patients. Aspirin does not improve cardiovascular outcomes and it significantly increases the risk of bleeding events.

STRENGTH OF RECOMMENDATION

B: Based on a single randomized controlled trial.

McNeil JJ, Wolfe R, Woods RL, et al. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. *N Engl J Med.* 2018;379:1509-1518.¹

ILLUSTRATIVE CASE

A healthy 72-year-old man with well-controlled hypertension on amlodipine 10 mg/d presents to you for an annual exam. He has no history of coronary artery disease or stroke. Should you recommend that he start aspirin for primary prevention of cardiovascular disease?

Cardiovascular disease (CVD) remains the leading cause of death in the United States.² Aspirin therapy remains the standard of care for secondary prevention of CVD in patients with known coronary artery disease (CAD).³ Aspirin reduces the risk of atherothrombosis by irreversibly inhibiting platelet function. At the same time, it increases the risk of major bleeding, including gastrointestinal bleeds and hemorrhagic strokes. Even though the benefit of aspirin in patients with known CAD is well established,

the benefit of aspirin as primary prevention is less certain.

Two recent large randomized controlled trials (RCTs) examined the benefits and risks of aspirin in a variety of patient populations. The ARRIVE trial looked at more than 12,000 patients with a mean age of 63 years with moderate risk of CVD (approximately 15% risk of a cardiovascular event in 10 years) and randomly assigned them to receive aspirin or placebo.⁴ After an average follow-up period of 5 years, researchers observed that actual cardiovascular event risk was < 10% in both groups, and there was no significant difference in the primary outcome of first cardiovascular event or all-cause mortality. There was, however, a significant increase in bleeding events in the group receiving aspirin.⁴

The ASCEND trial evaluated aspirin vs placebo in more than 15,000 adult patients with type 2 diabetes mellitus and a low risk of CVD (< 10% risk of cardiovascular event in 5 years).⁵ The primary endpoint of the study was first cardiovascular event. The authors found a significantly lower rate of cardiovascular events in the aspirin group, as well as more major bleeding events. Additionally, there was no difference between the aspirin and placebo groups in all-cause mortality after 7 years. The authors concluded that the benefits of aspirin in this group were counterbalanced by the harms.⁵

Currently, several organizations offer recommendations on aspirin use in people 40 to 70 years of age based on a patient's risk

of bleeding and risk of CVD.⁶⁻⁸ Recommendations regarding aspirin use as primary prevention have been less clear for patients < 40 and > 70 years of age.⁶

Elderly patients are at higher risk of CVD and bleeding, but until recently, few studies had evaluated elderly populations to assess the benefits vs the risks of aspirin for primary CVD prevention. As of 2016, the US Preventive Services Task Force (USPSTF) stated the evidence was insufficient to assess the balance of the benefits and harms of initiating aspirin use for primary prevention of CVD in patients older than 70 years of age.⁶ This trial focuses on aspirin use for primary prevention of CVD in healthy elderly adults.

STUDY SUMMARY

Don't use aspirin as primary prevention of CVD in the elderly

This secondary analysis of a prior double-blind RCT, which found low-dose aspirin did not prolong survival in elderly patients, examined the effect of aspirin on CVD and hemorrhage in 19,114 elderly patients without known CVD.¹ The patients were ≥ 70 years of age (≥ 65 years for blacks and Hispanics) with a mean age of 74 years and were from Australia (87%) and the United States (13%). Approximately one-third of the patients were taking a statin, and 14% were taking a non-steroidal anti-inflammatory drug (NSAID) regularly. Patients were randomized to either aspirin 100 mg/d or matching placebo and were followed for an average of 4.7 years.

■ Outcomes. The outcome of CVD was a composite of fatal coronary heart disease, nonfatal myocardial infarction (MI), fatal or nonfatal ischemic stroke, or hospitalization for heart failure, and the outcome of major adverse cardiovascular event was a composite of fatal cardiovascular disease (excluding death from heart failure), nonfatal MI, or fatal and nonfatal ischemic stroke.

■ Results. No difference was seen between the aspirin and placebo groups in CVD outcomes (10.7 events per 1000 person-years vs 11.3 events per 1000 person-years, respectively; hazard ratio [HR] = 0.95; 95% confidence interval [CI], 0.83-1.08) or major cardiovascular events (7.8 events per

1000 person-years vs 8.8 events per 1000 person-years, respectively; HR = 0.89; 95% CI, 0.77-1.03). The composite and individual endpoints of fatal cardiovascular disease, heart failure hospitalizations, fatal and non-fatal MI, and ischemic stroke also did not differ significantly between the groups.

The rate of major hemorrhagic events (composite of hemorrhagic stroke, intracranial bleed, or extracranial bleed), however, was higher in the aspirin vs the placebo group (8.6 events per 1000 person-years vs 6.2 events per 1000 person-years, respectively; HR = 1.4; 95% CI, 1.2-1.6; number needed to harm = 98).

WHAT'S NEW

Finding of more harm than good leads to change in ACC/AHA guidelines

Although the most recent USPSTF guidelines state the evidence is insufficient to assess the risks and benefits of aspirin for the primary prevention of cardiovascular disease in this age group, this trial reveals there is a greater risk of hemorrhagic events than there is prevention of cardiovascular outcomes with aspirin use in healthy elderly patients > 70 years of age.⁶ Because of this trial, the American College of Cardiology (ACC) and the American Heart Association (AHA) have updated their guidelines on the primary prevention of cardiovascular disease to recommend that aspirin not be used routinely in patients > 70 years of age.⁷

CAVEATS

Potential benefit to people at higher risk?

The rate of cardiovascular disease was lower than expected in this overall healthy population, so it is not known if cardiovascular benefits may outweigh the risk of bleeding in a higher-risk population. The trial also didn't address the potential harms of deprescribing aspirin. Additionally, although aspirin may not be protective for cardiovascular events and may lead to more bleeding, there may be other benefits to aspirin in this patient population that were not addressed by this study.



Because of this trial, the ACC and AHA have updated their guidelines on primary prevention of CVD to recommend against the routine use of aspirin in patients > 70 years of age.

CONTINUED

CHALLENGES TO IMPLEMENTATION**Popular beliefs and wide availability may make tide difficult to change**

Patients have been told for years to take a daily aspirin to “protect their heart”; this behavior may be difficult to change. And because aspirin is widely available over the counter, patients may take it without their physician’s knowledge.

JFP

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