Updated Recommendations on Daily Aspirin Use in Patients with Diabetes

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Literature search described? No

Evidence rating system used? Yes

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Persons with diabetes mellitus have two to four times the risk of cardiovascular events compared with persons of the same age and sex who do not have the disease. Coronary heart disease (CHD) is responsible for more than two-thirds of deaths in persons with diabetes who are older than 65 years. Although aspirin has been proven to reduce cardiovascular morbidity and mortality rates in high-risk patients with myocardial infarction or stroke, its benefit is unclear in patients without a history of cardiovascular events.

In 2007, the American Diabetes Association and American Heart Association recommended aspirin therapy (75 to 162 mg daily) for primary prevention in patients with diabetes who had increased CHD risk (e.g., older than 40 years, smoking, family history of cardiovascular disease). Since these recommendations were published, new evidence has raised questions about the effectiveness of this strategy. The U.S. Preventive Services Task Force recently recommended that physicians encourage aspirin use in men 45 to 79 years of age and in women 55 to 79 years of age, regardless of whether they have diabetes. To address the uncertainties about aspirin use in persons with diabetes, experts from the American Diabetes Association, American Heart Association, and American College of Cardiology Foundation reviewed the current evidence and updated the 2007 recommendations. The group organized its recommendations around the following questions:

- What is the evidence for aspirin in preventing initial cardiovascular events in patients with diabetes?
- How can the conflicting results of various primary prevention trials be reconciled?
- What are the risks of aspirin therapy, and are these risks similar for patients with diabetes compared with those for patients without the disease?
- What is the recommended dosage?
- How should the potential benefits and risks of aspirin therapy be integrated to determine which patients should take aspirin daily for the primary prevention of cardiovascular events?

The current evidence on aspirin therapy for prevention of cardiovascular disease includes three trials conducted in patients with diabetes, and six trials containing subgroups of patients with diabetes. None of these trials provides definitive results, so the group performed a meta-analysis to reconcile the available data. Data from subgroups of patients with diabetes from the six trials were included in a previous meta-analysis by the Antithrombotic Trialists' Collaboration. These were combined with data from the Japanese Primary Prevention of Atherosclerosis With Aspirin for Diabetes study, the Prevention of Progression of Arterial Disease and Diabetes trial, and the Early Treatment of Diabetic Retinopathy Study. A random-effects model showed that aspirin use is associated with nonsignificant decreases in the risk of CHD events (relative risk [RR] = 0.91; 95% confidence interval ▶

[CI], 0.79 to 1.05) and of stroke (RR = 0.85; 95% CI, 0.66 to 1.11). The results of the diabetes-specific analyses are consistent with the findings of the previous meta-analysis, and suggest that aspirin use likely reduces the risk of cardiovascular disease to a modest degree in patients with diabetes.

Adverse effects of aspirin therapy include intracranial bleeding (hemorrhagic stroke) and extracranial bleeding (mainly gastrointestinal [GI]). Several cardiovascular risk factors also increase the risk of extracranial bleeding, which suggests that persons at higher risk of CHD events are also at higher risk of aspirin-related adverse effects. Current evidence supports the use of proton pump inhibitors to decrease the risk of recurrent aspirin-related GI bleeding. However, routine use of these agents may not be cost-effective, and it is not clear whether they should be recommended for primary prevention of GI bleeding.

The optimal dosage of aspirin for prevention of CHD events is not clear. The average daily dosage used in primary prevention trials that included persons with diabetes ranged from 50 to 650 mg. The risk reductions achieved with low dosages (75 to 162 mg per day) seem to be similar to those obtained with higher dosages. Although platelets from patients with diabetes have altered function, it is not clear whether this affects the recommended dosage of aspirin for cardioprotection. There are alternate pathways for platelet activation and aggregation that are independent of thromboxane A_2 and are therefore not sensitive to the effects of aspirin. The evidence is insufficient to empirically recommend higher dosages of aspirin for patients with diabetes.

In adults with cardiovascular risk greater than 1 percent per year, the number of CHD events prevented will be approximately equal to or greater than the number of bleeding events induced, although these events (myocardial infarction, stroke, and GI bleeding) do not have equal effects on long-term health.

Recommendations

Low-dose aspirin therapy is reasonable in adults with diabetes and no history of vascular disease, whose 10-year risk of CHD events is greater than 10 percent, and who are not at increased risk of bleeding (i.e., no history of GI bleeding or peptic ulcer disease, and no concurrent use of other medications that increase bleeding risk). Adults with diabetes who are at increased risk of CHD events include most men older than 50 years and women older than 60 years who have at least one additional major risk factor (i.e., smoking, hypertension, dyslipidemia, albuminuria, or family history of premature cardiovascular disease).

Aspirin should not be recommended in adults with diabetes who are at low risk of cardiovascular events (men younger than 50 years and women younger than 60 years with no additional major risk factors). The potential adverse effects from bleeding offset the potential benefits in these patients.

Low-dose aspirin therapy may be considered for patients with diabetes who are at intermediate risk of CHD events (younger patients with at least one risk factor, older patients with no risk factors, or patients with a 10-year risk of 5 to 10 percent).

These recommendations depend on the accurate assessment of CHD risk. Not all patients with diabetes are at high risk, and the use of a risk prediction tool is essential. There are several Web-based tools available, such as the UK Prospective Diabetes Study Risk Engine (http://www.dtu.ox.ac.uk/riskengine/index.php) and the Atherosclerosis Risk in Communities CHD Risk Calculator (http://www.aricnews.net/riskcalc/html/RC1.html). Risk should be reassessed periodically, because patients may acquire additional risk factors over time. ■

Answers to This Issue's CME Quiz

Q1. C	**Q6.** C	**Q11.** A, D
Q2. C	**Q7.** A	**Q12.** A
Q3. B, D	**Q8.** A, C	**Q13.** A
Q4. A	**Q9.** C	**Q14.** B, C
Q5. A, B, C	**Q10.** D	