REVIEW

CME CREDIT

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Who should be taking aspirin to prevent coronary events?

ABSTRACT

The decision to prescribe aspirin to prevent a coronary event is not straightforward, and requires physicians to balance the risk of a coronary event with the risk of adverse events from aspirin. Although evidence-based medicine shows the way, it does not answer all the questions, especially for patients at intermediate risk.

KEY POINTS

Based on existing trial data and our knowledge of aspirin's antiplatelet effects, current guidelines recommend using low doses (75 to 100 mg), but it is not clear that lower doses reduce bleeding risk.

Key to deciding whether to give aspirin therapy is to estimate the patient's annual risk of a major coronary event, using the National Cholesterol Education Program's risk assessment tool.

While there has been no randomized trial of aspirin for the primary prevention of coronary disease events in patients with diabetes, subgroup analyses from larger randomized trials suggest a benefit.

ASPIRIN IS WIDELY PROMOTED as an effective, safe, and inexpensive means of preventing coronary disease events,[1–3] and a number of randomized trials[4–7] have demonstrated its efficacy. But aspirin therapy is not for everybody.[1] People at low risk of a coronary event do not need to take aspirin, and some people at high risk may not be candidates owing to bleeding problems or hypersensitivity to salicylates.

The decision is often not straightforward. However, estimating the patient's risk of a coronary event and following a simple algorithm (**FIGURE 1**) can help us make a reasonable, evidence-based decision.

I will present three brief examples of how to use the estimated coronary event risk and the algorithm in deciding whether to prescribe long-term aspirin therapy.

A QUICK CALCULATION OF CORONARY RISK

A key part of deciding whether to prescribe aspirin is to estimate the patient's annual risk of a major coronary event (ie, myocardial infarction or coronary death). This can be done quickly in the office with the National Cholesterol Education Program's risk assessment tool,[8,9] which is based on data from the Framingham Heart Study. I recommend the online version (**www.nhlbi.nih.gov/guidelines/cholesterol/index.htm**, then click on "10-Year Risk Calculator"). The calculator can also be downloaded.

After you enter the patient's age, sex, total cholesterol level, high-density lipoprotein (HDL) cholesterol level, and systolic blood pressure, and whether he or she smokes or is currently taking antihypertensive medication, click on "calculate the 10-year risk." In a few

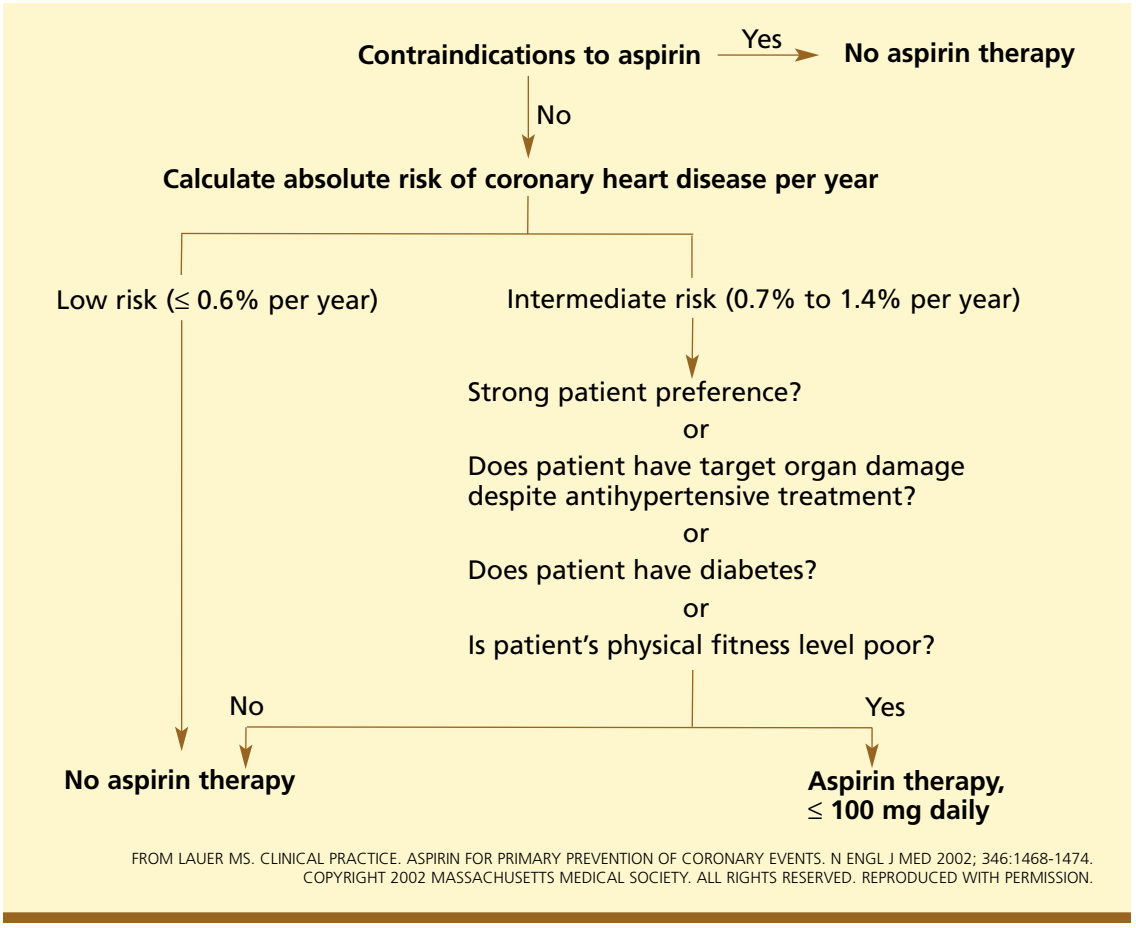

FIGURE 1. Algorithm for deciding whether to institute aspirin therapy for primary prevention. Contraindications to aspirin include renal failure, active peptic ulcer disease or gastrointestinal bleeding, and bleeding diathesis and/or platelet disorder. Relative contraindications include concurrent use of nonsteroidal anti-inflammatory drugs and inadequately controlled hypertension.

The decision is more complicated in those at intermediate risk

seconds the program gives you the estimated 10-year risk, which you divide by 10.

Classifying risk. Generally speaking:

- 1.5% per year or greater is high risk
- 0.7 to 1.4% is intermediate risk
- 0.6% per year or lower is low risk.

Most patients at high risk are good candidates for aspirin therapy, barring any contraindications. **Absolute contraindications** include:

- Renal failure
- Active peptic ulcer or gastrointestinal bleeding
- Bleeding diathesis and/or platelet disorder.

Relative contraindications include:

- Concurrent use of nonsteroidal anti-inflammatory drugs
- Inadequately controlled hypertension.

Those at low risk probably do not need aspirin therapy.

In patients at intermediate risk, the decision is less straightforward, and we need to consider other issues, eg:

- Is the patient's hypertension being adequately controlled?
- Does the patient have evidence of target-organ damage due to hypertension or diabetes?
- What is the patient's physical fitness level?
- What is the patient's risk of adverse effects from long-term aspirin therapy?
- What are the patient's personal preferences?[8,10–12]

The probability of experiencing a major coronary event is typically estimated by taking into account standard risk factors, but it may be modified by consideration of physical fitness,[12] end-organ damage related to hypertension,[1] and the presence of diabetes,[8] which is now considered a "coronary disease equivalent."

CASE 1: WHEN IS FITNESS TESTING HELPFUL?

A 55-year-old man is concerned about his risk for myocardial infarction: a number of his friends recently had premature heart attacks or underwent coronary artery bypass surgery.

Profile

- Total cholesterol level 250 mg/dL
- High-density lipoprotein (HDL) cholesterol level 60 mg/dL
- Systolic blood pressure 128 mm Hg, which is classified as "prehypertensive" in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7)
- He does not smoke
- He has never taken antihypertensive medications.

Coronary event risk

This patient's estimated 10-year risk is 8%, or 0.8% per year, which is intermediate.

The decision

As seen in the algorithm (FIGURE 1), this patient may be a candidate for aspirin therapy. Because his estimated risk is intermediate, we cannot tell him that there is definitive evidence that the benefits of aspirin exceed the risks, as the 1.5% estimate must be considered conservative.[4] On the other hand, we also cannot tell him that he would gain no benefit from aspirin therapy, as would be more likely among those patients with a risk of less than or equal to 0.6% per year.[3,4]

In this patient, other important factors to consider are his personal preferences and his level of physical fitness.[12] We recently showed that an impaired functional capacity is a strong predictor of reduced mortality associated with aspirin therapy.[12] Therefore, it may not be unreasonable to obtain an exercise treadmill test in this patient.[13]

If his functional capacity is preserved (ie, above the 20th percentile for his age and sex), we could reassure him that his risk of premature death or major cardiovascular event is quite low,[14,15] and that aspirin therapy would probably not be necessary. On the other hand, if his functional capacity is low (ie, in the lowest quintile for his age and sex), aspirin therapy might well be appropriate.[12]

It is important to recognize, though, that the use of exercise testing for risk stratification in the primary care setting is not established practice and requires further confirmation.[16]

CASE 2: DO WOMEN OBTAIN THE SAME BENEFITS AS MEN?

Women should benefit as much as men, though the data are limited

A 72-year-old woman wonders whether she should be taking aspirin, since her sister recently suffered a myocardial infarction. Until now, she has been healthy, except for hypertension, for which she takes medication.

Profile

- Systolic blood pressure 150 mm Hg
- Total cholesterol level 240 mg/dL
- HDL cholesterol level 40 mg/dL
- She does not smoke
- She is taking antihypertensive medication.

Coronary event risk

This woman's annual risk of a major coronary event is 1.5%, which is high.

The decision

This case raises an important uncertainty about the efficacy of aspirin for primary prevention of coronary events in women. Most patients enrolled in the primary prevention trials were men.[1] There are some data about the value of aspirin for primary prevention in women, but these data primarily derive from a large observational cohort.[17]

Nonetheless, given that coronary disease is the number-one cause of death in women, and given that some data are available, it seems reasonable to treat women no differently than men when considering aspirin therapy. An ongoing meta-analysis may help settle this question.

This woman's annual risk of a major coronary event is high, and aspirin therapy seems reasonable.[4] But I would also explain to her the risks of aspirin therapy and that the benefits of aspirin in women are not as established in women as in men.

Furthermore, I would make every effort to bring her blood pressure under better control: there is some evidence that the risk of intracranial hemorrhage associated with aspirin[18] may be higher when hypertension is not optimally controlled.[19] There is also evidence that aspirin therapy does not reduce the risk of myocardial infarction in patients whose hypertension is not well controlled.

CASE 3: ARE DIABETIC PATIENTS GOOD CANDIDATES?

A 64-year-old man with type 2 diabetes wonders whether he should be taking aspirin. He has no history of coronary disease.

Profile

- Systolic blood pressure 150 mm Hg
- Total cholesterol level 250 mg/dL
- HDL cholesterol level 30 mg/dL
- Triglyceride level 250 mg/dL (elevated)
- He smokes
- He is currently on drug therapy for hypertension
- He has no evidence of complications of diabetes, such as retinopathy, nephropathy, or albuminuria
- He has central abdominal obesity.

Coronary event risk

Since diabetes is a coronary disease equivalent, the risk equations do not apply to diabetic patients. However, even without doing the calculation, he is clearly at extremely high risk for premature mortality and major coronary events. Diabetes carries a mortality rate as high as that of established coronary disease.[20,21] Furthermore, he may well have the "metabolic syndrome," as he has diabetes, low HDL cholesterol, high triglycerides, hypertension, and central abdominal obesity.[8]

The decision

I would feel very comfortable prescribing aspirin in this patient, though I admit that we do not yet have definitive evidence regarding benefit.

This case raises another uncertainty about the use of aspirin for primary prevention of coronary events: its use in patients with diabetes. The coronary event risk calculator was not specifically designed for patients with diabetes. However, diabetes is currently considered a coronary artery disease equivalent.[20,21] Therefore, at least when deciding if lipid-lowering therapy is needed, we should consider patients with diabetes as already having coronary artery disease.

While there has been no randomized trial of aspirin for the primary prevention of coronary disease events in patients with diabetes, subgroup analyses from larger randomized trials suggest a benefit.[5,7,22] Furthermore, aspirin therapy has been shown to be safe in diabetes: ie, it apparently does not promote the progression of eye disease.[22]

Diabetes imparts the same risk of death as established coronary disease

WHICH ASPIRIN DOSE IS BEST FOR PRIMARY PREVENTION?

One final question worth addressing briefly is what dose of aspirin to prescribe for primary prevention.

There have been no randomized trials comparing different doses of aspirin. Based on existing trial data and our knowledge of aspirin's antiplatelet effects, current guidelines recommend low doses (75 to 100 mg).[23] Supporting this, a large meta-analysis recently showed that, among patients at high risk for vascular events (including many patients with pre-existing vascular disease), lower doses of aspirin, defined as 75 to 150 mg per day, were no less effective than higher doses.[24] On the other hand, it is not clear that lower doses necessarily reduce bleeding risk.[25]

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