

“Should I take ASA if I do not have blocked arteries?”

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The bulk of preventative measures for cardiovascular disease, such as the daily use of acetylsalicylic acid (ASA), have focused largely on controlling established modifiable cardiac risk factors (*i.e.*, hypertension, diabetes, smoking, sedentary lifestyle, weight management, and cholesterol).

The evidence clearly supports ASA therapy (or more potent blood-thinning agents) for individuals who already have blocked arteries. The protective benefit must be weighed against the possible harm of chronic ASA use (*i.e.*, gastrointestinal bleeding and hemorrhagic stroke). Large randomized, controlled trials (RCT) have been conducted to shed light on this issue.

Physicians' Health Trial

The Physicians' Health Trial, a randomized, double-blinded, placebo-controlled trial, randomized 22,071 healthy male physicians from the U.S. into four groups receiving various combinations of ASA, 325 mg every other day, beta-carotene, and placebo. A 44% reduction in heart attacks was

reported in the ASA group after an average followup time of 60.2 months.

Hypertension Optimal Treatment Study

The Hypertension Optimal Treatment (HOT) Study, a multicentre, randomized, controlled trial, looked at 18,790 hypertensive patients aged 50 to 80 with a mean cholesterol of 6.0 mmol/L (15,710 of whom were free of vascular disease at the start of the trial). Approximately half were assigned ASA, 75 mg daily. After an average followup of 3.8 years, ASA significantly reduced major cardiovascular events (defined as myocardial infarction [MI], stroke, and cardiovascular death) by 15% and heart attack by 36%, with no significant effect on stroke.

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Although there was no significant difference in fatal bleeding, with a rate of 1.3%, non-fatal bleeds were twice as common in the ASA-arm.

Overall, 1,000 patients/year need to be treated to prevent 1.6 vascular events (MI), or 1.4 non-fatal bleeds.

Finally, renal dysfunction has emerged as an important marker of future vascular disease. In HOT, a serum creatinine > 1.15 mmol/L should be considered for ASA therapy.

About the author...

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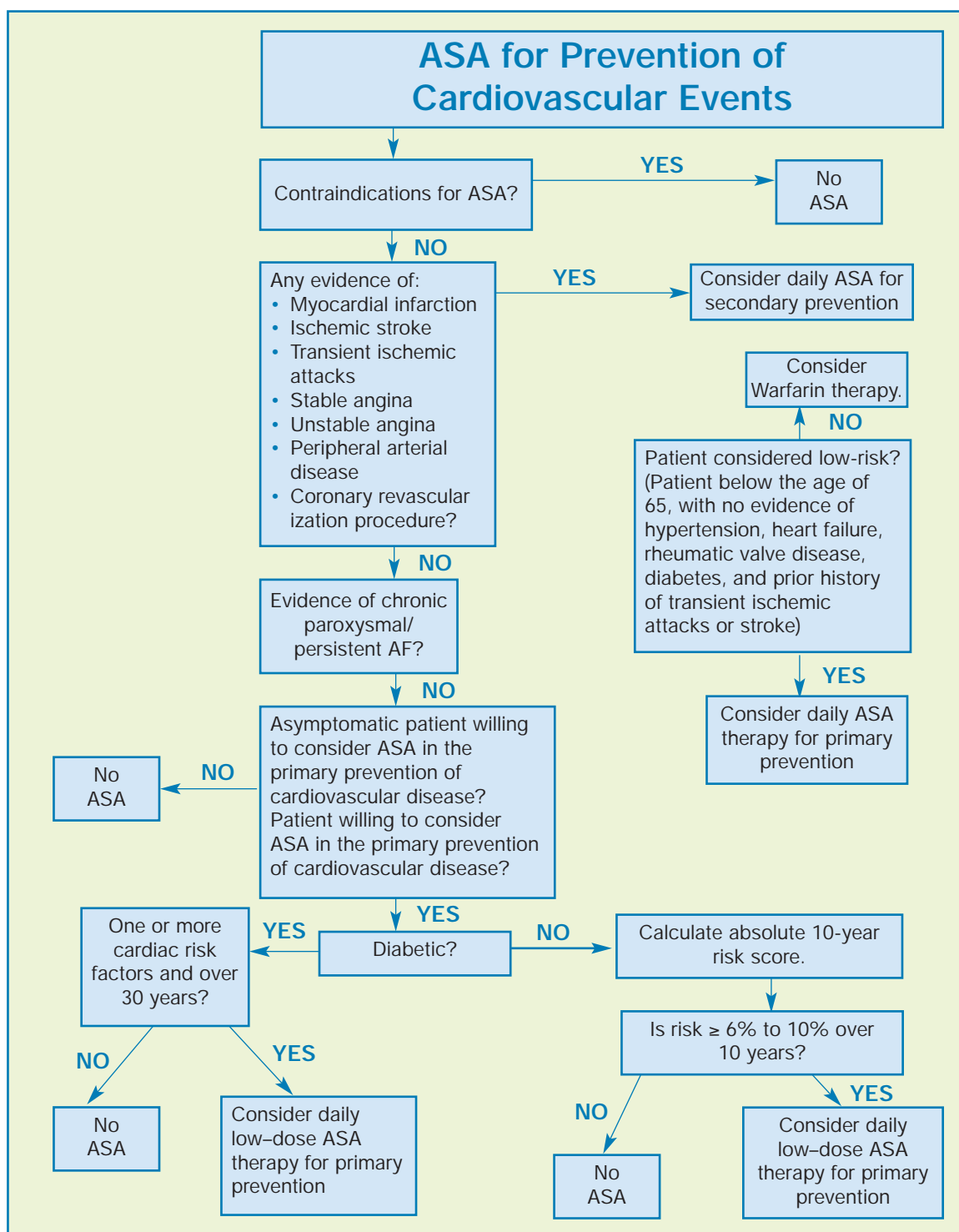


Figure 1. Suggested algorithm for the use of daily preventive ASA therapy.

Anti-Platelet Collaboration

A recent meta-analysis reported that while ASA significantly reduces the risk of coronary events by 28%, users had a non-significant trend towards an increased risk of hemorrhagic strokes and a significant increased risk of major stomach bleeding. The authors commented the net benefit of ASA increases with increasing cardiovascular risk.

The U.S. Preventive Services Task Force has updated their 2002 recommendations in response to these recent findings by stating the benefits of ASA are likely to outweigh the harm if a patient's estimated risk of heart attack over the next 10 years is at least 6%. They have also stated there is no single correct answer for all individuals and that the decision to take ASA depends on individual feelings about avoiding heart attacks, while accepting the possible complications of bleeding in the GI tract or brain.

In my practice, ASA therapy is recommended for patients at risk for heart disease (10-year risk of vascular disease > 10 %) who do not have a sensitive stomach, have controlled blood pressure, and possess little in the way of bleeding risk factors (Table 1).

What's the suggested ASA therapy?

Figure 1 outlines suggested use of daily preventive ASA therapy. The optimal dose of ASA needed to provide adequate primary cardiovascular protection appears to be 81 mg to 325 mg, which seems to be as effective as higher doses for long-term treatment.

It has been suggested that serious bleeding caused by ASA is dose-related. The American Diabetes Association has recommended low-dose ASA for patients over 30 with diabetes and one or more risk factors for cardiovascular disease.

Table 1

Risk factors for bleeding during ASA therapy

- Advanced age
- Uncontrolled hypertension
- Alcohol abuse
- Liver disease
- Kidney disease
- History of bleeding lesions (*i.e.*, peptic ulcer disease, diverticular disease, recent intracranial hemorrhage)
- Bleeding tendency (*i.e.*, abnormal platelets, coagulation defects)
- Concurrent use of drugs that increase bleeding (*i.e.*, NSAIDs, COX inhibitors)

NSAID: Non-steroidal anti-inflammatory drug

COX: Cyclooxygenase

What does the future hold?

The majority of individuals enrolled in ASA primary prevention trials are men; a RCT for women is forthcoming. The women's health study is currently comparing ASA, 100 mg every other day, versus placebo among 40,000 healthy post-menopausal women.

The introduction of clopidogrel into many treatment algorithms for vascular disease has prompted the initiation of the Clopidogrel for High Atherothrombotic Risk and Ischemic and Management and Avoidance (CHARISMA) trial. CHARISMA aims to determine whether or not the addition of clopidogrel to ASA is beneficial in preventing vascular events among patients at high risk of cardiovascular disease already taking ASA. 