

Low-Dose Aspirin for Primary Prevention of Cardiovascular Events in Japanese Patients 60 Years or Older With Atherosclerotic Risk Factors: A Randomized Clinical Trial

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FROM ABSTRACT

The objective of this study was to determine whether daily, low-dose aspirin reduces the incidence of cardiovascular events in older Japanese patients with multiple atherosclerotic risk factors.

14,464 patients aged 60 to 85 years, presenting with hypertension, dyslipidemia, or diabetes mellitus were followed up for about 5 years. They were randomized 1:1 to enteric-coated aspirin 100 mg/d or no aspirin in addition to ongoing medications. They were assessed for the incidence of death from cardiovascular causes (myocardial infarction, stroke, and other cardiovascular causes), nonfatal stroke (ischemic or hemorrhagic, including undefined cerebrovascular events), and nonfatal myocardial infarction. Secondary outcomes included TIA, angina pectoris, and arteriosclerotic disease requiring surgery or intervention.

This study was designed to assess whether primary prevention with once-daily, low-dose aspirin would reduce the combined risk of death from cardiovascular causes, nonfatal stroke, and nonfatal myocardial infarction in Japanese patients (aged ≥ 60 years) with hypertension, dyslipidemia, or diabetes mellitus.

KEY POINTS FROM THIS STUDY:

- 1) The World Health Organization estimates that annual global mortality due to cardiovascular diseases (including myocardial infarction and stroke) will approach 25 million by 2030.
- 2) "The 5-year cumulative primary outcome event rate was not significantly different between the groups."
- 3) "There was no statistically significant difference between the 2 groups in time to the primary end point—a composite of death from cardiovascular causes, nonfatal stroke, and nonfatal myocardial infarction."

- 4) In both the aspirin and no aspirin groups, 56 fatal events occurred.
- 5) Patients with an occurrence of nonfatal stroke totaled 114 in the aspirin group and 108 in the no aspirin group.
- 6) Aspirin "significantly increased the risk of extracranial hemorrhage requiring transfusion or hospitalization."
- 7) "Once-daily, low-dose aspirin did not significantly reduce the risk of the composite outcome of cardiovascular death, nonfatal stroke, and nonfatal myocardial infarction among Japanese patients 60 years or older with atherosclerotic risk factors."
- 8) In prior studies, aspirin increased major gastrointestinal and extracranial bleeding compared with controls that did not take aspirin.
- 9) The primary end point, the composite of death from cardiovascular causes, nonfatal stroke, and nonfatal myocardial infarction, were increased with these factors:
 - Being older than 70 years
 - Having diabetes mellitus
 - Smoking
 - Having hypertension
 - Being male
- 10) The primary end point, the composite of death from cardiovascular causes, nonfatal stroke, and nonfatal myocardial infarction, was ***NOT*** increased with these factors:
 - Having dyslipidemia
 - Having a BMI of 25 or higher
- 11) "The risk of a primary end point event was also not significantly lower with aspirin vs. no aspirin."
- 12) "When TIA, angina pectoris, and arteriosclerotic disease requiring surgery or intervention were added to the composite primary end point, the difference between the aspirin group and no aspirin group remained nonsignificant."

13) There were also no significant differences between the 2 study groups for time to any cause of death for aspirin vs. no aspirin:

- Death from cardiovascular disease
- Death from causes other than cardiovascular disease
- Nonfatal cerebrovascular disease (ischemic or hemorrhagic)
- Angina pectoris
- Arteriosclerotic diseases requiring surgery or intervention

14) Aspirin reduced the risk of nonfatal myocardial infarction by 28%.

15) Aspirin reduced the risk of TIA by 23%.

16) Aspirin increased the risk of extracranial hemorrhage requiring transfusion or hospitalization by 134%.

17) "Analysis of gastrointestinal adverse events of interest indicated that these events were reported in a higher proportion of patients receiving daily low-dose aspirin than in those not receiving aspirin."

18) The study was terminated early; however, even if it was not, "the clinical importance of aspirin in the primary prevention of cardiovascular events would have been less than originally assumed. Therefore, it appears that aspirin is unlikely to show a clinically important benefit in the overall population included in this study."

19) In this study, more patients treated with aspirin had nonfatal intracerebral hemorrhage or subarachnoid hemorrhage than those not receiving aspirin.

COMMENTS FROM DAN MURPHY

Often our patients ask our opinion as to the use of low-dose aspirin for the prevention of heart attacks and strokes.

This is our second Article Review questioning the use of low-dose aspirin for the prevention of heart attack and strokes. The other was **Article Review 05-13** Effect of Aspirin on Vascular and Nonvascular Outcomes; Meta-analysis of Randomized Controlled Trials; Archives of Internal Medicine; February 13, 2012; Vol. 172; No. 3; pp. 209-216.

It seems ironic that the major emphasis in reducing risks of heart attack and/or stroke are weight control, blood lipid control, and taking a daily low-dose aspirin. Yet in this study, none of these three factors made any difference in the incidence of these cardiovascular diseases.