

Aspirin Did Not Cut CV Risk in Younger Diabetics

At the same time, the data suggest that low-dose aspirin may reduce total events in older patients.

BY CAROLINE HELWICK
Contributing Writer

NEW ORLEANS — Aspirin therapy is commonly used for primary prevention of cardiovascular events in persons with type 2 diabetes, but a Japanese study of 2,539 subjects found no statistically significant reduction in the primary end point of total atherosclerotic events, except in patients aged at least 65 years.

The study, which is the largest primary prevention trial of aspirin in type 2 diabetes, was reported at the annual scientific sessions of the American Heart Association.

In the Japanese Primary Prevention of Atherosclerosis with Aspirin for Diabetes (JPAD) trial, the use of daily low-dose aspirin was associated with a 20% non-significant reduction in the risk of the combined end point of coronary, cerebrovascular, and peripheral vascular events in the population as a whole, and a 32% statistically significant reduction in events among those aged 65 and older, reported Dr. Hisao Ogawa of the Kumamoto (Japan) University.

Aspirin use also significantly reduced the composite of fatal coronary and fatal cerebrovascular events.

"Although the effect of low-dose aspirin was not statistically significant for the primary end point, a significant effect was demonstrated on fatal coronary and fatal cerebrovascular events. The trial also suggests that low-dose aspirin might reduce total events in older patients," he said at a late-breaking trials session.

The results were reported online simultaneously with Dr. Ogawa's presentation (JAMA 2008;300:2134-41).

Japanese investigators from 163 institutions examined the benefit of low-dose aspirin for preventing cardiovascular events in 2,539 patients with type 2 diabetes who had no history of atherosclerotic disease. Average age of the patients was 65 years and 55% were men.

The investigators randomly assigned 1,262 patients to receive 81-100 mg aspirin per day and 1,277 to receive no aspirin. The primary end point was the composite of all coronary, cerebrovascular, and peripheral vascular events.

After a median follow-up of 4.4 years, a total of 154 fatal and nonfatal atherosclerotic events had occurred: 68 in the aspirin group and 86 in the nonaspirin group. This represented a rate of 13.6 events 1,000 person-years, compared with 17.0 events per 1,000 person-years, for a 20% reduction in risk that was not statistically significant, Dr. Ogawa reported.

Benefit was, however, demonstrated in older patients taking aspirin. Among the 719 patients aged at least 65 in the aspirin arm, 45 events (6.3%) atherosclerotic events occurred, compared with 59 events (9.2%) in the 644 older patients in the nonaspirin group, representing a statistically significant 32% reduction in risk with aspirin use.

The combined secondary end point of fatal coronary events and fatal cerebrovascular events occurred in 1 patient (stroke) in the aspirin group and 10 patients (5 fatal myocardial infarctions and 5

fatal strokes) in the nonaspirin group, for a 90% statistically significant reduction in risk for that outcome.

Adverse effects occurred in 86 persons taking aspirin and in 14 who were not on aspirin. Hemorrhagic events were greater with aspirin (34 events, compared with 10), including an increase in gastrointestinal bleeding and the need for transfusion for severe GI bleeding in four patients, but there was no increase in hemorrhagic stroke.

"JPAD supports the safety of using low-dose aspirin in diabetics for primary prevention," he said.

The investigators cautioned that the findings should be interpreted in context of the low incidence of atherosclerotic disease in Japan and the aggressive management of cardiovascular risk factors.

"The event rate was lower than anticipated because the patients were so well treated," Dr. Ogawa said. "They saw their physicians every 2-4 weeks."

Dr. Marian Limacher, professor of medicine at the University of Florida, Gainesville, said JPAD was "a well-designed and well-conducted study" that aimed to address a question that "some may have thought did not need to be answered," given the widespread recommendation for the use of aspirin in diabetic patients.

"However, the evidence basis for this has been lacking until recently, and JPAD adds to this considerably," she commented at a press conference.

The findings are congruent with the recently completed Progression of Arterial Disease and Diabetes (POPADAD) study from Great Britain, she noted. POPADAD, involving 1,276 patients with asymptomatic peripheral arterial disease, found no evidence for aspirin's benefit on cardiovascular events and mortality.

As discussant of the paper, Dr. Limacher offered several possible explanations for the lack of effect on the study's primary end point. Among her suggestions were: the choice of population, which included a number of women who may respond differently to aspirin when compared with men; the dose, which may have been too low to be protective in some patients; a too-short duration of intervention; the effect of aspirin resistance in some patients; the use of concomitant risk factor-modifying medications; and lack of power to show an effect when event rates were so low.

"We may need to rethink the guidelines," she suggested, "especially for patients younger than 65."

"To come up with recommendations we also need to assess the risk/benefit ratio," she continued.

"Diabetes is a high-risk group for cardiovascular events, and Japanese patients are a high-risk group for the use of aspirin because of their risk of hemorrhagic stroke. Conducting this study in Japan, therefore, makes sense. ... The safety [in JPAD] was quite reasonable for low-dose aspirin," she said. ■

In 719 patients aged at least 65 in the aspirin arm, there were 45 atherosclerotic, events compared with 59 events in the 644 older patients in the nonaspirin group.

CT Angiography Shows Plaque in Patients at Low Clinical Risk

BY DIANA MAHONEY
New England Bureau

BOSTON — Direct screening for atherosclerosis using CT coronary angiography may provide a more accurate cardiovascular risk picture than do routine clinical predictors. However, the value of the imaging method in asymptomatic patients must be demonstrated in clinical trials before it can be used to modify therapy.

In a study designed to determine the prevalence of coronary atherosclerosis in patients with varying clinical predictors and to identify the limitations of traditional cardiac risk factors for predicting individual atherosclerotic burden, computed tomographic angiography (CTA) revealed evidence of calcific and noncalcific coronary atherosclerosis in a cohort of consecutive patients with low to intermediate Framingham risk scores.

This finding, together with the absence of atherosclerotic plaques in some patients with high FRS, suggests that the use of routine clinical predictors may be insufficient for identifying patients who might benefit from aggressive risk factor

modification, Dr. Benjamin Chow reported at the annual meeting of the American Society of Nuclear Cardiology.

Of 1,247 consecutive patients who underwent CTA at the University of Ottawa (Ont.) Heart Institute between February 2006 and March 2008, Dr. Chow and his coinvestigators identified 554 patients (mean age, 55 years) who did not have a history of myocardial infarction, revascularization, or diabetes mellitus, and who were not on current statin therapy. Approximately half of the patients were men, and the mean body mass index was 28.5 kg/m².

The mean pretest probability for obstructive coronary artery disease was 24.4%, he said.

Using a 17-segment model of the coronary arteries to assess for the presence of calcific or noncalcific plaque, the investigators calculated a total plaque score by summing the number of coronary segments with visible atherosclerotic plaque.

They calculated the Framingham risk scores using age, sex, total cholesterol, HDL cholesterol, smoking history, and blood pressure.

Based on the Framingham risk score, 408 of the patients were considered to have a very low (5% or less) or low (10% or less) 10-year risk for cardiac events, whereas 93 patients had an intermediate risk (11%-19%) and 53 were considered

Although the Framingham risk score was moderately predictive of plaque burden in this population, it might have underestimated the total plaque burden.

high risk (20% or greater), said Dr. Chow.

Of the patients who were found to be in the

very-low- and low-risk groups, more than half had visible evidence of atherosclerotic plaque on CTA, Dr. Chow said.

Additionally, about 9% of patients in the high-risk category had no evidence of calcific or noncalcific plaques.

"Although the mean atherosclerotic plaque burden did increase with the 10-year Framingham risk, the correlation between [the Framingham risk score] and plaque was fair," Dr. Chow reported.

The findings suggest that, although the Framingham risk score is moderately predictive of plaque burden in this patient population, "it may underestimate total plaque burden," he said.

The value of identifying subclinical coronary atherosclerosis through CT angiography has yet to be established in clinical trials, noted Dr. Chow of the University of Ottawa Heart Institute.

"Although many would argue that more aggressive risk-factor modification is warranted for patients with evidence of coronary atherosclerosis, prospective studies are needed to determine whether modifying therapy [based on imaging evidence] is appropriate."

Currently, the main suggested indication for CT angiography is for symptomatic individuals or those patients who have equivocal stress test findings, Dr. Chow noted.

CTA "is not currently indicated to screen for coronary atherosclerosis because the benefit of doing so has yet to be [proved]," he said.

Dr. Chow reported no conflicts of interest with respect to his presentation at the meeting. ■