

Benefits of Low-Dose Aspirin Alone Offset Costs

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WASHINGTON — Low-dose aspirin alone may be the most cost-effective antiplatelet therapy despite the risk of adverse gastrointestinal outcomes, according to an analysis presented at the annual Digestive Disease Week.

"In average-risk patients, aspirin alone optimized the economic balance between cardiovascular and GI outcomes," said Dr.

Martin Van Oijen of Radboud University, Nijmegen Medical Centre, the Netherlands.

Aspirin and clopidogrel, the two most commonly used antiplatelet therapies, increase the risk of GI bleeding, peptic ulcers, and dyspepsia. Concurrent use of proton pump inhibitors (PPIs) can reduce the risk of GI events, but at increased cost.

Dr. Van Oijen and his colleagues assessed the cost-effectiveness of various combinations of aspirin, clopidogrel, and PPIs. The base case for this analysis was a

60-year-old man with a 5-year MI risk of more than 3%. Six strategies were considered: aspirin alone, aspirin plus a PPI, clopidogrel alone, clopidogrel plus a PPI, aspirin in combination with clopidogrel, and the combination of aspirin, clopidogrel, and a PPI.

They derived probability estimates from a review of the literature. Costs were evaluated from the perspective of a third-party payer. Medicare reimbursement schemes and wholesale average drug

prices were used in the calculations. The primary outcome was the cost increment per quality-adjusted life year (QALY).

Aspirin alone optimized the economic balance between cardiovascular and GI outcomes. In contrast, clopidogrel-based strategies appeared to be cost ineffective.

The researchers hypothesized that the cost of PPIs would have an important effect on outcome. When the cost of a PPI became \$2.50 per tablet, the aspirin plus a PPI strategy became viable. ■

'Not Justified'

Homocysteine from page 1

B₁₂; folic acid and B₁₂; B₆ only; or placebo.

The mean baseline homocysteine level was 10.8 micromol/L. It fell by 28% in the groups receiving folate.

During a median 38 months there was a 13.7% incidence of the combined end point of all-cause mortality, unstable angina, or nonfatal stroke or MI, with no significant difference among the four treatment arms.

Discussant Dr. Salim Yusuf argued that it is too early to close the book on homocysteine lowering as preventive therapy because, despite the lack of evidence of an impact on ischemic heart disease events to date, there is a consistent, though modest, trend toward fewer strokes, with an average 14% relative risk reduction. WENBIT echoed this trend: there were 9 nonfatal strokes in patients assigned to folic acid plus vitamins B₆ and B₁₂, compared with 15 or 16 in each of the other study arms.

The stroke benefit in the studies reported thus far isn't statistically significant, but those studies were underpowered to show such an effect with the exception of the second Heart Outcomes Prevention Evaluation (HOPE-2), chaired by Dr. Yusuf.

"There was a nominally significant reduction in strokes with homocysteine lowering in HOPE-2, the only study with a significant number of stroke patients followed up longer than 3 years. When we wrote the paper we believed it was due to play of chance because we had looked at many end points, but perhaps we were wrong," added Dr. Yusuf, director of the Population Health Research Institute and professor of cardiology at McMaster University, Hamilton, Ont.

The argument that homocysteine lowering could have divergent effects in the coronary vascular and cerebrovascular trees has biologic plausibility. Within the next 1-2 years, two ongoing randomized trials are due to be completed: the Australian VITamins TO Prevent Stroke (VITATOPS) study, featuring 8,000 patients with recent stroke or transient ischemic attack, and the Oxford University-based Study of the Effectiveness of Additional Reductions In Cholesterol and Homocysteine (SEARCH) trial in more than 12,000 patients with various forms of occlusive vascular disease.

"We will have another 20,000 patients' worth of new data [and] twice as much follow-up. ... at the moment there is no reason to lower homocysteine. But it is too early to write off the hypothesis," Dr. Yusuf said.

WENBIT was funded by Norwegian nonprofit organizations. ■

Are her symptoms
more *typical*
than *atypical*?

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Although chest pain is the most common symptom of myocardial infarction among both sexes,¹ women often present with symptoms that are not typically seen in men.² Coronary heart disease can be different in women, and many challenges exist in risk stratification and decision making.^{3,4}

Myocardial perfusion imaging (MPI) can provide important risk stratification information in women.⁴ Approximately 40% of women referred for MPI are candidates for pharmacologic stress.³ For those unable to exercise adequately, Adenoscan stress provides interpretable MPI results in 98.7% of patients.⁵

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IMPORTANT SAFETY INFORMATION

Intravenous Adenoscan® (adenosine injection) is indicated as an adjunct to thallium-201 myocardial perfusion scintigraphy in patients unable to exercise adequately.

Approximately 2.6% and 0.8% of patients developed second- and third-degree AV block, respectively. All episodes of AV block have been asymptomatic, transient, and did not require intervention; less than 1% required termination of adenosine infusion.

Fatal cardiac arrest, sustained ventricular tachycardia (requiring resuscitation), and non-fatal myocardial infarction have been reported coincident with Adenoscan infusion. Patients with unstable angina may be at greater risk.

Side effects that were seen most often included flushing (44%), chest discomfort (40%), and dyspnea (28%). Side effects usually resolve quickly when infusion is terminated and generally do not interfere with test results.

Despite adenosine's short half-life, 10.6% of the side effects started several hours after the infusion terminated, and 8.4% of the side effects that began during the infusion persisted for up to 24 hours after infusion. In many cases, it is not possible to know whether these late adverse events are the result of Adenoscan infusion.

Please see brief summary of prescribing information on the next page.

1. Isaac D, et al. *Can J Cardiol*. 2001;17(suppl D):38D-48D. 2. Wenger NK. *Cardiovasc Res*. 2002;53:558-567. 3. Mieres JH, et al. *J Nucl Cardiol*. 2003;10:95-101. 4. Hachamovitch R, et al. *J Am Coll Cardiol*. 1996;28:34-44. 5. Cerqueira MD, et al. *J Am Coll Cardiol*. 1994;23:384-389.

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