

## PAD Deaths Reduced With Statins, Aspirin, Beta-Blockers

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DALLAS — Treatment with each of four drug classes—statins,  $\beta$ -blockers, aspirin, and ACE inhibitors—was associated with significant cuts in mortality in patients with peripheral artery disease during an average follow-up of 8 years, Dr. Harm H. Feringa reported at the annual scientific sessions of the American Heart Association.

“Patients with peripheral artery disease have, by definition, coronary artery disease. A patient with proven coronary artery disease should get” these drugs, commented Dr. Don Poldermans, a coinvestigator on the study and professor of medicine at Erasmus University in Rotterdam, the Netherlands. “You need to find a reason not to give these drugs to patients with peripheral artery disease,” he said.

The analysis reviewed 2,420 consecutive patients with peripheral artery disease seen at Erasmus University during 1983-2004. Their average age was 64 years, and 72% were men. The average ankle-brachial index was 0.58. At baseline, 19% of the patients were treated with a statin, 25% were treated with a  $\beta$ -blocker, 22% were on aspirin, and 26% received an ACE inhibitor.

During follow-up, 1,067 (44%) of the patients died, according to data from civil registry records. The investigators performed a multivariate analysis to determine the relative risk for all-cause

mortality associated with various clinical measures and with drug treatment.

The most powerful clinical association for death was renal failure, which increased mortality by 3.3 times. Hypercholesterolemia boosted mortality by 77%, a history of heart failure was linked with a 73% increased risk, and age of more than 70 years was linked with a 68% increased risk of death.

Treatment with a statin at baseline was linked with a 54% reduced risk of death. Treatment with a  $\beta$ -blocker was associated with a 32% reduced risk, aspirin was linked with a 28% reduced risk, and treatment with an ACE inhibitor was linked with a 20% reduced risk of death. All of these associations were statistically significant, said Dr. Feringa, an Erasmus University physician.

Treatment at baseline with a calcium channel blocker, warfarin (Coumadin), a diuretic, or a nitrate was not significantly associated with a reduced risk of death.

So far, the analysis has not looked for possible interactions between treatment with statins,  $\beta$ -blockers, aspirin, and ACE inhibitors.

During the period studied, use of all four drug classes increased. During 1983-1987, statins,  $\beta$ -blockers, aspirin, and ACE inhibitors were used by 13%, 17%, 15%, and 12% of all patients, respectively. During 2000-2004, the prescription rates for these drugs were 32%, 40%, 27%, and 30%, respectively, Dr. Feringa said. ■

## Pharmacy Service Helps PAD Patients Attain Lipid Control

BY MARK S. LESNEY  
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Patients with peripheral arterial disease often are undertreated with regard to atherosclerotic risk factor modification. Such patients can benefit from the use of a clinical pharmacy service in conjunction with physician recommendations for lipid control, according to Dr. Thomas F. Rehring and colleagues from the Kaiser Permanente Colorado Region and the University of Colorado Health Sciences Center in Denver.

In a cohort of 691 outpatients with peripheral arterial disease (PAD) validated by noninvasive arterial study, 90 patients were enrolled into a pharmacist-managed, physician-monitored algorithmic approach for the management of lipids, and 601 were given standard care, according to Dr. Rehring, of the vascular surgery department at Kaiser Permanente, and his colleagues. They presented the results of their research at the annual meeting of the Western Vascular Society in Deer Valley, Utah.

Low-density lipoprotein cholesterol (LDL-C) control goals were achieved by a significantly greater percentage of the pharmacist-managed group (79%) than the standard treatment group (54%). And a significant difference in the number of patients with LDL-C values over 130 mg/dL was noted between the treatment

(1.2%) and control (14%) groups. In the control group, nearly 52% of patients used statins, compared with 84% of the pharmacist-managed group, a statistically significant difference.

All patients in the study were members of a not-for-profit managed care system serving about 405,000 patients. Full outpatient records of medical, pharmacy, laboratory, and radiology information were stored electronically, allowing for “current and comprehensive analysis,” according to the researchers. Mean follow-up was slightly more than 17 months. Fasting lipid profiles were screened in 95% (86/90) of the patients in the algorithmic group and nearly 67% (402/601) of the standard care group.

All patients accepting enrollment in the algorithmic approach interacted regularly with a pharmacist-manager who collected data, monitored medication and laboratory compliance while making treatment plan adjustments, and kept the responsible primary care physician notified. Lipid control goals were those defined by the National Cholesterol Education Program Adult Treatment Panel III guidelines.

“Our current study demonstrates that improvements in lipid control and statin usage, and attainment of national lipid goals, are highly achievable in a PAD population that is treated in a disease management fashion,” the researchers stated. ■

**Of pharmacist-managed patients, 79% reached LDL cholesterol goals, compared with 54% in the control group.**

## CLINICAL CAPSULES

### Tooth Loss Linked to CHD

Loss of permanent teeth may raise the risk for coronary heart disease, and the risk could increase as the extent of tooth loss worsens, reported Catherine A. Okoro and her associates at the Centers for Disease Control and Prevention, Atlanta.

Epidemiologic studies have shown a link between coronary heart disease (CHD) and tooth loss due to periodontal or other oral disease, but other studies have cast doubt on this association. Ms. Okoro and her colleagues assessed tooth loss and CHD prevalence using data from a surveillance study involving 41,891 people aged 40-79 years in the general U.S. population.

The rate of CHD was 4.7% in subjects who had all their natural teeth but was 5.7% in those who were missing 1-5 teeth, 7.5% in those missing 6-31 teeth, and 8.5% in those missing all of their teeth due to tooth decay or gum disease.

In addition, patients with CHD were more likely to be missing several teeth (29.4%) or all of their teeth (23.6%) than were people who didn't have CHD (17.6% and 10.1%, respectively). Like other local infections, periodontal infections are thought to raise systemic levels of inflammatory mediators and thus promote inflammation-associated atherosclerotic processes, the investigators said (Am. J. Preventive

Med. doi:10.1016/j.amepre.2005.07.006).

This study was not designed to identify any possible causal links between tooth loss and CHD. It is possible that the findings simply indicate that people who are more health conscious have better oral health and lower CHD risk, they noted.

### Diesel Fumes Harm Vascular Function

Inhaling diesel exhaust impairs two complementary aspects of vascular function: the regulation of vascular tone and the performance of endogenous fibrinolysis.

This may be the mechanism by which air pollution exerts its well-known adverse effects on the cardiovascular system, reported Dr. Nicholas L. Mills of Edinburgh University and his associates.

Noting that transient exposure to road traffic appears to raise the risk of MI and that long-term residence near major highways increases cardiopulmonary mortality, Dr. Mills and his associates assessed the effects of diluted diesel exhaust inhalation on endothelial function in a study involving 30 healthy male nonsmokers aged 20-38 years.

Half of the subjects were randomly assigned to breathe diesel exhaust in a specially designed chamber while performing moderate exercise and resting. The other 15 subjects breathed normal room air and performed the same activities in the

chamber. In a second session 2 weeks later, all subjects were crossed over to the other group. The exhaust was produced by an idling diesel engine. Over 90% of it was shunted away, and the remainder was diluted with room air and fed into the testing chamber, the researchers said (Circulation 2005;112:3930-6).

Breathing diesel fumes was found to impair the vasomotor responses in the forearm vascular bed to both endothelium-dependent and endothelium-independent vasodilators, but it had no effect on the vasomotor response to a calcium channel antagonist. This suggests that the mechanism of vascular dysfunction involved increased consumption of nitrogen oxides, the investigators said.

### Binge Drinking Imperils MI Survivors

Binge drinking doubles short-term mortality in patients who have survived an MI, regardless of their usual level of drinking and the type of alcohol they consume, reported Dr. Kenneth J. Mukamal of Beth Israel Deaconess Medical Center, Boston, and his associates.

The researchers assessed mortality in a subset of patients who had participated in a multicenter cohort study on the causes of MI. The 1,919 patients had been interviewed about their drinking habits and other factors while they were hospitalized for an initial MI between 1989 and 1994.

A total of 318 of the patients died during a median of 3.8 years of follow-up. As expected, light and moderate drinking were found to protect against cardiovascular mortality and total mortality, as has been reported in previous studies, the investigators said (Circulation 2005;112:3839-45).

In contrast, binge drinking (consuming 3 or more drinks in 1-2 hours) was linked to a twofold increase in cardiovascular mortality and total mortality. This association held true for subjects who binged on beer, wine, liquor, or any combination of these drinks. It also persisted after the data were adjusted to account for differences in infarct size and severity; smoking status; and intake of coffee, tea, marijuana, and cocaine.

There also appeared to be a dose-response relationship, with mortality risk rising as the frequency of binge drinking episodes increased.

Binge drinking raised mortality among people who customarily were light drinkers as well as those who drank more heavily. This suggests that “any potential benefits of moderate drinking must be weighed against the risks of even occasional binge drinking,” Dr. Mukamal and associates said. “In our analyses, the apparent benefit associated with otherwise light drinking among patients with acute MI was completely eliminated by episodes of binge drinking.”

—Mary Ann Moon