LDL More Predictive Than Biomarkers

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BARCELONA — C-reactive protein was among 17 novel biomarkers of inflammation and atherosclerosis that failed to predict future cardiovascular events in statin-treated patients with established coronary heart disease, in a post hoc subanalysis of the landmark Treating to New Targets (TNT) study.

Indeed, only 1 of the 18 biomarkers assessed in the study proved predictive of major cardiovascular events: osteopontin. At baseline, when TNT participants had already been on atorvastatin (Lipitor) at 10 mg/day for 8 weeks, a low osteopontin level was associated with a significant 16% increase in the risk of cardiovascular events during the median 4.9 years of follow-up, Dr. John J.P. Kastelein reported at the annual congress of the European Society of Cardiology.

In marked contrast to the underperformance of the novel biomarkers, on-treatment levels of the traditional lipid risk factors—LDL cholesterol, HDL cholesterol, and triglycerides—were powerful predictors of major cardiovascular events. The implication is that the appropriate treatment strategy in patients with established CHD is to put them on a statin, titrate to a dose that achieves guideline-recommended lipid levels, and don't bother messing around with the novel biomarkers, which do not offer increased predictive power over the standard lipids.

"Until further evidence is available and/or guidelines recommend otherwise, clinical decisions around statin therapy might continue to focus on traditional contributors to cardiovascular risk," said Dr. Kastelein, professor of medicine and chairman of the department of vascular medicine at the Academic Medical Center of the University of Amsterdam.

In statin patients, novel biomarkers do not offer increased predictive power over the standard lipids.

DR. KASTELEIN

The post hoc nested case-control study utilized stored plasma samples from 507 TNT participants who experienced a major cardiovascular event—CHD death, nonfatal MI, fatal or nonfatal stroke, or resuscitated cardiac arrest—and 1,020 controls who did not. The biomarkers were measured in samples obtained after 8 weeks on low-dose atorvastatin during the study run-in period and again in samples gathered after 1 year of randomized treatment.

An on-treatment elevated LDL cholesterol level was associated with a 2.1-fold increased risk of major cardiovascular events. The main TNT trial as well as this analysis were sponsored by Pfizer. ■

Valsartan Cuts Cardiovascular Events by 45% in Heart Study

BARCELONA — Add-on valsartan for control of high-risk hypertension resulted in a highly significant 45% reduction in the incidence of the primary cardiovascular end point compared with non–angiotensin receptor blocker add-on therapy in the randomized Kyoto Heart Study.

The estimated number of patients who would need to be treated (NNT) with valsartan (Diovan) instead of an alternative antihypertensive drug for 3.27 years to prevent one additional adverse cardiovascular event was 21, Dr. Hiroaki Matsubara reported at the annual congress of the European Society of Cardiology.

The combined primary end point consisted of stroke, MI, angina, hospitalization for heart failure, coronary revascularization, renal failure, or peripheral artery disease. The overall 45% decrease in the valsartan group was driven chiefly by reductions of 55% in the risk of stroke and 49% for angina, noted Dr. Matsubara of Kyoto (Japan) Prefectural University School of Medicine.

The Kyoto Heart Study randomized 3,042 hypertensive Japanese subjects at high cardiovascular risk to open-label add-on valsartan or non-ARB antihypertensive therapy. High risk was defined by the presence of diabetes, ECG evidence of left ventricular hypertrophy, obesity, smoking, or a history of coronary artery disease. With add-on therapy, patients achieved identical blood pressure lowering, going from a mean baseline of 157/88 mm Hg to 133/76 mm Hg. Although the target dose for valsartan was 160 mg/day—the maximum in Japan—the average dose was 88 mg/day.

The trial was halted early, after a median 3.27 years of follow-up, for ethical reasons because the combined primary end point had been reached by 10.2% of control patients compared with 5.5% of those in the valsartan group.

There were 25 strokes in the valsartan arm, compared with 46 in controls. Moreover, the valsartan group had 22 cases of angina pectoris, as determined by a blinded end point committee on the basis of ECG evidence and confirmatory coronary angiography, compared with 44 cases in controls. The NNT to prevent one stroke was 72; the NNT to prevent one case of angina was 69.

New-onset diabetes, a prespecified secondary end point, occurred in 86 controls, compared with 58 valsartan-treated patients, a highly significant difference.

However, rates of MI, heart failure hospitalization, and all-cause mortality were not significantly different in the two treatment arms.

The Kyoto Heart Study was undertaken because of a dearth of clinical trial data on the use of ARBs in Asian patients. For example, Asians comprised less than 4% of participants in the landmark Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) and Valsartan Antihypertensive Long-Term Use Evaluation (VALUE) trials, and not a single Japanese patient was included in either of these very large studies, Dr. Matsubara noted.

Cardiovascular disease in the Japanese population differs from that in the United States and Europe. Cardiovascular mortality is one-third that in the United States; however, stroke mortality is at least 50% greater. The Japanese have a much lower average body mass index than do Americans, but their salt intake is 2.5-fold greater. While the prevalence of hypertension is comparable in Japan and the West, calcium channel blockers account for more than 60% of all antihypertensive drug prescriptions in Japan.

The Kyoto findings suggest valsartan may be considered a vascular-specific ARB. It has the greatest selectivity of any ARB for the angiotensin type-1 receptor, and it appears to be particularly useful in treating hypertensive patients who have angina or who are at risk for stroke, according to Dr. Matsubara.

The Kyoto Heart Study was funded by Kyoto Prefectural University. Dr. Matsubara reported having no financial conflicts of interest regarding their presentations. ■

High 3-Year Atherothrombotic Event Rates Seen in Registry

BARCELONA — Three-year follow-up data from the 44-nation REACH registry provide unprecedented insight into the course of atherothrombotic disease in contemporary community-based primary care medical practices around the world. And it's not a pretty picture.

Indeed, more than one-quarter of the 32,347 patients with baseline symptomatic atherothrombotic disease who were followed for 3 years experienced vascular death, nonfatal MI or stroke, or rehospitalization for a different vascular event during that time period, Dr. Mark J. Alberts reported at the annual congress of the European Society of Cardiology.

"Extrapolated across a global population, this really represents tens of millions—if not hundreds of millions—of events that are affecting these patients," said Dr. Alberts, professor of neurology and director of the stroke program at Northwestern University, Chicago.

REACH (Reduction of Atherothrombosis for Continued Health) is the largest worldwide registry of patients with all types of atherothrombotic disease. To participate in the observational registry, patients had to have stable established coronary artery disease (CAD), cerebrovascular disease, and/or peripheral artery disease (PAD), or at least three atherothrombotic risk factors. Although the overall 3-year rate of the combined end point of vascular death, nonfatal MI or stroke, or rehospitalization for a different vascular event was 28%, in patients with baseline PAD it was 40%. This was significantly greater than for patients with baseline atherothrombotic disease in other vascular beds. The PAD group had a particularly high rate of hospitalization for a vascular event other than MI, stroke, or death; hospitalizations accounted for more than three-quarters of the composite end points in the PAD group.

In the patients with monovascular, symptomatic disease at baseline, the 3-year rate of the combined end point was 26%, compared with 41% in those with baseline polyvascular disease.

'This really represents tens of millions—if not hundreds of millions—of events.'

DR. ALBERTS

Patients with PAD only at baseline were more likely than those with other forms of monovascular disease to progress to involvement of additional vascular beds during 3 years of follow-up. Indeed, nearly 10% of patients with PAD progressed to polyvascular disease, a rate Dr. Alberts called "alarming" in light of the very high vascular event rate associated with polyvascular disease. By comparison, only about 4% of patients with symptomatic monovascular CAD or cerebrovascular disease at enrollment progressed to polyvascular disease.

The high vascular event rates documented in REACH occurred despite high rates of guideline-recommended therapies. REACH is sponsored by Sanofi-Aventis, Bristol-Myers Squibb, and the Waksman Foundation for Microbiology. Dr. Alberts reported having received research grants, honoraria, and consulting fees from Sanofi-Aventis, Bristol-Myers Squibb, AstraZeneca, Genentech, Schering-Plough, and Boehringer Ingelheim. ■