Predictors of Plaque Build-Up in Lupus Identified

BY JEFF EVANS
Senior Writer

WASHINGTON — Atherosclerosis is more likely to progress in systemic lupus erythematosus patients when lupus is diagnosed at older ages or has existed for a long duration, and when high homocysteine levels are present, according to new research presented at the annual meeting of the American College of Rheumatology.

Other data at the meeting suggested the risk that women with SLE will develop carotid artery plaque may be determined by the presence of proinflammatory high-density lipoprotein (piHDL) cholesterol.

"We really don't know the rate and determinants of progression of carotid plaque in lupus," said Dr. Mary J. Roman of Cornell University, New York. She and her colleagues used serial ultrasound scans of the distal carotid artery and clinical assessments to evaluate the progression of atherosclerosis in 159 patients in the Hospital for Special Surgery's SLE registry.

After an average follow-up of 34 months, 28% of the patients had either developed first-time atherosclerotic plaque in the carotid since their baseline assessment or showed an increase in existing plaque since baseline. That is equivalent to progression of atherosclerosis in about 10% of SLE patients per year, Dr. Roman said. "We may use this observed rate of atherosclerosis progression in assessing the efficacy in future intervention trials."

Compared with patients who had progressive plaque build up, those without plaque progression were significantly younger at baseline (mean age 50 years vs. 36 years) and at diagnosis (mean 36 years vs. 21 years), as well as lower serum homocysteine levels at baseline. Patients without progression of atherosclerosis tended to have more aggressive treatment of disease than those with progression.

For each 10-year incremental increase in either age at diagnosis or disease duration, patients were about 3 times more likely to have plaque progression than no plaque or stable plaque. Progression of atherosclerosis occurred in 56% of patients in the highest tertile of baseline serum homocysteine levels (7.9 micromol/L or greater).

"Other than older age, traditional risk factors were not associated with progression of atherosclerosis," Dr. Roman noted.

In a separate presentation, Dr. Maureen McMahon of the department of rheumatology at the University of California at Los Angeles reported preliminary data from an ongoing study suggesting the development of carotid artery plaque in women with SLE is associated with the presence of piHDL.

After conducting B-mode ultrasound screening of the carotid artery and taking blood samples of women with SLE and healthy control women, Dr. McMahon and her colleagues found that 42 of 95 (44%) women with SLE had piHDL, compared with 3 of 52 (6%) age-matched control women. Significantly more SLE patients with carotid plaque had piHDL than did SLE patients without plaque (93% vs. 38%). But there was no significant difference in the presence of piHDL between control patients with and without plaque.

Oxidized low-density lipoprotein (LDL cholesterol) directly and indirectly promotes the production of inflammatory cytokines, the migration of monocytes into the subepithelial space of vessels, and the formation of macrophages that take up the oxidized LDL cholesterol and form foam cells that build an atherosclerotic plaque. Normal HDL cholesterol helps to reduce the effect of oxidized LDL cholesterol by promoting cholesterol efflux from cells and by inhibiting the oxidization of LDL cholesterol. During periods of acute inflammation, HDL cholesterol may become proinflammatory and unable to perform its usual protective function, she explained.

SLE patients with piHDL were 25 times more likely than control patients to have plaque after controlling for the traditional cardiovascular risk factors of hypertension, elevated LDL cholesterol, age, body mass index, diabetes, and high-sensitivity C-reactive protein. "Measurement of piHDL may be one tool to identify [SLE] patients at risk for the development of atherosclerosis," Dr. McMahon concluded.

The SLE patients had a mean age of about 43 years and were not selected for a history of cardiovascular disease. They were not allowed to take statins within 6 months of entry into the study. ■

Glucocorticoids Increase Artery Calcification Risk

BY NANCY WALSH
New York Bureau

WASHINGTON — Treatment with glucocorticoids was strongly associated with the presence of coronary calcification among patients with rheumatoid arthritis in a cross-sectional analysis, Dr. Jon T. Giles reported at the annual meeting of the American College of Rheumatology.

Coronary artery calcification, as measured by high-resolution computed tomography, is a quantifiable representation of coronary atherosclerotic burden and is predictive of future cardiovascular events in patients with subclinical atherosclerosis, according to Dr. Giles of Johns Hopkins University, Baltimore.

A group of 187 patients (115 women), underwent multidetector-row computed tomography of the chest with quantification of coronary artery calcification using the Agatston scoring method. The overall prevalence of calcification was 53%, and among men of all ages, it was 75% and among women, 39%.

Patients also underwent laboratory assessments including those for fasting glucose, cholesterol, triglycerides, C-reactive protein, and homocysteine. Data were collected on demographics, body composition, and medication history, and functional status was evaluated on the health assessment questionnaire (HAQ). Depression was rated on the basis of a Center for Epidemiologic Study depression score. A multivariate logistic regression analysis determined the association of individual characteristics with the presence of coronary artery calcification.

After controlling for demographic and conventional risk factors, the presence of any coronary artery calcification was significantly associated with increased levels of clinical depression (odds ratio 1.05), HAQ score (OR 1.71), and high waist:hip ratio (OR 1.21). Most notable was that when compared with no exposure, any history of glucocorticoid exposure was associated with an odds ratio of 2.98 for calcification, even after adjusting for demographic and cardiovascular risk factors, Dr. Giles wrote in a poster session.

Rheumatoid arthritis disease duration and current disease activity such as C-reactive protein were not associated with calcification, while increased education was associated with a decreased odds ratio of 0.71.

"These data would suggest that careful [use] of glucocorticoids in the clinical setting, avoidance of central obesity, and efforts to improve physical functioning and to promote psychological well-being … may be effective strategies in reducing the burden of atherosclerosis in RA patients," he concluded. ■

Functional Disability Is a Marker for Cardiovascular Mortality in Arthritis

BY NANCY WALSH
New York Bureau

WASHINGTON — Early functional disability is predictive of all-cause and cardiovascular mortality in patients with inflammatory polyarthritis, Dr. Tracey M. Farragher reported at the annual meeting of the American College of Rheumatology.

An association between early functional disability, as measured by the Health Assessment Questionnaire (HAQ), and later mortality has previously been noted. But whether the baseline HAQ score or the HAQ score at 1 year, at which time disease modifying antirheumatic drug (DMARD) therapy is likely to have been initiated, represents a more accurate predictor of mortality has not previously been investigated, according to Dr. Farragher of the University of Manchester (England).

But now, analysis of longitudinal data from the Norfolk (England) Arthritis Register has determined that HAQ score at 1 year is a stronger predictor of mortality, particularly from cardiovascular causes, than is baseline HAQ score.

The register enrolled 1,010 patients with new-onset inflammatory polyarthritis between 1990 and 1994. They were assessed at 1, 5, 7, and 10 years, with structured interviews and clinical examinations. Patients were stratified according to HAQ score as being less than 1 (none or mild disability), 1-2 (moderate disability), or greater than 2 (severe disability).

By 1 year, 40% of the patients had been treated with a DMARD, which was reflected in changes in HAQ scores: In the 590 patients in the group with the lowest HAQ scores, the median swollen and tender joint count was one at baseline and none at year 1. In the 331 in the moderate HAQ group, the median swollen and tender joint counts were 6 at baseline and 2 at year 1, and in the 89 in the severe HAQ group, these counts were 10.5 at baseline and 5 at year 1.

Mortality rates per 1,000 person-years were calculated according to HAQ scores, and information on numbers and causes of death was obtained by the Office for National Statistics. By the end of 10 years, 170 patients had died, 69 (41%) of cardiovascular causes, with the highest mortality rates in the severe HAQ group at both time points.

The increase in the all-cause mortality rate per unit increase in HAQ score was about 25% greater using the 1-year score rather than the baseline score, Dr. Farragher wrote in a poster session. The hazard ratio for all deaths at baseline was 1.32, compared with 1.61 at year 1. The corresponding numbers for cardiovascular deaths were 1.29 and 1.96.

The 1-year HAQ score is a marker of residual disease activity and, by implication, physical activity, which may account for its predictive capacity for cardiovascular disease and mortality, wrote Dr. Farragher and her colleagues (Ann. Rheum. Dis. 2006 Nov 7 [Epub doi:10.1136/ard.2006.056390]). ■

Mortality per 1,000 Patients

	HAQ Score		
	Less Than 1 (n = 590)	1-2 (n = 331)	Greater Than 2 (n = 89)
All-Cause Mortality			
Baseline	11.5	21.8	39.0
Year 1	11.9	23.2	40.7
CVD Mortality			
Baseline	5.3	9.5	17.5
Year 1	5.0	12.0	16.2

Source: Dr. Farragher

ELSEVIER GLOBAL MEDICAL NEWS