

Heart Disease in SLE Called 'Startlingly Worrying'

BY NANCY WALSH
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LONDON — The incidence of coronary heart disease among young women with systemic lupus erythematosus is “startlingly worrying,” Ian Bruce, M.D., said at the Sixth European Lupus Meeting.

Studies have shown that the annual incidence of ischemic heart disease in lupus patients is 1.3%-1.5%. In comparison, the incidence among those with newly diagnosed type 2 diabetes and among those who have had a first myocardial infarction is 2%-2.2% per annum. “This latter number may be higher, but you have to remember that these are men in their mid-to late 50s, while the lupus patients in these studies are women whose average age is 35-37,” said Dr. Bruce, of the University of Manchester (England).

The prevalence of myocardial infarction or angina in lupus cohorts ranges from 7% to 10%, depending on patient age and duration of follow-up, he said.

Moreover, as survival improves, the prevalence of the disease increases, as does the proportion of lupus patients who are older and at even greater risk for cardiovascular disease, he said.

Some epidemiologic work has suggested that the peak age of onset also is increasing and now occurs between the fifth to seventh decades. Damage accrues more quickly among patients who are older at onset, he added.

Atherosclerosis also occurs much earlier in women with lupus than in healthy women. “In women younger than 45 in the general population, you virtually do not see plaque, whereas women with lupus are beginning to acquire plaque at that early age,” Dr. Bruce said.

Classic risk factors clearly are implicat-

ed in the premature atherosclerosis and coronary heart disease seen in lupus. There is a much higher prevalence of hypertension, diabetes, and renal impairment, and lupus patients typically have other risk factors such as higher levels of LDL cholesterol and triglycerides (*Arthritis Rheum.* 2003;48:3159-67).

And these risk factors do have an impact. “In a cohort study, we stratified patients according to their total cholesterol levels and found that among those with persistently elevated cholesterol, 24% developed a cardiac event during 12 years of follow-up, compared with 3% whose cholesterol level was normal or varied only

slightly with disease flares,” Dr. Bruce said at the meeting, sponsored by the British Society for Rheumatology.

But classic risk factors do not tell the whole story. (See box.) In the general population, risk for a cardiac event increases as risk factors accumulate. “Lupus patients, however, seem to be set at an intrinsically higher baseline, and the accumulation of risk factors has an even more devastating effect,” he said.

A great need exists for properly conducted clinical trials of potential interventions for these patients. “We need to see if what we think will work actually does work and what the magnitude of risk

reduction is with a particular intervention,” he said.

Statins are an example. “Everywhere they have been used so far, they have been associated with a reduction in risk of coronary-disease events by about 30%. You could assume that also might be the case in lupus, but that could be a dangerous assumption, because these drugs might not be as well tolerated by lupus patients,” he said.

The larger scope of the disease also must be addressed. Future work must focus on the worldwide burden of atherosclerosis in lupus and consider the ethnic gradient of risk, which might reveal some interesting things about the pathogenesis, he said. ■

Classic Risk Factors Don't Tell the Whole Story

As the magnitude and severity of atherosclerosis and heart disease in systemic lupus erythematosus (SLE) become clearer, so do some possible mediators and markers. A series of posters presented at the meeting by researchers from the Karolinska Institute, Stockholm, explored various potential contributing factors:

► **LDL cholesterol.** Increased LDL-cholesterol oxidation contributes to lupus-related cardiovascular disease, reported Anna Cederholm, M.D. She compared levels of several risk and protective factors in three groups: 26 women with lupus plus cardiovascular disease, 26 women with lupus but no clinical manifestations of cardiovascular disease, and 26 normal controls. Circulating levels of oxidized LDL cholesterol were increased in both lupus groups, as was platelet-activating factor acetylhydrolase (PAF-AH). Levels of

oxidized LDL cholesterol and PAF-AH also were significantly higher in the lupus patients with cardiovascular disease than in those with lupus and no heart disease. Because PAF-AH binds to LDL cholesterol, it also may contribute to atherogenesis, Dr. Cederholm said.

► **Anti-HDL cholesterol antibodies.** SLE-related dyslipidemia showed a surprising pattern in a study of women with a history of cardiovascular disease, reported J. Su, M.D. Large, rather than small, LDL- and HDL-cholesterol particles characterized the dyslipidemia profile. This was not an expected atherogenic lipid profile, Dr. Su explained.

Antibodies against apolipoprotein A₁ in HDL cholesterol also were elevated and were associated with the presence of tumor necrosis factor. Whether these anti-apo A₁ antibodies play a pathogenic role—for example, by inhibiting the anti-inflammatory proper-

ties of HDL—is under investigation, Dr. Su said.

► **Homocysteine.** Hyperhomocysteinemia in patients with lupus correlates with markers of inflammatory activity and is a risk factor for cardiovascular disease, said Elisabet Svenungsson, M.D. In fasting blood samples obtained from a cohort of 208 patients, homocysteine levels were associated with acute phase reactants including C-reactive protein, serum amyloid A protein, fibrinogen, and complement.

Hyperhomocysteinemia also correlated with the presence of arterial disease and nephritis. “It may cause endothelial activation and damage and thus adds to the inflammatory burden that we believe renders SLE patients highly susceptible to cardiovascular disease,” she said.

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Cervical Dysplasia Common Among Patients With Lupus

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LONDON — Women with lupus face an elevated risk of having cervical dysplasia, but the underlying cause of such pathology is still unclear, Michelle T. McHenry, M.B., said at the Sixth European Lupus Meeting.

Unlike the situation for healthy women, there appeared to be no association between cervical dysplasia and other traditional risk factors, such as a history of sexually transmitted disease, in a cohort of 221 women with systemic lupus erythematosus (SLE) identified through hospital records and the Northern Ireland pathology database.

Among this entire cohort, 74 (33%) had a lifetime history of having had at least one abnormal cervical smear, Dr. McHenry reported.

Of those, 45% had had more than one abnormal smear and 26% had had a high-grade abnormality, she said.

From the entire cohort, 141 patients agreed to participate in a study that involved answering a risk factor question-

naire and providing a current cervical smear. Adequate smears were obtained from 133 patients.

Low-grade abnormalities were found on 22 (17%) of these smears, which is twice the expected incidence, according to the Northern Ireland department of health statistics. High-grade abnormalities were identified on six (5%), which is three times the expected incidence, said Dr. McHenry, a rheumatologist at Queen's University Musculoskeletal Education and Research Unit, Belfast.

The abnormality was detected after the time of diagnosis of lupus in 63% of patients.

“Patients with SLE are at increased risk of cervical cancer but the reasons why are unclear, whether it is related to having the disease itself, to having active disease, [or] to the treatments we administer, or if tra-

ditional cervical cancer risk factors have a part to play,” Dr. McHenry said.

“When we assessed these patients for traditional cervical cancer risk factors, we found they were more likely to have had more sexual partners and more children,” she said at

Other risk factors, including age at first sexual contact and history of ever having used oral contraceptives, were not associated with increased risk of cervical dysplasia. “And surprisingly, there was no association between abnormal cervical smear history and tobacco smoking,” she said. (See chart.)

Although a correlation was seen between high disease activity scores and history of cervical smear abnormality, there was no correlation with lupus damage scores or duration of disease.

Exposure to corticosteroids and immunosuppressive agents also did not differ between patients with and without abnormal cervical smear histories.

Further analyses will consider cumulative immunosuppressive doses and will compare human papillomavirus DNA findings between lupus patients and controls. ■

Risk Factors and Pap History

Risk Factor	Patients With Abnormal Cervical Smear History	Patients With Normal Cervical Smear History
Age at first sexual contact	18.8 yr	20.4 yr
History of smoking	58%	56%
<2 Sexual partners	29%	62%
Nulliparity	10%	35%
History of STD	13%	8%

Source: Dr. McHenry

the meeting, which was sponsored by the British Society for Rheumatology.

There also was an increased risk of having a cervical smear abnormality among patients who had more active disease as reflected by the Systemic Lupus Activity Measure (SLAM) score, she said.