Guidelines Spell Out Optimal Lupus Monitoring

BY SALLY KOCH KUBETIN

New guidelines issued by the European League Against Rheumatism on the monitoring of patients with systemic lupus erythematosus offer advice for clinicians and recommendations for the design of observational studies.

The document includes recommendations on 10 components of patient monitoring. An appendix to the document contains a core set of data to be collected in routine clinical practice. Having such standardized data would be a significant help to research, according to Dr. Marta Mosca of the University of Pisa (Italy) and her fellow authors. The panel included rheumatologists, internists, dermatologists, and a nephrologist. They arrived at the following recommendations after a systematic literature review and numerous consultations:

► **Patient assessment.** Every visit should include assessments of the patient's disease activity, using a validated index; quality of life, determined either by history alone or in addition to a patient-completed measure such as a 0-10 visual analog scale; and comorbidities and drug toxicity. Organ damage should be assessed yearly.

► **Cardiovascular risk factors.** Cardiovascular disease (CVD), including related factors such as smoking, vascular events, physical activity level, oral contraceptive use, hormone therapies, and family history of CVD, should be assessed at baseline and monitored at least once a year thereafter. Similarly, lupus patients also need yearly blood tests for blood cholesterol and glucose levels as well as blood pressure measurement and determination of either body mass index or waist circumference. Patients on glucocorticoids and other lupus patients at particularly high risk for CVD may require more frequent assessment.

► **Other comorbidities.** All patients with SLE should be assessed for osteoporosis risk factors, including adequate calcium and vitamin D intake, regular exercise, and smoking habit. They should be screened and followed for osteoporosis according to either of two existing sets of guidelines: those for postmenopausal women or those for patients on glucocorticoids or other medications that reduce bone mass, such as methotrexate. Cancer screening (including Pap smears) is recommended according to guidelines for the general population.

► **Infection risk.** Lupus patients should be screened for HIV, hepatitis C virus, and hepatitis B virus, especially before the start of immunosuppressive drugs; for tuberculosis, according to local guidelines and especially before the initiation of immunosuppressive drugs; and for cytomegalovirus. Lupus patients should receive inactivated vaccines for influenza and pneumococcus in accordance with guidelines for immunosuppressed patients issued by the Centers for Disease Control and Prevention. It is ideal to do the immunization when the lupus is inactive. The use of other vaccines should be considered on a case-by-case basis. To determine the exact risk for infection, lupus patients should be monitored for neutropenia, severe lymphopenia, and low IgG.

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► **Frequency of assessments.** Assessment every 6-12 months is adequate in patients with no disease activity, no organ damage, and no comorbidities. Preventive measures should be stressed during these visits. The committee found no data to suggest an optimal frequency of clinical and laboratory assessment in patients with lupus.

► **Laboratory assessment.** The committee recommended that baseline lab assessment include monitoring antinuclear antibody, anti–double-stranded DNA, anti-Ro, anti-La, anti-RNP, anti-Sm, antiphospholipid, C3, and C4. Reevaluation of antiphospholipid antibodies is necessary in previously negative patients prior to pregnancy, surgery, transplant, and estrogen-containing treatments, or in the presence of a new neurologic or vascular event. Before pregnancy, anti-Ro and anti-La antibodies also should be monitored. Remeasurement of anti-dsDNA and low levels of C3 or C4 may support evidence of disease activity or remission.

At 6- to 12-month intervals, patients with inactive disease should have the following lab tests: complete blood count, erythrocyte sedimentation rate, C-reactive protein, serum albumin, serum creatinine (or EGFR), urinalysis, and urine protein:creatinine ratio. Any patient on a specific drug treatment should have that drug monitored as well.

► **Mucocutaneous involvement.** Cutaneous manifestations include lupus erythematosus (LE)–specific lesions, including acute cutaneous LE (CLE), subacute CLE, chronic CLE, and intermittent CLE lesions, and LE-nonspecific lesions. Many conditions may mimic LE and therefore may require an evaluation by an experienced dermatologist as well as a skin biopsy for histologic analysis. Follow-up rebiopsy is recommended if there is a change in the clinical morphology of the lesions, or if there is a lack of response to treatment.

► **Kidney.** Patients with a persistently abnormal urinalysis or raised serum creatinine should have urine protein:creatinine ratio tests, urine microscopy, and renal ultrasound, and should be considered for biopsy referral. Patients with established nephropathy should have protein:creatinine ratio and immunologic tests, urine microscopy, and blood pressure evaluations at least every 3 months for the first 2-3 years. Patients with established chronic renal disease should be followed according to the National Kidney Foundation guidelines for chronic kidney disease (www.kidney.org).

► **Neuropsychiatric manifestations.** Neurologic involvement (central, peripheral, or autonomic) occurs frequently in SLE. The most frequent syndromes observed are headache, mood disorders, seizures, cognitive impairment, and cerebrovascular disease. The assessment of neurologic symptoms is difficult, and no specific instrument has been evaluated in clinical practice. Therefore, the guidelines recommend that patients should be monitored by clinical history. Cognitive impairment may be assessed by evaluating memory, attention, concentration, and word-finding difficulties (Ann. Rheum. Dis. 2009 Nov. 5 [doi:10.1136/ard.2009.117200]).

► **Eye assessment.** The incidence of retinopathy among SLE patients who are treated with antimalarial drugs is low (0.5%). Risk factors are age older than 60 years, presence of macular degeneration, retinal dystrophy, obesity, liver disease, renal insufficiency, duration of therapy longer than 5 years, daily dose of hydroxychloroquine greater than 6.5 mg/kg, or chloroquine greater than 3 mg/kg. Recommendations on screening for antimalarial retinopathy include a baseline eye assessment according to published guidelines (Ophthalmology 2002;109:1377-82).

Thereafter, in low-risk patients, no further testing is required for the next 5 years; after the first 5 years of treatment, eye assessment is recommended yearly. In high-risk patients, an eye assessment is recommended yearly. In addition, an eye assessment may be required if there are symptoms suggesting eye involvement by lupus. ■

Depression Linked to Atherosclerosis in Women With SLE

BY MITCHEL L. ZOLER

PHILADELPHIA — Patients with systemic lupus erythematosus who are also diagnosed with depression were nearly four times more likely to have subclinical atherosclerosis than were lupus patients without depression in a cross-sectional study with 161 women with lupus.

"Depression may be a component of the 'lupus factor' that increases risk for cardiovascular disease," Carol M. Greco, Ph.D., said at the annual meeting of the American College of Rheumatology. "Depressive symptoms may add to the inflammatory burden" of systemic lupus erythematosus, said Dr. Greco, a clinical psychologist at the lupus center of the University of Pittsburgh.

Finding evidence of a role for depression in causing atherosclerosis in patients with SLE is important because depression is a modifiable risk factor that can be targeted for intervention, she added. Her group's next step is to follow these interactions in a longitudinal clinical study.

To examine correlates of preclinical atherosclerosis in women with SLE, Dr. Greco and her associates studied 161 lupus patients with no history of a cardiovascular event. The women had enrolled in the HEARTS (Heart Effects on Atherosclerosis and Risk of Thrombosis in SLE) study at the University of Pittsburgh. At their baseline examination in 2001-2005, their average age was 50 years, and 88% were white. Their average waist:hip ratio (a measure of adiposity) was 0.85, 55% were hypertensive, and 36% had a history of smoking. Their average duration of SLE was 16 years, with an average SLE disease activity index of 2.0. Two-thirds of the women received steroid treatment, and among these patients the median duration on a steroid was 10 years.

The researchers assessed depression with the 20-item CES-D (Centers for Epidemiologic Study–Depression) scale. In Dr. Greco's analysis, patients who scored 16 or higher on the CES-D were diagnosed with depression, and among the 161 patients in the study 27% met this criterion. Depression may be relatively common among patients with SLE as a manifestation of central nervous system involvement of the disease, or because medications used to treat SLE may contribute to mood symptoms, she said.

The researchers diagnosed atherosclerosis by two measures: coronary artery calcium detected by electron beam CT, and carotid artery plaque visualized with ultrasound. Patients with either a coronary artery calcium Agatston score greater than zero or a carotid plaque index score of at least 1, or both, were considered to have atherosclerosis. In the study, 63% of the patients met this standard for having atherosclerosis.

In a multivariate analysis, six parameters had a significant association with atherosclerosis: age, years of education, hypertension, a waist:hip ratio of 0.868 or greater, serum level of C reactive protein, and depression.

Depression was among the strongest factors. Lupus patients with a CES-D score of 16 or higher had a significant and independent 3.85-fold greater risk for atherosclerosis, compared with patients without depression.

Depression may contribute to atherosclerosis in women with SLE by leading to sedentary behavior or poor diet, and depression is also associated with increased systemic inflammation, Dr. Greco said. ■