PsA, Others Join Diabetes as CVD Risk Factors

BY MITCHEL L. ZOLER

COPENHAGEN — Psoriatic arthritis, rheumatoid arthritis, and ankylosing spondylitis are as strong as diabetes as risk factors for cardiovascular disease, prompting a European League Against Rheumatism task force to issue the group's first consensus recommendations for managing cardiovascular risk in these patients.

"In our view, rheumatoid arthritis [RA], ankylosing spondylitis [AS], and psoriatic arthritis [PsA] should be seen as new, independent cardiovascular risk factors," Dr. Michael T. Nurmohamed said at the annual European Congress of Rheumatology. "The risk is comparable to type 2 diabetes," added Dr. Nurmohamed, of Free University Medical Center in Amsterdam.

"Cardiovascular risk management is absolutely necessary" in patients with RA, AS, or PsA, and should involve assessing and treating conventional cardiovascular disease (CVD) risk factors as well as suppressing the underlying inflammatory process by treatment with disease-modifying antirheumatic drugs (DMARDs). "Most important is to decrease the inflammatory burden as much as possible," through the use of biologic and/or synthetic DMARDs, he said in an interview. "The extent to which antirheumatic treatment decreases the risk is not known."

Just as cardiovascular disease is now the most feared outcome of diabetes, it may be time to expand the definition of the clinical impact of RA, AS, and PsA to include the extra CVD burden they trigger, Dr. Nurmohamed said.

Designation of RA, AS, and PsA as CVD risk factors by a task force of the European League Against Rheumatism (EULAR) is the first time a major medical group has singled out these conditions in this way.

The extra risk from these disorders is substantial.

When a clinician uses the European SCORE (Systemic Coronary Risk Evaluation) formula to calculate an RA patient's 10-year risk for cardiovascular disease death, the number should be increased by 50% to get the patient's actual risk when at least two of three criteria are present: disease duration more than 10 years, positivity for rheumatoid factor or anti–cyclic citrullinated peptide antibody, or extra-articular manifestations.

Dr. Nurmohamed based his recommendation on findings from an analysis done with his associates that found a greater than twofold increased risk for CVD in patients with RA, compared with people without RA. The higher level of conventional risk factors among the RA patients in the study explained roughly half of the doubled risk. The other half of the increased risk was directly attributable to RA, he said.

Similarly, a person's Framingham risk score for having a cardiovascular event should also be boosted by about 50% if RA, AS, or PsA is present, he said.

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Major evidence for the impact of rheumatoid diseases on cardiovascular risk came in data on findings—from 294 patients with RA, 194 patients with type 2 diabetes, and 258 controls, all aged 50-75 years—that Dr. Nurmohamed and his associates first reported last year.

In an analysis that controlled for age, sex, and cardiovascular risk factors, patients with RA had a 2.7-fold increased risk for cardiovascular disease events, compared with controls, and patients with type 2 diabetes had a twofold increased risk (Ann. Rheum. Dis. 2008 Aug. 12 [doi:10.1136/ard.2008.094151]).

These and other findings prompted Dr. Nurmohamed to convene an 18-member task force for EULAR that included rheumatologists, cardiologists, internists, and epidemiologists from nine European countries. The panel wrote nine evidence- and expert-opinion–based recommendations for the management of cardiovascular risk in these patients.

The key recommendation is that patients with RA, AS, or PsA should be considered at high risk for developing CVD because of both an increased prevalence of traditional CVD risk factors and their inflammatory burden.

"The increased CVD risk in patients with inflammatory arthritis is now well recognized. Everyone is aware that something should be done," he said in the interview. But the extent to which the new guidelines are already routinely followed in Europe by physicians who manage these patients is variable. In some countries, CVD risk management in patients with rheumatoid diseases is uncommon.

He acknowledged that the evidence supporting a CVD effect is stronger for RA than for AS and PsA, but added that adequate evidence exists to support including AS and PsA in the recommendations.

Dr. Nurmohamed itemized the other eight task force recommendations:

► Adequate control of rheumatoid disease activity is necessary to lower a patient's CVD risk.

► A CVD risk assessment following evidence-based EULAR guidelines is recommended annually for all RA patients, and should be considered for all patients with AS and PsA.

► CVD risk score models should be multiplied by 1.5 when an RA patient has at least two of the following three criteria: disease duration of more than 10 years, positivity for rheumatoid factor or anti–cyclic citrullinated peptide antibody, and extra-articular manifestations.

► The total cholesterol:HDL cholesterol ratio should be used in the formula for estimating CVD risk.

► Interventions with lipid-lowering drugs and with antihypertensive medications should follow national guidelines.

► Statins, ACE inhibitors, and angiotensin receptor blockers are the preferred treatment agents because of their pleiotropic effects. Therapy with 40 mg atorvastatin daily in patients with RA was shown to produce a modest but significant improvement in RA disease activity (Lancet 2004;363:2015-21).

► The role of cyclooxygenase-2 selective inhibitors (coxibs) and most NSAIDs in most CVD is not well established and needs further investigation; therefore, these agents should be prescribed with caution.

► When corticosteroids are prescribed, they should be at the lowest dose possible.

Dr. Nurmohamed reported having no financial conflicts. ■

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damage, and no comorbidities. The treating clinician should emphasize prevention at the time of these assessments, Dr. Mosca said.

► **Laboratory assessment.** According to the guidelines, baseline laboratory assessment should include testing for antinuclear antibodies (ANA), anti-phospholipid (aPL) antibodies, Complement 3 (C3) and Complement 4 (C4), as well as the following autoantibodies: anti-double stranded DNA (anti-dsDNA), anti-Ro, anti-La, and anti-ribonuclear protein (RNP).

Prior to pregnancy, previously negative patients should be re-evaluated for aPL, anti-Ro, and anti-La antibodies. Prior to surgery, transplant, or the initiation of estrogen-containing treatments, or in the presence of a new neurologic or vascular event, previously negative patients should be tested for aPL, according to Dr. Mosca.

At 6- to 12-month intervals in patients with inactive disease, "we recommend performing a complete blood cell count, erythrocyte sedimentation rate, C-reactive protein, serum albumin, serum creatinine, and urinalysis," she said. "Monitoring should be tailored to specific treatment drugs, when necessary."

► **Mucocutaneous involvement.** "Mucocutaneous lesions should be characterized, according to existing classification systems, as to whether they may be lupus-specific, lupus nonspecific, lupus mimickers, or drug related," Dr. Mosca reported. "All lesions should be assessed for activity and damage using validated indexes."

► **Kidney involvement.** Monitoring recommendations in this domain depend on kidney status.

"Patients with persistently abnormal urinalysis or creatinine should have a urine protein/creatinine ratio or 24-hour proteinuria [test], urine microscopy, renal ultrasound, and be considered for biopsy referral," Dr. Mosca said. "Patients with established nephropathy should have urine protein/creatinine ratio or 24-hour proteinuria [test], immunological studies [C3, C4, anti-dsDNA], and urine microscopy at least every 3 months for the first 2-3 years; and patients with established chronic kidney disease should be followed according to the National Kidney Foundation guidelines for chronic kidney disease."

► **Neuropsychological manifestations.** Although the rate of neurocognitive impairment in SLE is high, "monitoring neurocognitive status is difficult because there are no standardized assessment tools for this population," Dr. Mosca stated.

All SLE patients should be monitored for neuropsychological symptoms using a focused history. Additionally, "cognitive impairment may be assessed by evaluating memory, attention, concentration, and word finding difficulties; and if there is suspicion of cognitive impairment, the patient should be referred to a specialist for a more detailed assessment," she said.

► **Eye assessment.** Eye damage in patients with lupus varies from minor problems to severe retinopathy. A small percentage of lupus patients develop scleritis, retinal vasculitis, cotton wool spots at the back of the eyeball, or retinal bleeding and swelling of the optic disc.

According to the guidelines, patients on steroids or antimalarial drugs should undergo a baseline eye examination according to standard recommendations.

Annual follow-up eye exams are recommended in selected patients taking steroids and those at high risk for eye problems.

"In patients taking antimalarial drugs who are low risk for eye problems, no further testing is required until after 5 years from baseline, at which point yearly examinations are recommended," Dr. Mosca said.

In addition to facilitating good clinical practice, the recommendations for monitoring SLE are expected to "improve the quality control of care for lupus patients and to standardize the collection and comparison of data in observational studies," Dr. Mosca concluded.

The recommendations, which are expected to be published in the Annals of Rheumatic Disease later this year, were developed by an expert panel using a three-staged consensus approach comprising a discussion of relevant categories, a comprehensive literature review and level of evidence assessment, and the integration of the evidence with expert opinion, said Dr. Mosca.

She reported having no financial conflicts of interest to disclose. ■