New Criteria May Speed Dx of Spondyloarthritis

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BY MITCHEL L. ZOLER

A worldwide team of spondyloarthritis experts published a new set of criteria for classifying the axial form of the disease, an action expected to dramatically expand the number of patients identified with axial spondyloarthritis and enable physicians to flag affected patients sooner and start them on treatment.

A major hope is that earlier treatment, either with nonsteroidal anti-inflammatory drugs (NSAIDs) or tumor necrosis factor (TNF) inhibitors, will help patients by slowing progression of axial spondyloarthritis (SpA).

But this anticipated benefit has yet to be supported by study results.

The landmark step in formalizing the early identification of axial SpA was taken by a primarily Eurocentric organization, the Assessment of Spondyloarthritis International Society (ASAS). With the new ASAS classification criteria now published (Ann. Rheum. Dis. 2009; 68:770-6; 778-83), it remains unclear whether most U.S. rheumatologists and primary care physicians will buy into the criteria and apply them.

The report, published in June, showed that the new classification criteria (see box) identified people with axial SpA with a sensitivity of 83% and a specificity of 84% when tested on 649 patients. The new classification criteria were compared against identification by expert rheumatologists.

If implemented, the new criteria would "increase the frequency of diagnosing [axial SpA] by probably threefold, to as high as 1.5%" of the adult U.S. population," said Dr. John D. Reveille, professor of medicine and director of the division of rheumatology and clinical immunogenetics at the University of Texas at Houston. He based his estimate on the application of the new axial SpA criteria to a representative sample of the U.S. population collected in the National Health and Nutrition Examination Survey (NHANES).

"The new criteria will be helpful in identifying more patients with the disease, and also for recognizing the disease very early," agreed Dr. Muhammad A. Khan, professor of medicine at Case Western Reserve University in Cleveland.

"The new criteria are much better than older criteria, which require x-ray evidence of abnormalities in the sacroiliac joints. With the new criteria, you can make the diagnosis [even] when the x-ray is normal, provided you have MRI evidence," Dr. Khan said in an interview. Dr. Khan was the sole U.S.-based member of ASAS to serve on the expert panel that devised the new classification criteria.

Axial SpA has typically gone undetected until much later in the course of the disease, when it has progressed to ankylosing spondylitis with its characteristic spinal-bone changes that are visible on plain x-ray films.

"The old classification criteria required patients to have x-ray changes of sacroiliitis, which take 6-10 years to develop after patients have other symptoms," said Dr. Atul Deodhar, medical director of the rheumatology clinics at the Oregon Health and Science University in Portland.

"We definitely need new criteria; we can't call it ankylosing spondylitis if the patient doesn't have x-ray changes. The diagnosis of axial spondyloarthritis is completely new," Dr. Deodhar said in an interview. "We think that some—but not all—patients with axial spondyloarthritis will progress to ankylosing spondylitis."

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Identification of inflammation in axial joints using MRI is a key element in the new axial SpA classification. Axial joint inflammation is often hard to diagnose without MRI because the affected joints are in locations that are impossible to palpate, Dr. Deodhar said.

Early diagnosis that is made possible, at least in part, by MRI evidence of inflammation is vital for timely treatment. Without it, physicians wait to see x-ray evidence of ankylosing spondylitis.

A wait of up to 10 years "is a long period of time to deny patients access to medications that have been shown to work in this disease," Dr. Reveille commented.

"We think that if we intervene sooner, we can prevent some of the significant morbidity and disability associated with this condition," said Dr. John A. Flynn, professor of medicine at Johns Hopkins University in Baltimore.

Some rheumatologists "have been doing this [using MRI to help make an early diagnosis of axial SpA] for 5-10 years," Dr. Flynn added. "Now clinical science is catching up with that experience, saying we realize that the time from symptom onset to diagnosis has been very long" when the diagnosis relies on x-ray changes.

"If the [patient's clinical presentation] sounds good for the condition but the x-rays don't show anything, we should push to get the MRI," he said.

But Dr. Flynn and Dr. Deodhar stressed that the appearance of axial joint inflammation on MRI is not enough to make the diagnosis, as this can occur in people without axial SpA.

Other key factors include age younger than 45 years, slow onset of symptoms, reduced spine mobility, stiffness and pain that worsens with rest but improves with exercise (unlike mechanical back pain that improves with rest and worsens with exercise), and exacerbation of pain and stiffness while sleeping that takes several hours to improve on awakening.

"I'm not getting an MRI on the majority of my patients [with back pain] because the back pain that I see is usually not inflammatory; it's mechanical," Dr. Flynn said.

U.S. experts share concern about how widely the criteria will be applied by other U.S. rheumatologists and, perhaps more importantly, by U.S. primary care physicians who see the bulk of these patients initially.

"There clearly is a difference of opinion [in the United States and in Europe]," Dr. Flynn said. "I was amazed when I looked at the centers" that participated in the ASAS study that validated the new axial SpA criteria. "None were in the United States."

The validation study used patients from 25 centers in 16 countries, with 14 of the centers in Europe, 5 in Asia, 4 in Turkey, 1 in Canada, and 1 in Columbia (Ann. Rheum. Dis. 2009;68:777-83).

One possible reason why European rheumatologists have been more active in developing the new criteria is that their population contains a higher proportion of people with the HLA B27 genotype, who are most susceptible to developing axial SpA.

"The question is, Are the Europeans not only seeing more, but do they see different patients?" Dr. Flynn noted. "I think you've got to validate [the new criteria] with U.S. patients too."

"American rheumatologists are still not as well versed in spondyloarthritis as our European colleagues," Dr. Khan said.

But if the new classification criteria for SpA were followed, it would result in better patient care, Dr. Reveille said.

Treatment today for axial SpA starts with an NSAID, followed by a course with a second NSAID of a different type if the first fails.

If both NSAID regimens fail to produce satisfactory results within 3 months, current standards say the next step is treatment with a TNF inhibitor. In the United States, those include adalimumab (Humira), etanercept (Enbrel), infliximab (Remicade), and golimumab (Simponi). Although none has Food and Drug Administration approval for use in axial SpA, all four are approved for treating ankylosing spondylitis.

Ideal treatments for axial SpA don't include nonbiologic disease-modifying drugs, such as methotrexate and sulfasalazine.

No study results have yet documented that early treatment with an NSAID or with a TNF inhibitor slows or stops progression of axial SpA, but specialists are optimistic that such is the case, and that these data will eventually exist.

"We suspect early treatment might have better outcomes; there is the precedent with rheumatoid arthritis," Dr. Khan said.

In addition, even without evidence of slowed progression, early treatment "clearly improves quality of life and function and reduces time lost from work," Dr. Flynn said.

The importance of early identification and treatment of spondylitis has been recognized by the leadership of the Spondylitis Association of America (SAA).

Researchers working with SAA sponsorship developed a screening tool aimed at helping people with chronic back pain self-identify whether they have indications of an inflammatory process that needs medical evaluation.

A report on the development of the SAA screening tool for ankylosing spondylitis is scheduled to appear in the January issue of Arthritis Care and Research, and then the SAA will publicize it as an Internet-based tool, said SAA executive director Laurie Savage. ■

New Classification Criteria for SpA

Patients with back pain for at least 3 months and with an age of onset younger than 45 years are classified as having spondyloarthritis if they have sacroiliitis on imaging plus at least one spondyloarthritis feature (see below), or if they are HLA B27 positive and have at least two other spondyloarthritis features.

Sacroiliitis on imaging is defined as one of the following:

- ► Active acute inflammation on MRI highly suggestive of sacroiliitis associated with spondyloarthritis.
- ► Definite radiographic sacroiliitis, according to the modified New York criteria.

The features of spondyloarthritis include the following characteristics:

- ► Inflammatory back pain
- ► Arthritis
- ► Enthesitis
- ► Uveitis
- ► Dactylitis
- ► Psoriasis
- ► Crohn's disease/ulcerative colitis
- ► Good response to NSAIDs
- ► Family history of spondyloarthritis
- ► HLA B27 positive
- ► Elevated C-reactive protein level (in the context of chronic back pain)

Source: Ann. Rheum. Dis. 2009;68:777-83