

Entheses on US Can Predict Spondyloarthritis

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RHEUMATIC DISEASES

A power Doppler ultrasound examination may provide the most accurate early diagnosis of spondyloarthritis, with a sensitivity of 76% and a specificity of 81% upon the visualization of at least one vascularized enthesis.

The finding may be particularly valuable to rheumatologists because the existing spondyloarthritis diagnostic criteria have, at best, a limited ability to accurately identify the disease in its earliest stages, Dr. Maria Antoinette D’Agostino and her colleagues wrote.

Although the test itself is a “delicate technique,” it is within the reach of most ultrasound technicians, said Dr. D’Agostino of Versailles Saint-Quentin-en-Yveline (France) University.

The 2-year prospective cohort study comprised 118 patients with symptoms suggestive of spondyloarthritis. These included inflammatory back pain (48); arthritis or arthralgia (38); enthesitis or dactylitis (12); and HLA B27 plus acute anterior uveitis (20). Their median age was 40 years; the median disease duration at baseline was 2 years.

All patients underwent a standard

VITALS

Major Finding: One vascularized enthesis seen on ultrasound predicted SpA within 2 years with a sensitivity of 76% and a specificity of 81%. An ultrasound finding of a nonvascularized enthesis, combined with positive Amor criteria, predicted the disorder at 2 years with a sensitivity of 90% and a specificity of 77%.

Data Source: A prospective cohort study of 118 patients with symptoms suggestive of spondyloarthritis.

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clinical examination by a rheumatologist who was blinded to the diagnosis of the referring physician. All had provided a pelvic x-ray not more than 6 months old for the scoring of sacroiliitis; if the radiologic findings were equivocal or if there was persistent buttock pain, the patients underwent a pelvic CT scan.

Every patient had a power Doppler ultrasound examination of peripheral entheses by a sonographer who was blinded to the patients’ data. Areas examined included plantar fascia, Achilles tendon, patellar ligament on the patella apex, quadriceps femoris, gluteus medius tendon, and the common extensor and common flexor tendons on the lateral

and medial epicondyle of the elbow.

Important findings included any morphologic or structural abnormalities and vascularization at bony insertion points. The study evaluated three criteria: any vascularized enthesis, the number of abnormal entheses, and the global ultrasound score.

The referring physician’s diagnosis was used as the clinical standard in evaluating ultrasound’s diagnostic capability; after 2 years, the patients were reevaluated for a final diagnosis, which the investigators then compared with the original diagnosis to compute ultrasound’s diagnostic capability. At the end of the follow-up period, patients were reclassified by their referring rheumatologist (51 diagnosed with SpA, 48 not diagnosed as SpA, and 19 unclassified).

In building the prediction model, the investigators examined the ultrasound findings in light of the final diagnoses. Ultrasound found at least one abnormal enthesis in 88 (75%) of the patients; the enthesis was vascularized in 56 of these patients. At least one vascularized enthe-

sis occurred in 76% of those with an SpA diagnosis, 19% of those with a non-SpA diagnosis, and 42% of unclassified patients (Ann. Rheum. Dis. 2011;70:1433-40).

Ultrasound detected significantly more abnormal and vascularized entheses in SpA patients than in non-SpA patients. Those with a SpA diagnosis also had significantly higher ultrasound global scores than did the other groups.

Overall, two factors independently predicted a final diagnosis of SpA: Patients who had at least one vascularized enthesis on ultrasound were 12 times more likely to have a final diagnosis of SpA, and patients with an Amor criteria score of 6 or greater were nearly nine times more likely to have SpA than patients with a lower score. Further analysis confirmed that the baseline presence of at least one vascularized enthesis predicted SpA at 2 years with a 76.5% sensitivity and an 81% specificity. If there were no vascularized entheses at baseline, SpA could still be predicted with a combination of ultrasound and positive Amor criteria score, the authors said; this method yielded a sensitivity of 90% for SpA and a specificity of 77%. “Strikingly, we confirmed that vascularization of the enthesis insertion by [ultrasound] is a landmark feature for SpA, even in suspected cases,” the authors said.

Live Vaccines Live vaccines should not be given concurrently with HUMIRA [see Warnings and Precautions].

USE IN SPECIFIC POPULATIONS

Pregnancy Pregnancy Category B - There are no adequate and well-controlled studies in pregnant women. Because animal reproduction and developmental studies are not always predictive of human response, HUMIRA should be used during pregnancy only if clearly needed.

Pregnancy Registry: To monitor outcomes of pregnant women exposed to HUMIRA, a pregnancy registry has been established. Physicians are encouraged to register patients by calling 1-877-311-8972.

Nursing Mothers It is not known whether adalimumab is excreted in human milk or absorbed systemically after ingestion. Because many drugs and immunoglobulins are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from HUMIRA, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use Safety and efficacy of HUMIRA in pediatric patients for uses other than juvenile idiopathic arthritis (JIA) have not been established.

Juvenile Idiopathic Arthritis In the JIA trial, HUMIRA was shown to reduce signs and symptoms of active polyarticular JIA in patients 4 to 17 years of age. HUMIRA has not been studied in children less than 4 years of age, and there are limited data on HUMIRA treatment in children with weight <15 kg.

The safety of HUMIRA in pediatric patients in the JIA trial was generally similar to that observed in adults with certain exceptions [see Adverse Reactions].

Post-marketing cases of malignancies, some fatal, have been reported among children, adolescents, and young adults who received treatment with TNF-blockers including HUMIRA [see Warnings and Precautions].

Geriatric Use A total of 519 rheumatoid arthritis patients 65 years of age and older, including 107 patients 75 years of age and older, received HUMIRA in clinical studies RA-I through IV. No overall difference in effectiveness was observed between these subjects and younger subjects. The frequency of serious infection

and malignancy among HUMIRA treated subjects over 65 years of age was higher than for those under 65 years of age. Because there is a higher incidence of infections and malignancies in the elderly population in general, caution should be used when treating the elderly.

OVERDOSAGE

Doses up to 10 mg/kg have been administered to patients in clinical trials without evidence of dose-limiting toxicities. In case of overdosage, it is recommended that the patient be monitored for any signs or symptoms of adverse reactions or effects and appropriate symptomatic treatment instituted immediately.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility Long-term animal studies of HUMIRA have not been conducted to evaluate the carcinogenic potential or its effect on fertility. No clastogenic or mutagenic effects of HUMIRA were observed in the *in vivo* mouse micronucleus test or the *Salmonella-Escherichia coli* (Ames) assay, respectively.

PATIENT COUNSELING INFORMATION

Patients or their caregivers should be provided the HUMIRA “Medication Guide” and provided an opportunity to read it and ask questions prior to initiation of therapy. The healthcare provider should ask the patient questions to determine any risk factors for treatment. Patients developing signs and symptoms of infection should seek medical evaluation immediately.

Patient Counseling Patients should be advised of the potential benefits and risks of HUMIRA. Physicians should instruct their patients to read the Medication Guide before starting HUMIRA therapy and to reread each time the prescription is renewed.

• **Infections** Inform patients that HUMIRA may lower the ability of their immune system to fight infections. Instruct patients of the importance of contacting their doctor if they develop any symptoms of infection, including tuberculosis, invasive fungal infections, and reactivation of hepatitis B virus infections.

• **Malignancies** Patients should be counseled about the risk of malignancies while receiving HUMIRA.

• **Allergic Reactions** Patients should be advised to seek immediate medical attention if they experience any symptoms of severe allergic reactions. Advise latex-sensitive patients that the needle cap of the prefilled syringe contains latex.

• **Other Medical Conditions** Advise patients to report any signs of new or worsening medical conditions such as congestive heart failure, neurological disease, autoimmune disorders, or cytopenias. Advise patients to report any symptoms suggestive of a cytopenia such as bruising, bleeding, or persistent fever.

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