Dr. Seidman replies

To the Editor:

We are pleased to note the interest that Van Hoovels and colleagues have for our SpACE Capsule study[1], and read with interest their investigation of the clinical utility of assaying fecal calprotectin (FC) to assist in the diagnosis of spondyloarthritis (SpA)[2]. Rheumatologists traditionally proclaim that the extraarticular manifestations of SpA include inflammatory bowel disease (IBD)[3]. IBD, including Crohn disease (CD) and ulcerative colitis, are analogously associated with various extraintestinal manifestations (EIM). The most common EIM is articular involvement, reported in 16–33% of patients with IBD[4]. Thus, gastroenterologists often decree SpA as an EIM of IBD. Regardless of which side of this "chicken and egg" debate one adheres to, the unifying message is that SpA and IBD often coexist and need to be assessed, because jointly they modify management strategies[5,6].

FC is established as an excellent biomarker of intestinal inflammation[7]. Van Hoovels, *et al* investigated the value of FC in diagnosing suspected SpA. FC, in combination with imaging studies [plain radiograph and/or magnetic resonance imaging (MRI)], improved the diagnostic sensitivity of SpA[2]. In patients with both radiological and HLA-B27 testing, sensitivity and specificity were 67% and 84%, respectively. Adding FC increased the sensitivity to 74%, with specificity unchanged[2]. Based on their findings, the authors recommend endoscopic investigation of SpA patients with an elevated FC. Their observation is in keeping with our prospective SpACE Capsule study, which showed that FC was clinically useful in screening for IBD in established SpA[1]. We found that an elevated FC was associated with CD (OR 4.5, sensitivity 74%). We reported a significantly higher detection rate of CD in patients with SpA using videocapsule endoscopy (42%), compared to traditional colonoscopy (11%). No correlation was observed with the presence of GI symptoms, C-reactive protein, or IBD serology. Finding CD in patients with SpA led to a change in management in 65% of cases[1].

There are certain limitations to the Van Hoovels group's conclusions. The FC level, although elevated in the group diagnosed with SpA, was within the normal range for most patients. Moreover, there are concerns regarding the potential to overdiagnose axial spondyloarthritis (axSpA). In the Van Hoovels study, the final diagnosis of SpA was based on expert opinion[2]. Recently, Ez-Zaitonie, *et al*[8] prospectively investigated whether patients presenting with chronic back pain (CBP) of short duration and many SpA features are uniformly diagnosed with axSpA by the rheumatologist, and to what extent fulfillment of the Assessment of Spondyloarthritis international Society (ASAS) axSpA criteria is associated with an axSpA diagnosis. Data from 500 patients of the Spondyloarthritis Caught Early cohort, which includes patients with CBP (≥ 3 mos, ≤ 2 yrs, onset < 45 yrs) were analyzed. Importantly, all patients underwent a complete diagnostic examination, including MRI of the sacroiliac joints (MRI-SI) and radiographs of the sacroiliac joints (radiograph-SI). They reported[8] that of 230 patients with a positive ASAS classification, 17.4% did not have a diagnosis of axSpA. HLA-B27 positivity (OR 5.6) and any positive imaging (MRI-SI and/or radiograph-SI OR 34.3) were strong determinants of an axSpA diagnosis. That study points out that neither the presence of numerous SpA features nor fulfillment of the ASAS classification criteria automatically led to a diagnosis of axSpA. Moreover, positive imaging was considered particularly important in making a diagnosis of axSpA. In the Van Hoovels study, 80% of patients underwent imaging studies, and only 67% had both imaging and HLA testing.

A recent French nationwide study showed that rheumatologists' confidence in the diagnosis of SpA in patients with CBP had limited agreement with classification criteria[9]. The authors concluded that currently, the best way to classify SpA should be the association of at least 1 classification criterion and a diagnosis of SpA according to the rheumatologist[9].

Positive and negative predictive values (PPV and NPV) are the proportions of positive and negative results that are true positive and negative results, respectively. The PPV and NPV describe the clinical performance of a diagnostic test. However, when considering predictive values of diagnostic or screening tests, it is important to recognize the effect of the prevalence of disease in the study population. A test in a population with higher prevalence increases PPV. Conversely, increased prevalence results in decreased NPV. In the Van Hoovels study, the clinical diagnosis of SpA was reported in 52% of patients tested[2]. The clinical performance of FC to detect IBD is underscored by its very high NPV[7]. In the context of its added value to support a diagnosis of SpA, further prospective studies using rigorously classified SpA in cohorts with high and low prevalence of disease are needed. However, given their frequent coexistence, clinicians should be aware that FC testing is a useful tool for rheumatologists to screen for IBD in cases with an established diagnosis of SpA.

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