Letters to the Editor

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Re: Surgery in rheumatoid arthritis

Sir, I read with great interest the review on published studies of hand surgery in rheumatoid arthritis by Ghattas et al. [1], which gives the state of the art on the literature for this topic. In their key messages (p. 841), the authors state that medical therapy has reduced the need for surgery in rheumatoid arthritis. Unfortunately they do not provide any data or references which support this statement. Could the authors clarify this point, which might be responsible for misunderstandings between rheumatologists and orthopaedic surgeons.

The author has declared no conflicts of interest.

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Surgery in rheumatoid arthritis: reply

Sir, The correspondence by Dr Trieb raises the important issue of whether and to what extent medical therapy has reduced the need for surgery in rheumatoid arthritis (RA). Recently introduced drugs have effectively slowed down disease progression in RA patients, thus delaying the onset of disabilities and improving the overall quality of life [1, 2]. These improvements in medical treatment may explain, at least in part, the reduced need for surgery that has been reported in large cohorts of RA patients [3, 4]. It should be noted, however, that the indications for surgical treatment in the setting of RA remain uncertain and somewhat controversial [5]. It is hoped that further clinical investigation may soon provide a better assessment of the role of surgery in the clinical management of RA patients.

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Positive and negative predictive values from published studies can be misleading for decision-making in clinical practice

Sir, There are few laboratory tests which may be of help in diagnosing ankylosing spondylitis (AS) [1]. With interest we read the article by Duftner and co-workers on the presence and mean concentrations of antibodies cross-reacting with a purified 28 kDa Drosophila antigen in patients with AS, patients with other inflammatory conditions and healthy controls [2]. The authors concluded that a positive test result has a high predictive value, thus offering an additional tool for further diagnostic decision-making. Although this antibody test may in fact have some additional diagnostic value in AS and other spondylarthropathies, we strongly disagree with the conclusion that this test is of diagnostic relevance because of a high positive predictive value (PPV), as is suggested by the title, the abstract and throughout the discussion. We disagree because the PPV is highly dependent on the test setting, in particular on the prevalence of the disease (pretest probability) in the test setting, and therefore is subject to change. A high PPV in one setting can drop dramatically in another setting, although both the sensitivity and the specificity of the test do not change!

Using a cut-off level of ≥75 U/ml, the authors found 30.7% of 371 AS patients to be positive for this antibody cross-reacting with the 28 kDa antigen, whereas only 3 of 37 (8.1%) healthy controls were positive, resulting in a PPV of 97.4%. The PPV for a cut-off level of ≥60 U/ml was 95.7% (sensitivity 36.1%, specificity 83.8%).

The high PPV reported by the authors mainly resulted from the high prevalence of the disease in their study population (90.9%) who underwent the test. If instead of 37 controls, 370 healthy controls had been included, for example, the PPV for a cut-off level ≥75 U/ml would have dropped from 97.4 to 79.1%, applying the same sensitivity (30.7%) and specificity (91.9%) to the test.

The authors suggest using this test as a diagnostic tool in patients with suspected AS. If this test is being applied to all patients with chronic back pain in primary care, no more than 5% of such patients can be expected to have AS or early AS according to Underwood and Dawes [3]. If we consider that the 371 AS patients investigated by the authors constitute the 5% of patients with chronic back pain who have AS, a total of 7049 patients with non-inflammatory (mechanical) back pain would have been
tested for this antibody as well (constituting 95% of all patients with chronic back pain; total population, 7420). Assuming that for a cut-off level of ≥75 U/ml the frequency of a positive test result (8.1%) is the same in patients with non-inflammatory back pain as in healthy controls, 371 of 7049 patients with non-inflammatory back pain can be expected to be positive, whereas the percentage of AS patients with a positive test result would again be 30.7% (114 out of 371 positive). In this setting of 371 AS patients and 7049 controls (5% prevalence of AS), the PPV would be only 16.6%, and the PPV would be 10.5% if a cut-off level ≥60 U/ml had been chosen.

Such low PPVs may tell the reader that this test is not useful at all. Moreover, the resulting negative predictive values (NPV) of 96.2 and 96.1%, respectively, in this setting would suggest that in clinical practice a negative test result might be more helpful in ruling out AS than would a positive test result in ruling in AS. However, ruling out the disease by a negative test result is not appropriate either, as correctly discussed by the authors, because 64–70% of AS patients are negative for this antibody!

The authors are rather vague as to the question of which population of patients should be tested—all patients with chronic back pain or only patients with inflammatory back pain? The latter suggestion can only be found in the key messages at the end of the paper and is not discussed elsewhere in the paper. If only patients with inflammatory back pain (IBP) were tested (sensitivity and specificity of IBP in AS are both around 75%), the PPV calculated by us was 91.4% and the NPV was 30.6%. However, 93 of 371 AS patients (25%) would not have undergone testing for this antibody because around 25% of AS patients had not fulfilled criteria for IBP [1,4,5].

The examples above illustrate the heavy dependence of positive and negative predictive values on the prevalence of the disease within the population tested, i.e. on the number of subjects tested in each group (patients and controls), although the sensitivity and specificity of the test that is applied stay absolutely the same. Thus, a high PPV, such as 95%, by no means implies that this test is helpful in clinical practice. Following this line of argument, PPVs and NPVs are of highly limited value and are best avoided since they can strongly mislead the clinician reader.

Instead, the likelihood ratio (LR) is a much better description of the value of any diagnostic test [6,7]. The LR is much more robust since the LR does not depend on the number of patients or controls tested, and thus does not depend on the prevalence of the disease. Using a cut-off level of ≥75 U/ml, the antibody test cross-reacting with the 28 kDa Drosophila antigen had a positive (LR +) of 3.8, which is comparable to the diagnostic value of the presence of IBP [1,5], enthesitis of the heel, or peripheral arthritis [1,4]. The LR + of 2.2 for a positive test result using a lower cut-off level of ≥60 U/ml implies a relatively small diagnostic gain [8], which, in the case of suspected AS, is comparable to the diagnostic gain of an elevated ESR or CRP [1].

We agree with the authors that the test for antibodies cross-reacting with 28 kDa Drosophila antigen may be of additional diagnostic value in suspected AS, assuming a LR + of 3.8 if the high cut-off level of >75 U/ml is chosen. Pending results from future studies on sensitivity in early disease and on specificity, this antibody may expand the diagnostic laboratory armamentarium in early AS, which is currently limited to ESR/CRP (LR + 2.5) and HLA-B27 (LR + 9.0) [1].

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Positive and negative predictive values from published studies can be misleading for decision-making in clinical practice: reply

SIR, The letter to the editor by Rudwaleit and Sieper points out the important role of the likelihood ratio (LR) as a description of the diagnostic value of any diagnostic test in comparison to the restricted usefulness of positive and negative predictive values. The authors demonstrate in various examples the dependence of the positive and negative predictive values on the prevalence of the disease within the population tested. We totally agree with the conclusion of Rudwaleit and Sieper that highlighting the positive predictive value of specific antibodies cross-reacting with a 28 kDa Drosophila antigen in ankylosing spondylitis (AS) patients [1] may be misleading for clinical decision-making.

We also share the opinion that testing patients suspicious for AS for the presence of antibodies cross-reacting with the 28 kDa Drosophila antigen may have an additional diagnostic value. The positive LR s, provided in Table 2, were calculated to be 1.9, 2.2 and 3.8 for the cut-off levels of ≥50, ≥60 and ≥75 U/ml, respectively. Choosing a higher cut-off of ≥125 U/ml results in a further increase in the positive LR (7.3, Du et al., unpublished) but decreases the sensitivity of this test below 20%. Then the question arises whether such a gain in the positive LR, paralleled with poor sensitivity, is helpful in clinical practice. Using a cut-off of ≥75 U/ml, the positive LR of 3.8 is comparable with the diagnostic value of inflammatory back pain, enthesitis of the heel or peripheral arthritis [2], with a sensitivity of 30.7%. [1] As serological signs of inflammation measured by the ESR and CRP levels are often absent in AS patients [3] and diagnosis of AS in HLA-B27 negative patients is unacceptably delayed, [4] a positive enzyme-linked immunosorbent assay (ELISA) test result can contribute to the diagnostic evaluation of these patients, expanding the diagnostic laboratory assessments available so far.

Notably, in this study the presence of antibodies cross-reacting...