Easy assessment of axial spondyloarthritis (early ankylosing spondylitis) at the bedside

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Making a diagnosis of ankylosing spondylitis in patients with chronic back pain can be difficult at an early stage—that is, before radiographic sacroiliitis is definitely present (also referred to as axial spondyloarthritis (SpA) at the preradiographic state). We recently proposed to diagnose patients at this early stage by probability estimations[1] based on a pretest probability (p_{pre}) of 5% in patients with chronic back pain.[2] To facilitate the probability calculation in each patient, we subsequently[3] proposed the use of likelihood ratios (LR).[4] We suggested that the diagnosis could be considered definite if the post-test probability (p_{post}) is ⩾90% (LR product ⩾171), probable if the post-test probability is 80–90% (LR product 76–171) and unlikely if the post-test probability is ⩽10–20% (LR product <2–4).[1 3]

Mainly because of the complicated mathematics, we previously[3] concentrated on the use of positive likelihood ratios—that is, in case the parameter is present. However, when making a diagnosis in daily practice, a negative test result (absence of a certain parameter) sometimes helps to rule out a diagnosis. In axial SpA, a few parameters, if absent, clearly render the diagnosis less likely. These include negativity for human leucocyte antigen-B27, a negative magnetic resonance image (showing no signs of inflammation), the absence of the inflammatory type of back pain, a normal C reactive protein level or erythrocyte sedimentation rate, no good response to non-steroidal anti-inflammatory drugs and, probably, a negative family history (discussed already by Rudwaleit *et al*[1]). On the other hand, other mostly clinical parameters should not be considered to be definitely absent if not present at disease onset, as these may occur later in the disease course and therefore are rather a function of disease duration. These include peripheral arthritis, enthesitis, dactylitis, acute anterior uveitis, psoriasis and inflammatory bowel disease. These parameters are helpful in increasing the disease probability if present, but should be ignored if absent at an early disease stage.

Table 1 shows the list of LR+ values for positive test results supplemented by LR− values for negative test results. The likelihood ratio product is calculated by multiplying the relevant LR+ and LR− values as derived from table 1, according to the presence or absence of particular features as appropriate. The final post-test probability can be read from fig 1, which presents a probability curve showing the dependency of the post-test probability on the LR product, again based on a pretest probability of 5%. The curve in fig 1 has been calculated using the formula

$$p_{post} = \frac{\Pi_{LR} \times p_{pre}}{1 + (\Pi_{LR} - 1) \times p_{pre}}$$

where p_{post} is the post-test probability, Π_{LR} the product of likelihood ratios and p_{pre} the pretest probability.

Thus, taking into account all positive and negative diagnostic test results as appropriate, the disease probability of axial SpA at the preradiographic stage in a patient with chronic back pain can now be easily assessed at the bedside with the help of table 1 and fig 1.

Table 1 Representative values of sensitivity and specificity for several tests relevant for axial spondyloarthritis as evaluated previously,[1 3] along with the resulting LR+ and LR−*

Parameter	Sensitivity (%)	Specificity (%)	LR+	LR−
Inflammatory type of back pain[5 6]	75	76	3.1	0.33
Heel pain (enthesitis)	37	89	3.4	(0.71)†
Peripheral arthritis	40	90	4.0	(0.67)†
Dactylitis	18	96	4.5	(0.85)†
Iritis or anterior uveitis	22	97	7.3	(0.80)†
Psoriasis	10	96	2.5	(0.94)†
IBD	4	99	4.0	(0.97)†
Positive family history for axial SpA, reactive arthritis, psoriasis, IBD or anterior uveitis	32	95	6.4	0.72
Good response to NSAIDs	77	85	5.1	0.27
Raised acute-phase reactants (CRP/ESR)	50	80	2.5	0.63
HLA-B27‡	90	90	9.0	0.11
Sacroiliitis shown by magnetic resonance imaging	90	90	9.0	0.11

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HLA, human leucocyte antigen; IBD, inflammatory bowel disease; LR+, positive likelihood ratio; LR−, negative likelihood ratio; NSAID, non-steroidal anti-inflammatory drugs; SpA, spondyloarthritis.
*LR+ = sensitivity/(1 − specificity); LR− = (1 − sensitivity)/specificity.
†As enthesitis, dactylitis, uveitis, peripheral arthritis, psoriasis and IBD may not be present at disease onset but may develop later, it is recommended to ignore a negative test result of these tests in an early state of possible axial SpA. The LR− of parameters, which should be ignored, are shown in brackets.
‡The figures for sensitivity and specificity of HLA-B27 refer to a European Caucasian population. In European Caucasian patients with psoriasis or IBD, a sensitivity of 50%, a specificity of 90%, an LR+ of 5.0 and an LR− of 0.56 for HLA-B27 should be applied. In other ethnic populations, sensitivity and specificity of HLA-B27 may be different, resulting in different LR+ and LR− (also discussed by Rudwaleit *et al*[1]).

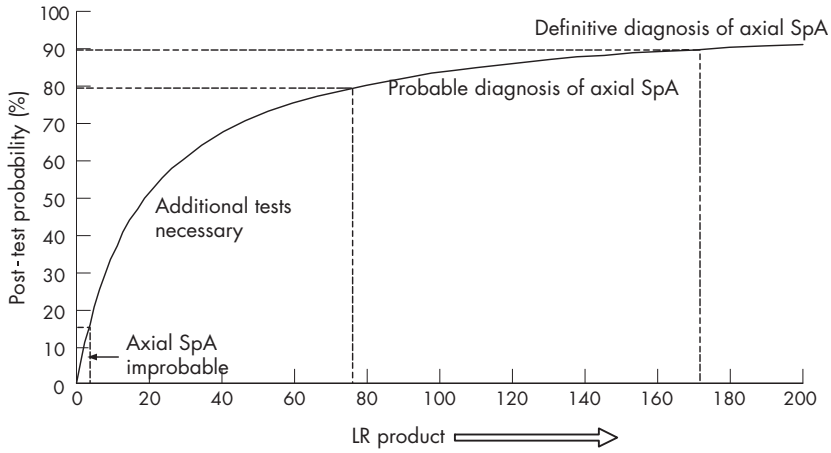

Figure 1 Dependency of the post-test probability of axial spondyloarthritis (SpA) on the resulting likelihood ratio (LR) product for an assumed pretest probability of 5% (according to Underwood and Dawes[2]). This probability curve is meant to be applied in patients with chronic back pain suspected to have axial SpA.

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Examining the exhaled levels of hydrogen peroxide in rheumatoid arthritis: a pilot study

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Previous studies have assessed airway inflammation in rheumatoid arthritis by using bronchoalveolar lavage (BAL).[1 2] To widen the scope of the study, a biomarker that is less invasive and less expensive is necessary. Recent studies have shown that exhaled breath condensate (EBC), a measure that is minimally invasive and substantially less expensive than BAL, can be used to assess inflammation in the lower respiratory tract.[3 4] To assess the utility of this measure, we compared the levels of EBC hydrogen peroxide (H_2O_2) in patients with rheumatoid arthritis with values in controls.

Patients with rheumatoid arthritis (n = 22) meeting the disease classification criteria[5] and controls (n = 23) were studied. As smoking influences EBC measures of inflammation,[6] we assessed smoking status (current smoker *v* non-smoker), excluding subjects self-reporting a diagnosis of chronic lung disease or those taking inhaled drugs indicative of such a diagnosis.

Specimens were collected by using EcoScreen (Erich Jaeger, Hoechberg, Germany), which uses a portable unit that freezes exhaled air and permits the participants to breathe normally from room air. Levels of H_2O_2 were measured by using an assay with a 0.1 μM/ml detection threshold, a measure based on the H_2O_2-dependent oxidation of homovanillic acid to a highly fluorescent dimmer.[7] Group comparisons of H_2O_2 values were carried out using analysis of variation, adjusting for age. Levels of H_2O_2 in all patients with rheumatoid arthritis were compared with those in all controls, subsequently stratifying analyses by smoking status. H_2O_2 values falling below the assay sensitivity were given the default value of 0.1 μmol/ml.

Table 1 shows the characteristics of patients with rheumatoid arthritis (n = 22) and controls (n = 23). Patients with rheumatoid arthritis had higher levels of EBC H_2O_2 (0.302 μmol/ml (standard deviation (SD) 0.202) *v* 0.202 μmol/ml (SD 0.159); p = 0.05) than controls. Differences in levels of exhaled H_2O_2 were most pronounced

Abbreviations: BAL, bronchoalveolar lavage; EBC, exhaled breath condensate; H_2O_2, hydrogen peroxide