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HOW TO CITE THIS ARTICLE
Mannoja A, Pekkola J M, Hämäläinen M T. Lumbosacral radiographic signs in patients with previous entero- or uroarthritis Ann Rheum Dis Published Online First [date of publication]*. doi: 10.1136/ard.2004.027086

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LUMBOSACRAL RADIOGRAPHIC SIGNS
IN PATIENTS WITH PREVIOUS ENTERO- OR UROARTHRITIS

(extended report)

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ABSTRACT
OBJECTIVE: To investigate if there are differences in radiological findings in lumbosacral spine radiographs between different subgroups of patients with previous reactive arthritis.

METHODS: 95 patients with previous enteroarthritis (n=53), uroarthritis (n=37) or etiologically unknown Reiter’s syndrome (n=5) were included in the study. Lumbosacral radiographs were taken 7-38 years after the initial arthritis. Three independent observers read the radiographs. Spinal changes included squaring of vertebrae, Romanus lesions, syndesmophytes and osteophytes. Sacroilitis was recorded according to the New York and Stoke methods. In addition, signs of enthesitis in the iliacal crest and disc space narrowing were recorded. Interobserver reliability and intraobserver reproducibility were determined.

RESULTS: 23% of patients had grade 2-4 sacroilitis (New York criteria) and 14% had syndesmophytes. In uroarthritis, as compared with enteroarthritis, there was more frequent sacroilitis (32% vs. 13%) and the number and occurrence of syndesmophytes were higher (mean 0.54 vs. 0.15 per patient, 24% vs. 6%, respectively). In other radiological features, no significant differences were present between the groups. In the whole material, patients with grade 2 or greater sacroilitis had significantly lesser number and occurrence of disc space narrowing. Inter- and intraobserver agreement calculated using Cohen’s kappa method varied from 0.2 to 1. CONCLUSION: In patients with previous uroarthritis, syndesmophytes and sacroilitis are more frequent, but radiological findings in lumbosacral spine radiographs are characteristically similar to those in patients with previous enteroarthritis.

KEY WORDS: SPONDYLARTHROPATHIES, REACTIVE ARTHRITIS, SPINE, SACROILIAC JOINT, and RADIOLOGY.
INTRODUCTION

Reactive arthritis (ReA) is a subgroup of spondylarthropathies other members of which are ankylosing spondylitis, arthritis associated with inflammatory bowel disease (IBD), psoriatic arthritis and undifferentiated spondylarthropathy (1). ReA was described as a sterile arthritis occurring after a primary infection remote from the joint at another site such as the gastrointestinal or urogenital tract (2). Several criteria for diagnosing ReA have been proposed, but at the moment there is no complete agreement on their use (3,4,5).

ReA can be divided classically into uroarthritis and enteroarthritis – arthritides following urogenital and enteral infection, respectively. The most common pathogens underlying enteroarthritis are Yersinia, Salmonella, Campylobacter and Shigella species (6), and for uroarthritis Chlamydia trachomatis (7).

Spondylarthropathies differ in radiological findings of the spine. In 1974, McEwen et al. (8) made a distinction in the radiological characteristics of the spine between so called Category 1 (ankylosing spondylitis and spondylarthropathy associated with IBD) and Category 2 (Reiter’s disease and psoriatic arthritis). Later on, Helliwell, Hickling and Wright (9) confirmed some but not all of these differences. The asymmetry of syndesmophytes, less severe changes and distinctive form of syndesmophytes in psoriatic arthritis compared with ankylosing spondylitis and spondylarthropathy associated with IBD were confirmed. However, the subgroup of ReA in this later study was so small that definite conclusions about ReA in relation to other subgroups could not be made. The most commonly affected segments of the spine in Reiter’s disease are the lower dorsal and upper lumbar regions (8,10).

Radiography is still the standard for diagnosing chronic sacroilitis (11). Radiological signs of spondylarthropathy (syndesmophytes and/or sacroilitis) are observed in 10-30 % of patients with previous ReA (12,13). The aim of this study was to determine whether proportions of types of syndesmophytes and characteristics of other spondylarthropathy-
related signs, such as sacroilitis, differ between uro- and enteroarthritis in lumbosacral radiographs of patients with previous definite ReA.

PATIENTS AND METHODS

Patients
The material of this study included radiographs of 95 Finnish patients with diagnosis of ReA or Reiter’s syndrome. Patients were treated at the Helsinki University Central Hospital, Department of Medicine. The acute phase of ReA or Reiter’s syndrome began in 1955-1986. A follow-up study with lumbosacral radiographs was performed in 1991-1995. The average age of the patients at the time of radiography was 48.7 (range 30-86) years. There were 60 men and 35 women in the study. The patients were grouped into one of three categories: enteroarthritis, uroarthritis or etiologically unknown Reiter’s syndrome. The enteroarthritis group (n=53) consisted of 46 patients with Yersinia, 5 with Salmonella and 2 with etiologically unknown enteritis as the triggering infection. The uroarthritis group (n=37) consisted of 13 patients with Chlamydia trachomatis, 16 with nongonococcal urethritis, 6 with gonococcal urethritis and 2 with etiologically unknown prostatitis as the triggering infection or focus. Five patients who had complete or incomplete Reiter’s syndrome but no known preceding infection formed the etiologically unknown Reiter’s syndrome group. HLA-B27 status was available for 89 patients.

All patients had a typical clinical picture of ReA. Diagnosis of Chlamydia trachomatis was based on urethral/cervix culture and/or serology by immunofluorescence, of gonococcus on urethral/cervix culture and of Yersinia and Salmonella on stool culture and/or serology.
Table 1. Characteristics of the patients

<table>
<thead>
<tr>
<th></th>
<th>Enteroarthritis</th>
<th>Uroarthritis</th>
<th>Reiter’s syndrome, etiology unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>53</td>
<td>37</td>
<td>5</td>
<td>95</td>
</tr>
<tr>
<td>Male/female</td>
<td>21/32</td>
<td>34/3</td>
<td>5/0</td>
<td>60/35</td>
</tr>
<tr>
<td>Age, mean (range), years at followup</td>
<td>49.5 (30-86)</td>
<td>47.5 (33-63)</td>
<td>48.2 (34-61)</td>
<td>48.7 (30-86)</td>
</tr>
<tr>
<td>Duration of followup, mean (range), years</td>
<td>18.4 (7-24)</td>
<td>19.2 (14-34)</td>
<td>21.1 (14-38)</td>
<td>18.9 (7-38)</td>
</tr>
<tr>
<td>Total number of arthritic attacks, median (range)*</td>
<td>1 (1-6)</td>
<td>1 (1-10)</td>
<td>2 (1-3)</td>
<td>1 (1-10)</td>
</tr>
<tr>
<td>HLA-B27+</td>
<td>40/50 (80%)</td>
<td>30/36 (83%)</td>
<td>2/3 (67%)</td>
<td>72/89 (81%)</td>
</tr>
</tbody>
</table>

* Data available for 88 patients.

For patients with negative cultures and serology, history of preceding symptomatic urological infection or gastroenteritis was applied in classifying patients into entero- or uroarthritis groups. Patients had no clinical or microbiological evidence of purulent arthritis, and exclusion of other rheumatic diseases was performed according to routine clinical practice.

The general characteristics of the groups are described in Table 1. The study is a part of the
long-term outcome study of ReA. The study protocol was approved by the Ethics Committee of the Helsinki University Central Hospital.

Methods

Conventional lumbosacral plain radiography with anteroposterior and lateral projections was used. The lumbosacral radiographs were read by three independent observers in 2002. Observers did not know the ReA subgroup and clinical features of patients. Two of the observers were radiologists (MH and JP) and one an orientated general practitioner (AM). A structured form was used in interpreting radiographs. Before reading the radiographs, observers participated in a common session where typical findings were discussed and use of the form was practised with an experienced radiologist (LL). A preliminary reading of the material of 10 patients was performed, followed by a practical session with advice on filling out the form. After first reading the entire material, radiographs of 20 randomly selected patients were read again in 2003 by the same three observers blinded to name and day of birth of patients (year of birth was available) to assess intraobserver reproducibility.

Spinal changes were assessed from Th12 to S1. Squaring of vertebrae and Romanus lesions were interpreted with regard to vertebrae, and in the case of Romanus lesions, also upper anterior and lower anterior corners of vertebrae. In later analysis, this data was converted to either the presence or the absence of these signs in a patient. Marginal and nonmarginal syndesmophytes and osteophytes were recorded with regard to every intervertebral space so that location could be anterior, right lateral, left lateral or posterior. For any given location no more than one of these three options (nonmarginal/marginal syndesmophytes and osteophytes) could be recorded. Syndesmophytes were graded from 1 to 3. Grade 1 was used when a syndesmophyte did not reach over the intervertebral border of a vertebra, grade 2 when a syndesmophyte reached over the border but was not bridging and grade 3 when there was a bridging syndesmophyte. Osteophytes were not graded. In the analysis, the grade of a syndesmophyte was determined as a rounded average of grades of the
observers. Syndesmophytes were considered as bilateral asymmetric when a difference was found in type or grade of lateral syndesmophytes at the same level. Symmetry of anterior and posterior syndesmophytes was not determined. In the analysis a radiological sign was considered to be present when at least two of the observers noticed it.

Sacroilitis was assessed using both the modified New York (NY) and Stoke methods (14,15). In case of disagreement between the three readers, a majority decision was made. In further analysis sacroilitis was grouped in two groups: a) grades 0-1 and 2-4 or b) grades 0-2 and 3-4.

Iliacal enthesitis was looked for separately on the left and right sides. Disc space narrowing was determined with regard to every intervertebral space. Inter- and intraobserver agreement on nonmarginal syndesmophytes, marginal syndesmophytes, osteophytes, disc space narrowing and iliacal enthesitis was calculated with respect to every recorded location on the spine.

Statistics

Statistical differences between the groups were calculated pairwise using the Pearson Chi-Square method (and Fisher’s Exact Test for small groups when needed) or the Mann-Whitney U–test. Interobserver reliability and intraobserver reproducibility were calculated using Cohen’s kappa method. The cut-off point for statistical significance was P<0.05. In all calculations, SPSS version 11.0 statistical software was used.

RESULTS

No significant differences in average age of patients during acute ReA, in duration of follow-up, total number of arthritic attacks or in HLA-B27 positivity were found between the uroarthritis, enteroarthritis and etiologically unknown Reiter’s syndrome groups. The proportion of male patients in the uroarthritis and etiologically unknown Reiter’s syndrome groups was significantly higher than in the enteroarthritis group.
**Table 2.** Spinal radiographic signs in the groups

<table>
<thead>
<tr>
<th></th>
<th>Entero-arthritis</th>
<th>Uro-arthritis</th>
<th>Reiter’s syndrome, etiology unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(53)</td>
<td>(37)</td>
<td></td>
<td>(95)</td>
</tr>
<tr>
<td>Squaring of vertebrae, presence (%)</td>
<td>5 (9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Romanus lesions, presence (%)</td>
<td>1 (2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Syndesmophytes, presence (%)</td>
<td>3 (6)*</td>
<td>9 (24)*</td>
<td>1 (20)</td>
<td>13 (14)</td>
</tr>
<tr>
<td>Nonmarginal/marginal, presence</td>
<td>2/1</td>
<td>7/2</td>
<td>0/1</td>
<td>9/4</td>
</tr>
<tr>
<td>Syndesmophytes, mean number per patient (range)</td>
<td>0.15*</td>
<td>0.54*</td>
<td>0.40</td>
<td>0.32</td>
</tr>
<tr>
<td>Nonmarginal/marginal syndesmophytes, number (% nonmarginal)</td>
<td>5/3</td>
<td>17/3</td>
<td>1/1</td>
<td>23/7</td>
</tr>
<tr>
<td>Anterior syndesmophytes, number (%)</td>
<td>4 (50)</td>
<td>9 (45)</td>
<td>0 (0)</td>
<td>13 (43)</td>
</tr>
<tr>
<td>Unilateral syndesmophytes, number (%)</td>
<td>3 (38)</td>
<td>7 (35)</td>
<td>1 (50)</td>
<td>11 (37)</td>
</tr>
<tr>
<td>Bilateral asymmetric syndesmophytes, number (%)</td>
<td>0 (0)</td>
<td>2 (10)</td>
<td>1 (50)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>Mean number of syndesmophytes in patients with syndesmophytes (range)</td>
<td>2.7 (2-3)</td>
<td>2.2 (1-6)</td>
<td>2 (2)</td>
<td>2.3 (1-6)</td>
</tr>
<tr>
<td>Mean grade of syndesmophytes in patients with syndesmophytes (range)</td>
<td>2.5 (1-3)</td>
<td>2.3 (1-3)</td>
<td>3.0 (3)</td>
<td>2.4 (1-3)</td>
</tr>
<tr>
<td>Osteophytes, presence (%)</td>
<td>22 (42)</td>
<td>13 (35)</td>
<td>2 (40)</td>
<td>37 (39)</td>
</tr>
<tr>
<td>Disc space narrowing, presence (%)</td>
<td>15 (28)</td>
<td>13 (35)</td>
<td>0 (0)</td>
<td>28 (29)</td>
</tr>
</tbody>
</table>

*Statistically significant difference between the groups (P<0.05).

Presence of syndesmophytes was significantly more frequent in the uroarthritis group (24%) than in the enteroarthritis group (6%, P=0.010). In the uroarthritis group, patients had significantly more syndesmophytes than in the enteroarthritis group (P=0.014).
There were no statistically significant differences in marginality/nonmarginality, location (anterior, posterior, lateral), symmetry or mean number of syndesmophytes in patients with syndesmophytes when comparing the groups (Table 2). Also the average grade of syndesmophytes was fairly similar. There were no posterior syndesmophytes.

The presence of sacroilitis grades 2-4 using NY criteria was significantly more frequent in the uroarthritis group (32%) than in the enteroarthritis group (13%, P=0.028). When using Stoke criteria, the difference was not statistically significant but was consistent with the results obtained with NY criteria. When stricter criteria for sacroilitis were used, there were no significant differences in frequency of sacroilitis grade 3-4 (Table 3). No significant differences were present in unilaterality of sacroilitis.

All the squaring of vertebrae and Romanus lesions were in the enteroarthritis group, but there were no significant differences between the groups. The frequency of iliacal enthesitis did not differ between the groups (Table 3).

The frequency and number (data not shown) of osteophytes and disc space narrowing were not significantly different between the main groups. In the whole material, patients with sacroilitis by NY or Stoke grades 2-4 or 3-4 had statistically significantly lower occurrence and number of disc space narrowing (P<0.05). The mean age of patients with sacroilitis grades 2-4 using the NY system (47.8 years, SD 7.1) was not significantly different when compared to patients without sacroilitis grades 2-4 (48.9 years, SD 9.2). Neither were there any statistically significant differences in the mean duration of follow-up between those with sacroilitis grades 2-4 (mean 19.4 years, SD 5.0) and those without sacroilitis grades 2-4 (18.6 years, SD 3.7). The analysis by dividing patients with respect to sacroilitis grades 0-2 vs. 3-4 by NY criteria or applying the Stoke criteria did not change the results (data not shown). The results of radiographic findings are described in Tables 2 and 3.
When comparing the subgroups (Yersinia, Salmonella, Chlamydia, Gonococcus, NGU, prostatitis, etiologically unknown enterocystitis and etiologically unknown Reiter’s syndrome) of the three main groups, there were no statistically significant differences with

**Table 3. Sacroilitis and iliacal enthesitis in the groups**

<table>
<thead>
<tr>
<th></th>
<th>Enteroarthritis (53)</th>
<th>Uroarthritis (37)</th>
<th>Etiologically unknown Reiter’s syndrome (5)</th>
<th>Total (95)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sacroilitis (NY) grade 2-4 (%)</td>
<td>7 (13)*</td>
<td>12 (32)*</td>
<td>3 (60)</td>
<td>22 (23)</td>
</tr>
<tr>
<td>Sacroilitis (Stoke) grade 2-4 (%)</td>
<td>8 (15)</td>
<td>11 (30)</td>
<td>3 (60)</td>
<td>22 (23)</td>
</tr>
<tr>
<td>Sacroilitis (NY) grade 3-4 (%)</td>
<td>4 (8)</td>
<td>8 (22)</td>
<td>2 (40)</td>
<td>14 (15)</td>
</tr>
<tr>
<td>Sacroilitis (Stoke) grade 3-4 (%)</td>
<td>4 (8)</td>
<td>6 (16)</td>
<td>3 (60)</td>
<td>13 (14)</td>
</tr>
<tr>
<td>Unilateral sacroilitis (NY) grade 2-4 (%)</td>
<td>1/7 (14)</td>
<td>4/12 (33)</td>
<td>0/3 (0)</td>
<td>5/22 (23)</td>
</tr>
<tr>
<td>Unilateral sacroilitis (Stoke) grade 2-4 (%)</td>
<td>3/8 (38)</td>
<td>3/11 (27)</td>
<td>0/3 (0)</td>
<td>6/22 (27)</td>
</tr>
<tr>
<td>Iliacal enthesitis (%)</td>
<td>2 (4)</td>
<td>3 (8)</td>
<td>1 (20)</td>
<td>6 (6)</td>
</tr>
</tbody>
</table>

*Statistically significant difference between the groups (P<0.05). NY = New York criteria for sacroilitis. Stoke = Stoke criteria for sacroilitis.

respect to sacroilitis, syndesmophytes, iliacal enthesitis, Romanus lesions or squaring of vertebrae (data not shown).
One of the gonococcal urethritis subgroup patients had a serological and one culture based evidence of simultaneous chlamydial infection. If other gonococcal urethritis cases were omitted from comparison between the uro- and enteroarthritis groups, statistical significance of the difference of the presence of syndesmophytes, grades 2-4 NY sacroilitis or the number of syndesmophytes did not change (data not shown).

Interobserver reliability and intraobserver reproducibility varied from 0.2 to 1 (data not shown).

**DISCUSSION**

A mean of 19 years after acute ReA, 14% of patients had syndesmophytes in the lumbosacral spine radiograph and 14-15% had grade 3-4 sacroilitis. This study supports the view that group of reactive arthritides is uniform in character of radiological findings but there are differences in frequency of certain signs between uro- and enteroarthritis groups. In patients with previous uroarthritis, syndesmophytes and sacroilitis were found to be more frequent when compared to enteroarthritis. This difference reflects a poorer prognosis and more frequent relapses of uroarthritis in this comparison and is in accordance with other studies (12,13,16,17).

Before the onset of the study, we had a hypothesis that in *Chlamydia trachomatis* - triggered arthritis and in uroarthritis nonmarginal syndesmophytes would be more common than in enteroarthritis. This was not confirmed and our result suggests that the course of entero- and uroarthritis is very similar. In patients with syndesmophytes, the average number per patient and the average grade of syndesmophytes were also similar. Osteophytes were also analysed in our study because sometimes it is hard to distinguish syndesmophytes (especially nonmarginal) and osteophytes. Distribution of number and frequency of occurrence were similar between the groups, suggesting that osteophytes did not bring a major bias factor in the study.
Assessment of agreement when interpreting enthesophytes (syndesmophytes and osteophytes) has not been common in earlier studies. In one study, interobserver and intraobserver agreement of radiologists on the presence of bridging syndemophytes on lumbar spine with regard to intervertebral spaces varied between 0.19 and 0.66 (18). Their kappa values are not directly comparable with ours (interobserver agreement 0.39-0.51 and intraobserver agreement 0.67-0.76) because of differences in methods and definitions.

Grading of sacroiliac joints is considered difficult, and kappa statistics to express intraobserver and interobserver variation has ranged from 0.07 to 1.0 and from 0.19 to 0.79, respectively (19,20,21,22,23). In the analysis of this study, the original grading was divided into a dichotomous classification, with a cut-off point between grades 1 and 2 or 2 and 3. This was done to enable us to make majority decision with regard to sacroiliac joint when disagreement existed. Only independent blind readings were taken into account and reconciliation was not used, as it has been found to introduce an additional dimension to the variation, and fails to provide a recipe for stable interpretations (21). In the determination of sacroilitis a cut-off point between grades 1 and 2 has provided good agreement (kappa 0.77 and 0.765) between radiologists when reading conventional radiographs (24,25,26).

Intraobserver agreement has been reported to be good (kappa 0.765) (25). In this study, the inter- and intraobserver agreement in sacroilitis grades 2-4 was from fair to good (0.53-0.75 and 0.52-0.75, respectively). Analysis with a cut-off point between 2 and 3 was also included because it has been considered pragmatically and statistically best choice (21). In this comparison, inter- and intraobserver agreement improved to the good-excellent range (0.70-0.80 and 0.77-0.84, respectively). Use of the Stoke method of grading did not improve inter- or intraobserver agreement, and with regard to reliability or reproducibility it cannot be seen superior to the NY grading system.

The association between grade 2-4 and grade 3-4 sacroilitis (NY or Stoke) and the absence and a lesser number of disc space narrowing in the material was an unexpected
finding. There was no significant difference in the average age of the patients and age did not seem to be a source of bias. Somehow, sacroilitis gradus 2 and greater seems to be a protective factor against disc space narrowing. This relationship may be associated with mechanical factors, such as influence of inflammatory spinal disease on posture, as well as genetic factors.

In conclusion, the lumbosacral radiographic features in patients with previous uro- or enteroarthritis are characteristically similar, but in uroarthritis there is more syndesmophytes (occurrence and number) and sacroilitis present. In the future, more sophisticated imaging methods (such as MRI) are anticipated to shed more light on this subject.
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APPENDIX

Table 4. Interobserver reliability and intraobserver reproducibility with regard to radiological sign

<table>
<thead>
<tr>
<th></th>
<th>Interobserver A B</th>
<th>Interobserver A C</th>
<th>Interobserver B C</th>
<th>Intraobserver A</th>
<th>Intraobserver B</th>
<th>Intraobserver C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syndesmophytes and osteophytes</td>
<td>0.39</td>
<td>0.42</td>
<td>0.51</td>
<td>0.67</td>
<td>0.76</td>
<td>0.76</td>
</tr>
<tr>
<td>(marginal/ nonmarginal/ osteophyte)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sacroilitis (NY) grade 2-4</td>
<td>0.75</td>
<td>0.53</td>
<td>0.55</td>
<td>0.52</td>
<td>0.75</td>
<td>0.66</td>
</tr>
<tr>
<td>Sacroilitis (Stoke) grade 2-4</td>
<td>0.76</td>
<td>0.47</td>
<td>0.48</td>
<td>0.52</td>
<td>0.76</td>
<td>0.40</td>
</tr>
<tr>
<td>Sacroilitis (NY) grade 3-4</td>
<td>0.80</td>
<td>0.74</td>
<td>0.70</td>
<td>0.84</td>
<td>0.77</td>
<td>0.77</td>
</tr>
<tr>
<td>Sacroilitis (Stoke) grade 3-4</td>
<td>0.83</td>
<td>0.66</td>
<td>0.62</td>
<td>0.84</td>
<td>0.77</td>
<td>0.68</td>
</tr>
<tr>
<td>Iliacal enthesitis</td>
<td>0.43</td>
<td>0.23</td>
<td>0.20</td>
<td>0.79</td>
<td>0.69</td>
<td>1.0</td>
</tr>
<tr>
<td>Disc space narrowing</td>
<td>0.53</td>
<td>0.38</td>
<td>0.59</td>
<td>0.64</td>
<td>0.59</td>
<td>0.86</td>
</tr>
</tbody>
</table>