High Prevalence of Symptomatic Enthesopathy of the shoulder in Ankylosing Spondylitis
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Azar Bahrami, PGY4
Introduction

AS

- HLA B27 associated chronic inflammatory disease of axial skeleton, with unknown etiology.
- Characterized by Sacroilitis and spondylitis.
- Age: 15-35 years (mean 27)
- Prevalence: 0.1%
Ankylosing Spondylitis

- Involvement of:
  - Axial skeleton
  - Appendicular skeleton
    - Peripheral joints
    - Synovial
    - Cartilaginous
    - Enthesopathy
Ankylosing Spondylitis

- Peripheral joints
  - 10-20% eventually up to 50%
- Most common:
  - Shoulder
  - Hips
- Knees, hands, wrists and feet
Enthesis: site of the attachment of tendon ligament, fascia or articular capsule to the bone.

- A complex structure that extends into the bone and bone marrow cavity.

- 4 histologic zones:
  - Collagen fibers (tendon, ligament)
  - Unmineralized fibrocartilage
  - Mineralized fibrocartilage
  - Bone
Histologic Zones

Figure 1

Photomicrograph outlines the four zones of an enthesis. 1 = tendon; 2 = unmineralized fibrocartilage; 3 = mineralized fibrocartilage; 4 = lamellar bone. (H&E × 210) [Reproduced from Resnick and Niwayama (4) with permission of the publisher]
Enthesis histologic zones
Enthesopathy

Pathological changes at the enthesis

- Inflammatory
  - SPA: AS, Psoriatic, Reiter, Undifferentiated

- Non inflammatory
  - Degenerative: OA, Rotator Cuff Syndrome, DISH

- Traumatic

- Metabolic
Enthesopathy

In different type of joints:

- Synovial articulation (shoulder, knee)
- Cartilaginous articulation (SP, MS, DV)
- Juxta-articular nonsynovial (GT, patella, calcaneus)
Enthesitis/Enthesophyte

- **Enthesitis:**
  - Edema and inflammation of enthesis, adjacent to the bone marrow.

- **Enthesophyte:**
  - Bony excrescence/ossification at the enthesis
    - Calcaneus, ulnar olecranon and patella.
Enthesophyte
Enthesitis

Sites:
- Shoulder: GT, acromion, distal clavicle
- Pelvis: Iliac crest, ischial tuberosities, femoral trochanters, SP
- Knee: Patella, tibial tuberosity
- Foot: Calcaneus
- Spine: Spinous processes, discovertebral
Histology: Enthesopathy

- Marked capillary proliferation
- Cellular infiltration
  - Fibroblasts
  - Chondrocytes
  - Plasma cells
  - Lymphocytes
    - CD8
    - T lymphocytes
Enthesopathy

- Subchondral cellular infiltrates invading the cartilage.
- Fibroblasts and activated lymphocytes.
- Calcification and bone formation.
Shoulder Anatomy
Shoulder Enthesopathy

X-Ray changes:

- Osseous erosions
- Reactive bone formation
- Bony outgrowth at enthesis
  - Bony excrescence
  - Enthesophyte
**Figure 4:** Humeral enthesopathy. Anterior radiograph of the left shoulder in a woman suffering from recurrent episodes of “shoulder periarthritis”. Erosions and reactive bone sclerosis are clearly visible at the humeral head.
Ultrasound Enthesopathy

- Periarticular soft tissue abnormalities
  - Early stage:
    - Enthesal edema and thickening
  - Late stage:
    - Subentheseal erosion
    - New bone formation (Enthesophyte)
      - As spikes of high echogenicity with a variable acoustic shadowing depending on enthesophyte bone maturity.
Shoulder Enthesopathy

Figure 2  Erosive arthropathy of the left shoulder in a patient with ankylosing spondylitis. (A and B) Oblique coronal ultrasound image through superior aspect of greater tuberosity left humerus showing subentheseal erosive changes and entheseal new bone formation consistent with involvement in a patient with an SpA.
Study

- This is the first systematic controlled evaluation by clinical exam and MRI of shoulder disorder in AS pts.

- This study demonstrates the major MRI findings in the shoulder of AS pts with shoulder pain compared with the control group of symptomatic non inflammatory arthropathy.
Study

Purpose of the study:
- Prevalence and characteristics of clinically defined shoulder disease in AS.
- Sensitivity and specificity of MRI findings in shoulder of AS pts.
Study Rationale

- Shoulder pain in AS presumed to be due to synovitis, bursitis or structural joint damage.

- No studies have systematically examined the etiology of shoulder pain in a controlled format.

Study Rationale

- Radigraphic study of peripheral non-synovial enthesopathy. (K.P. Vodouris et al, 2003)
  - Pelvic EN was the most frequent EN in both SPA and degenerative disease.
  - Humeral head EN more significant in non-inflammatory diseases.
  - Not sensitive for early stage enthesitis.
  - Not specific
  - Doesn’t show intensity
Study Rationale

- U/S of the plantar fascia (Gibbon W, et al, 1999)
  - 46% of pts with symptomatic plantar fascitis and SPA showed abnormal echogenicity within the thickened plantar fascia
  - 40% had associated retro calcaneal bursitis
  - Specificity wasn’t examined for etiology.
MRI Entheseal changes of knee synovitis in SPA. (McGonagle et al, 1997)

- Entheseal BM edema in the knee is specific for SPA.
- That allowed differentiation of people, who ultimately develop AS vs RA.
Study Rationale

MRI:

- Bone Marrow abnormalities adjacent to an enthesis.
- Fat suppression sequence technique
- Entheseal and nonenthesal BM edema and synovitis.
Patients and Methods

- **Cohort A:**
  - Retrospective chart review of 400 AS pts for prevalence of shoulder disease in AS (69.5% male, mean age 43, mean duration 18 y)

- **Cohort B:**
  - 100 pts from cohort A randomly selected for systemic clinical evaluation. Those with shoulder pain > 1 month within specific area, further evaluated by MRI.

- **Cohort C:**
  - AS pts being followed prospectively at U of Alberta, examined for the same AS specific shoulder lesions identified in cohort B pts through MRI.
Patients and Methods

- Control cohort A:
  - Consecutive pts age >18 y attending a primary care practice in Edmonton for unrelated complaints.

- Control Cohort B:
  - Computer generated list of shoulder MRI’s over the last 18 m from 4 local hospitals and clinics.
## Prevalence of shoulder disorders in AS Clinical Evaluation Cohort B (n=100)

Table 3. Prevalence of shoulder disorders in AS patients (n = 73) and primary care practice controls (n = 285) as defined by the Southampton physical exam schedule*

<table>
<thead>
<tr>
<th>Shoulder disorder</th>
<th>AS patients No. (%)</th>
<th>Controls No. (%)</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All disorders</td>
<td>18 (24.7)</td>
<td>12 (4.2)</td>
<td>8.2 (3.1–21.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>RCT</td>
<td>11 (15.1)</td>
<td>10 (3.5)</td>
<td>8.2 (2.7–25.1)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ACJ</td>
<td>5 (6.8)</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCT</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GH</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not determined</td>
<td>2</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*AS = ankylosing spondylitis; OR = odds ratio adjusted for age and sex; 95% CI = 95% confidence interval; RCT = rotator cuff tendinitis; ACJ = acromioclavicular joint disease; BCT = bicipital tendinitis; GH = glenohumeral joint disease.
### MRI evaluation

<table>
<thead>
<tr>
<th>MRI feature</th>
<th>AS patients (n = 17)</th>
<th>Controls (n = 94)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACJ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthrosis</td>
<td>16 (94.1)</td>
<td>64 (68.1)</td>
<td>94.1</td>
<td>31.9</td>
<td>0.04</td>
</tr>
<tr>
<td>Subchondral</td>
<td>11 (64.7)</td>
<td>37 (39.4)</td>
<td>64.7</td>
<td>60.6</td>
<td>0.07</td>
</tr>
<tr>
<td>BME</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GHJ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effusion</td>
<td>1 (5.9)</td>
<td>13 (13.8)</td>
<td>5.9</td>
<td>86.2</td>
<td>0.69</td>
</tr>
<tr>
<td>Synovitis</td>
<td>2 (11.8)</td>
<td>3 (3.2)</td>
<td>11.8</td>
<td>96.8</td>
<td>0.17</td>
</tr>
<tr>
<td>Arthrosis</td>
<td>2 (11.8)</td>
<td>4 (4.3)</td>
<td>11.8</td>
<td>95.7</td>
<td>0.23</td>
</tr>
<tr>
<td>Greater tuberosity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosion</td>
<td>11 (64.7)</td>
<td>13 (13.8)</td>
<td>64.7</td>
<td>86.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Erosion plus BME</td>
<td>10 (58.8)</td>
<td>8 (8.5)</td>
<td>58.8</td>
<td>91.5</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Rotator cuff</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tear</td>
<td>7 (41.2)</td>
<td>46 (48.9)</td>
<td>41.2</td>
<td>51.1</td>
<td>0.61</td>
</tr>
<tr>
<td>Tendinosis</td>
<td>12 (70.6)</td>
<td>54 (57.4)</td>
<td>70.6</td>
<td>42.6</td>
<td>0.42</td>
</tr>
<tr>
<td>Enthesal BME</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any site</td>
<td>12 (70.6)</td>
<td>18 (19.1)</td>
<td>70.6</td>
<td>80.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Intense BME</td>
<td>9 (52.9)</td>
<td>2 (2.1)</td>
<td>52.9</td>
<td>97.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>A/C BME</td>
<td>8 (47.1)</td>
<td>1 (1.1)</td>
<td>47.1</td>
<td>99.0</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*MRI = magnetic resonance imaging; AS = ankylosing spondylitis; ACJ = acromioclavicular joint; BME = bone marrow edema; GHJ = glenohumeral joint; A/C = acromial and/or clavicular.*
Results: MRI evaluation

Acromial and clavicular entheseseal BM edema at the Deltoid origin was significant in AS patients with the specificity of 99%.
Partial RCT/ deltoid enthesitis

Figure 1. Magnetic resonance image of right shoulder of 35-year-old male control subject with shoulder pain. A, Coronal turbo spin-echo T2 image. Note small partial-thickness tear of supraspinatus tendon at its insertion (black arrow). B, Coronal short tau inversion recovery image. Abnormal bright signal is seen in and around the acromioclavicular joint with bone marrow edema in the clavicle better seen on the fat suppression sequence (long white arrow). Note the subtle focus of bone marrow edema in the greater tuberosity of the humerus (short white arrows) associated with the supraspinatus tendon tear. HH = humeral head; DM = deltoid muscle; SS = supraspinatus; ACR = acromion process.
Figure 2. Magnetic resonance image of the right shoulder of a 41-year-old man with a 9-year history of ankylosing spondylitis and a 6-month history of right shoulder pain diagnosed as rotator cuff tear on clinical evaluation. A large erosion in the greater tuberosity of the humerus demonstrates loss of marrow fat and is of relatively low signal intensity on both sequences (long arrows). A, Coronal turbo spin-echo T2 image. B, Coronal short tau inversion recovery (STIR) image. Intense inflammation/edema in bone surrounding the erosion is better seen on STIR acquisition (short arrow). HH = humeral head.
Acromion at deltoid origin

Figure 3. Magnetic resonance image of the right shoulder of a 49-year-old man with a 21-year history of ankylosing spondylitis and bilateral shoulder pain of 1 year’s duration. Sagittal short tau inversion recovery image at the level of the acromion process. Intense bright signal in bone marrow is present along the superior edge and in the posterior aspect of the acromion process at the origins of the deltoid muscle (arrows). Other images confirmed that this bone marrow abnormality was clearly separated from the acromioclavicular joint. ANT = anterior; POST = posterior; HH = humeral head; DM = deltoid muscle.

Figure 5. Magnetic resonance image of the right shoulder of the same patient as in Figure 3. Coronal short tau inversion recovery image. Increased signal intensity in the greater tuberosity of the humerus is typical of edema/inflammation at insertion of supraspinatus tendon (arrow).
Figure 4. Magnetic resonance image of the right shoulder of a 31-year-old woman with a 9-year history of ankylosing spondylitis and right shoulder pain of 2 year’s duration. Sagittal short tau inversion recovery image at the level of the acromion process. Abnormal bright signal is present in the posterior aspect of the acromion process at the deltoid attachment (arrow) and focally within adjacent soft tissue. ANT = anterior; POST = posterior; HH = humeral head; DM = deltoid muscle.

Figure 6. Magnetic resonance image of the right shoulder of a 48-year-old man with an 18-year history of ankylosing spondylitis and bilateral shoulder pain of 1 year’s duration. Sagittal short tau inversion recovery image at the level of the acromion process. Intense inflammation in the posterior aspect of the acromion process is associated with marked increase in signal intensity in the deltoid muscle at its origin along the posterior aspect of the scapular spine/acromion process (arrow). (Radiofrequency type artifact is projected over the lower part of the illustration). ANT = anterior; POST = posterior; HH = humeral head; DM = deltoid muscle.
Discussion

Erosion of the GT with or without adjacent BM edema had the best combination of sensitivity (58-65%) and specificity (86-92%).
Discussion

- Intense entheseseal BM edema at the acromial or calvicular origin of the deltoid muscle in the absence of significant injury is a finding specifically associated with AS.

Specificity 99%
Discussion

- Primary GH joint involvement is not a feature of AS.

- Narrowing of the GH joint likely reflect the elevation of humeral head in glenoid due to:
  - Rotator cuff disease
  - Secondary OA of the GH joint.
Conclusion

In the absence of the significant rotator cuff injury, entheseseal BM edema, especially intense, or erosive changes with adjacent BM edema strongly suggests AS!
Appraisal:

- Methodological flaws:
  - Only studied AS patients and no other SPA.
  - Control group were all non inflammatory pts with shoulder pain.
References

Clinical evaluation

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Diagnostic criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotator cuff tendinitis</td>
<td>History of pain in the deltoid region and pain on resisted active movement (abduction–supraspinatus; external rotation–infraspinatus; internal rotation–subscapularis)</td>
</tr>
<tr>
<td>Bicipital tendinitis</td>
<td>History of anterior shoulder pain and pain on resisted active flexion or supination of forearm</td>
</tr>
<tr>
<td>Shoulder capsulitis</td>
<td>History of pain in the deltoid area and equal restriction of active and passive glenohumeral movement with capsular pattern (external rotation &gt; abduction &gt; internal rotation)</td>
</tr>
<tr>
<td>Acromioclavicular joint disease*</td>
<td>Pain on shoulder abduction and point tenderness localized to the joint</td>
</tr>
<tr>
<td>Glenohumeral joint disease*</td>
<td>Pain on passive internal rotation of the shoulder with the elbow flexed and the arm held by the side</td>
</tr>
</tbody>
</table>

*Not defined in the Southampton examination schedule. See reference 25 for description.
# MRI imaging definition

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>Rotator cuff tear</td>
<td>Abnormal signal in rotator cuff tendon that is increased on all T2 images—similar to joint fluid.</td>
</tr>
<tr>
<td>Rotator cuff tendinosis</td>
<td>Abnormal signal in rotator cuff tendon that is increased on all T2 images—less intense than joint fluid.</td>
</tr>
<tr>
<td>Tuberosity cyst</td>
<td>Abnormal signal in the tuberosity of the humeral head that is well-circumscribed and of increased signal on T2 sequences similar to joint fluid. The overlying cortex is intact and there is complete loss of marrow fat signal on the T1 sequence.</td>
</tr>
<tr>
<td>Tuberosity erosion</td>
<td>Abnormal signal in the tuberosity of the humeral head that is well-circumscribed and of variable signal on T2 sequences; less intense than joint fluid. Overlying cortex is destroyed and marrow fat signal is completely lost on T1 sequence.</td>
</tr>
<tr>
<td>Bone marrow edema</td>
<td>Abnormal signal in bone marrow that is increased on T2 sequences and is best appreciated when fat suppression is employed. Overlying cortex is intact and there is partial loss of fat signal on T1 sequence.</td>
</tr>
<tr>
<td>Joint or bursal fluid/effusion</td>
<td>Increased volume of material in the appropriate space that is of signal character similar to joint fluid.</td>
</tr>
<tr>
<td>Joint or bursal inflammation</td>
<td>Increased volume of material in the appropriate space that demonstrates increased signal on T2 sequences but is not as bright as joint fluid.</td>
</tr>
<tr>
<td>Arthrosis</td>
<td>Hyaline cartilage thinning, labral abnormality, subchondral sclerosis, or subchondral cyst. In the acromioclavicular joint, this also includes capsular thickening.</td>
</tr>
</tbody>
</table>
# W. Gibbon Study

## Table 1 Quantitative changes in the plantar fascia

<table>
<thead>
<tr>
<th>Study group</th>
<th>Number (n)</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Plantar fascia thickness (mm)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean</td>
<td>Range</td>
<td>Male</td>
</tr>
<tr>
<td><strong>1. Controls</strong></td>
<td>96</td>
<td>48</td>
<td>21–67</td>
<td>20</td>
</tr>
<tr>
<td>Difference between heels</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td><strong>2. Plantar fasciitis</strong></td>
<td></td>
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</tr>
<tr>
<td>A. Unilateral</td>
<td>83</td>
<td>53</td>
<td>24–78</td>
<td>45</td>
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<tr>
<td>Symptomatic</td>
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</tr>
<tr>
<td>Asymptomatic</td>
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<tr>
<td>Difference between heels</td>
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<tr>
<td>B. Bilateral</td>
<td>214</td>
<td>54</td>
<td>17–72</td>
<td>63</td>
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<tr>
<td>Difference between heels</td>
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<tr>
<td><strong>3. Arthropathy</strong></td>
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<td>Rheumatoid –ve</td>
<td>70</td>
<td>55</td>
<td>32–74</td>
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<tr>
<td>Rheumatoid +ve</td>
<td>32</td>
<td>44</td>
<td>34–49</td>
<td>3</td>
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<td><strong>4. Achilles tendon disease</strong></td>
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</tr>
<tr>
<td><strong>5. Ankle injury</strong></td>
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</table>