CRITICALLY APPRAISED TOPIC

Is Ultrasonography a Valid Diagnostic Tool to Detect a Shoulder Synovitis in Patients with Rheumatoid Arthritis?

Appraised by Drs. Michel Kandel (kandel.physio@bluewin.ch), November 16, 2016

Clinical bottom line

The level of evidence and bias (internal validity) in this study make it impossible to answer the clinical question convincingly, despite moderate results and good external validity. More research, especially in bigger samples and the combination of ultrasonographic findings of axillary- and posterior synovitis, compared with MRI, needs to be done.

Clinical question: A female patient, 48-years-old suffers from rheumatoid arthritis for more than 10 years (according to criteria defined by the American College of Rheumatology). Her major problems are morning stiffness lasting more than one hour, pain, swelling and restricted function in hand and fingers. The patient has also difficulties in activities like walking, rising after sitting and several hand activities like grasping, lifting, writing, etc. Besides work disability she had to reduce her walking and horseback riding activities and give up cycling and playing volleyball. To suppress the inflammation she gets a medical treatment consisting of Adalimumab (Humira) 40mg subcutaneous every two weeks and 7.5 mg Methotrexat once a week. The health problem and clinical outcome of this patient was plotted in a RPS-Form, which enables an ICF analysis and a multidisciplinary approach\(^1\).

Since 3 weeks, she additionally complains of pain in the right shoulder (VAS 60/100) and impaired function in overhead movements. Physical examination showed limited movements in abduction/elevation, external and internal rotation. Synovial inflammation is a primary causal event, resulting in possible humeral head erosions and rotator cuff lesions\(^2\). A complementary examination to obtain objective information of inflammation could be useful and define a special treatment. Ultrasononography is an imaging modality used to visualize, identify and quantify soft tissue pathology. The question is, if ultrasonography is a valid modality to detect synovial inflammation in patients with rheumatoid arthritis.
Search strategy: Pubmed / Cochrane Library

Evidence: There is little information about the validity of ultrasonography in synovial inflammation. There was no secondary literature (Cochrane Library / same search terms) and only one study, reporting the validation of ultrasonography for synovial inflammation in patients with rheumatoid arthritis.


Summary of key evidence
The authors of this article compared ultrasonography (US) and magnetic resonance imaging (MRI) findings of synovial inflammation (axillary synovitis and posterior recess synovitis) in 9 patients with rheumatoid arthritis carried out by 11 rheumatologists. The MRI findings were defined as gold standard. Besides estimation of the intern validity, they also examined the intra- and inter observer reliability in these items, as each rheumatologist examined each patient twice. The results of the US findings compared with the MRI findings were presented in a table (as seen in table 1):
The critical appraisal of this validation study was made by using the Quadas-2 checklist and the “Diagnose Checklist 4.2” from Scholten et al.

**Strengths**
* The observers (rheumatologists) were experienced in musculoskeletal US and had a training session to get familiar with the scoring system.
* The definition of having a synovitis was clearly described (>3mm of effusion/synovial hypertrophy)
* All observers were blinded for the MRI results.
* Time between US and MRI was within 2 weeks.
* MRI was used as gold standard, which is appropriate for detecting synovial inflammation.
* With the available data it was possible to make a 2x2 diagram and recalculate the research findings.
* The intra observer reliability for detecting a synovitis was moderate (kappa 0.59) to good (kappa 0.62).
* The inter observer reliability for detecting a synovitis was moderate (kappa 0.52) to excellent (kappa 0.97).

**Threads**
* The including criteria were outpatients with RA according to the criteria of the American College of Rheumatology with “shoulder involvement”, which was unspecified.
* By recalculating the data, some inconsistencies were found. At first sight it was obvious that in an axillary synovitis a NPV of 0.43 at a prevalence of 33% is impossible. The NPV should at least be over 0.67 (pre-test probability for not having an axillary synovitis). In clinical terms a NPV of 0.43 would indicate that in case of absence of an axillary synovitis in US, the patient is more likely to have the disease (33% to 57%)! The recalculated and corrected NPV was 0.82 as seen in table 2.
* Time between US and MRI was within 2 weeks (possible disease pro- or regression bias, as it is unknown how fast the presence of synovitis can alter in RA).
* Nine patients and one healthy control were recruited. The healthy control was not considered in the results. The reason was not provided in the study.
* Each of the 11 rheumatologists examined each of the 9 patients twice. Each examination was counted as a case; so they artificially lifted the population from 9 to 198 samples. Consequently, the confidence interval of the results became much better (clustering bias).
* The study design of the research was more appropriate for testing the inter observer reliability, than testing the diagnostic accuracy of ultrasonography in shoulder synovitis. There were more observers (11) than patients (9).
* The authors failed to compare the combined findings of US axillary- and posterior synovitis with the MRI findings.

<table>
<thead>
<tr>
<th></th>
<th>Axillary synovitis</th>
<th>Posterior synovitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.60 (0.53-0.67)</td>
<td>0.93 (0.86-1.00)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.88 (0.78-0.97)</td>
<td>0.49 (0.36-0.61)</td>
</tr>
<tr>
<td>PPV</td>
<td>0.88 (0.80-0.96)</td>
<td>0.36 (0.31-0.42)</td>
</tr>
<tr>
<td>NPV</td>
<td>0.43 (0.41-0.45)</td>
<td>0.97 (0.94-1.00)</td>
</tr>
<tr>
<td>MRI findings</td>
<td>3 present, 6 absent</td>
<td>2 present, 7 absent</td>
</tr>
</tbody>
</table>

Table 1: Values are the mean (95% confidence interval)
PPV = positive predictive value
NPV = negative predictive value
Clinical evaluation

The calculations of the 2 x 2 table for ultrasonography in detecting axillary and posterior synovitis are shown in table 2 and 3. The relatively good specificity (0.88) in axillary synovitis indicates, that the test could be used as a SPIN, to confirm patients having an axillary synovitis. The moderate sensitivity (0.60), however, causes substantial false negative findings. In posterior synovitis a good sensitivity (0.93) was found, which implies that according to SNOUT, a negative test would rule out its presence. The poor specificity, however, leads to a few negative and many false positive findings. Unfortunately, the sensitivity and specificity of the test combination remains unknown.

The characteristics of the patient in this clinical question are almost identical to the researched population (sex, disease duration, medication; except age (48 to 55-76)). She would have perfectly fit into the including criteria of this study.

The prevalence of shoulder pain in patients with rheumatoid arthritis is 83.8%6. In this study 33% of these patients had an axillary synovitis, 22% a posterior synovitis. In a “Graph of Conditional Probabilities” the post-test probabilities of ultrasound in axillary synovitis (Fig. 1) and posterior synovitis (Fig. 2) can be shown. Despite these moderate changes in absolute probabilities, the bias in this study (clustering bias, small sample, measurement errors) makes it impossible to answer the clinical question.

<table>
<thead>
<tr>
<th>MRI</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
<td></td>
</tr>
<tr>
<td>Axillary synovitis</td>
<td>56</td>
</tr>
<tr>
<td>No axillary synovitis</td>
<td>142</td>
</tr>
<tr>
<td>Total</td>
<td>198</td>
</tr>
</tbody>
</table>

Table 2:
Sensitivity: 0.60
Specificity: 0.88
PPV: 0.71
NPV: 0.82
Prevalence: 0.33
LR+: 5
LR-: 0.45

<table>
<thead>
<tr>
<th>MRI</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasonography</td>
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</tr>
<tr>
<td>Posterior synovitis</td>
<td>59</td>
</tr>
<tr>
<td>No posterior synovitis</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
<td>198</td>
</tr>
</tbody>
</table>

Table 3:
Sensitivity: 0.93
Specificity: 0.49
Prevalence: 0.22
PPV: 0.35
NPV: 0.96
LR+: 1.82
LR-: 0.14
Figure 1: Graph of Conditional Probabilities showing the post-test probability of axillary synovitis at different prevalence's. The red line shows the post-test probability after a positive test result. The green line shows the post-test probability after a negative test result. The more distance to the indifferent test result (blue line) the bigger the change in absolute probability is. The black vertical line indicates the prevalence in this study (0.33 or 33%).

Figure 2: Graph of Conditional Probabilities showing the post-test probability of posterior synovitis at different prevalence's. The red line shows the post-test probability after a positive test result. The green line shows the post-test probability after a negative test result. The more distance to the indifferent test result (blue line) the bigger the absolute probability is. The black vertical line indicates the prevalence in this study (0.22 or 22%).

(Figure 1 and 2: Illustration & calculations by Michel Kandel)
Literature


