Ultrasound to Guide Treatment Decisions in Rheumatoid Arthritis

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INTRODUCTION AND OBJECTIVE

Ultrasound (US) detects synovitis more accurately than clinical examination in people with rheumatoid arthritis (RA). This review aimed to investigate the use of US, compared to clinical examination alone, in treatment strategies for RA, and to estimate its potential to be cost-effective in making treatment decisions.

METHODS

Systematic reviews were conducted of studies where US-detected synovitis had been used to inform prediction of treatment response or treatment tapering when compared with clinical examination assessed synovitis; and to identify papers assessing the cost-effectiveness of US to monitor synovitis. To inform the model, a systematic search sought studies of tapering RA treatment regardless of the involvement of US. The following electronic databases were searched from inception to October 2015 as part of a larger project:1 MEDLINE AND MEDLINE In-Process Citations Ovid; EMBASE Ovid; Cochrane Database of Systematic Reviews; Cochrane Central Register of Controlled Trials; Health Technology Assessment Database; Database of Abstracts of Reviews of Effects; NHS Economic Evaluation Database; Science Citation Index Expanded; Science Citation Index and Conference Proceedings Index; Clinical Trials.gov; European League Against Rheumatism Abstract Archive searched via Web of Science; American College of Rheumatology and Association of Rheumatology Health Professionals searched via Web of Science; OMERACT conference abstracts searched via Web of Science. The full search strategy and details of the full project will be available from the HTA website in the future.1

A model was constructed to investigate the potential cost-effectiveness of US in i) selecting patients suitable for treatment tapering; ii) avoiding treatment escalation.

RESULTS

Searches of electronic databases from a larger project1 yielded 2724 results. Following title and abstract sifting, 71 treatment-related articles were assessed for eligibility, and nine studies were included at full-text sift.

Seven prospective cohort studies (Table 1) found US-assessed synovitis at baseline could significantly predict treatment response as measured by clinical outcomes such as EULAR response or radiological progression (significance levels ranging from p=0.020 to p=0.04), and power Doppler US could predict treatment tapering or discontinuation failure as measured by relapse or disease flare (p=0.0005 to p=0.06), whereas in most cases clinical measures alone could not. Two RCTs identified suggested US added to DAS-based treatment strategies did not significantly improve primary outcomes (Table 1, ARCTIC p=0.54, TaSER p=0.72 and p=0.33 respectively), but was associated with improved rate of DAS remission (TaSER p=0.03).

Table 1 Characteristics of included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population and joints</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dougados 2013</td>
<td>Prospective cohort</td>
<td>59 RA bDMARD</td>
<td>Weekly</td>
<td>vdHSS van der Heijde-modified total Sharp Score, RAMRIS rheumatoid arthritis magnetic resonance imaging scoring system.</td>
</tr>
<tr>
<td>Ellegaard 2011</td>
<td>Prospective cohort</td>
<td>109 RA</td>
<td>Every 6 months</td>
<td>Clinical remission (no DAS28 &gt; 32) and reduction in disease activity (DAS28, CRP, ESR).</td>
</tr>
<tr>
<td>Inanc 2014</td>
<td>Prospective cohort</td>
<td>32 RA</td>
<td>Any</td>
<td>Clinical remission (no DAS28 &gt; 32) and reduction in disease activity (DAS28, CRP, ESR).</td>
</tr>
<tr>
<td>Dale 2013</td>
<td>Prospective cohort</td>
<td>150 RA</td>
<td>Any</td>
<td>Clinical remission (no DAS28 &gt; 32) and reduction in disease activity (DAS28, CRP, ESR).</td>
</tr>
</tbody>
</table>

The search for tapering studies identified nineteen papers.1 The evidence showed that some patients (proportions varied widely) who had achieved low disease activity could have treatment tapered, with no, or little, short term harm to the patient.

For patients where the clinician was contemplating reducing the dose the model estimated the reduction in treatment costs at which point the addition of monitoring synovitis with US became cost-neutral. For patients where the physician was thinking of increasing dosage the reduction in patients escalating treatment at which US was cost-neutral was calculated.

The model estimated (Table 3) that an average reduction of 2.46% in the costs of biological disease-modifying anti-rheumatic drug (bDMARDs) was sufficient to cover the costs of performing US every three months. Assuming a price reduction of 50% (estimated as appropriate if use of biosimilars becomes widespread) then an average reduction of approximately 4.93% in the costs of bDMARDs would render quarterly US monitoring cost neutral.

Table 3 The reduction in drug costs at which using US to monitor synovitis became cost-neutral

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DAS28</th>
<th>DAS28DMARD</th>
<th>DAS28DMARD</th>
<th>DAS28DMARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No tapering or escalation</td>
<td>£218.17</td>
<td>£218.17</td>
<td>£218.17</td>
<td>£218.17</td>
</tr>
<tr>
<td>Tapering costs of bDMARDs are 50%</td>
<td>10.0%</td>
<td>10.0%</td>
<td>10.0%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Assuming a 2 year trial</td>
<td>0.2%</td>
<td>0.2%</td>
<td>0.2%</td>
<td>0.2%</td>
</tr>
</tbody>
</table>

CONCLUSIONS

Use of US to monitor synovitis could potentially be a cost-effective approach, given that the proportions of patients for whom clinicians consider amending treatment, would need to taper bDMARD treatment, or not escalation to bDMARDs to negate the costs of US monitoring are low. US could provide clinicians with more confidence in reducing drug burden. However, there is considerable uncertainty in this conclusion due to lack of robust data relating to key parameters.

REFERENCES