The detection of subclinical synovitis by ultrasound in oligoarticular juvenile idiopathic arthritis: a pilot study

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Abstract

Objectives. Adult studies have demonstrated that ultrasonography (US) is more sensitive at detecting synovitis than clinical examination. The detection of subclinical disease has implications for deciding which patients receive more aggressive therapy from the outset. This study aimed to determine whether children with clinically diagnosed oligoarticular juvenile idiopathic arthritis (JIA) had US-detectable subclinical synovitis.

Methods. This was a cross-sectional pilot study conducted in a tertiary paediatric rheumatology clinic. Seventeen children with a median age of 10 years (range 3–13 years) and with oligoarticular disease of duration <12 months (median 5 months) were recruited. All subjects were DMARD and oral/i.v. corticosteroid naïve. A core set of 40 joints was clinically examined for synovitis and then scanned by a rheumatologist trained in joint US and blinded to all clinical data, at the same appointment.

Results. In total, 680 joints were examined both clinically and by US. Twenty-three joints were found to have clinical synovitis, and of these only 17 had synovitis confirmed by US. A further 15 joints were found to have synovitis on US examination alone. Overall, subclinical synovitis was detected in 6/17 children, mostly in the hands and feet. One child was reclassified as having polyarticular disease.

Conclusions. This pilot study has highlighted a discrepancy between clinical examination and ultrasound when assessing the joints of children with JIA. US is a feasible tool for examining multiple joints and identifying subclinical synovitis, particularly when considering the small joints of the hands and feet.

Key words: Ultrasound, Subclinical synovitis, Juvenile idiopathic arthritis, Oligoarticular, Paediatric.

Introduction

Subclinical synovitis is well recognized in adults with inflammatory arthritis and has been demonstrated by several imaging modalities, including ultrasonography (US) [1–3], MRI [4] and arthroscopy [5]. Our group has previously demonstrated the presence of US-detected subclinical synovitis in a population of 80 adults with early-onset oligoarticular disease. It showed that two-thirds of patients had subclinical disease and one-third of patients could be reclassified as having polyarticular disease [6].

In children, the concept of subclinical disease has been infrequently studied with imaging. MRI has previously demonstrated involvement of clinically unaffected knees in children with monoarthritis, which has been shown to predict disease extension [7]. However, it is not feasible to use MRI for multiple joint assessments of children in a clinical setting. US has been shown to be more sensitive than clinical examination for detecting synovitis in the knee [8–10] and hip [10] and to correlate with MRI in the knee [11]. It is an ideal tool for examining multiple joints in relatively short periods of time and is acceptable by children.

Early identification of synovitis in children would potentially enable earlier treatment, on the evidence that...
a shorter interval between symptom onset and the start of treatment is associated with a favourable therapeutic outcome in children with juvenile idiopathic arthritis (JIA) [12, 13] and adult-onset arthritis [14–17]. It is equally important not to over treat children and US has been demonstrated to be valuable in detecting tenosynovitis, rather than tibiotalar synovitis in clinically swollen joints [18].

The objectives of this pilot study in children with oligoarticular JIA were to identify the potential of US to detect subclinical synovitis when examining multiple joints and to evaluate its importance as an adjunct to clinical examination. The data were further examined to determine whether there are any differences between those joints where synovitis was detected both clinically and by US, and those that were assessed to have synovitis by clinical examination or US alone.

Methods

Patients

Children were recruited from a tertiary paediatric rheumatology centre. All had a diagnosis of oligoarthritis with clinical synovitis in four or less joints as determined by a consultant paediatric rheumatologist. All children were within 12 months of diagnosis and were DMARD and oral/i.v. corticosteroid naïve. No child had received any IA steroid injection (IACS) in the preceding month.

Study protocol

This study received local ethics committee approval (Leeds West Research Ethics Committee) and all parents gave written valid consent. Each child had a detailed clinical history taken, full clinical examination of all the joints and physicians global assessment of disease activity score (PGAS) [19] of 0–10, by a paediatric rheumatology specialist registrar. A joint was defined as having active synovitis clinically, if there was swelling of the joint, or if there was limitation of range of movement of the joint accompanied by heat, pain or tenderness (LROM+), as per ACR criteria [20]. A visual analogue scale (VAS) assessment of well-being and pain [0 cm (best) to 10 cm (worst)] and child HAQ (CHAQ) [21] scoring 0–3 were completed by each patient/parent. Details of previously symptomatic joints, corticosteroid injected joints and current drug therapy were recorded. Results of ANA and RF were also recorded.

At the same appointment a consultant rheumatologist trained in joint US, blinded to all clinical information, performed a detailed US examination in a minimum of two planes (longitudinal and transverse) of a standard set of 40 joints. Joints examined were knees, ankles, wrists, elbows, MCP, PIP, MTP and mid-foot. US was performed with an ATL HDI 3000 (Advanced Technologies Laboratories, Bothel, WA, USA) employing a 10–5 MHz transducer, or Philips 5000 US machine employing 15–8 or 12–5 MHz transducers. For small joints, a ‘hockey style’ transducer was used. Gel was applied to the skin to provide an acoustic interface.

The diagnosis of US-detected synovitis was defined by the presence of an abnormal, partially compressible hypo-echoic joint space, representing synovial hypertrophy and/or the presence of a compressible anechoic space within the joint, representing fluid (Figs 1 and 2) [22]. Synovitis detected by US was graded as mild, moderate or severe (score from 0 to 3).

Statistics

The number of joints with clinical synovitis or US-detected synovitis was not normally distributed and therefore the means, medians and ranges are reported. For statistical calculations, US was taken as the standard against which clinical examination was compared.

Results

Demographic data

Seventeen patients were recruited into the study, nine males, with median age 10 years (range from 3 years to 12 years).
3 months to 13 years 11 months). Mean disease duration was 5 months (range 1–12 months), with mean number of clinically synovitic joints 1.4 (range 0–4). Seven of the children were on regular NSAIDs at the time of the study. Of the 16 children tested, 8 were ANA positive and all were RF negative. On the day of assessment, the majority of children felt well (13 children had VAS score ≤4), in little pain (12 children had VAS score ≤4) with minimal impact of their disease on their ability to function (all CHAQ ≤1.0), and were all felt by the physician to be well (all PGAS <2).

Clinical and US findings

In total, 680 joints were examined both clinically and by US as seen in Table 1. Twenty-three joints were found to have clinical synovitis and of these only 17 had synovitis confirmed by US. US-detected synovitis in 15/657 joints assessed as clinically normal. If US is taken as the standard against which clinical examination is compared, the sensitivity of clinical assessment of a joint is the highest for the ankle, wrist and mid-foot, with high specificity for all the joints examined. Subclinical disease was detected by US in 6/17 children assessed. US changed the joint count in 9/17 of patients assessed, with 5/17 having an increased joint count on US assessment. One child could be reclassified as having polyarticular disease on the basis of US findings.

The data were examined in more detail to determine whether there was any difference in the joints where synovitis was detected both clinically and by US, when compared with the joints where synovitis was only detected by either clinical examination or US. In the 17 joints with synovitis detected both clinically and by US, almost one-third of joints had obvious evidence of synovitis with both swelling and LROM+. In comparison, in the six joints with synovitis detected clinically but not by US, no joint on clinical examination had both swelling and LROM+. Four of them (three ankles, one knee) were in three different patients in which the contralateral ankle/knee was assessed as clinically synovitic, and confirmed on US.

In the joints with synovitis detected both clinically and by US, 13/17 had synovitis US Grade 2 or 3. In comparison, of the 15 joints detected by US only, there were no Grade 3 and 8/15 Grade 2 joints on US. The most apparently difficult joints to assess clinically in terms of ‘missing’ synovitis were in the hands (5/15) and feet (6/15). Twelve out of 17 joints in the US and clinical correlation group had a history of previous intra-articular corticosteroids (IACS), compared with 3/21 joints where there was disagreement between clinical and US findings.

Conclusions

Imaging modalities, such as US and MRI, are evolving in the pursuit of identifying clinical and subclinical synovitis. This pilot study has highlighted the potential value of US in paediatric rheumatology, both in confirming the presence of synovitis and in detecting subclinical synovitis when assessing multiple joints. We do not yet fully know the clinical significance of synovitis detected on US in children.

TABLE 1 Number of joints that had synovitis detected simultaneously by clinical assessment and US, clinically only or by US only

<table>
<thead>
<tr>
<th>Joint (no. examined)</th>
<th>Clinical and US synovitis</th>
<th>Clinical synovitis only</th>
<th>US synovitis only</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee (34)</td>
<td>8</td>
<td>2</td>
<td>3</td>
<td>0.73</td>
<td>0.91</td>
</tr>
<tr>
<td>Ankle (34)</td>
<td>5</td>
<td>3</td>
<td>0</td>
<td>1.0</td>
<td>0.8</td>
</tr>
<tr>
<td>Wrist (34)</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1.0</td>
<td>0.91</td>
</tr>
<tr>
<td>Elbow (34)</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>–</td>
<td>1.0</td>
</tr>
<tr>
<td>MCP (170)</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>–</td>
<td>1.0</td>
</tr>
<tr>
<td>PIP (170)</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0.5</td>
<td>1.0</td>
</tr>
<tr>
<td>Mid-foot (34)</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>MTP (170)</td>
<td>1</td>
<td>0</td>
<td>6</td>
<td>–</td>
<td>1.0</td>
</tr>
<tr>
<td>Total (680)</td>
<td>17</td>
<td>6</td>
<td>15</td>
<td>0.53</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Sensitivity and specificity of clinical vs US examination of the joint have been calculated when US examination findings are considered as the gold standard.
and further longitudinal studies are needed. However, identification of subclinical disease potentially alerts the physician to monitor the patient more closely and could allow earlier, more aggressive treatment with the aim of reducing long-term damage.

In this study, clinical examination was most accurate for detecting synovitis in the wrist, ankle and mid-foot when compared with US. However, we recognize that there are limitations in the interpretation of sensitivity and specificity of small numbers in this pilot study and also the use of US as the standard measure. The knee was the most commonly involved joint, with one-third of all patients having synovitis demonstrated on US. One-quarter of the joints assessed to have clinical synovitis did not have synovitis detected on US. Of these joints, one-third had IACS administered with symptomatic relief in the 6/52 post-US. It is uncertain how far in advance of symptoms US findings may be demonstrated. The ability of US to differentiate between acute or chronic synovial hyper trophy is unclear [10, 23]. A study looking at US of the knee in children with JIA and controls, found that out of 17 children with JIA and clinically quiet knees, 35% had knee in children with JIA and controls, found that out of 17 children with JIA and clinically quiet knees, 35% had US evidence of synovial hypertrophy and 21% effusion, compared with clinically active patients (n=19), where 93% had synovial hypertrophy and 66% effusion [8]. The principle aim of our study was to detect early synovi tis, and hence the patient population in this study were all within the first 12 months of diagnosis decreasing the chances of chronic synovial hypertrophy.

Subclinical synovitis was detected in just over one-third of our patients, but only one child could be reclassified as having polyarticular disease. Most subclinical synovitis was detected in the hands and feet, which is a similar finding to our adult study [6]. Early detection of synovitis in the small joints can impact significantly in the active joint count and hence disease classification.

There are several limitations to this pilot study, relating to both ultrasound and clinical examination. With respect to US, there are no reliability data and it may have been beneficial for a second ultrasonographer to carry out a blinded examination. However, it was not felt that the resultant lengthened scanning time would be acceptable for the child. In future studies, the capture of video clips may partly overcome this difficulty. Of note, subclinical synovitis was mostly detected in the MCP and MTP joints, in which interobserver agreement rates with US have been demonstrated to be high in adults [24]. We recognize the value of power Doppler in the detection of subclinical synovitis [25], but did not use it in all our patients due to the limitations of the first US machine used in the study. Doppler may have allowed better differentiation between cartilage and synovial thickening in some patients. Imaging assessment (US or MR) of synovitis in the paediatric population is also challenging, with a lack of normative data relevant to the impact of different ages, stages of growth and puberty.

Clinical limitations include having only one clinical observer and no control group of children without JIA. Bias may have been introduced to the clinical examiner with knowledge that a joint previously had had an IACS, particularly when a clinically borderline joint may be regarded as having active synovitis. The ultrasonographer may not have been completely blinded from clinical evaluation as the joint is handled during US examination. In the group of joints with synovitis detected clinically but not by US, three ankles and one knee had US confirmed clinical synovitis in the contralateral joint. This may suggest bias on clinical examination, or alternatively these patients may have presented with some swelling/tenderness, due to increased mechanical load through the contralateral joint to compensate for less weight bearing on the synovitic side.

Overall, this pilot study has shown US to be a potentially valuable tool in our paediatric clinical practice and demonstrated discrepancies in clinical vs US detection of synovitis in joints of children with oligoarticular JIA. We highlight the value of US in the assessment of the small joints of the hands and feet, in children where the joint may be tender but does not fulfil ACR criteria with additional LROM+, if tenosynovitis [18, 26] is considered and in the child with excess subcutaneous tissue. However, prospective studies are still required to determine the full significance of US-detected subclinical synovitis in children.

References


