Joint Imaging and Management in Haemophilia
Objectives

• Review Imaging options in Haemophilia Arthropathy

• Role of imaging in joint care

• Expand on the use of Ultrasound
  – Utility of US in decision making process

• Demonstration of Ultrasound of the Elbow
Introduction

• Recurrent Haemarthropathy is a destructive process that often results in debilitating joint disease and functional impairment

• Pathophysiological mechanism not entirely understood and likely multifactorial
  – Direct effects of blood leading to chondrocyte damage and inflammatory arthritis
  – Changes to biomechanics of joints arising from altered bone formation

• Episodes of bleeding often begin in early life
  – Elbow: age 2-5

• Haemophiliac arthritis contributes the greatest morbidity and cost

• Most common sites include the elbow, ankle, and knee
What’s the purpose of imaging Joints?

• Detect site and severity of joint damage

• Detect changes prior to irreversible damage
  – Predict the risk of further bleeding

• Provide a tailored approach to the management of HA

• Evaluate the joint for an acute haemarthrosis

• Monitor effects of treatment:
  – What should be the schedule
    • Adults: 12 monthly
    • Children: 6 monthly
Plain Radiography

- Excellent assessment of late disease
  - Valuable in the planning for joint replacement surgery

- Poor sensitivity for early changes

- Limited visualisation of haemarthrosis

- No ability to visualise synovitis

*Has limited role in the modern approach to evaluating treatment efficacy*

- There are two scales to evaluate changes on radiographs
Scoring scales

Table 1. The Arnold-Hilgartner Scale

<table>
<thead>
<tr>
<th>Stage</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal joint</td>
</tr>
<tr>
<td>I</td>
<td>No skeletal abnormalities, soft tissue swelling is present</td>
</tr>
<tr>
<td>II</td>
<td>Osteoporosis and overgrowth of the epiphysis, no cysts, no narrowing of the cartilage space</td>
</tr>
<tr>
<td>III</td>
<td>Early subchondral bone cysts, squaring of the patella, widened notch of the distal femur or humerus, preservation of the cartilage space</td>
</tr>
<tr>
<td>IV</td>
<td>Findings of stage III, but more advanced; narrowed cartilage space</td>
</tr>
<tr>
<td>V</td>
<td>Fibrous joint contracture, loss of the joint cartilage space, extensive enlargement of the epiphysis, substantial disorganization of the joint</td>
</tr>
</tbody>
</table>

Table 2. The Pettersson Score

<table>
<thead>
<tr>
<th>Radiographic Finding</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osteoporosis</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Enlarged epiphysis</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Irregular subchondral surface</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Partly involved</td>
<td>1</td>
</tr>
<tr>
<td>Totally involved</td>
<td>2</td>
</tr>
<tr>
<td>Narrowing of joint surface</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Joint space &gt; 1 mm</td>
<td>1</td>
</tr>
<tr>
<td>Joint space &lt; 1 mm</td>
<td>2</td>
</tr>
<tr>
<td>Subchondral cyst formation</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>1 cyst</td>
<td>1</td>
</tr>
<tr>
<td>&gt; 1 cyst</td>
<td>2</td>
</tr>
<tr>
<td>Erosion of joint margins</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Present</td>
<td>1</td>
</tr>
<tr>
<td>Gross incongruence of articulating bone ends</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
</tr>
<tr>
<td>Pronounced</td>
<td>2</td>
</tr>
<tr>
<td>Joint deformity (angulation or displacement or both between articulating bones)</td>
<td></td>
</tr>
<tr>
<td>Absent</td>
<td>0</td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
</tr>
<tr>
<td>Pronounced</td>
<td>2</td>
</tr>
</tbody>
</table>

• The A-H Stage is determined by most severe feature present  
  • Easy to use

• The Pettersson Score is an additive score  
  • Highest score is 13  
  • Discrimates change best  
  • Higher interobserver reliability  
  • Recommended by WHF
Typical X-ray Projections
MRI

• Widely considered the Gold standard modality in evaluation of HA
  – Albeit for the elbow can be less sensitive
  – Clinical significance of early changes in HA yet to be established

• Can differentiate between simple effusion and haemorrhage

• Validated scoring system developed
  – International Prophylaxis Study Group scale
  – Separates soft tissue from osteochondral disease
    • As such will likely give meaningful insight into pathophysiology of HA progression

  – Reflects progression from early disease to advanced arthropathy
    • Although performs relatively poorly at differentiating mild from moderate and severe disease

• Limitations are;
  – Expense
  – Access
  – Need for sedation in children

Cross S, et al. Semin Ultrasound CT MRI 2013; 34:516-524
Ultrasound

- Allows the evaluation of soft tissue changes in HA including:
  - Reasonable ability to differentiate effusion from haemarthrosis
    - Useful in the evaluation of an acutely swollen joint
  - Inexpensive, accessible, fast, real time, dynamic and no sedation required
  - Does not provide detailed evaluation of cartilage or bone

<table>
<thead>
<tr>
<th>Children US vs MRI</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synovial Hypertrophy</td>
<td>&gt;90%</td>
<td>&gt;90% knees</td>
</tr>
<tr>
<td></td>
<td></td>
<td>50% ankles</td>
</tr>
<tr>
<td>Effusion and Haemarthrosis</td>
<td>70% ankles</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>&gt;90% knees</td>
<td></td>
</tr>
<tr>
<td>Haemosiderin deposition</td>
<td>100%</td>
<td>67% ankles</td>
</tr>
<tr>
<td>Cartilage damage</td>
<td>&gt;85%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Useful in planning prophylaxis and assessing early treatment efficacy
Ultrasound in the detection of subclinical disease

- Subclinical joint bleeds do occur
  - Despite compliance with prophylactic factor replacement
  - More common in those with inhibitors

- Early detection may provide opportunity to intervene prior to irreversible joint damage

- Evaluated the ability of US (HEAD-US protocol) to detect subclinical disease

- Studied 167 patients (976 joints) with no history of joint bleeds

- Found;
  - 25% of patients with HJHS score of 0 had evidence of joint changes
  - Chondral changes were the most common abnormalities detected
  - The most affected joint appears to be the ankle
  - There were no predictors towards joint changes identified in patient characteristics

*Ultrasound is a sensitive tool in detecting joint changes relating to subclinical disease*
Ultrasound in Acute Setting

• Currently the general approach to acute swollen joint is empiric
  – Patient usually decides whether to;
    • Administer factor replacement therapy
    • Use conservative measures if chronic arthritis presumed the cause of pain

• Symptoms of an acute bleed are non-specific
  – Haemarthrosis vs haemophilic arthritis

• Rapid point-of-care US has a role in this setting
  – Can readily distinguish simple from complex (bloody) effusion
How to distinguish blood from synovium

- attached to the walls (peripheral)
- irregular margins
- some vasculature may be detected

- detached from the walls (central)
- smooth margins
- free of color flow signals at Doppler imaging
Ultrasound in Acute Setting

• Ceponis, et al, evaluated 30 patients who presented to HA clinic with acute joint pain

  – Assessment within 48 hrs of pain /swelling onset
    • Physical examination
    • Ultrasound

  – Patients proceeded with usual care

  – Treatment adjusted according to US findings

Ultrasound in Acute Setting

Findings

- 40 episodes of acute joint pain were evaluated
  - Median time to evaluation 10 hr
  - 70% assessed within 24 hrs
  - Patient perceived aetiology correct in only ≈ 33%
  - Physician perceived diagnosis not much better
    - Correct in only 18 or 40 episodes
  - Agreement between patient and physician occurred in only 9 cases!!!
    - Of which only 4 were confirmed on US as correct

Ultrasound in Acute Setting

• Impact on Decision Making
  – Directly changed treatment in 29 of 40 episodes of acute joint pain
    • Symptoms poorly controlled for painful episodes at time of presentation to clinic
    • US guided decision resulted in symptom improvement in 65% of cases
    • In confirmed non-bleeding, factor replacement was not initiated in 12 or discontinued in 10
      – Prompted other conservative interventions such as Physiotherapy, NSAIDs, and/or I/A steroid injections
    • Study probably under-estimates the episodes of ‘arthritic’ pain that were instead haemarthrosis – representing a further missed opportunity to prevent further damage
Ultrasound in Acute Setting

• Case 1:
  – 37yo male Haemophilia A
  – Knee pain, warmth and swelling
  – Thought a bleed
  – US synovitis
    • Non compressible
    • Positive power Doppler signal

• Case 2
  – 23yo severe Haemophilia B
  – Ceased prophylaxis, choosing on demand treatment
    • ‘most are ‘arthritic’ pains
  – Painful ankle
  – US: Acute haemarthrosis
    • Complex effusion
    • Compressable
    • No power Doppler signal
  – Confirmed on aspiration
  – Commenced Prophylaxis again
Ultrasound

• Furthermore, in most episodes of haemarthrosis

  • Persistent effusion is noted on Ultrasound evaluation despite resolution of symptoms
    – Lack of agreement in 57.8% between symptoms and US findings

  • Effusion typically resolves after 7 days post bleed

*Questioning duration of factor replacement therapy post bleed*

• If effusion persists >2 weeks after acute bleed then presume fluid relates to chronic synovial hypertrophication / synovitis

*In summary, in appears that the current practice of decision making based on patient and/or physician opinion is inadequate for modern haemophilia care*
Ultrasound Protocols

• Numerous Ultrasound protocols proposed
  – Aim is to address operator-dependent evaluation by providing a standardised approach

• HEAD US
  – Haemophilia Early Arthritis Detection with UltraSound
  – Simple scanning procedure and scoring method
  – Aims:
    • Increase sensitivity to detect early signs of joint involvement
    • Easy technique
    • Quick to perform
    • Integrate US in the routine practice of Haemophilia centers

HEAD US

- Procedure evaluates:
  - Joint recesses to assess for an effusion and synovial thickening
  - 1 view of the cartilage and bone to assess for damage

- Additive scoring method
  - Synovium
  - Cartilage
  - Bone
  - Maximum score of 8 for each joint

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<table>
<thead>
<tr>
<th>Disease activity (synovitis)</th>
<th>Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrophic synovium</td>
<td></td>
</tr>
<tr>
<td>0. Absent/Minimal</td>
<td>0</td>
</tr>
<tr>
<td>1. Mild/Moderate</td>
<td>1</td>
</tr>
<tr>
<td>2. Severe</td>
<td>2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease damage (articular surfaces)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cartilage</td>
</tr>
<tr>
<td>0. Normal</td>
</tr>
<tr>
<td>1. Echotexture abnormalities, focal partial/full-thickness loss of the articular cartilage involving &lt;25% of the target surface*</td>
</tr>
<tr>
<td>2. Partial/full-thickness loss of the articular cartilage involving at least ≤50% of the target surface*</td>
</tr>
<tr>
<td>3. Partial/full-thickness loss of the articular cartilage involving &gt;50% of the target surface*</td>
</tr>
<tr>
<td>4. Complete cartilage destruction or absent visualization of the articular cartilage on the target bony surface*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>0. Normal</td>
</tr>
<tr>
<td>1. Mild irregularities of the subchondral bone with/without initial osteophytes around the joint</td>
</tr>
<tr>
<td>2. Deranged subchondral bone with/without erosions and presence of prominent osteophytes around the joint</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Inter-observer</th>
<th>k</th>
<th>95% CI</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elbow</td>
<td>0.80</td>
<td>0.70–1.00</td>
<td>0.09</td>
</tr>
<tr>
<td>Knee</td>
<td>0.81</td>
<td>0.69–0.78</td>
<td>0.02</td>
</tr>
<tr>
<td>Ankle</td>
<td>0.66</td>
<td>0.21–0.91</td>
<td>0.06</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th>Intra-observer</th>
<th>k</th>
<th>95% CI</th>
<th>SE</th>
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<tbody>
<tr>
<td>Elbow</td>
<td>0.80</td>
<td>0.61–0.98</td>
<td>0.10</td>
</tr>
<tr>
<td>Knee</td>
<td>0.80</td>
<td>0.67–0.94</td>
<td>0.07</td>
</tr>
<tr>
<td>Ankle</td>
<td>0.69</td>
<td>0.46–0.93</td>
<td>0.12</td>
</tr>
</tbody>
</table>

K values are reported as weighed with linear weights. 95% CI, 95% confidence interval; SE, standard error.

HEAD US

• A: Evaluate the fossa for effusion / synovitis
  – Medial = coronoid fossa
  – Lateral = radial fossa

• B: Evaluate cartilage of distal humeral epiphysis
  – Medial = concave trochlea
  – Lateral = capitellum

• C: Evaluate radial-capitellar joint
  – Assess radial fossa and annular fossa for effusion / synovitis
  – Assess cartilage and bone

• D: Evaluate the trochlea-ulnar joint
  – Assess coronoid fossa for effusion / synovitis
  – Assess cartilage and bone

• E: Evaluate posterior elbow joint
  – Assess the olecranon fossa for effusion / synovitis

HEAD-US Scoring Scale – interpretation rules

ELBOW – joint distension

GRADE-0

- Concavity
- No synovium on the floor
HEAD-US Scoring Scale – interpretation rules

ELBOW – joint distension

GRADE-0

- capitellum
- olecranon
- trocheal

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ELBOW – joint distension

GRADE-I

convexity

concavity

synovium on the floor

HEAD
CAPITELLUM

OLECRANON
TROCHLEA

HEAD-US Scoring Scale – interpretation rules

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HEAD-US Scoring Scale – interpretation rules

ELBOW – joint distension

GRADE-I

POSTERIOR ELBOW

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ELBOW – joint distension

GRADE-II

continuous involvement over the anterior aspect of the joint

distension of the annular recess

convexity

synovium on the floor
HEAD-US Scoring Scale – interpretation rules

ELBOW – joint distension

GRADE-II

POSTERIOR ELBOW

olecranon

joint line

humerus

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