PREVENTION OF PATHOLOGICAL FRACTURE

14TH NOVEMBER 2013
PREVENTION OF PATHOLOGICAL FRACTURE (PPF) GUIDELINE DEVELOPMENT GROUP

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SESSION OUTLINE

• Overview
• Existing Standards
• Updated Standards & Guidelines
• Mr Paul Cool - External Review
PROVENANCE

• April 2005 – initial guidelines produced

• 3rd May 2012 – Review meeting of MCPCNAG, majority quorate vote to review guidelines

• Meetings of membership of Prevention of Pathological Fracture (PPF) guideline development group
  – 17th July 2012
  – 25th September 2012
  – 13th November 2012
  – 11th June 2013
  – 12th September 2013
  – 16th October 2013
  – 4th November 2013

• Presentation of Literature Review on 4th July 2013
LITERATURE REVIEW

- Main changes to evidence base:
  - Mirels Score
    - upgraded to Level 2+ evidence
  - Denosumab licensed for PPF
    - Breast cancer and solid tumours if bisphosphonates would otherwise be prescribed
    - Not used in prostate cancer
    - Level 1+ Evidence
EXISTING STANDARDS & AUDIT RESULTS
REVISED GUIDELINES FOR THE PREVENTION OF PATHOLOGICAL FRACTURES IN PALLIATIVE CARE
1. GENERAL PRINCIPLES (1)

• Bone is one of the commonest sites of metastatic disease. The most likely primary tumours to spread to bone are breast, bronchus, kidney, thyroid and prostate. The axial skeleton (skull, ribs, spine and pelvis) is more likely to develop metastatic disease than the appendicular skeleton. ¹

• The major associated morbidities of bone metastases include pain (the most common symptom occurring in 70% of patients), pathological fractures (occurring in 8-30% of patients) and hypercalcaemia.² ³

• Advances in hormonal treatments, use of bisphosphonates and chemotherapy treatments have meant that the prognosis of patients with bone metastases, without visceral metastatic disease, has greatly improved. ⁴
1. GENERAL PRINCIPLES (2)

- Survival rates for people with bone metastases vary depending on the primary tumour type. In breast cancer, median survival is 24 months with a 5-year survival rate of 20% and in prostate cancer there is a 5-year survival rate of 25% and a median survival of 40 months\(^5\).

- Prediction of pathological fractures before the event is a relevant clinical problem. Prophylactic fixation of long bone metastases is generally easier for the surgeon and less traumatic for the patient. Therefore, prophylactic fixation of long bones prior to radiotherapy should be considered. Stabilisation of impending pathological fractures is likely to result in shorter hospital stays, with patients more likely to be discharged to their own homes.\(^9\)

- The prevention and management of pathological fractures should be within the context of a multi-disciplinary team. \(^5,\!^{10}\)
2. GUIDELINES
2.1 Investigation of bone pain (1)

- Pain may be described as a dull ache to a deep intense pain; pain at rest; pain exacerbated by weight bearing and importantly, pain which is worse at night. Patients should be encouraged to report skeletal symptoms promptly.

- Bone pain may be due to structural damage, periosteal irritation, nerve entrapment or secretion of chemical mediators causing osteolysis e.g. prostaglandins and cytokines. These mediators activate both osteoclasts and nociceptors.

- The clinical conundrum is to determine which pains are due to new or existing metastatic disease and which of these lesions may progress to a pathological fracture. As such, reports of bone pain should be investigated following the British Association of Surgical Oncology (BASO) Guidelines (see Table 2.1).
# BASO Guidelines for the Investigation of Bone Pain\(^\text{10} [\text{Level 4}]\)

<table>
<thead>
<tr>
<th>Level of clinical suspicion of metastatic disease</th>
<th>Clinical features</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Minimal</strong></td>
<td>Known cause for pain. Resolves well usually 2-3 weeks from onset.</td>
<td>Normal outpatient review. Return to GP if resolution not complete.</td>
</tr>
<tr>
<td><strong>Low</strong></td>
<td>Probable cause known. Good resolution over 4-6 weeks.</td>
<td>Plain radiograph. If negative: no action. If positive: follow advice regarding the need for orthopaedic assessment.</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td>No clear cause for pain which is persistent but not progressive.</td>
<td>Plain radiographs, serum calcium and bone scan within 10 working days. Review one week later. If all negative, review in 8 weeks if symptomatic. If one or more tests positive, follow advice regarding the need for orthopaedic assessment.</td>
</tr>
<tr>
<td><strong>High</strong></td>
<td>No identified cause for pain. Night pain, severe and / or progressive pain. Neurological symptoms and signs.</td>
<td>Plain radiographs, serum calcium and bone scan within 10 working days. Review one week later. If all negative but suspicion high, review in 1 week (appendicular skeleton). If pain in spine, then arrange MRI. If one or more tests positive, then follow advice regarding need for orthopaedic assessment.</td>
</tr>
</tbody>
</table>
2.1 Investigation of bone pain (2)

- Plain radiographs should be of the entire bone, including the joint above and below the site of pain. Specific radiographs should be centralised over the painful area in an AP and lateral view.

- Bone metastases may be described as osteolytic (bone appears less dense on imaging), osteoblastic (where bone looks denser or whiter on imaging) or mixed in nature.\(^4\) [Level 4]

- Any plain radiograph report that details the presence of a lytic lesion in a long bone should be discussed with a radiologist regarding its size and degree of cortical involvement, if not already stated.\(^7, 8, 10\) [Level 4]

- Plain radiographs are relatively insensitive at detecting bone metastases.\(^19\) Thus if clinical suspicion is high and radiographs are normal, further imaging is warranted. This should be an isotope scan if the appendicular skeleton is suspected, and an MRI if the spine is potentially involved.\(^19\)
2.1 Investigation of bone pain (3)

- Areas of increased uptake in any long bones on an isotope bone scan should be followed up by plain radiographs of the whole bone in two planes at 90° to each other, to assess for size and cortical involvement.\textsuperscript{10} [Level 4]

- Patients with symptomatic bone metastases should be referred urgently to an orthopaedic clinic or be discussed at a site-specific multidisciplinary team meeting if they have any of the following:
  - Structurally significant bone destruction.
  - Uncertainty whether the destruction is significant.
  - Pain of sudden onset (or change in character) that is exacerbated by movement.\textsuperscript{10} [Level 4]
PREDICTION OF PATHOLOGICAL FRACTURE

- Clinical features of impending pathological fracture include pain on movement, persistent pain and increasing pain. Pain in an area which has already been treated with radiotherapy, but has not responded, may also be considered as a clinical indicator of possible impending fracture.\(^7,8\)

- The risk of a pathological fracture occurring, and therefore the need to consider prophylactic fixation, may be assessed using either Mirels scoring system (for use in long weight bearing bones) or Harrington's classic definitions (use restricted to the proximal femur).\(^7\)

- In Mirels scoring system (Table 32.2) [Level 2+], the maximum possible score is 12. If a lesion scores 8 or above, then prophylactic fixation is recommended *prior* to radiotherapy.
<table>
<thead>
<tr>
<th>Score Clinical features</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td>Upper limb</td>
<td>Lower limb</td>
<td>Peritrochanteric</td>
</tr>
<tr>
<td>Pain severity</td>
<td>Mild</td>
<td>Moderate</td>
<td>Functional</td>
</tr>
<tr>
<td>Type of lesion</td>
<td>Blastic</td>
<td>Mixed</td>
<td>Lytic</td>
</tr>
<tr>
<td>Size (Maximum destruction of cortex in any view as seen on plain x-ray)</td>
<td>&lt;1/3</td>
<td>1/3-2/3</td>
<td>&gt;2/3</td>
</tr>
</tbody>
</table>

Table 32.2  Mirels scoring system for the prediction of pathological fractures [Level 2+]
ANY ONE OF HARRINGTON'S CLASSIC DEFINITIONS INDICATES A HIGH RISK OF PATHOLOGICAL FRACTURE IN THE PROXIMAL FEMUR (SEE TABLE 2.3).¹ [LEVEL 3].

<table>
<thead>
<tr>
<th>Table 2.3  Harrington's classic definitions. Risk of a pathological fracture 8 [Level 3]</th>
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<tr>
<td>1. 50% of circumferential cortical bone has been destroyed.</td>
</tr>
<tr>
<td>2. Where pain with weight bearing stresses persists, increases or recurs, despite adequate local irradiation.</td>
</tr>
<tr>
<td>3. Lesions in the proximal femur in excess of 2.5cm in any dimension.</td>
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<tr>
<td>4. Lesions in the proximal femur associated with avulsion of the lesser trochanter.</td>
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</table>
2.3 ROLE OF ORTHOPAEDIC SURGEON

• A lead orthopaedic surgeon for appendicular metastatic bone disease should be identified in each local NHS trust. ⁴ [Level 4]

• Referral to an orthopaedic surgeon is appropriate in the following situations:
  - Prophylactic fixation of metastatic deposits when there is a high risk of fracture i.e. Mirels score equal or greater than 8 (see Table 32.2) or the presence of any one of Harrington's classic definitions (see Table 32.3).
  - Stabilisation or reconstruction after pathological fracture.
  - Decompression of the spinal cord and nerve roots and / or stabilisation for spinal instability. ⁴ [Level 4] (see Guidelines on the Management of Metastatic Spinal Cord Compression).
2.4 **RADIOThERAPy**

- Radiotherapy has a major role in the treatment of bone metastases. 70% of patients will achieve pain relief with palliative external beam radiotherapy. It may also prevent additional bone destruction, help to maintain function, prevent neurological compromise and maintain quality of life.\(^6\)

- Following nailing of a bone, radiotherapy should be considered by appropriate specialists within the context of the multidisciplinary team.\(^5, 11, 12\) [Level 2-]
2.5 OTHER TREATMENT MODALITIES (1)

- Bisphosphonates should be considered, where clinically appropriate, for the prevention of skeletal related events and treatment of malignant bone pain in patients with bone metastases from breast cancer or hormone refractory prostate cancer, and also patients with multiple myeloma.\textsuperscript{13} [Level 1+] Decisions to treat should be based on an assessment of their general medical condition and expected survival time (see Guidelines on the Use of Bisphosphonates in the Management of Malignant Bone Disease). [Level 4].

- Radiofrequency ablation of bone metastases is an emerging alternative therapy for the management of bony metastatic disease. Referral to an appropriate specialist may be beneficial for effective pain palliation and local control of disease. \textsuperscript{15} [Level 3]
2.5 OTHER TREATMENT MODALITIES (2)

- Percutaneous cementoplasty is indicated for patients with painful vertebral metastases. It is a minimally invasive technique involving injection of polymethylmethacrylate to strengthen a vertebra. It may provide fast pain relief for patients when traditional surgical options are considered to be too invasive. ¹⁶,¹⁷ [Level 3]

- Denosumab is recommended as an option for preventing skeletal-related events from breast cancer and from solid tumours, if bisphosphonates would otherwise be prescribed. It can be used in poor renal function. It is however not recommended by NICE for use in prostate cancer, and carries the risk of potential osteonecrosis of the jaw⁵. [Level 1+]
2.3 **STANDARDS**

1. Reports of bone pain should be promptly and appropriately investigated following British Association of Surgical Oncology (BASO) Guidelines.\(^{10}\) [Grade D].

2. If there is evidence of significant risk of a pathological fracture, urgent orthopaedic review should be **considered**.\(^4,^{10}\) [Grade D]

3. Following any orthopaedic intervention (prophylactic stabilisation or fracture management) a patient **should be discussed with an oncologist regarding the possibility of further therapy**.\(^{10}\) [Grade D]

4. Patients presenting with a **NEW OR SYMPTOMATIC** lesion due to metastatic bone disease must be discussed with an oncologist for consideration of further therapy (e.g. hormonal manipulation, bisphosphonates, chemotherapy, radiotherapy) regardless of orthopaedic intervention.\(^{10}\) [Grade C]
2.4 REFERENCES (1)

2.4 REFERENCES (2)


