Guidelines for the Prevention of Pathological Fractures in Palliative Care

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Quick Reference Summary

Metastatic bone disease (MBD) is common and has a damaging effect on quality of life. Pathological fracture can impact on survival in advanced cancer. It is essential that people at risk of pathological fracture are identified for management that can reduce risk of fracture and its associated morbidity.

4.1 Assessment and Investigation of Bone Pain

- People with cancer, regardless of the presence of metastatic bone disease, should be encouraged to report bone pain promptly ⁴,8 [Level 4]
- Bone pain should be investigated following the British Association of Surgical Oncology (BASO) Guidelines (see Table 2) ⁴,8 [Level 4]

4.1.1 Imaging

- Plain radiographs should be of the entire bone, including the joint above and below the site of pain ⁴,6 [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 on the report ⁸,12,13 [Level 4]
- Plain radiographs may not detect all bone metastases. ⁴,6 If clinical suspicion of metastatic bone disease is high and radiographs are normal, use NM Isotope, CT or MRI ¹⁵ [Level 4]

4.2 Determining Risk of Pathological Fracture

- The risk of a pathological fracture occurring may be assessed using either Mirels scoring system ¹² [Level 2+] (for use in long weight bearing bones) or Harrington’s classic definitions (use restricted to the proximal femur) ¹³ [Level 3]

4.3 Management of Patients at Increased Risk of Pathological Fracture

4.3.1 Orthopaedic Surgery

- Patients with symptomatic bone metastases who may benefit from intervention should be referred urgently to an orthopaedic clinic or be discussed at a site-specific multi-disciplinary team meeting if they have any of the following [Level 4]:
  - Structurally significant bone destruction ⁸
  - Uncertainty whether the destruction is significant ⁸
  - Pain of sudden onset (or change in character) that is exacerbated by movement
  - Solitary bone metastasis (to exclude different primary) ⁴
- Referral to an orthopaedic surgeon is appropriate in the following situations [Level 4]:
  - Prophylactic fixation of metastatic deposits when there is a high risk of fracture i.e. Mirels score equal or greater than 8 (see Table 3) or the presence of any one of Harrington’s classic definitions (see Table 4) ¹²,13
  - Stabilisation or reconstruction after pathological fracture ¹⁵
  - Decompression of the spinal cord and nerve roots and / or stabilisation for spinal instability. ⁴ (See Guidelines on the Management of Metastatic Spinal Cord Compression.
  - A lead orthopaedic surgeon for appendicular metastatic bone disease should be identified at each acute NHS Trust ⁴ [Level 4]

4.3.1.1 Other surgical interventions

- Referral to an interventional radiologist for radiofrequency ablation of bone metastases may be beneficial ¹⁶,¹⁷ [Level 3]
- Referral to a spinal orthopaedic surgeon for assessment of the role of percutaneous cementoplasty may be advisable ¹⁶,¹⁷ [Level 3]

4.3.2 Oncology

- Following orthopaedic intervention, radiotherapy and other oncology treatments (e.g. hormonal manipulation, chemotherapy) should be considered by appropriate specialists within the context of the multidisciplinary team ⁴, ²¹, ²² [Level 2+]
- Oncologists will consider the use of bisphosphonates and denosumab in preventing skeletal related events. Use will depend on the goals of treatment and the cancer type ⁴, ²³ [Level 1-]
Section 1: Introduction

- Bone is one of the commonest sites of metastatic disease.\(^1\) The most likely primary tumours to spread to bone are breast, bronchus, kidney, thyroid and prostate.\(^1\) 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 are described as skeletal related events which are defined as:\(^2,3,\)
  - severe bone pain requiring palliative radiotherapy or analgesics (70% of people with metastatic bone disease)\(^2\)
  - pathological fractures (8-30% of people with metastatic bone disease)
  - spinal cord compression
  - bone instability requiring orthopaedic surgery

- Advances in hormonal treatments, use of bisphosphonates and chemotherapy have meant that the prognosis of patients with bone metastases, without visceral metastatic disease, has greatly improved.\(^4\) 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%\(^5\)
  - In prostate cancer, median survival is 40 months with a 5-year survival rate of 25%\(^5\)
  - In lung cancer, the presence of bone metastases confers a shorter prognosis with a median survival of six months in those experiencing skeletal related events. This is extended to 12 months for those with metastatic bone disease who do not have skeletal related events\(^6\)

- Therefore, prevention of pathological fractures before the event is a relevant clinical problem. It has a significant impact on the experience of people living with cancer. Stabilisation of impending pathological fractures is likely to result in shorter hospital stays, with patients more likely to be discharged to their own homes compared to those who sustain a pathological fracture.\(^7\)

- The prevention and management of pathological fractures should be managed within the context of a multi-disciplinary team.\(^4,8\)
Section 2: Scope and Purpose

- The following guidance is an update of *Guidelines for the Prevention of Pathological Fractures in Palliative Care* developed in 2005 and reviewed in 2009.  

- This guideline is aimed primarily at practitioners in specialist palliative care including doctors, nurses, physiotherapists, occupational therapists and pharmacists. The guidelines will also be of benefit to generalist providers of palliative care such as general practitioners, district nurses and those in secondary care.

- The aims of this guideline are to:
  - Enhance the identification of patients at risk of pathological fracture
  - Reduce the associated morbidities of pathological fracture including pain and impairment of function

- Table 1 summarises the scope and purpose of this guideline.

<table>
<thead>
<tr>
<th>Table 1: Scope of guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
</tr>
<tr>
<td>Adults with incurable advanced cancer experiencing bone pain</td>
</tr>
<tr>
<td><strong>Populations not covered</strong></td>
</tr>
<tr>
<td>Under 18 years of age, potentially curable disease</td>
</tr>
<tr>
<td><strong>Healthcare setting</strong></td>
</tr>
<tr>
<td>People in their usual place of residence</td>
</tr>
<tr>
<td>Primary and community care</td>
</tr>
<tr>
<td>Secondary care</td>
</tr>
<tr>
<td>Hospice care</td>
</tr>
<tr>
<td><strong>Topics</strong></td>
</tr>
<tr>
<td>Investigation of bone pain in the presence of advanced cancer</td>
</tr>
<tr>
<td>Assessment and prediction of risk of pathological fracture in this population</td>
</tr>
<tr>
<td>The multi-disciplinary management of people at risk of pathological fracture of metastatic bone disease</td>
</tr>
<tr>
<td><strong>Topics not covered</strong></td>
</tr>
<tr>
<td>Management of those that have sustained a pathological fracture due to metastatic bone disease</td>
</tr>
<tr>
<td>Reduction of risk in other types of pathological fracture (e.g. from osteoporotic disease, infection, benign cysts or inherited bone disorders such as osteogenesis imperfecta)</td>
</tr>
</tbody>
</table>
Section 3: Methods

- The guideline is based on the AGREE II criteria and can be found in detail in the Cheshire and Merseyside Palliative and End of Life Care Network Audit Group Guideline Development Manual.\(^1\)

3.1 Clinical Questions & Interventions

- Clinical questions were derived from the previous guidance published in 2005 and reviewed in 2009. These were then refined by the Guideline Development Group which has authored this guideline. The clinical questions were used to guide the literature review in PICO (Patient, Intervention, Control and Outcome) format are:
  
  - How should patients with advanced cancer and bone pain be assessed and investigated by palliative care health professionals?
  - How can palliative care health professionals predict the risk of pathological fracture?
  - What interventions can reduce the risk of pathological fracture?

3.1.1 Outcomes

- To reduce associated morbidities of pathological fracture including pain and impairment of function.

3.2 Literature Search

- Systematic electronic database searches were done to find potentially relevant articles. Ovid MEDLINE, EMBASE, CINAHL and Cochrane databases were searched in June 2013. A full explanation of the search strategy, results and appraisal of evidence can be found on the Cheshire and Merseyside Palliative and End of Life Care Network Audit Group website. Grading of level of evidence and recommendations follows the Cheshire and Merseyside Palliative and End of Life Care Network Audit Group Guideline Development Manual and uses SIGN criteria.\(^1\)

Section 4: Guideline Recommendations

4.1 Assessment and Investigation of Bone Pain

- Bone pain may be due to structural damage, periosteal irritation, nerve entrapment and / or secretion of chemical mediators causing osteolysis e.g. prostaglandins and cytokines. These mediators activate both osteoclasts and nociceptors producing pain and bone destruction.\(^2\)

- Pain may be described as \(^2\):
  - a dull ache to a deep intense pain
  - pain at rest
  - pain exacerbated by weight-bearing
  - importantly, pain which is worse at night

- In order to facilitate the assessment and earlier identification of lesions requiring oncological or orthopaedic intervention, patients should be encouraged to report bone pain promptly.\(^4\) [Level 4]
The clinical conundrum is to determine which pains are due to new or existing metastatic disease and which lesions may progress to a pathological fracture.\textsuperscript{4, 8}

The British Association of Surgical Oncology (BASO) Guidelines (see Table 2) have been developed for the treatment of metastatic bone disease in breast cancer.\textsuperscript{8} The British Orthopaedic Association and the British Orthopaedic Oncology Society consensus statement has reviewed these guidelines and feel they are appropriate for management of metastatic bone disease from all cancers.\textsuperscript{4} [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>Minimal</td>
<td>Known cause for pain&lt;br&gt; Resolves well, usually 2-3 weeks from onset</td>
<td>Normal outpatient review&lt;br&gt; Return to GP if resolution not complete</td>
</tr>
<tr>
<td>Low</td>
<td>Probable cause known.&lt;br&gt; Good resolution over 4-6 weeks</td>
<td>Plain radiograph. If negative no action required.&lt;br&gt; If positive follow advice regarding the need for orthopaedic assessment</td>
</tr>
<tr>
<td>Moderate</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&lt;br&gt; If all negative, review in 8 weeks if symptomatic&lt;br&gt; If one or more tests positive, follow advice regarding the need for orthopaedic assessment</td>
</tr>
<tr>
<td>High</td>
<td>No identified cause for pain.&lt;br&gt; Night pain, severe and / or progressive pain&lt;br&gt; Neurological symptoms and signs</td>
<td>Pain in Appendicular Skeleton&lt;br&gt; Plain radiographs, serum calcium and bone scan within 10 working days. Review one week later&lt;br&gt; If all negative but suspicion high, review in 1 week&lt;br&gt; If one or more tests positive, then follow advice regarding need for orthopaedic assessment&lt;br&gt; Pain in Spine&lt;br&gt; If pain in spine, then arrange MRI of the whole spine within one week&lt;br&gt; If pain in spine and neurological symptoms or signs suggestive of MSCC arrange MRI of the whole spine within 24 hours</td>
</tr>
</tbody>
</table>

Table 2 BASO guidelines for the investigation of bone pain including NICE Guidelines on Metastatic Spinal Cord Compression (MSCC) \textsuperscript{4, 8, 11} [Level 4]
4.1.1 Imaging

4.1.1.1 Plain Radiographs

- 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.\textsuperscript{4} [Level 4]

- Radiograph reports may describe bone metastases as osteolytic (bone appears less dense on imaging), osteoblastic (where bone looks denser or whiter on imaging) or mixed in nature.\textsuperscript{2,4}

- 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 on the report (see 4.2 – Determining Risk of Pathological Fracture).\textsuperscript{8,12,13} [Level 4]

- Plain radiographs may not detect all bone metastases.\textsuperscript{14} If clinical suspicion of metastatic bone disease 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.\textsuperscript{15} [Level 4]

4.1.1.2 Isotope Bone Scans

- Unless plain radiographs have been normal, 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{8} [Level 4]

4.1.1.3 Computerised Tomography (CT)

- Where plain radiographs have been normal and there is increased uptake on an isotope bone scan, CT should be used as it can detect cortical destruction not seen on plain radiographs.\textsuperscript{15} [Level 4]

- CT may also be useful where MRI is contraindicated or not tolerated.\textsuperscript{15} [Level 4]

4.1.1.4 Magnetic Resonance Imaging (MRI)

- MRI is the imaging with the highest sensitivity and specificity in detecting metastatic bone disease. However, the cost, time, tolerability and contraindications to use bar it from first line use.\textsuperscript{15} [Level 4]

- The exception is in suspected metastatic spinal cord compression where MRI is the imaging modality of choice.\textsuperscript{11} [Level 1]

4.2 Determining Risk 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.\textsuperscript{12,13} [Level 4]
The risk of a pathological fracture occurring, and therefore the need to consider prophylactic fixation, may be assessed using either Mirels scoring system \(^{12}\) [Level 2+] (for use in long weight bearing bones of the upper and lower limbs) or Harrington's classic definitions (use restricted to the proximal femur).\(^ {13}\) [Level 3]

### 4.2.1 Mirels Score

In Mirels scoring system (Table 3), the maximum possible score is 12.\(^ {12}\) If a lesion scores 8 or above, then prophylactic fixation is recommended prior to radiotherapy.\(^ {12}\) [Level 2+].

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site</td>
<td></td>
<td>Upper limb</td>
<td>Lower limb</td>
<td>Peritrochanteric</td>
</tr>
<tr>
<td>Pain severity</td>
<td></td>
<td>Mild</td>
<td>Moderate</td>
<td>Functional</td>
</tr>
<tr>
<td>Type of lesion</td>
<td></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>
<td></td>
</tr>
</tbody>
</table>

### 4.2.2 Harrington’s Criteria for Risk of a Pathological Fracture in the Proximal Femur \(^ {13}\)

- Any one of Harrington's classic definitions indicates a high risk of pathological fracture in the proximal femur (see Table 4).\(^ {13}\) [Level 3]

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Harrington’s Criteria for Risk of a Pathological Fracture in the Proximal Femur (^ {13}) [Level 3]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>50% of circumferential cortical bone has been destroyed</td>
</tr>
<tr>
<td>2.</td>
<td>Where pain with weight-bearing stresses persists, increases or recurs, despite adequate local irradiation</td>
</tr>
<tr>
<td>3.</td>
<td>Lesions in the proximal femur in excess of 2.5cm in any dimension</td>
</tr>
<tr>
<td>4.</td>
<td>Lesions in the proximal femur associated with avulsion of the lesser trochanter</td>
</tr>
</tbody>
</table>
4.3 Management of Patients at Risk of Pathological Fracture

4.3.1 Orthopaedic Surgery

- Patient with symptomatic bone metastases who may benefit from intervention should be referred urgently to an orthopaedic clinic or be discussed at a site-specific multi-disciplinary team meeting if they have any of the following:[Level 4]
  - Structurally significant bone destruction
  - Uncertainty whether the destruction is significant
  - Pain of sudden onset (or change in character) that is exacerbated by movement
  - Solitary bone metastasis (to exclude different primary)

- Referral to an orthopaedic surgeon is appropriate in the following situations [Level 2+]:
  - Prophylactic fixation of metastatic deposits when there is a high risk of fracture i.e. Mirels score equal or greater than 8 (see Table 3) or the presence of any one of Harrington's classic definitions (see Table 4)
  - Stabilisation or reconstruction after pathological fracture
  - Decompression of the spinal cord and nerve roots and / or stabilisation for spinal instability. (See Guidelines on the Management of Metastatic Spinal Cord Compression)

- A lead orthopaedic surgeon for appendicular metastatic bone disease should be identified at each acute NHS Trust. [Level 4]

4.3.1.1 Other surgical interventions

- Radiofrequency ablation of bone metastases (the use of high frequency electrical currents to destroy cancer cells) is an emerging alternative therapy for the management of bony metastatic disease. Access to this modality is limited and varies across the United Kingdom. Referral to an appropriate interventional radiologist may be beneficial for effective pain palliation and local control of disease into the future.

- 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. Referral to a spinal orthopaedic surgeon for assessment may be advisable.

4.3.2 Oncology

4.3.2.1 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. Following orthopaedic intervention, radiotherapy should be considered by appropriate specialists within the context of the multidisciplinary team. [Level 2-]

4.3.2.2 Bisphosphonates

- Bisphosphonates should be considered, where clinically appropriate, for the prevention of skeletal related events in people with bone metastases from breast cancer and those with multiple myeloma. [Level 1+]

- There is further information on the use of bisphosphonates for malignant bone pain in Guidelines on the Use of Bisphosphonates in the Management of Malignant Bone Disease. [Level 4]

4.3.2.3 Denosumab

- Denosumab is recommended as an option for preventing skeletal-related events from solid tumours, if bisphosphonates would otherwise be prescribed. It is however not recommended by NICE for use in prostate cancer. [Level 1+]

- Similar to bisphosphonates, denosumab carries the risk of potential osteonecrosis of the jaw. It can be used in patients with poor renal function. [Level 1+]

- The choice of use of a bisphosphonate or denosumab in mitigating skeletal related events should be made by the treating oncologist. [Level 1+]

4.3.2.4 Other Medication

- There are a number of medications which in some animal models can impair bone healing or are associated with human osteoporotic fractures, including NSAIDs, corticosteroids and proton pump inhibitors. Currently there is insufficient evidence in pathological fractures in humans to influence prescribing of these medications. [Level 4]

Section 5: Standards

1. Reports of bone pain should be investigated following British Association of Surgical Oncology (BASO) Guidelines. [Grade D]

2. If Mirels’ Score or Harrington’s Criteria deem there is significant risk of a pathological fracture, a decision about orthopaedic review should be made based on fitness for surgery and patient preference. The outcome of the decision should be recorded in the case notes. [Grade D]

3. Following any orthopaedic intervention (prophylactic stabilisation or fracture management) patients with a performance status of 2 or less should be discussed with an oncologist regarding the possibility of further therapy. The outcome of the decision to refer or not refer should be recorded. [Grade D]

4. Patients with a performance status of 2 or less presenting with a new or symptomatic lesion due to metastatic bone disease should be discussed with an oncologist for consideration of further therapy (e.g. hormonal manipulation, bisphosphonates, chemotherapy, radiotherapy), regardless of orthopaedic intervention. [Grade C]
Section 6: Applications and Implications

Economic modelling performed by NICE of bisphosphonate and denosumab therapy has suggested that implementing these therapies is cost-effective.\(^5\) A similar review of the effectiveness of surgical prophylaxis has not been carried out. There is no evidence of the impact of this on cost-effectiveness of palliative care services. Intuitively, reduction of risk and therefore actual pathological fracture is likely to reduce pain and morbidity. This has implications of improved quality of life and therefore reduction of use of prescribed analgesia, therapy services, equipment and domiciliary and nursing care through NHS Continuing Healthcare funding.

The most pressing implication is of education and training of palliative care professionals as demonstrated in audit results.\(^2\)\(^7\) The Cheshire and Merseyside Cancer Network have resources to support education in implementing this guideline at [http://www.cmscnsenate.nhs.uk/strategic-clinical-network/our-networks/palliative-and-end-life-care/audit-group/](http://www.cmscnsenate.nhs.uk/strategic-clinical-network/our-networks/palliative-and-end-life-care/audit-group/).

Recommendations for research and service improvement include:

- Reviewing the BASO guidance given the changing availability of imaging modalities
- The BASO guidelines primarily extrapolate the experience of managing metastatic breast cancer – is there a different natural history in different types of cancer?
- Design, implementation and evaluation of resources and interventions to support people with cancer in reporting bone pain to determine clinical and cost effectiveness

Section 7: Acknowledgments

We acknowledge the work of the following in supporting these guidelines:

- Dr Helen Emms, Consultant in Palliative Medicine, Wirral Hospice St John’s and Mr Nicholas Emms, Consultant Orthopaedic Surgeon at St Helens and Knowsley Hospitals NHS Trust, who developed the initial guidelines in 2005
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Section 8: Declarations of Interest

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Section 9: Review Date

The guidelines will be reviewed three years after publication as outlined in the Cheshire and Merseyside Palliative and End of Life Care Network Audit Group Guideline Development Manual.
References


