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Impending fracture: A difficult diagnosis

Andrea Piccioli [a], Maria Silvia Spinelli [b,*], Giulio Maccauro [b]

[a] Orthopedics Oncology, "Palazzo Baleani", Teaching Hospital Policlinico Umberto I, Rome, Italy
[b] Department of Orthopaedic Oncology, Agostino Gemelli Hospital, Catholic University of Rome, Largo Francesco Vito 1, Rome, Italy

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ABSTRACT

Introduction: The concept of impending fracture has been developed to help address this difficult skeletal-related problem. There is no consensus on the subject in the literature and a specific definition of impending fracture has not been outlined.
Discussion: There is disagreement in the literature on the best criteria for the diagnosis of impending fracture. A method of discrimination for patients who need preventative treatment for a metastatic lesion has not yet been established.
Conclusions: Current score systems consider variables like size, location and treatment response and are easy to remember. However, these score systems have never been evaluated prospectively and rigorously, their sensitivity is low and they do not take into account potentially relevant factors that can influence patient prognosis. A consistent tool to evaluate impending fractures would be of great value to guide the treatment of metastatic bone disease.

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Introduction

Bone is the third most common site of metastases after lungs and liver [1,2]. Bone metastases occur in up to 70% of advanced breast and prostate cancers and 15–30% of other common cancers, such as those of the lung, colon, bladder, rectum, kidney or uterus [3]. The spine is the most common site of skeletal metastases, followed in order of frequency by pelvic bones, ribs, and upper and lower extremities [4,5].

Pathological fracture in patients with metastatic bone disease is a severe emergency that should be avoided [6]. The median survival of patients without fracture is significantly longer than that of patients with fracture and underlines the presence of a fracture as a negative prognostic factor. These results indicate that prophylactic osteosynthesis is an important goal before fractures occur [7]. A pathological fracture has severe complications, including rapid decrease in autonomy, pain, hospitalisation, and interruption of chemotherapy (or other adjuvant therapies). Furthermore, performing useless surgical procedures in these patients could be dangerous. The orthopaedic oncologist has to achieve the goal of a correct diagnosis of impending fracture. Prophylactic osteosynthesis may potentially minimise complications and maximise patient quality of life, but there is no consensus on the best criteria for the diagnosis of impending fracture [8].

Complications of metastatic bone disease dramatically affect patient quality of life and prognosis and add to the resource utilisation and costs of metastatic bone disease. The improved survival of cancer patients is likely to be associated with an increase in the prevalence of bone metastases and consequently the emphasis should be placed on maintaining quality of life. Prophylactic treatment to prevent fracture will help to maintain patient function and mobility [9]. Moreover, prophylactic fixation can be technically easier than reactive surgery, and is likely to be associated with less patient morbidity, better recovery, and shorter postoperative care and length of hospital stay [10]. However, despite the advances in the field of orthopaedics and the availability of many surgical options, there is still a lack of objective criteria to select patients who would benefit most from surgery. The management of metastatic patients should comprise a multidisciplinary and coordinated approach that involves orthopaedic surgeons and radio-oncologists.

Discussion

Impending fracture

The concept of impending fracture has been developed to help address this difficult skeletal-related problem. There is no

* Corresponding author at: Largo A. Gemelli, 1, 00168 Rome, Italy.
Tel.: +39 06 30154248; fax: +39 06 3051161.
E-mail address: msilviaspinelli@yahoo.it (M.S. Spinelli).

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consensus on the subject in the literature and a specific definition of impending fracture has not been outlined.

The authors define the concept of impending fracture as a pathological condition of imminent fracture risk on a pre-existent bone lesion. Impending fracture refers to the state of a bone where a pathological fracture appears almost certain if no preventative action is taken [11]. Pathological fractures occur mainly in the femur (72.5%) and humerus (18.1%) and only rarely in the spine (2.7%) [12]. Severity of pain and tumour characteristics, including site and size, both affect risk of fracture. Accurate prediction of peripheral fracture is necessary to guide the surgeon in the decision-making process. For this reason, several scoring systems have been developed, including Mirels' scoring system [13] and Harrington's criteria [14]. However, there is currently no definitive and valuable tool that can be used universally to objectively quantify the risk of sustaining a pathological fracture through a metastatic lesion in a long bone. The ideal classification system would be a clear communication tool that guides treatment planning, enables prediction of prognosis, and has excellent inter- and intra-observer reliability. Use of this ideal system would help circumvent unnecessary surgery and prevent pathological fracture; these are critical priorities when aiming to minimise the morbidity of metastatic bone disease.

Mirels' scoring system

Mirels' scoring system is the most commonly used scoring system for the risk of pathological fracture on a known metastasis. The British Orthopaedic Association recommends the use of Mirels' system when determining the need for prophylactic surgery [15]. This scoring system combines several radiological and clinical factors, such as location (upper limb, lower limb, peritrochanter), radiographic appearance (lytic, blastic, or mixed), size of the lesion (<1/3, 1/3–2/3, >2/3), and accompanying pain (mild, moderate, functional). Each parameter is scored from 1 to 3, resulting in a total score from a minimum of 4 to a maximum of 12. The initial validation study retrospectively analysed 78 metastatic long bone lesions [13]. At 6 months, 51 lesions did not fracture and 27 fractured. As the score increased above 7, so did the percentage risk of fracture. Lesions with scores ≤ 7 had a low risk (5%) of fracture within a 6-month period, thus can be safely irradiated. Lesions with a score of 8 had 15% risk of fracture, so clinical judgement is required to determine the best course of action as this is a grey zone. Lesions with scores ≥ 9 had very significant risk (33%) that justifies prophylactic fixation. Reproducibility, validity and application of Mirels' score across various experience levels and training backgrounds were investigated successively [16]. Twelve femoral metastatic lesions (before treatment or fracture) were analysed by 53 participants, including musculoskeletal radiologists, orthopaedic attending physicians, fellowship-trained practicing orthopaedic oncologists, and radiation or medical oncologists. Excluding the radiation and medical oncologists, there was significant agreement across experience categories for overall Kappa and for the concordance for individual and overall scores. Radiation and medical oncologists had the greatest variability in score (SD, 1.54) and also significantly underscored the lesions. The medical professionals in these categories often see metastatic patients first and need a good screening tool to select patients who should be referred to higher experience level groups for final decisions regarding prophylactic stabilisation. The overall sensitivity of the applied Mirels' system was 91% for determining the likelihood of pathological fracture, which across all experience categories was greater than the sensitivity of using clinical judgement alone. This tool is therefore helpful to rule out an impending fracture. The overall specificity was 35%, which means the score would overestimate the risk of fracture and a strict application of the Mirels' guidelines would potentially result in unnecessary procedures in two out of three of the patients. This limitation was confirmed in 2003 by Van der Linden et al. [17] who studied the prognostic value of conventional risk factors and the scoring system of Mirels in 102 patients with femoral metastases who were treated conservatively. Only axial cortical involvement >30 mm ($p = 0.01$), and circumferential cortical involvement >50% ($p = 0.03$) were predictive of fracture. Mirels' scoring system was insufficiently specific to predict a fracture ($p = 0.36$). The use of axial cortical involvement instead of Mirels' scoring system or other conventional risk factors seems to reduce the number of patients referred for unnecessary prophylactic osteosynthesis. Moreover, one subsequent study showed that Mirels' scoring system is not applicable indistinctly to various sites [18]. The considerable differences in load-bearing requirements between the upper and lower extremities, for example, mean that the humerus has a different fracture susceptibility profile compared with the femur. A total of 17 case histories and plain radiographs of 16 patients with humeral metastases were presented through a web-based survey to 39 physicians with varying training and experience. Mirels' threshold of 9 points resulted in a sensitivity level of 14.5% and specificity level of 82.9%. Lowering the threshold to 7 for the humerus preserved the same level of sensitivity and specificity that the Mirels' rating system displays for other long bones. Sensitivity for correctly predicting a humeral fracture increased to 81%, but at a cost of reducing specificity to 32%. This means that 10% to 20% of impending pathological fractures may be missed using these definitions, and also unnecessary prophylactic stabilisation may be performed as reported for femoral lesions.

Although Mirels' scoring system had been independently validated twice before [16,18], it was not as consistent as the conventional system in classifying impending pathological fractures [19]. The conventional system was introduced by Carnesale and recommended prophylactic surgery for tumour with transverse and longitudinal diameters > 3 cm or cortices involvement $> 50\%$. El-Husseiny and Coleman [19] examined the intra- and inter-observer reliability of these scoring systems and showed better inter- and intra-observer agreement of the conventional system compared with Mirels' scoring system; this may be because the conventional system was simple and easier to reproduce and had fewer variables. However, neither system assesses patient prognosis after the procedure, or considers life expectancy or the patient's situation relative to the possible complications and risks of the intervention. Underlying diagnosis, comorbidities, previous radiotherapy treatment, and other sites of disease should be taken into account. Patients with slowly growing primary malignancies appear to recover well from prophylactic procedures [20], while the presence of visceral, cerebral or multiple skeletal metastases, a poor Eastern Cooperative Oncology Group (ECOG) status, and the use of previous chemotherapy all reduce survival rate [21]. Weber et al. [22] reported that Mirels' score "does not take into account the functional demands of patients, their anticipated longevity, or their baseline osteoporosis"; they suggested to use Mirels' score along with assessments of cortical destruction and the overall functional status of the patient. Numerous factors should be considered to develop a new consistent rating system that could predict impending fractures and guide the management of metastatic patients.

Harrington's criteria

Prior to Mirels' publication, Harrington [23] proposed a definition of impending pathological fracture of the long bones. The definition included the following parameters: cortical bone destruction greater than 50%, lesion larger than 2.5 cm, a pathological avulsion fracture of the lesser trochanter, and persisting stress pain despite irradiation. These were all considered

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