Clin Orthop Relat Res (2010) 468:2825–2827
DOI 10.1007/s11999-010-1326-4

IN BRIEF

In Brief

Classifications in Brief

Mirels' Classification: Metastatic Disease in Long Bones and Impending Pathologic Fracture

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Published online: 30 March 2010

History

The earliest efforts to predict the risk of an impending fracture in the presence of tumor dates to the 1960s [1–3, 10, 11]. Although some of the earlier studies made positive contributions, they lacked supportive statistical evidence. Later, several larger and well-documented studies were designed to identify the features of an impending pathologic fracture [4, 7, 8]. Although the statistical power of the later studies was improved, they failed to reach an agreement regarding specific criteria on which to base the decision of prophylactic fixation. It was not until 1989 when Hilton Mirels proposed a rating system to classify pathologic fracture risk [12].

Purpose

Metastasis is the most common malignant process affecting the bones. Of all the new cases of invasive carcinoma diagnosed annually in the United States, approximately 50% eventually metastasize to bones [7]. Current advances in treatment options have improved the mean survival for patients with disseminated disease [13]. These metastatic lesions and other destructive processes affecting bones such as myeloma and lymphoma, predispose the bone to an impending fracture [16]. Such a high-risk lesion can be treated with radiotherapy, drugs (bisphosphonates), and surgery [20]. Surgery usually is reserved for lesions at the highest risk of fracture or intractable pain. A pathologic fracture in these settings would expose the patient to extreme pain, urgent hospitalization, and the risk of surgery in less than ideal circumstances. Thus, predicting an impending fracture and prophylactic fixation in an elective setting are critical to avoid debilitating complications. An ideal staging system should be practical, reproducible, and accurately predict risk.

Mirels' Staging System

Mirels proposed a scoring system based on four characteristics: (1) site of lesion; (2) nature of lesion; (3) size of lesion; and (4) pain. All the features were assigned progressive scores ranging from 1 to 3 (Table 1).

Site of lesion includes three categories: upper extremity, lower extremity, and peritrochanteric area of femur (peritrochanteric). These sites were assigned increasing scores from 1 to 3, respectively. It is commonly believed that lesions in the peritrochanteric area are high risk for fracture [6]. It is also believed chances of pathologic fractures are greater for weightbearing bones than for nonweightbearing bones [15]. However, in Mirels' original investigation, these commonly held beliefs were not confirmed and site of lesion did not independently predict a fracture [12].

The nature of the lesion is also subdivided into three categories with increasing scores (1–3): blastic, mixed, and lytic. In the original investigation by Mirels, the rates of fracture in the three categories were 0%, 32%, and 48%, respectively [12].

Each author certifies that he or she has no commercial associations (eg, consultancies, stock ownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

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Table 1. Mirels' scoring system

Score	Site of lesion	Size of lesion	Nature of lesion	Pain
1	Upper limb	< ⅓ of cortex	Blastic	Mild
2	Lower limb	⅓–⅔ of cortex	Mixed	Moderate
3	Trochanteric region	> ⅔ of cortex	Lytic	Functional

(Adapted and published with permission of Lippincott Williams & Wilkins from Mirels H. Metastatic disease in long bones: a proposed scoring system for diagnosing impending pathologic fractures. *Clin Orthop Relat Res.* 1989;249:256–264.)

Size of lesion is expressed as a fraction of the cortical thickness. Progressively increasing scores (1–3) are assigned to lesions/cortex ratios of < ⅓, ⅓ to ⅔, and > ⅔. In the original evaluation, the rate of pathologic fracture was 0% for lesions less than ⅓ the size of the cortex, 5% for lesions between ⅓ to ⅔ the size of the cortex, and 81% for lesions occupying more than ⅔ of the cortex [12].

Pain is the only subjective variable in this classification system. Mild, moderate, or functional pain is assigned scores from 1 to 3, respectively. Rate of fracture was only 10% among patients with mild to moderate pain. However, all the patients with functional pain progressed to a fracture. Mirels also reported an association between pain and the size of the lesion [12].

Based on an overall score, a recommendation for or against prophylactic fixation of a lesion is given. According to Mirels' recommendation, prophylactic fixation is highly indicated for a lesion with an overall score of 9 or greater. A lesion with an overall score of 7 or less can be managed using radiotherapy and drugs. An overall score of 8 presents a clinical dilemma. The probability of fracture is only 15% and Mirels recommended the attending physician use clinical judgment in such cases and consider prophylactic fixation [12] (Table 2).

The classic guidelines for treating lower extremity bone metastases have been attributed to Harrington [7]. Before Mirels' classification, Harrington recommended prophylactic stabilization of an impending fracture based on the findings of earlier studies [6, 7, 15, 17]. The variables deemed important by Harrington included size and nature of the lesion, association with progressively increasing pain, or radiographic progression. He defined an impending fracture as a 'lytic' bony lesion, involving more than ½ the diameter of the bone, greater than 2.5 cm in greatest diameter, or as associated with persistent pain or radiographic progression after radiation [7].

Table 2. Mirels' clinical recommendations

Mirels' score	Clinical recommendation
≤ 7	Radiotherapy and observation
8	Use clinical judgment
≥ 9	Prophylactic fixation

Confirmation/Validation

Mirels' classification system for impending pathologic fracture has been confirmed in two studies: (1) intramurally by Mirels [12] (78 lesions) and (2) extramurally in a study conducted by Damron et al. [5] (12 lesions).

Damron et al. [5] performed an evaluation to determine the reproducibility, validity, and applicability across various experience levels and training backgrounds of physicians (53 physicians). The individual Mirels' score component that showed the greatest variability was pain because of its subjective nature. Concordance was statistically significant across all examiners of all experience categories. Validity was assessed by separately analyzing the data from seven patients who did not have prophylactic femur stabilization. The pooled odds ratio in favor of being predicted correctly to produce fracture using Mirels' scoring system was 4.56; greater than the pooled odds ratio (2.13) based on an independent clinical judgment. Overall sensitivity was 91% and specificity was 35%. The study concluded Mirels' system is reproducible, valid, and more sensitive than clinical judgment across all experience levels [5].

Limitations

The limitations of Mirels' classification system include the following. (1) There is a treatment dilemma at a total score of 8 regarding whether to use prophylactic fixation for the patient or to treat nonsurgically. Strict application of Mirels' recommendation would result in unnecessary prophylactic fixation in ⅔ of the patients [5]. Specific criteria are needed to predict impending fracture at borderline scores. (2) Although the reported sensitivity for Mirels' classification is 91%, a modest specificity of 35% increases the chances of false positives and thus unnecessary procedures. (3) In the study by Damron et al. [5], medical and radiation oncologists had the greatest variability in their scores. The role of additional education regarding Mirels' system among this group of physicians is yet to be determined. As a patient with a bony metastasis is more likely to present to a medical or a radiation oncologist, the availability of a useful screening tool for this group of physicians is imperative. (4) Inclusion of site as a criterion

in the Mirels' staging system is contradictory to the findings of his study [12]. There was no association reported between site and development of fracture in the above-mentioned study. However, there was an association between histology of the primary lesion and development of fracture, a factor not included in the classification system. Similarly, there was an association between size of lesion and development of pain and both factors have been included as a part of the classification system. (5) Numerous other factors should be investigated as predictors of fracture including previous radiotherapy treatment, comorbidities, expected duration of survival, other sites of disease, activity level, and bone mineral density [5]. (6) Mirels' classification is applicable only to metastatic lesions in long bones. It cannot be applied to the vertebral column. The spine is the most common location for metastatic breast cancer and an alternative noninvasive approach was suggested by Snyder et al. [18].

Conclusions/Uses

Mirels' classification system for impending pathologic fracture is a valid screening tool that is reasonably reproducible only for metastatic lesions in long bones. It has been assessed independently and proved superior to clinical judgment alone [5]. However, there is room for improvement and more specific parameters are needed. Recent advancements in CT-based structural rigidity analysis have allowed for assessment of densitometric, morphometric, and mechanical characteristics of the human skeleton. There have been reports claiming sensitivity of 100% and specificity as much as 70% in prediction of fracture risk in patients with metastatic spine lesions using this technology [9, 14, 19]. In the future, this technology potentially can be applied to the lesions of long bones.

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