ISTANBUL UNIVERSITY PRESS

RESEARCH / ARAŞTIRMA
DOI: 10.26650/IUITFD.1037033
İst Tıp Fak Derg 2022 / J Ist Faculty Med 2022

INTER- AND INTRA-OBSERVER RELIABILITY OF THE MIRELS' SCORING SYSTEM FOR THE DETERMINATION OF PATHOLOGICAL FRACTURE RISK IN METASTATIC BONE LESIONS AMONG ORTHOPEDIC SURGEONS WITH DIFFERENT LEVELS OF EXPERTISE

METASTATİK KEMİK LEZYONLARINDA PATOLOJİK KIRIK RİSKİNİN BELİRLENMESİNDE KULLANILAN MİRELS SKORLAMASININ FARKLI KIDEMLERDEKİ ORTOPEDİK CERRAHLAR ARASINDAKİ GÜVENİLİRLİĞİ

Emre KOCAZEYBEK[1], Emre MERİÇ[2], Hasan Memet CHOUSEIN[3], Ahmet Müçteba YILDIRIM[3], Yavuz SAGLAM[3], Ali ERŞEN[3], Ahmet SALDUZ[3]

[1]Haseki Training and Research Hospital, Department of Orthopedics and Traumatology, Istanbul, Turkiye
[2]Basakşehir Cam and Sakura City Hospital, Department of Orthopedics and Traumatology, Istanbul, Turkiye
[3]Istanbul University, Istanbul Faculty of Medicine, Department of Orthopedics and Traumatology, Istanbul, Turkiye

ORCID IDs of the authors: E.K. 0000-0001-5861-8653; E.M. 0000-0003-0968-0500; H.M.C. 0000-0002-9518-6623; A.M.Y. 0000-0003-4460-815X; Y.S. 0000-0003-4475-8211; A.E. 0000-0001-6241-2586; A.S. 0000-0001-9448-6416

Cite this article as: Kocazeybek E, Meric E, Chousein HM, Yildirim AM, Saglam Y, Ersen A, et al. Inter- and intra-observer reliability of the Mirels' scoring system for the determination of pathological fracture risk in metastatic bone lesions among orthopedic surgeons with different levels of expertise. J Ist Faculty Med 2022;85(4):510-6. doi: 10.26650/IUITFD.1037033

ABSTRACT

Objective: To assess inter- and intra-observer reliability of Mirels scoring for the determination of pathological fracture risk in metastatic bone lesions of 30 patients among six different levels of experienced orthopedic surgeons who were trained in the same university clinic.

Material and Methods: Thirty patients were randomly selected from oncology unit consultations. Six observers were selected in accordance to their orthopedic experience. Mirels parameters except pain were evaluated by observers on two different times without the observers being aware of each other.

Results: The Fleiss' Kappa values were detected as κ=0.21, p<0.0001, and κ=0.15, p<0.0001 by inter-observers at the first and second observational points, respectively. The Kappa values were in perfect (κ=0.95), fair (κ=0.27) and fair (κ=0.10) agreements for the region, size and type of the metastatic involvement by inter-observers at the first observational point. The same parameters had similiar scores as κ=0.83, κ=0.13 and κ=0.28 for region, size and type for the second observation. Fair (κ=0.333), moderate (κ=0.413), fair (κ=0.225), slight (κ=0.035), fair (κ=0.369

ÖZET

Amaç: Bu çalışmanın amacı, metastatik kemik lezyonları nedeniyle oluşan patolojik kırık riskinin tespiti için geliştirilmiş Mirels skorlamasının, metastatik lezyon tanısı alan 30 hastada aynı üniversite kliniğinde eğitim almış altı farklı tecrübedeki ortopedist arasındaki güvenilirliğini değerlendirmekti.

Gereç ve Yöntem: Şiddetli veya en az orta derecede ekstremite ağrısı nedeniyle onkoloji birimi tarafından konsülte edilen rastgele 30 hasta seçildi. Ağrı dışındaki parametreler gözlemciler tarafından bir ay arayla birbirlerinden habersiz olarak değerlendirildi.

Bulgular: Gözlemciler arasındak Fleiss' Kappa değerleri, sırasıyla birinci ve ikinci gözlem noktalarında κ=0,21, p<0,0001 ve κ=0,15, p<0,0001 olarak tespit edildi. İlk değerlendirmede gözlemciler arası metastatik tutulumun lokalizasyonu, boyutu ve tipi için Kappa değerleri sırasıyla mükemmel (κ=0,95), zayıf (κ=0,27) ve zayıf (κ=0,10) olarak bulundu. Aynı parametreler bir ay arayla ikinci kere değerlendirildiğinde ise lezyonun lokalizasyonu, boyutu ve tipi için κ=0.83, κ=0.13 ve κ=0.28 olarak benzer puanlara sahipti. Gözlemcilerin kendi içlerinde, iki farklı zaman diliminde

Corresponding author/İletişim kurulacak yazar: Emre KOCAZEYBEK – emrekcz@gmail.com

Submitted/Başvuru: 19.12.2021 • **Revision Requested/Revizyon Talebi:** 24.01.2022 •
Last Revision Received/Son Revizyon: 30.05.2022 • **Accepted/Kabul:** 13.07.2022 • **Published Online/Online Yayın:** 17.08.2022

and poor (κ=0.030) evidence of agreements were detected in the comparison of the first and second observations for total scores in seniority order.

Conclusions: Kappa analysis showed perfect agreement for region, but slight to fair for size and type. There was a significant difference in overall scores across experience levels for the most and least experienced observers. A new rating system with revised parameters may be required to predict impending fractures.

Keywords: Pathological fractures, mirels, bone metastasis

ağrı olmadan diğer parametrelere verdikleri cevapların toplamdaki skorları kıdem sırasına göre zayıf (κ=0,333), orta (κ=0,413), zayıf (κ=0,225), önemsiz düzeyde (κ=0,035), zayıf (κ=0,369) ve kötü (κ= -0,030) olarak görüldü.

Sonuç: Kappa analizine göre gözlemciler arasında lezyonun lokasyonu için mükemmel uyum görülürken, lezyonun tipi ve boyutu içinse önemsiz düzeyde ve zayıf bir uyum görülmüştür. Total skorlarda en deneyimli ve en az deneyimli gözlemciler arasında önemli bir fark tespit edilmiştir. Bu sebeple yaklaşan (impending) kırıkları öngörmek ve hastaların prognozunu dikkate almak için parametrelerinin revize edildiği yeni bir derecelendirme sistemi gereklidir.

Anahtar Kelimeler: Patolojik kırıklar, mirels, kemik metastazı

INTRODUCTION

More than 75% of diagnosed carcinoma patients exhibit an evidence of skeletal metastases during their treatment (1). The most prevalent etiology of skeletal system metastases are lung and breast cancers (2). Once cancer spreads to the skeleton, cure can rarely be attained (3). The most common regions of metastases are the spine and the pelvis, followed by the femur (4). The diagnosis is based on signs, symptoms, clinical findings and radiological imaging. The mobility of these patients usually decreases due to severe pain. Spinal cord compression due to pathologic vertebral fracture and pathologic fractures of a lower extremity are two major reasons of morbidity which may have devastating consequences for their ongoing oncological treatment (5).

With the increase in the global life expectancy of patients with bone metastasis, it is crucial to determine the appropriate protocols aiming to improve the quality of patients life. This has to be done even before the occurrence of a pathologic fracture, and to preserve such stabilization for the rest of their life (6).

Prediction of bone fracture risk due to metastasis, a scoring system including four parameters including region, pain, type (blastic, lytic or mixed) and the lesion size was described by Mirels et al (7). The rating system is based on 4 parameters, each scored from 1 to 3 (Table 1). The individual scores are added for a final total score. Treatment modalities are based on the risk of fracture according to the final score (Table 2).

Table 1: Mirels' scoring system (7)

Parameter	Score		
	1	2	3
Site	Upper limb	Lower limb	Peritrochanter
Pain	Mild	Moderate	Severe
Lesion	Blastic	Mixed	Lytic
Size	<1/3	1/3-2/3	>2/3

Table 2: Mirels' definitions and treatment recommendations (7)

Risk of pathological fracture	Total score	Treatment recommendations
Impending	≥9	Prophylactic stabilization
Borderline	8	Consider stabilization
Not impending	≤7	Nonoperative care

In this study, we aimed to investigate the intra- and inter-observer reliabilty of Mirels' scoring for the determination of pathological fracture risk in metastatic bone lesions of 30 patients among six different levels of experienced orthopedic surgeons who were trained in the same orthopedics clinic.

MATERIAL AND METHODS

This retrospective study was performed in accordance with the principles of the Declaration of Helsinki. The review included 30 patients radiologic demonstrations who were under oncologic treatment for a primary cancer diagnosed with bone metastasis at a single tertiary referral center. This study was approved by the ethics committee of the Istanbul Faculty of Medicine Clinical Research Ethics Committee, Istanbul University (Date: 11.02.2022, No: 03).

The thirty patients included in this study were randomly selected from oncology unit consultations. Patients with a pathological fracture at the time of initial presentation, patients without a standard radiograph of the painful extremity and patients with previous adjuvant radiotherapy (RT) to metastatic lesion were excluded from study. Plain radiographs of the 30 patients were obtained from the archives of our hospital server.

Six observers were selected in accordance to their orthopedic experience as following; one senior orthopedic oncologist; one senior orthopaedic surgeon of shoulder and elbow, one senior orthopedic surgeon, one junior orthopaedic surgeon, one senior resident of orthopedics and also one junior resident of orthopedics.

All observers were blinded to patients' data. Scoring was done to the region (upper extremity, lower extremity and trochanteric region), size (<1/3, 1/3-2/3, >2/3) with electronic ruler and type (blastic, mixed, lytic) of metastatic lesions by evaulating plain radiographs individually according to the Mirels' scoring system. To remove possible biases, pain criteria was not evaluated and other parameters of the Mirels Classification were based on by observers (8, 9). Therefore, scores were recorded from nine instead of twelve. Parametres were evaulated on two different times without the observers being aware of each other.

Statistical evaluation

The Fleiss' Kappa statistic was used for inter-observer agreement in each two time points (one month interval) individually. The intraclass correlation coefficient (ICC), shows how strongly units in the same group resemble each other and indicates the reliability of inter-observer agreement in each time point. The Kappa statistic (Cohen's Kappa coefficient) was used for intra-observer agreement (Table 3) (10). SPSS 24.0 was used for statistical analyses to evaluate intra observer variability and ICC value, but Stata 13.0 was performed for determining Fleiss Kappa coefficient.

RESULTS

Region scores for the first and second observational points were shown in Table 4, respectively. The Fleiss' Kappa value was detected as 0.95, z=27.47, p<0.0001, according to the region of metastatic bone involvement by inter-observers (Table 5). The Kappa coefficient was in perfect agreement for the region by inter-observers. The intraclass correlation coefficient (ICC) was calculated as 0.93, and it indicates a good reliability of ratings by inter-observers (high similarity between ratings from the same group). Similar results were detected at the second observational time between scores by inter-observers as the Fleiss' Kappa=0.83, z=24.09, p<0.0001 and ICC=0.99.

Table 3: The Kappa statistic agreement scores (10)

Value of κ	Agreement
<0	Poor agreement
0.00-0.20	Slight agreement
0.21-0.40	Fair agreement
0.41-0.60	Moderate agreement
0.61-0.80	Substantial agreement
0.81-1.00	Almost perfect agreement

The second criteria that was evaluated by observers was the size (<1/3, 1/3-2/3, >2/3) of the metastatic lesions. Scores given for the size of the lesions for the first and second observational time, are shown in Table 4. The Fleiss' Kappa value was detected as 0.27, z=7.32, p<0.0001, according to the size of metastatic bone involvement by inter-observers respectively (Table 5). The Kappa coefficient was detected as fair agreement for the size of lesion by inter-observers. Intraclass correlation coefficient (ICC) was calculated as 0.83, and it indicates a good reliability of ratings by inter-observers. Similar

Table 4: Inter-observer scores of Mirels criteria

	Region			Size			Type		
	UE	LE	PT	<1/3	1/3-2/3	>2/3	Blastic	Mixed	Lytic
	F/S	F/S	F/S	F/S	F/S	F/S	F/S	F/S	F/S
Orth. Onco	15/15	6/7	9/8	11/1	11/5	8/24	1/8	2/12	27/10
Sho&Elb Orth	15/15	5/7	10/8	3/15	8/7	19/8	2/1	11/11	17/18
Senior Orth	15/15	6/7	9/8	1/2	6/13	23/15	1/0	13/9	16/21
Junior Orth.	15/15	5/4	10/11	2/4	6/4	22/22	6/5	11/4	13/21
Sen. Orth Res	15/15	5/4	10/10	2/2	16/12	12/16	1/1	5/14	24/15
Jun Ort. Res.	15/15	7/8	8/9	2/0	9/8	19/22	3/4	8/9	19/7
Total: 30									

F/S: First observational point/Second observational point, UE: Upper Extremity, LE: Lower extremity, PT: Pertrochanteric, Ort. Onco: Orthopedic Oncologist, Sho&Elb Orth: Senior Shoulder and Elbow Surgeon, Senior Orth: Senior Orthopedic Surgeon, Junior Orth: Junior Orthopedic Surgeon, Sen Orth Res: Senior Orthopedic Resident, Jun Ort. Res.: Junior Ort hopedic Resident results (slight agreement) were detected at the second observational time between scores by inter-observers as the Fleiss' Kappa=0.13, z=3.34, p<0.0001 and ICC=0.76.

The third criteria evaluated by the observers was type (blastic, mixed, lytic) of the metastatic lesion. Scores given for type of the lesions for the first and second observational times are shown in Table 4. The Fleiss' Kappa value was detected as 0.10, z=2.72 p=0.0032, according to the type of lesions by inter-observers (Table 5). The Kappa coefficient was detected as slight agreement for the type by inter-observers. The intraclass correlation coefficient (ICC) was calculated as 0.50, and it indicates a moderate reliability of ratings by inter-observers. Similar but a little better results (fair agreement) were found at the second observational time between scores by inter-observers as the Fleiss' Kappa=0.28, z=7.57, p<0.0001 and ICC=0.78.

Lastly, total scores for the first and second observational times are shown in Table 6. The Fleiss' Kappa value was detected as 0.2, z=8.05, p<0.0001 by inter-observers (Table 5). The Kappa value was detected as fair agreement by inter-observers, and decreased due to decreasing seniority. The intraclass correlation coefficient (ICC) was calculated as 0.87, and it indicates a good reliability of ratings by inter-observers. Similar but a little lower results (slight agreement) were detected at the second time (two months) between scores by inter-observers as the Fleiss' Kappa=0.15, z=6.14, p<0.0001 and ICC=0.86.

For the orthopedic oncologist, there was a fair evidence of agreement in the comparison of the first and second observational times for total scores (κ=0.333, p<0.001), region (κ=0.947, p<0.0001), size (κ=0.019, p=0.821), and type (κ=0.097, p=0.160) (Table 7).

For the senior orthopedic surgeon of shoulder and elbow, there was a moderate evidence of agreement in the comparison of the first and second observational times for total scores (κ=0.413, p<0.0001), region (κ=0.947, p<0.0001), size (κ=0.209, p=0.134), and type (κ=0.427, p<0.007) (Table7).

For the senior orthopedic surgeon, a fair evidence of agreement was detected in the comparison of the first and second observational time-points for total scores (κ=0.225, p<0.012), region (κ=0.893, p<0.0001), size (κ=-0.074, p=0.588), and type (κ=0.195, p=0.237) (Table 7).

For the junior orthopedic surgeon, a slight evidence of agreement was detected in the comparison of the first l and second observational times for total scores (κ=0.035, p<0.012), region (κ=0.945, p<0.0001), size (κ=-0.172, p=0.210), and type (κ=0.024, p=0.840) (Table 7).

Table 5: Inter-observer analysis in each of the observational point for all observers

Subsets	First observational point				Second observational point			
	κ-statistic	z-score	ICC	P value	κ-statistic	z-score	ICC	p value
Overall	0.21	0.05	0.87	p<0.0001	0.15	6.14	0.86	p<0.0001
Site	0.95	27.47	0.93	p<0.0001	0.83	24.09	0.99	p<0.0001
Size	0.27	7.32	0.83	p<0.0001	0.13	3.34	0.76	p=0.0004
Type	**0.10**	**2.72**	**0.50**	**p=0.0032**	**0.28**	**7.57**	**0.78**	**p<0.0001**

Table 6: Results of total scores for intra-observer analysis

Total Scores	Orth. Onco	Sho&Elb Orth	Senior Orth	Junior Orth.	Sen. Orth Res	Jun Ort. Res.
	F/S	F/S	F/S	F/S	F/S	F/S
Score 3	0/0	0/0	0/0	1 /0	0/0	0/0
Score 4	0/1	0/0	1 /0	2 /1	0/0	1 /0
Score 5	4 /5	3 /3	0/1	3 /5	2 /3	1 /2
Score 6	10 /7	6 /7	6/7	4/4	6/8	8 /6
Score 7	11 /10	16/14	15/14	12/9	16/13	14 /13
Score 8	4 /6	2/6	6/6	4 /5	4/4	3 /7
Score 9	1/1	3 /2	2 /2	4 /6	0/2	3 /2
				Total: 30		

F/S: First observational point/Second observational point, Ort. Onco: Orthopedic Oncologist, Sho&Elb Orth: Senior Shoulder and Elbow Surgeon, Senior Orth: Senior Orthopedic Surgeon, Junior Orth: Junior Orthopedic Surgeon, Sen Orth Res: Senior Orthopedic Resident, Jun Ort. Res.: Junior Orthopedic Resident

Table 7: Intra-observer analyses for the comparison of two observational points

Observers	Subset	κ-statistic	p value
Orthopedic Oncologist	Overall	0.333	p<0.0001
	Site	0.947	p<0.0001
	Size	0.019	p=0.821
	Type	0.097	p=0.160
Senior orthopedic surgeon of shoulder and elbow	Overall	0.413	p<0.0001
	Site	0.947	p<0.0001
	Size	0.209	p=0.134
	Type	0.427	p<0.007
Senior orthopedic surgeon	Overall	0.225	p< 0.012
	Site	0.893	p<0.0001
	Size	-0.074	p=0.588
	Type	0.195	p=0.237
Junior orthopedic Surgeon	Overall	0.035	p<0.012
	Site	0.945	p<0.0001
	Size	-0.172	p=0.210
	Type	0.024	p=0.840
Senior resident of orthopedics	Overall	0.369	p<0.0001
	Site	0.945	p<0.0001
	Size	0.180	p=0.231
	Type	0.104	p=0.424
Junior resident of orthopedics	Overall	-0.030	p=0.769
	Site	0.740	p<0.0001
	Size	-0.049	p=0.761
	Type	0.026	p=0.851

For the senior resident of orthopedics, a fair evidence of agreement was detected in the comparison of the first and second observational times for total scores (κ=0.369, p<0.0001), for region (κ=0.945, p<0.0001), size (κ=0.180, p=0.231), and type (κ=0.104, p=0.424) (Table 7).

For the junior resident of orthopedics, a poor evidence of agreement was detected in the comparison of the first and second observational times for total scores (κ=-0.030, p=0.769) as well as comparing the scores for region (κ=0.740, p<0.0001), size (κ=-0.049, p=0.761), and type (κ=0.026, p=0.851) (Table 7).

DISCUSSION

Metastatic bone disease may cause a pathologic fracture with severe pain, hospitalization, and inevitably a surgery with high risks. Moreover, perioperative morbidity may be increased because of an established fracture. Prophylactic procedures such as surgical fixation become a necessity for patients with high pathological fracture risk. The main objective is to identify impending pathologic fractures that require surgical fixation prior to irradiation in clinical settings (8). Mirels created a scoring system to predict the metastatic bone fracture risk in 1988. He suggested as the score increased above a score of seven, the percentage of pathological fractures increased, but a score of nine is the most diagnostic value threshold to predict pathological fractures (7). However, Howard et al. found that a Mirels score of nine has a specificity of 35%, and they concluded that if the Mirels score is used as an indicator for surgery, two thirds of patients would have unnecessary surgery (9, 11). An impending pathologic fracture has some characteristics such as having a proximal femur lesion of ≥2.5 cm, and to occupy 50% or more of the bone diameter, and there is an adjacent lesser trochanteric fracture nearby (12). In our study, kappa and the Fleiss' kappa coefficient with intraclass correlation coefficient were used to score 30 patients with lesions according to the Mirels' rating system. We excluded the scoring of pain severity to remove subjectivity (8,15).

In the literature review, there are a few studies related to intra- and inter-observer variability scores in the prediction of metastatic lesions. Howard et al. conducted a study with four participants and 62 patients (9). Same as in our study, objective parameters of the Mirels classification were assessed two weeks apart, inter- and intra-observer reliability scores were calculated using the Fleiss' kappa statistic. Kappa values of scores for the inter-observer were detected as k=0.554 for region, k=0.342 for size, k=0.443 for radiographic view, and k=0.294 for the total score, similar to our results. The authors concluded that there was a fair to moderate agreement between observers at the first observational time, and moderate to substantial agreement after two weeks. They mentioned that the Mirels' score system is not objective and does not have reproducibility for the risk prediction of pathological fractures (9). Similarly in our study, the most experienced observers had the highest and the least experienced observer had the least agreement but the other observers had different agreement levels that do not belong to their experience level. In another study by Damron et al., they evaluated the intra- and inter-observer scores of 53 orthopedic surgeons or oncologists for 12 patients (12). They reported that the kappa values for the inter observer variability indicated a high agreement for region (k=0.752), moderate agreement for radiographic view, and fair agreement for size, similar to our results except for pain. Their overall sensitivity and specificity were 91% and 35%, respectively.

Furthermore, four orthopedic surgeons and four radiol ogists scored radiographs of 47 patients having bone metastases at the time of admission and after 12 weeks in the study of El-Husseiny and Coleman (14). Evans et al. suggested that the Mirels' ratings system may give false positive results leading patients to undergo an unnecessary prophylactic surgery (15). In the study by Mac Niocaill et al., radiographs with 35 lesions of 28 patients were scored twice by three orthopedic oncologists (8). In their study, inter-observer agreement of the lesions were found for size (κ=0.27–0.60), region (κ=0.77–1.0) and type of the lesion (κ=0.55–0.81). Unlike us, Damron et al. and Macniocaill et al. stated that the Mirels scoring system is a reliable and reproduceable clinical tool (8, 12). However, their kappa values indicated slight and moderate to high agreement for the size and radiographic view, and perfect agreement for the region.

Borderline scores, such as score of 8, is problematic in the Mirels' classification system, and makes treatment options uncertain for the selection of prophylactic fixation or surgery. Therefore, the clinically use of Mirels' recommendation may cause unnecessary fixation in approximately 2/3 of the patients (16). Damron et al. reported that oncologists had scored very inconstantly, and they were advised to have an additional education (12). This is also true for our group but we had only one orthopedic oncologist. Today's golden standard, the Mirels' score, may lead to over treatment. Therefore, new methods such as finite element analysis and computed tomography-based structural rigidity analysis could be useful in the prediction of impending pathological fractures. Computed tomography-based structural rigidity analysis calculates the reduction of 35% or more in the affected femur rigidity with 100% sensitivity and 61% specificity for the prediction of pathological fractures (17). Finite element analysis measures the bone mineral density (11). These analyses are complex and difficult to use in clinical settings. One of the conflicting results of this study was that of not obtaining scores from pain. Our aim was to evaluate objective parameters of the classification, as no objective definitions were clarified related to this integral part of the original classification. So, it might be considered a highly subjective variable, and excluded from assessment.

CONCLUSION

In conclusion, the difference between clinicians with different backgrounds and experience may partly influence the scores. There was a significant difference in overall scores across experience levels for the most and least experienced observers but not for other observers. We believe that the Mirels' scoring system doesn't consider important factors such as comorbidities, radiotherapy, underlying diseases and expected survival. Moreover, there is a need for more specific guidelines for selectively fracture risk in metastatic lesions of long bones. New and more specific parameters and a satisfactorily revised rating system is required to predict impending fractures.

Ethics Committee Approval: This study was approved by the ethics committee of the Istanbul Faculty of Medicine Clinical Research Ethics Committee, Istanbul University (Date: 11.02.2022, No: 03).

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- Y.S., C.M.C.; Data Acquisition- C.M.C., A.M.Y.; Data Analysis/Interpretation- E.K., A.M.Y.; Drafting Manuscript- E.M., E.K.; Critical Revision of Manuscript- E.K., Y.S.; Final Approval and Accountability- Y.S., A.E., A.S.; Material or Technical Support- A.S., Y.S.; Supervision- A.E., A.S.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Coleman RE. Skeletal complications of malignancy. Cancer 1997;80(8 Suppl):1588-94. [CrossRef]
2. Cecchini MG, Wetterwald A, van der Pluijm G, Thalmann GN. Molecular and biological mechanisms of bone metastasis. EAU Update Series 2005;3(4):214-26. [CrossRef]
3. Macedo F, Ladeira K, Pinho F, Saraiva N, Bonito N, Pinto L, et al. Bone Metastases: An Overview. Oncology reviews 2017;11(1):321. [CrossRef]
4. Sharma H, Bhagat S, McCaul J, Macdonald D, Rana B, Naik M. Intramedullary nailing for pathological femoral fractures. J Orthop Surg (Hong Kong) 2007;15(3):291-4. [CrossRef]
5. Coleman RE. Metastatic bone disease: clinical features, pathophysiology and treatment strategies. Cancer Treat Rev 2001;27(3):165-76. [CrossRef]
6. Narazaki DK, De Neto Alverga CC, Baptista AM, Caiero MT, De Camargo OP. Prognostic factors in pathologic fractures secondary to metastatic tumors. Clinics (Sao Paulo) 2006;61(4):313-20. [CrossRef]
7. Mirels H. Metastatic disease in long bones. A proposed scoring system for diagnosing impending pathologic fractures. Clinical orthopaedics and related research. 1989;(249):256-64. [CrossRef]
8. Mac Niocaill RF, Quinlan JF, Stapleton RD, Hurson B, Dudeney S, O'Toole GC. Inter- and intra-observer variability associated with the use of the Mirels' scoring system for metastatic bone lesions. Int Orthop 2011;35(1):83-6. [CrossRef]
9. Howard EL, Shepherd KL, Cribb G, Cool P. The validity of the Mirels score for predicting impending pathological fractures of the lower limb. Bone Joint J 2018;100-B(8):1100-5. [CrossRef]
10. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33(1):159-74. [CrossRef]
11. Anez-Bustillos L, Derikx LC, Verdonschot N, Calderon N, Zurakowski D, Snyder BD, et al. Finite element analysis and CT-based structural rigidity analysis to assess failure load in bones with simulated lytic defects. Bone 2014;58:160-7. [CrossRef]
12. Damron TA, Morgan H, Prakash D, Grant W, Aronowitz J, Heiner J. Critical Evaluation of Mirels' Rating System for Impending Pathologic Fractures. Clin Orthop Relat Res 2003;415(Suppl):S201-7. [CrossRef]
13. Dawson R, Currow D, Stevens G, Morgan G, Barton MB. Radiotherapy for bone metastases: A critical appraisal of outcome measures. J Pain Symptom Manage 1999;17(3):208-18. [CrossRef]

14. El-Husseiny M, Coleman N. Inter- and intra-observer variation in classification systems for impending fractures of bone metastases. Skeletal Radiol 2010;39(2):155-60. [CrossRef]
15. Evans AR, Bottros J, Grant W, Chen BY, Damron TA. Mirels' rating for humerus lesions is both reproducible and valid. Clin Orthop Relat Res 2008;466(6):1279-84. [CrossRef]
16. Jawad MU, Scully SP. In brief: classifications in brief: Mirels' classification: metastatic disease in long bones and impending pathologic fracture. Clin Orthop Relat Res 2010;468(10):2825-7. [CrossRef]
17. Damron TA, Nazarian A, Entezari V, Brown C, Grant W, Calderon N, et al. CT-based Structural Rigidity Analysis Is More Accurate Than Mirels Scoring for Fracture Prediction in Metastatic Femoral Lesions. Clin Orthop Relat Res 2016;474(3):643-51. [CrossRef]