Journal of Biomedical Engineering and Medical Devices

OPEN ACCESS Freely available online

Perspective

Predicting Pathologic Fracture Risk in Patients with Metastatic Prostate Cancer

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DESCRIPTION

In the landscape of musculoskeletal oncology, few challenges are as complex as predicting which metastatic bone lesions will lead to a catastrophic fracture. For patients with metastatic prostate cancer, the skeleton is the primary site of dissemination, with the proximal femur being a particularly vulnerable location for weight-bearing failure. Traditional methods for evaluating fracture risk have long relied on clinical and radiographic scoring systems; however, emerging research from 2025 and 2026 suggests that a more nuanced, "multi-modal" approach-integrating serum biomarkers, genetic profiles and advanced computational imaging-is essential for accurate prediction and the prevention of unnecessary surgical interventions.

For decades, the scoring system has been the gold standard for predicting pathologic fractures. This system assigns points based on the site of the lesion, the level of pain, the radiographic appearance (lytic, blastic, or mixed) and the size of the cortical involvement. While Mirels' criteria are highly sensitive-meaning they rarely miss a potential fracture they suffer from notoriously low specificity. In many cases, patients with a "high-risk" score of 8 or 9 never actually fracture, leading to "over-treatment" where patients undergo invasive prophylactic stabilization surgery that they might not have needed.

In prostate cancer specifically, the challenge is amplified because these metastases are often osteoblastic (bone-forming) rather than osteolytic (bone-destroying). While blastic lesions may appear "denser" on an X-ray, they are often structurally brittle and lack the mechanical integrity of healthy bone. This unique biology means that traditional size-based cutoffs often fail to reflect the true fracture potential in this specific patient population.

The most significant shift in 2026 research is the inclusion of systemic biomarkers to refine risk assessment. Recent studies, notably those presented at the Orthopaedic Research Society (ORS), have demonstrated a strong correlation between Prostate-Specific Antigen (PSA) levels and fracture risk. A PSA level significantly above 100 ng/mL, for instance, has been identified as a critical threshold for increased fracture odds. This suggests that the overall tumor burden and systemic activity of the cancer are just as important as the physical appearance of a single bone lesion.

Furthermore, next-generation sequencing (NGS) is allowing clinicians to look at the "genetic signature" of the tumor. Mutations in genes such as *BRCA2*, *RB1* and *PTEN* are currently being investigated as predictors of bone-metastatic aggressive tendencies. While no single mutation acts as a "smoking gun" for fracture, the combination of these genetic markers with clinical data provides a more comprehensive picture of disease progression. For example, patients with RB1 mutations may exhibit more aggressive bone remodeling, potentially weakening the trabecular architecture faster than those with standard metastatic profiles.

Beyond biology, the technological frontier of 2026 involves CT-based Structural Rigidity Analysis (CTRA) and Finite Element Analysis (FEA). Unlike a static X-ray, these tools allow for "patient-specific" biomechanical modeling. CTRA quantifies the reduction in bone rigidity by comparing the affected limb to the healthy contralateral side. If a lesion causes more than a 35% reduction in rigidity, the risk of fracture is deemed critical, regardless of the Mirels' score.

FEA takes this a step further by simulating mechanical loads-such as walking or climbing stairs-on a digital "twin" of the patient's bone. This allows surgeons to see exactly where stress concentrations occur. By combining these engineering metrics with PSA levels and genetic risk scores, the medical community is moving toward a Precision Oncology Model. This allows for a "watchful waiting" approach for low-risk patients, while fast-tracking high-risk individuals for prophylactic fixation, ultimately improving survival rates and maintaining a higher quality of life.

CONCLUSION

Predicting pathologic fracture in metastatic prostate cancer is no longer solely the domain of the radiologist. It is a collaborative effort involving oncology, orthopaedic surgery and bioinformatics. By leveraging the synergy between mechanical simulation and molecular biomarkers, clinicians can now move past the "one-size-fits-all" scoring of the past, ensuring that surgical intervention is reserved for those who truly need it to stay mobile and pain-free.

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Received: 30-Apl -2025, Manuscript No. BEMD-25-39964; **Editor assigned:** 05-May -2025, PreQC No. BEMD-25-39964 (PQ); **Reviewed:** 19-May-2025, QC No. BEMD-25-39964; **Revised:** 26-May-2025, Manuscript No. BEMD-25-39964 (R); **Published**: 02-Jun-2025. DOI: 10.35248/2475-7586.25.10.324

Citation: Ciatti C (2025). Predicting Pathologic Fracture Risk in Patients with Metastatic Prostate Cancer. J Biomed Eng Med Dev. 09:324.