

# CORR Insights®: Thirty-day Postoperative Complications After Surgery for Metastatic Long Bone Disease Are Associated With Higher Mortality at 1 Year

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## Where Are We Now?

The primary objectives in the management of most patients with osseous metastases are to reduce pain, increase mobility, and improve quality of life. During the past several years, studies have reported a clear benefit to the use of anti-resorptive therapy in preventing skeletal-related events (pathologic fracture, use of

radiation therapy or prophylactic stabilization, spinal cord compression, or hypercalcemia of malignancy) in such patients [4, 13]. As improvements in systemic therapy help patients with osseous metastases to live longer with their disease, the stabilization of long bones becomes increasingly important.

Although most long-bone stabilization procedures are palliative, prophylactic stabilizations are associated with longer patient survival [12], and with lower rates of early postoperative complications [3] compared with post-fracture stabilization. Studies have demonstrated associations between several factors, including hypoalbuminemia, Katagiri tumor type [7], and duration of survival after surgical treatment of appendicular skeletal metastases [5, 8]. The PathFX system is a widely available prognostic tool for predicting the probability of survival with bone metastases by using a Bayesian network; the system has been validated in numerous global populations [5, 6, 11]. PathFX identifies a key role for Katagiri grouping, as well as for several laboratory values [5]. Interestingly, the surgeon's estimation of survival duration is possibly the

most predictive variable in models of prognostication [10]. Perhaps experienced oncologic surgeons can synthesize patient- and disease-specific information and make informed judgments about the health of a potential surgical patient, which may influence treatment decisions. The current analysis helps inform a more objective assessment of perioperative risk in this complex patient population.

In the current analysis, Bindels and colleagues [1] identify potentially modifiable comorbidities associated with early postoperative complications and demonstrate the association of these early postoperative complications with 1-year mortality. In using the Clavien-Dindo classification of adverse events, the authors noted complications in 31% of surgically treated patients within 30 days after surgery. Although many of the identified comorbidities are outside the control of patients and clinicians (lesion location, primary malignancy type), others may be modifiable, particularly nutritional insufficiency and laboratory abnormalities.

## Where Do We Need To Go?

To improve the care of patients with skeletal metastases, we need to mitigate the risk of pathologic fracture, refine how we choose who can benefit

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from surgery for metastatic bone disease, and improve both safety and efficacy of surgical interventions in this complex population. Increased awareness of the role of anti-resorptive therapy, together with an integrated approach between medical oncology and radiation oncology, already appear to reduce the risk of skeletal-related events in patients with osseous metastases and multiple myeloma. However, anti-resorptive medications are still not used routinely in patients with skeletal metastases [9].

Regarding the “decision tree” for identifying patients who might benefit from surgery for these diagnoses, much progress has been made. CT-based structural rigidity analysis has improved discrimination of the impending pathologic fracture [2], and the PathFX tool has improved prognostication for survival [5].

Although the current analysis improves our understanding of which patients are likely to develop postoperative complications [1], it does not indicate which patients may benefit from not having surgery. Perhaps this determination is somewhat philosophical, reflecting the art of medicine rather than the science. Our increased attention to measures of quality and safety for evaluating performance and determining payment necessitates careful evaluation of modifiable risk factors. Still, when offering palliative surgical care, some patients with unmodifiable comorbidities deserve access to surgical procedures that are likely to result in complications.

Whereas other authors have demonstrated the prognostic role of the Katagiri diagnostic groups [5, 7] as it relates to survival, the current study [1] suggests that the Katagiri diagnostic group is also related to early postoperative complications. This relationship may reflect the disease state, in

which morbidity and mortality risk are related to the underlying quality of health. Each type of primary malignancy has unique attributes that are important in determining a clinical management strategy. Metastatic prostate carcinoma is often sclerotic, warranting mechanical considerations related to both fracture risk and the methods of surgical treatment. Renal cell carcinoma and bladder carcinoma are likely to be radioresistant, with rich vascularity leading to disease-specific decision-making for osseous metastases. Limitations in our case volumes may dictate the need for consolidation of data across primary malignancies for adequately powered analyses, though decision trees will likely need to consider more than biologic aggressiveness groupings like those of Katagiri. Rather, disease processes, such as myeloma, lymphoma, and breast carcinoma (including hormone status), may ultimately require analysis on a patient-by-patient basis to improve surgical treatment decisions and planning.

It may be simplistic to consider factors such as hyponatremia and hypoalbuminemia, or even anemia, to be signs of an overall advanced disease state with possible malnutrition or cachexia. As the authors note [1], albumin and sodium levels are potentially modifiable with preoperative and perioperative management. We need to determine whether improvement in these factors reduces the risk of early morbidity and death at 1 year.

### How Do We Get There?

As with most high-quality studies, the current analysis answers key questions and asks others. For example, does preoperative optimization improve early postoperative complication rates after surgical treatment of long bone

metastases [1]? The authors note that albumin data were missing for many patients and needed to be imputed. Perhaps the first step toward improving the health of patients is recognizing which patients need, and are capable of, improvement before surgery. In addition to routine evaluation of these laboratory tests, assessment of the potential benefit of improvement in nutrition, fluid management, and inflammation may be possible.

Considering that it took 18 years to accrue this large group of patients at a high-volume center, further investigation of improvement strategies will likely require collaboration and coordination among centers. Researchers may consider using the Musculoskeletal Tumor Society Registry or the International Bone Metastasis Registry to achieve larger sample sizes. In addition, these large registries may help researchers establish disease-specific indications and prognosticators that discriminate more finely than the Katagiri diagnostic groups allow. Despite some clear similarities, multiple myeloma is not a carcinoma, for example, and perhaps should be analyzed separately. Our institutional databases remain limited in the volume of patients they include, necessitating the aggregation of disparate disease processes for adequate statistical power to reach meaningful conclusions. However, with the benefit of collaboration across institutions, the numbers of patients with hormone-responsive prostate carcinoma may be large enough to establish actionable recommendations for preoperative clinical optimization to improve short-term complication rates and long-term survival after orthopaedic stabilization. With such information, we may be able to provide truly patient-specific surgical decision-making, prognostication, and perioperative improvement.

## References

1. Bindels BJJ, Thio QCBS, Raskin KA, Ferrone ML, Lozano Calderón SA, Schwab JH. Thirty-day postoperative complications after surgery for metastatic long bone disease are associated with higher mortality at 1 year. *Clin Orthop Relat Res*. 2019;in press.
2. Damron TA, Nazarian A, Entezari V, Brown C, Grant W, Calderon N, Zurakowski D, Terek RM, Anderson ME, Cheng EY, Aboulafia AJ, Gebhardt MC, Snyder BD. CT-based structural rigidity analysis is more accurate than Mirels scoring for fracture prediction in metastatic femoral lesions. *Clin Orthop Relat Res*. 2016; 474:643-651.
3. El Abiad JM, Raad M, Puvanesarajah V, Rao SS, Morris CD, Levin AS. Prophylactic versus postfracture stabilization for metastatic lesions of the long bones: a comparison of 30-day postoperative outcomes. *J. Am. Acad. Orthop. Surg*. 2019;27:e709-716.
4. Fizazi K, Carducci M, Smith M, Damiao R, Brown J, Karsh L, Milecki P, Shore N, Rader M, Wang H, Jiang Q, Tadros S, Dansey R, Goessl C. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. *Lancet*. 2011;377: 813-822.
5. Forsberg JA, Wedin R, Bauer HC, Hansen BH, Laitinen M, Trovik CS, Keller JO, Boland PJ, Healey JH. External validation of the Bayesian Estimated Tools for Survival (BETS) models in patients with surgically treated skeletal metastases. *BMC Cancer*. 2012;12:493.
6. Forsberg JA, Wedin R, Boland PJ, Healey JH. Can we estimate short- and intermediate-term survival in patients undergoing surgery for metastatic bone disease? *Clin Orthop Relat Res*. 2017; 475:1252-1261.
7. Katagiri H, Takahashi M, Wakai K, Sugiura H, Kataoka T, Nakanishi K. Prognostic factors and a scoring system for patients with skeletal metastasis. *J. Bone Joint Surg. Br*. 2005;87:698-703.
8. Kotian RN, Puvanesarajah V, Rao S, El Abiad JM, Morris CD, Levin AS. Predictors of survival after intramedullary nail fixation of completed or impending pathologic femur fractures from metastatic disease. *Surg. Oncol*. 2018;27:462-467.
9. McGrath LJ, Overman RA, Reams D, Cetin K, Liede A, Narod SA, Brookhart MA, Hernandez RK. Use of bone-modifying agents among breast cancer patients with bone metastasis: evidence from oncology practices in the US. *Clin Epidemiol*. 2018;10:1349-1358.
10. Nathan SS, Healey JH, Mellano D, Hoang B, Lewis I, Morris CD, Athanasian EA, Boland PJ. Survival in patients operated on for pathologic fracture: Implications for end-of-life orthopedic care. *J. Clin. Oncol*. 2005;23: 6072-6082.
11. Ogura K, Gokita T, Shinoda Y, Kawano H, Takagi T, Ae K, Kawai A, Wedin R, Forsberg JA. Can a multivariate model for survival estimation in skeletal metastases (PATHFx) be externally validated using Japanese patients? *Clin Orthop Relat Res*. 2017;475:2263-2270.
12. Ristevski B, Jenkinson RJ, Stephen DJ, Finkelstein J, Schemitsch EH, McKee MD, Kreder HJ. Mortality and complications following stabilization of femoral metastatic lesions: A population-based study of regional variation and outcome. *Can. J. Surg*. 2009;52:302-308.
13. Stopeck AT, Lipton A, Body JJ, Steger GG, Tonkin K, de Boer RH, Lichinitser M, Fujiwara Y, Yardley DA, Viniegra M, Fan M, Jiang Q, Dansey R, Jun S, Braun A. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. *J. Clin. Oncol*. 2010;28:5132-5139.