

CORR Insights®: Is Total Femur Replacement a Reliable Treatment Option for Patients With Metastatic Carcinoma of the Femur?

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Where Are We Now?

In their well-written and thoughtful report, Sevelde and colleagues [8] review their institution's 30-year experience in treating patients with osseous metastases to the femur with total femur replacement. As the authors note, this is a highly selected cohort of 11 patients with strict surgical indications, including no other appropriate reconstructive options and an estimated

duration of survival of at least 6 months. This study's contribution is especially meaningful considering little is known about the results of this procedure in patients with metastatic disease.

However, in this series, eight of the 11 patients died before 6 months, which was the minimum estimated duration of survival for patients to be indicated for the procedure. This highlights the difficulty in predicting survival in patients with metastatic cancer. In a previous analysis of 191 patients treated for pathologic fracture in the setting of osseous metastases, Nathan and colleagues [4] found that the orthopaedic oncologic surgeon's estimate was the single strongest predictor of the duration of patient survival after surgery. More recently, Bayesian belief network models have proven more reliable at predicting the probability of surviving for a given duration and have been validated through multiple international databases [2, 5].

metastases is manifest. What is also evident is the difficulty in predicting the timeline and completeness of recovery after surgery. The current study has little information on baseline functional status at the time of surgery. One presumes that many of these patients' preoperative Musculoskeletal Tumor Society scores were even lower than their reported final postoperative functional scores. Although the authors note that most patients did not recover fully, it remains unclear whether these patients still gained some clinical benefit during their lifetimes. Furthermore, we have little appreciation of the natural history of such a patient's pain and function in the absence of surgery. These highly selected patients had no reasonable alternative to total femur replacement other than amputation or palliative care; however, the duration of survival, quality of life, and overall healthcare costs and burdens associated with each of these options are not fully established for this unique patient population.

Recent trends in the treatment of patients with cancer exhibit a progressive increase in duration of survival with metastatic disease to bone, presumably as a result of advances in systemic treatment options [7, 9]. With the routine use of antiresorptive therapy, the rates of skeletal-related events can be mitigated somewhat. However, as patients live longer with osseous metastatic disease, the burden of skeletal-related events will likely increase. Although there are few data to

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Where Do We Need to Go?

The complexity of the clinical factors that help inform estimates of patient survival in the setting of skeletal

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prove the trend, we note anecdotally that diseases such as renal cell carcinoma appear to respond to receptor tyrosine kinase inhibition and immunotherapy to a greater degree in the viscera than in the skeleton [6]. This probably results in the continued progression of osseous disease, particularly in transitional cell carcinomas, as suggested in recent reports [1, 3].

In the current study [8], most of the indications for total femur replacement were pathologic fracture adjacent to previous hardware or local progression of disease. Xing and colleagues [10] have questioned the historical “one bone, one operation” mantra in suggesting that long-stem fixation is not always necessary in arthroplasty for proximal femur metastasis. However, no algorithm can tell us which patients are likely to outlast their initial implants. We also have only a limited ability to predict the length of each patient’s oncologic survival, his or her ability to recover from surgery, the best timelines for surgical palliation, and the time each patient will take to return to function. These factors are critical in determining the right clinical strategy for each patient.

How Do We Get There?

Although the results of this study appear to argue against performing such large reconstructions in patients with metastatic carcinoma, these data more clearly highlight the need to better understand the course of osseous metastatic disease in this era of rapid pharmaceutical advancement. The lessons learned in this cohort are inherent in the treatment of patients with less aggressive surgical options, as well. Although substantial progress has been made with antiresorptive therapy in reducing skeletal-related

events, evaluation of the role of novel anabolic agents, such as anti-sclerostin and anti-DKK1 antibodies, may prove valuable in the future treatment of skeletal metastases.

Even in the absence of additional systemic therapy options to limit the damage and progression of bone metastases, our ability to more accurately predict the right treatment for the right patient would benefit from improved data regarding these patients and their oncologic outcomes. Appropriately planned and designed efforts toward international registries that include implant data and clinical factors, as well as validated functional measures for the oncologic population, may help surgeons predict implant survival like the way in which PATHFx has augmented our prognostication of patient survival in this population. Similarly, the routine collection of patient-reported outcome measures and the sharing of these data across institutions can help inform surgeons regarding the timeline and completeness of pain control and functional improvement after surgical palliation in skeletal metastases. With a calculated and coordinated assembly of information regarding how patients actually perform over time, our ability to use the power of computational analysis and Bayesian belief networks to predict which patients are likely to outlast their implants can likely be greatly improved. This information, together with a better understanding of the costs associated with the various operative and nonoperative modalities, would allow large steps forward toward truly informed decision-making.

References

- Escudier BJ, Motzer RJ, Powles T, Tannir NM, Davis ID, Donskov F, Grunwald V, Heng DY, Hutson T, Melichar B, Nosov D, Rini BI, Salman P, Sternberg CN, Szczylik C, Wolter P, Arroyo AM, Mangeshkar M, Agarwal N, Choueiri TK. Subgroup analyses of METEOR, a randomized phase 3 trial of cabozantinib versus everolimus in patients (pts) with advanced renal cell carcinoma (RCC). *J Clin Oncol*. 2016;34:499.
- 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.
- Molina AM, Jia X, Feldman DR, Hsieh JJ, Ginsberg MS, Velasco S, Patil S, Motzer RJ. Long-term response to sunitinib therapy for metastatic renal cell carcinoma. *Clin Genitourin Cancer*. 2013;11:297–302.
- 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.
- 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.
- Plimack ER, Tannir N, Lin E, Bekele BN, Jonasch E. Patterns of disease progression in metastatic renal cell carcinoma patients treated with anti-vascular agents and interferon: Impact of therapy on recurrence patterns and outcome measures. *Cancer*. 2009;115: 1859–1866.
- Rogoz B, Houzé de l’Aulnoit A, Duhamel A, Houzé de l’Aulnoit D. Thirty-year trends of survival and time-varying effects of prognostic factors in patients with metastatic breast cancer—A single institution experience. *Clin Breast Cancer*. [Published online ahead of print September 1, 2017]. DOI: 10.1016/j.clbc.2017.08.012.
- Sevela F, Waldstein W, Panotopoulos J, Kaider A, Funovics PT, Windhager R. Is total femur replacement a reliable treatment option for patients with metastatic carcinoma of the femur? *Clin Orthop Relat Res*. [Published online ahead of print]. DOI: 10.1007/s11999.000000000000125.

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9. Vaishampayan U, Vankayala H, Vigneau FD, Quarshie W, Dickow B, Chalasani S, Schwartz K. The effect of targeted therapy on overall survival in advanced renal cancer: A study of the national surveillance epidemiology and end results registry database. *Clin Genitourin Cancer*. 2014;12:124–129.
10. Xing Z, Moon BS, Satcher RL, Lin PP, Lewis VO. A long femoral stem is not always required in hip arthroplasty for patients with proximal femur metastases. *Clin Orthop Relat Res*. 2013;471:1622–1627.