Clin Orthop Relat Res (2018) 476:1600-1602
DOI 10.1097/CORR.0000000000000345

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

CORR Insights

Published online: 12 May 2018

CORR Insights®: External Validation and Optimization of the SPRING Model for Prediction of Survival After Surgical Treatment of Bone Metastases of the Extremities

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Where Are We Now?

In order to recommend an appropriate treatment for patients with skeletal metastases, the physician needs to make an accurate estimate of the patient's anticipated survival. Unfortunately, these predictions are difficult to make. Because pathologic fractures caused by metastatic lesions often do not heal, internal fixation may be an insufficient treatment for patients who survive for longer durations [3, 10]. On the other hand, endoprosthetic reconstruction may be too much surgery for patients whose remaining lifespan is short. The treatment goals should be "one bone, one procedure," with immediate relief of symptoms and restoration of full weight bearing, as little risk as possible of morbidity and perioperative mortality, and a reconstructive or internal fixation construct that outlasts the patient [7].

In the current study, Sørensen and colleagues [8] improved upon an already-strong, and previously examined [9], prediction model for estimating survival following resection and reconstruction of skeletal metastases. The current study allows reasonably precise estimates of the remaining lifespan of these patients, which, while limited to patients undergoing resection and reconstruction, can help surgeons choose an operative plan that meets the "one bone, one procedure" standard I mentioned earlier. The study is strengthened by external validation from a consecutive, prospective patient database and closed patient population with no loss of followup. Interpreted with other recently published (ostensibly competing) prognostic models [2, 11], we now have compelling evidence that we can predict, with a reasonable degree of certainty, the likelihood of short- and intermediate-term survival of patients with symptomatic skeletal disease prior to surgery.

Where Do We Need To Go?

As noted, the model created and now updated by Sørensen and colleagues [8] demonstrates strong performance in their patients, but the model is not without limitations. First, as acknowledged by the authors, its data derive from a relatively homogeneous population (Denmark) and the conclusions were based on a relatively limited number of patients, all of whom were treated with surgical resection and reconstruction (perhaps limiting its applicability in patients who might be better candidates for internal fixation). Next, the presence of pathologic fracture was not associated with survival. While this finding disagrees with some prior research and, indeed, one other model [2], it seems to make little sense to leave a variable that was not

This CORR Insights® *is a commentary on the article* "External Validation and Optimization of the SPRING Model for Prediction of Survival After Surgical Treatment of Bone Metastases of the Extremities" *by Sørensen and colleagues available at:* DOI: 10.1097/01.blo.0000534678.44152.ee.

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This *CORR* Insights® comment refers to the article available at DOI: 10.1007/s11999.0000000000000293.

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statistically associated with survival in the model. Following from this concern, the present study did not attempt to improve the model by reanalyzing it and, if necessary, changing the variables analyzed. Rather, they augmented their existing model with additional data to strengthen statistical relationships and then revalidated it.

The next steps can then be directly derived from these limitations. The model should be further refined to reevaluate variables and relationships and then validated with more patients in additional populations, ideally treated with a variety of surgical modalities and/or radiation alone. Next, while recent models differ in methodology—one is a categorical treatment guide, one is a nomogram, and one utilizes a Bayesian Belief Network (BBN) to generate a probability of survival for a given time point [2, 8, 11]—the models should be directly compared for accuracy and validity. However, because nomograms and tables cannot tolerate missing data, this may be difficult using often incomplete, retrospective data.

Next, as Sørensen and colleagues note, online model access is needed. Because treatments for metastatic disease are frequently changing in ways that (hopefully) improve patient survival, these models each will require frequent, if not real-time, curation, revision, and updates. Eventually, we should seek to create online prognostic platforms that are frequently monitored and updated, and that are sufficiently robust to guide treatment. We then should determine whether use of these platforms improves patient-reported outcomes and quality of life, reduces treatment variability or costs, or even modestly improved survival (through appropriate treatment and minimizing perioperative mortality of patients approaching their end of life).

How Do We Get There?

This is conceptually easy given the above, but time and toil will be required. Online access must be established, as already exists for at least one model [2], and comparative studies should be performed. As part of these efforts, further prospective study and international collaboration to collect data from more patients and additional populations is needed. For example, the PATHFx BBN model has been validated in several countries [2, 6], while the categorical guideline-based model included more than 1500 patients [11]. These efforts could lead to a feedback loop within the models using a data-collection portal, such that model performance can be continuously improved. As part of this process, "old" data (based on antiquated treatments), which will eventually weaken rather than augment model performance, will need to be retired as they gradually become obsolete [1]. One example of this is refinement in diagnostic (rather than histologic) grouping, which is relatively crude and should be modified as more-precise diagnostic groups are created. Another example is the transition of metastatic melanoma from a "fast" to a "slow" grower because of the efficacy of checkpoint inhibitors [5].

These improved models will still require frequent refinements and modifications of the included variables and relationships as better information becomes available. For an additional example (and area that I believe requires future scrutiny), it is well documented that perioperative mortality increases in patients undergoing concurrent treatment of multiple disease sites, just as the perioperative morbidity and mortality of resection and endoprosthetic reconstruction may exceed that of closed intramedullary stabilization [4]. Likewise, I consistently counsel patients with skeletal metastases and their families that my role is to minimize pain and preserve function and quality of life for as long as possible, but that any treatment I render is unlikely to increase overall survival. However, as the performance of our prognostic models improves, we may need to ask ourselves if the proposed treatment itself should be included in the models as a variable. All existing models seek to guide treatment by predicting patient survival but, by either under- or overtreating patients, we may be altering the prognosis through local disease progression and construct failures (undertreatment) or perioperative complications and early death (overtreatment). Regardless, when these goals have been achieved, we will have widely available, accurate prognostic models to guide treatment in virtually any patient with a high degree of certainty. This should facilitate the right treatments for the right patients and, with that, the potential for improved outcomes—even for disease processes that will eventually prove fatal.

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