Systemic Therapy in Metastatic Long-Bone Disease: How do Treatment Patterns Influence Survival Prediction by the Skeletal Oncology Research Group Algorithm?

Tom Maarten De Groot, Joris Hendriks[1], Michelle Riyo Shimizu[2], Olivier Quinten Groot, Santiago Andres Lozano Calderon[3], Job N Doornberg[4], Paul C Jutte, Joseph Hasbrouck Schwab[5]
[1]Orthopedic Surgery, [2]Massachusetts General Hospital, [3]Massachusetts General Hospital - Harvard Medical S, [4]University Medical Centre Groningen, [5]MGH Dept. of Ortho Surg.

INTRODUCTION:
The prevalence of metastatic bone disease (MBD) is expected to increase due to improvements in diagnostics and oncologic treatment. Accurate survival prediction of patients with MBD is important for surgical decision making. Recently, the Skeletal Oncology Research Group (SORG) machine learning algorithm (MLA) has been developed and validated in cohorts from three different continents. However, on temporal validation using patients from 2017-2021, its performance showed to have decreased. This decrease in performance was especially present in patients treated with novel therapeutic agents. This study aimed to investigate the added value of treatment variables for survival prediction of patients who receive surgical treatment for MBD.
METHODS: All patients who underwent surgery for a metastatic bone lesion of the extremities between 1999 and 2020 were retrospectively included in the study. Patients who received revision surgery, or surgery for a primary bone tumor were excluded from the analysis. The primary outcome was postoperative survival. Treatment variables, which included preoperative use of checkpoint inhibitors, targeted therapy, and chemotherapy as well as demographics, clinical variables, and tumor variables were manually collected from the electronic health records. Statistical analysis was performed using multivariate logistic regression and Cox regression. The added value of treatment variables was assessed using the log-likelihood test and by comparing the area under the receiver operating curve (AUC) of a logistic regression model including all explanatory variables.
RESULTS: In total, 1,495 patients were included in the study. Preoperative chemotherapy use was associated with worse survival (HR=1.45; 95%CI=1.26-1.65; p<0.01). Preoperative checkpoint inhibitor (HR=0.74, 95%CI=0.57-0.96; p=0.03) and targeted therapy (HR=0.74; 95%CI=0.61–0.90; p<0.01) were associated with better overall survival. Incorporating the more granular approach resulted in a 0.022 increase for 90-day survival (AUC 0.776 versus 0.798; p<0.01) and a 0.024 increase in discriminative performance of a prediction model for 1-year survival (AUC 0.758 versus 0.782; p<0.01).
DISCUSSION AND CONCLUSION:
This study found that respective treatment modalities had varying effects on patients' survivorship in metastatic long-bone disease. The findings of this study also suggest that adding the use of targeted treatment as a variable in a prediction model can have a positive effect on the models' performance. Overall, this study highlights the importance of continuous updating of machine learning models and identifying new predictive variables to maintain predictive performance while treatment regimens evolve.

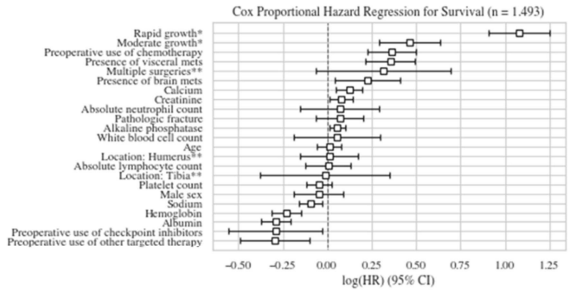

Figure 1. Cox proportional hazards regression for survival of patients who undergo surgery for a metastatic long-bone lesion. HR = Hazard Ratio; CI = Confidence Interval; *Primary tumor histology grouped according to the Katagiri tumor grouping.[24] **Compared to reference value of femoral location.

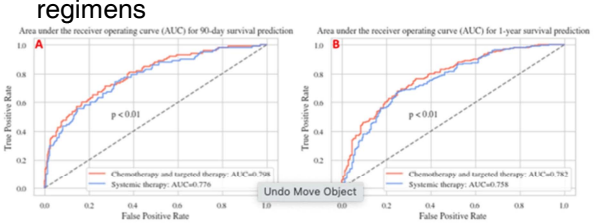

Figure 2. Area under the receiver operating curve (AUC) of logistic regression survival prediction models of patients on 90-day (A) and 1-year survival (B). Dividing systemic treatment into targeted therapy and chemotherapy improved the AUC of this simple prediction model by 0.024 in predicting 1-year survival and 0.022 in predicting 90-day survival. Both differences are statistically significant in favor of the more granular approach.