

Risk of Breast Cancer-Related Lymphedema: Development and Validation of a Clinically-Relevant, Patient-Facing Prediction Model

Danielle H. Rochlin, MD¹, Andrea V. Barrio, MD¹, Sarah A. McLaughlin, MD², Kimberly J. Van Zee, MD¹, Michelle R. Coriddi, MD¹, Joseph H. Dayan, MD MBA¹, Babak J. Mehrara, MD¹

¹Memorial Sloan Kettering Cancer Center, New York, NY, USA. ²Mayo Clinic Florida, Jacksonville, FL, USA.

Background

- Breast cancer-related lymphedema (BCRL) is a common complication of axillary lymph node dissection (ALND) that can also develop after sentinel lymph node biopsy (SLNB).
- Several models have been developed to predict risk of BCRL; however, all have shortcomings that include omission of key variables (e.g., SLNB and race/ethnicity) and inclusion of datapoints that are not readily available to patients.
- Purpose: To develop **simple and accurate prediction models for BCRL that can be used to estimate preoperative and postoperative risk.**

Methods

- Prospective cohort study at Memorial Sloan Kettering Cancer Center (MSKCC) and Mayo Clinic of women with breast cancer who underwent SLNB and/or ALND from 1999-2021
- Lymphedema diagnosed via arm circumference measurements or relative volume change
- Two predictive models formulated using logistic regression: a **preoperative model (model 1)** and a **postoperative model (model 2)**
 - Model variables selected based on the combination of clinically-meaningful variables that optimized the area under the curve (AUC) of receiver operating characteristic (ROC) curves for respective models
- Validation performed using a cohort of 34,438 patients with an ICD diagnosis of breast cancer (model 1, external validation) or 10-fold cross validation (model 2, internal validation)

Results

- 1,882 patients
- Mean follow-up 3.9±1.8 years
- ALND 43.5%, SLNB 56.5%
- BCRL rate 11.6%

Table 1. Preoperative Model (Model 1)

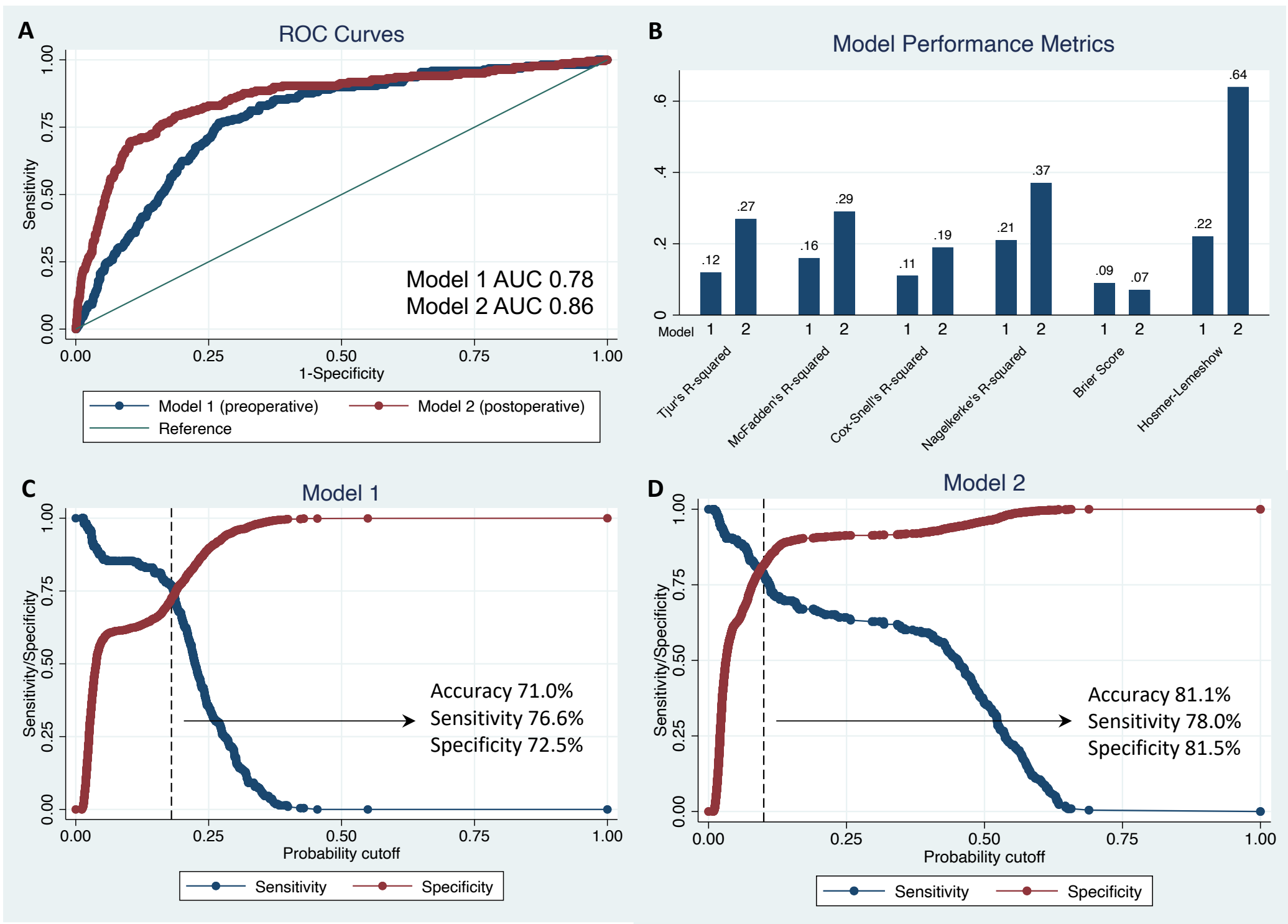
Variable	p-value	OR	95% CI
Baseline age [per 1-year increase]	0.130	1.01	1.00 – 1.02
Baseline weight [per 1-kg increase]	0.009	1.01	1.00 – 1.02
Height [per 1-cm increase]	0.104	0.98	0.96 – 1.00
Race [ref: White]			
Other	0.799	1.11	0.49 – 2.51
Black	0.047	1.53	1.01 – 2.32
Asian	0.987	0.99	0.48 – 2.06
ALND [ref: SLNB]	<0.001	7.89	5.14 – 12.10
Any radiation therapy [ref: no]	0.430	1.17	0.79 – 1.73
Any chemotherapy [ref: no]	0.036	1.66	1.03 – 2.68

Table 2. Postoperative Model (Model 2)

Variable	p-value	OR	95% CI
Current age [per 1-year increase]	0.002	1.02	1.01 – 1.04
Current weight [per 1-kg increase]	0.503	1.00	0.99 – 1.01
Race [ref: White]			
Other	0.894	0.94	0.39 – 2.29
Black	0.335	1.26	0.79 – 2.00
Asian	0.632	1.22	0.54 – 2.72
ALND [ref: SLNB]	<0.001	3.62	2.25 – 5.83
Any chemotherapy [ref: no]	0.047	1.68	1.01 – 2.81
Do you have swelling now? [ref: no]			
Yes	<0.001	10.85	7.48 – 15.74
Unknown	0.772	1.14	0.46 – 2.76

CI, confidence interval. OR, odds ratio.

Figure 1. ROC Curves and Performance Metrics



C and D show performance metrics as a function of optimal probability cutoff based on the Youden index for respective models: model 1=18%, model 2=10% (dashed lines).

Figure 2. Calibration and Validation ROC Plots

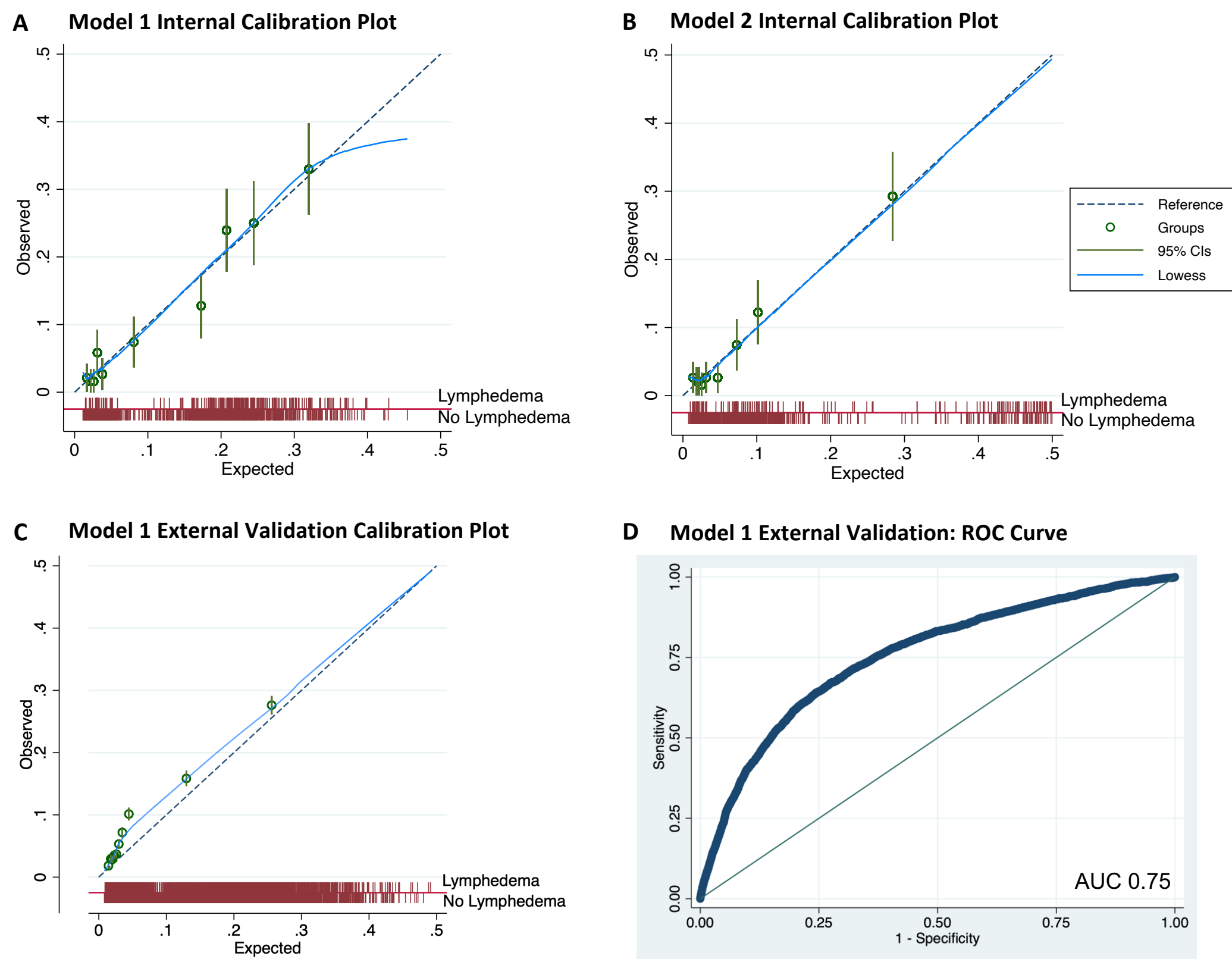
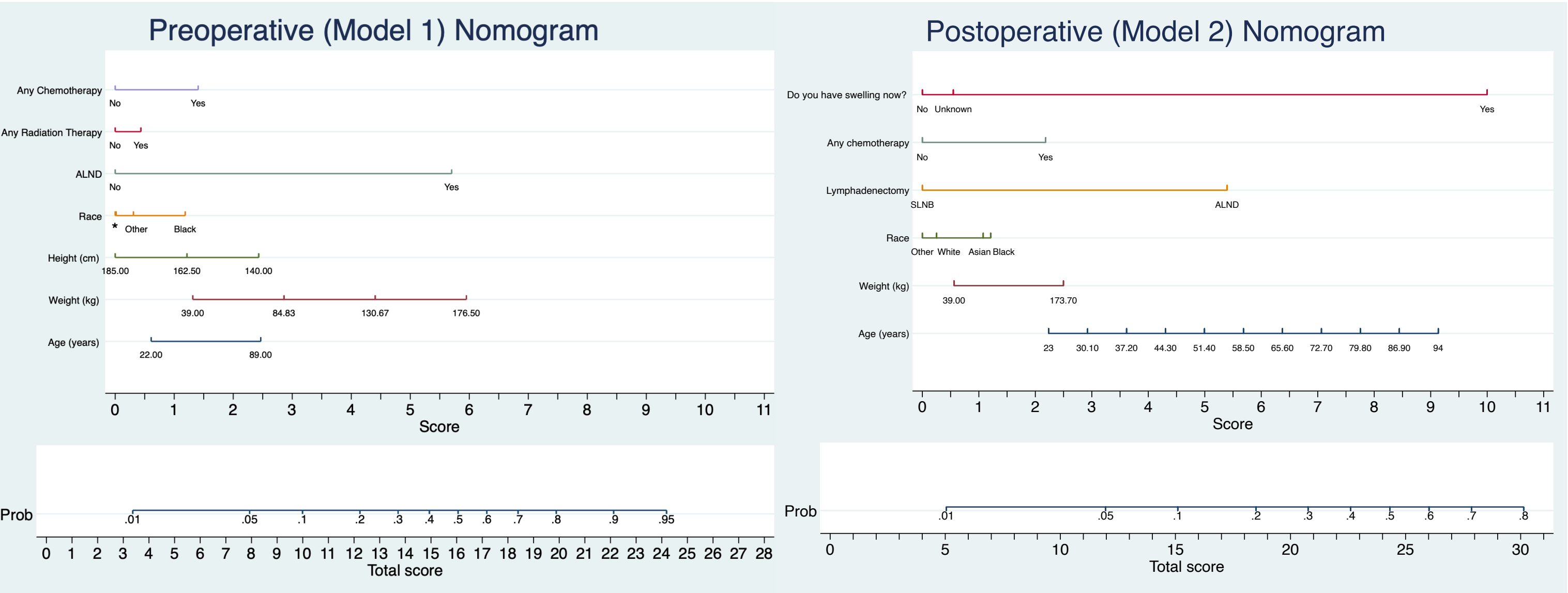


Figure 3. Nomograms for Predictive Models



*Race: White=0 points, Asian=0.3 points.

Conclusions

- With 73.0% accuracy (86.5% accuracy on external validation), the preoperative model (model 1) identifies patients with an 18% risk of developing BCRL.**
 - This model can be used to target high-risk patients for perioperative risk reduction measures and early institution of postoperative preventive therapies.
- With 81.1% accuracy, the postoperative model (model 2) identifies patients with a 10% risk of developing BCRL.**
 - This model identifies patients that should be closely monitored and similarly targeted for preventive and early therapeutic measures, thereby reducing the need for lymphedema surveillance with in-person limb measurements.
- The developed preoperative and postoperative prediction models for BCRL are highly accurate and clinically relevant tools comprised of accessible inputs that can connect patients with appropriate interventions.