# Supplemental Online Content

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Univariable and Multivariable Logistic Regression Modeling Lymphedema Development

| Variable	Univariable analysis			Multivariable analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Baseline age [per 1-year]	0.99	0.98 – 1.00	0.094	0.91	0.65 – 1.26	0.553
Follow-up age [per 1-year]	0.99	0.98 – 1.00	0.072	1.12	0.80 – 1.55	0.507
Baseline weight [per 1-kg increase]	1.01	1.01 – 1.02	<0.001	0.78	0.52 – 1.17	0.234
Follow up weight [per 1-kg increase]	1.01	1.01 – 1.02	<0.001	1.30	0.86 – 1.95	0.213
Weight change [per 1-kg increase]	1.00	0.98 – 1.02	0.749	0.78	0.52 – 1.17	0.227
Height [per cm]	1.00	0.98 – 1.02	0.797	0.98	0.96 – 1.00	0.110
Follow up years [per year]	0.95	0.88 – 1.03	0.249	1.07	0.77 – 1.50	0.675
Race [ref: white]						
Other	1.54	0.71 – 3.23	0.270	1.23	0.51 – 2.94	0.644
Black	2.51	1.72 – 3.68	<0.001	1.85	1.20 – 2.86	0.005
Asian	1.27	0.64 – 2.50	0.499	1.08	0.51 – 2.30	0.836
Mastectomy/BCT [ref: BCT]	1.97	1.48 – 2.62	<0.001	1.23	0.82 – 1.85	0.311
Tumor size [per cm]	1.20	1.12 – 1.28	<0.001	1.02	0.94 – 1.10	0.669
No. nodes removed [per LN]	1.08	1.07 – 1.09	<0.001	1.02	1.00 – 1.04	0.115
No. positive nodes [per 1-LN positive]	1.09	1.06 – 1.12	<0.001	1.01	0.98 – 1.05	0.496
ALND/SLNB [ref: SLNB]	9.47	6.42 – 13.95	<0.001	6.12	3.45 – 10.85	<0.001
Any radiation therapy [no]	1.66	1.15 – 2.40	0.007	1.38	0.83 – 2.30	0.215
Any chemotherapy [no]	4.50	2.95 – 6.86	<0.001	1.62	0.98 – 2.66	0.058
Neoadjuvant chemotherapy [no]	3.11	2.31 – 4.19	<0.001	1.21	0.79 – 1.86	0.379
Do you have swelling now? [ref: no]						
Yes	18.89	13.54 – 26.35	<0.001	-	-	-
Unknown	1.39	0.59 – 3.30	0.452	-	-	-
Have you had infections? [ref: no]						
Yes	2.47	1.40 – 4.35	0.002	-	-	-
Unknown	0.37	0.15 – 0.93	0.034	-	-	-

Patient-reported outcomes excluded from multivariable analysis. ALND, axillary lymph node dissection. BCT, breast conserving therapy. CI, confidence interval. LN, lymph node. OR, odds ratio. Ref, reference. SLNB, sentinel lymph node biopsy.

eFigure 1. Margins Plots for Model 1 by Variable
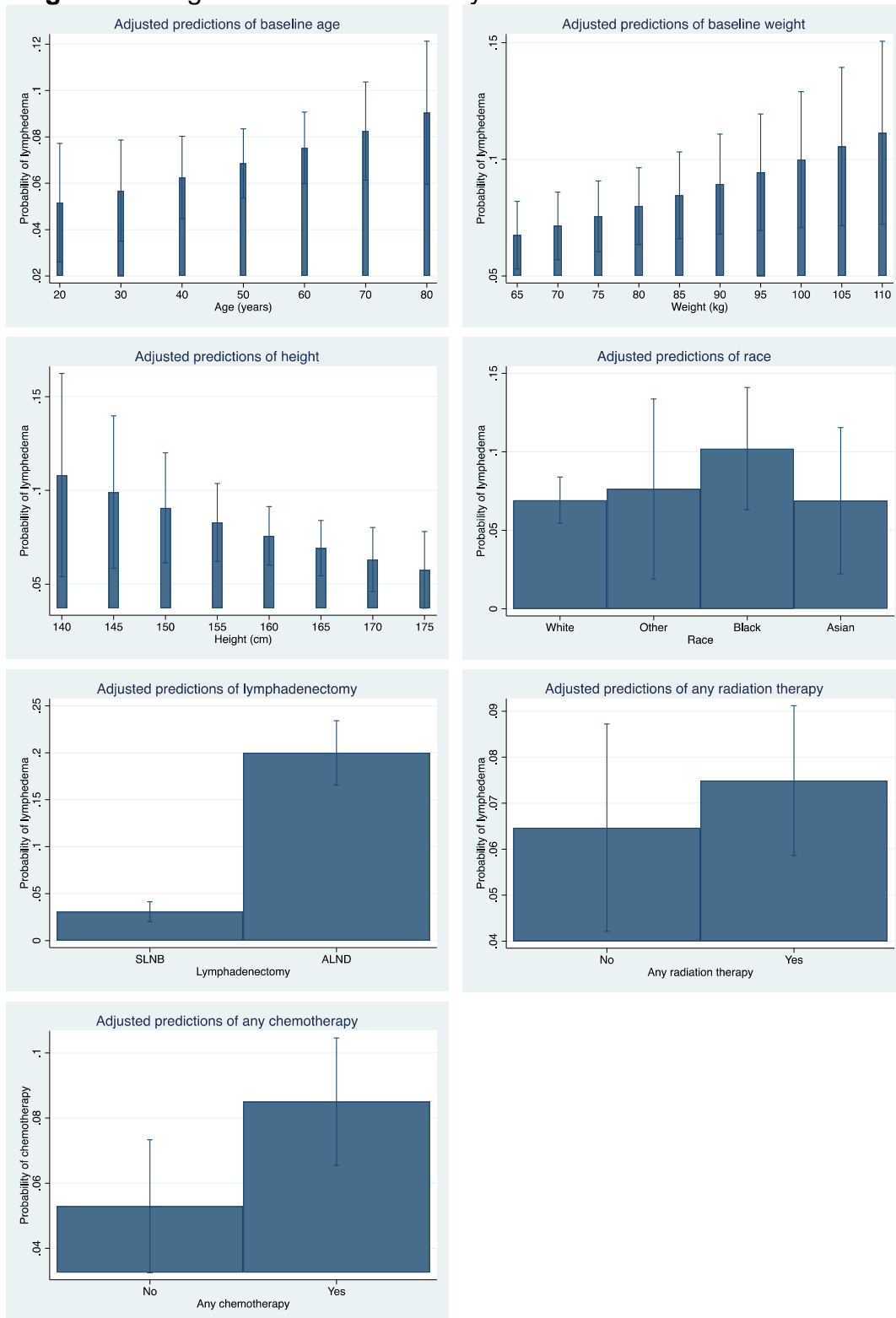
Adjusted predicted margins are computed at sample means. Each column represents the probability that a patient with a given characteristic has lymphedema with the rest of the predictors in the model set at their mean values. For instance, the probability of BCRL in a patient who underwent ALND is 20.0% compared to 3.1% for SLNB, when all other predictors are at their average value. Bars represent 95% confidence intervals.

eFigure 2. Margins Plots for Model 2 by Variable
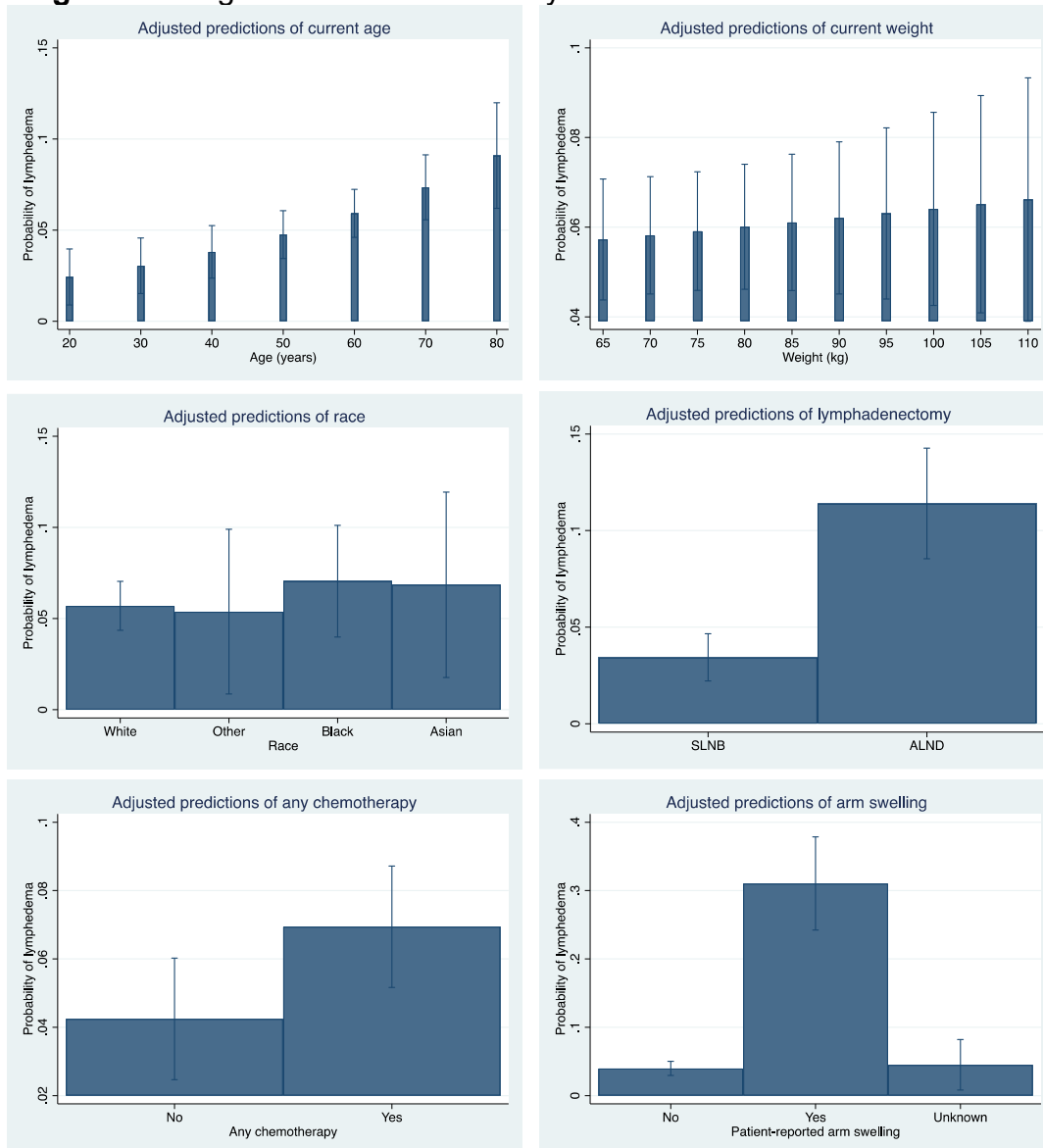
Adjusted predicted margins are computed at sample means. Each column represents the probability that a patient with a given characteristic has lymphedema with the rest of the predictors in the model set at their mean values. For instance, the probability of BCRL in a patient who underwent ALND is 11.4% compared to 3.4% for SLNB, when all other predictors are at their average value. Bars represent 95% confidence intervals.

eTable 2. Sensitivity Analysis: Bayesian Logistic Regression

| Variable	OR	95% Credible Interval	MCSE
Preoperative Model (model 1)			
Baseline age [per 1-year increase]	1.01	1.00 – 1.02	0.0034
Baseline weight [per 1-kg increase]	1.01	1.00 – 1.02	0.0003
Height [per 1-cm increase]	0.98	0.97 – 0.99	0.0006
Race			
White [ref]	-	-	-
Other	1.08	0.45 – 2.04	0.0305
Black	1.57	1.10 – 2.18	0.0341
Asian	0.99	0.47 – 1.73	0.0668
Lymphadenectomy			
SLNB [ref]	-	-	-
ALND	8.26	5.45 – 12.62	0.2067
Any radiation therapy			
No [ref]	-	-	-
Yes	1.20	0.78 – 1.78	0.0126
Any chemotherapy			
No [ref]	-	-	-
Yes	1.64	1.16 – 2.24	0.0387
Postoperative Model (model 2)			
Current age [per 1-year increase]	1.03	1.01 – 1.04	0.0011
Current weight [per 1-kg increase]	1.00	0.99 – 1.01	0.0003
Race			
White [ref]	-	-	-
Other	1.34	0.64 – 2.44	0.0477
Black	1.39	0.88 – 2.04	0.0239
Asian	1.46	0.61 – 2.58	0.0953
Lymphadenectomy			
SLNB [ref]	-	-	-
ALND	4.20	2.95 – 5.99	0.01587
Any chemotherapy			
No [ref]	-	-	-
Yes	1.39	0.93 – 2.00	0.0574
Do you have swelling now?			
No [ref]	-	-	-
Yes	11.95	9.07 – 15.85	11.813
Unknown	1.07	0.55 – 2.20	0.9786

ALND, axillary lymph node dissection. MCSE, Monte Carlo standard error. OR, odds ratio. Ref, reference. RT, radiation therapy. SLNB, sentinel lymph node biopsy. Random-walk Metropolis-Hastings sampling. Markov Chain Monte Carlo (MCMC) iterations=12,500, Burn-in=2,500. MCMC sample size=10,000.

eTable 3. Patient Demographic and Clinical Data for MSKCC *ICD* Validation Cohort

Variable	MSKCC ICD (n=34,438)
Age at surgery (years)	55.2 ± 12.4
Height (cm)	161.3 ± 6.6
Weight at surgery (kg)	71.4 ± 16.7
BMI at surgery (kg/m^2)	27.5 ± 6.2
Follow up (years)	6.2 ± 5.0
Lymphedema	
Yes	2,787 (8.1%)
No	31,651 (91.9%)
Race	
Asian	2,695 (7.8%)
Black	3,160 (9.2%)
White	27,670 (80.4%)
Other	913 (2.7%)
Lymphadenectomy	
ALND	5,927 (17.2%)
SLNB	28,511 (82.8%)
Any radiation therapy (yes)	16,606 (48.2%)
Any chemotherapy (yes)	13,575 (39.4%)
Neoadjuvant chemotherapy (yes)	2,502 (7.3%)

ALND, axillary lymph node dissection. ICD, International Classification of Diseases. MSKCC, Memorial Sloan Kettering Cancer Center. SLNB, sentinel lymph node biopsy.

eFigure 3. Ten-Fold ROC Curves for Model 2 Internal Validation

Model 2 Internal Validation
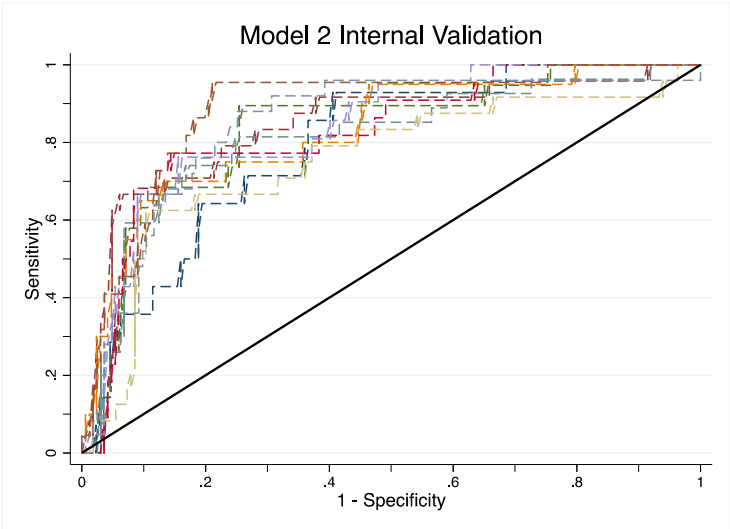
Cross-validated mean AUC (cvAUC)=0.82, bootstrap bias corrected 95% CI=0.79 – 0.85, cross-validated standard deviation (cvSD)=0.04, k=10.

eTable 4. Literature Review of Predictive Models for Breast Cancer-Related Lymphedema (BCRL)

Source	Definition of Lymphedema	Cohort	Predictive Model	Nomogram	Accuracy/Validation
Soran et al. 2011	N/A	51 women with lymphedema compared to 126 controls matched based on age, radiation therapy, and type of operation (lumpectomy, mastectomy +/- reconstruction). SLNB/ALND not reported.	Model constructed using Bayes' theorem and published estimates of lymphedema incidence, based on combinations of 3 modifiable risk factors: - Upper extremity infection - Level of occupational/hobby hand use - BMI ≥25	No	N/A
Bevilacqua et al. 2012	Volume difference of ≥200 ml between arms at ≥6 months postoperative	1,054 women with breast cancer who underwent lumpectomy or mastectomy and ALND. BCRL cumulative incidence 30.3% over 5 years.	Model predicts 5-year probability at each time point, derived from hazard ratios (Cox regression). Model 1: preoperative - Age, BMI, number cycles neoadjuvant chemotherapy in ipsilateral arm Model 2: within 6 months of surgery - Model 1 factors + level of axillary dissection, radiotherapy field Model 3: ≥6 months from surgery - Model 2 factors + seroma, early edema	Yes	C-index=0.71–0.74 External (Li et. al 2017): AUC=0.71 Hosmer-Lemeshow test p=0.0634 External (Soran et al. 2016): AUC=0.60–0.61
Kim et al. 2013	Grading system based on patient perception of arm edema, and arm circumference measurement	772 patients with breast cancer who underwent mastectomy or BCS and ALND. 127 developed BCRL (cumulative incidence 17% over 5 years). Excluded if neoadjuvant chemotherapy.	Model based on hazard ratios (Cox regression) using combinations of: - Number of dissected axillary nodes - Adjuvant chemotherapy - Supraclavicular radiation therapy Divided into low-, intermediate-, and high-risk groups based on number of risk factors. Each group with lymphedema rate at 5 years.	No	N/A

Source	Definition of Lymphedema	Cohort	Predictive Model	Nomogram	Accuracy/Validation
Wang et al. 2016	Circumferential arm measurement	358 women with breast cancer who underwent ALND. 31.8% incidence of lymphedema at 12 months.	Scoring system derived from odds ratios (logistic regression). Model factors: • Level of ALND • Hypertension • Surgery on dominant arm • Radiotherapy • Surgical infection, seroma, and/or early edema	No	AUC=0.88
Basta et al. 2017	ICD-9 code	3,136 women with breast cancer diagnosis and mastectomy in institutional electronic medical records. BCRL in 325 (10.4%) with average follow-up of 4.2 years (range 1.0-14.8). ALND in 39.4%, no report of SLNB.	Model 1 (based on adjusted hazard ratios, Cox regression): Risk Factor Model • Invasive cancer, post-mastectomy radiation, age >65, ALND, WHO Class 2 or 3 obesity, neoadjuvant chemotherapy, bilateral mastectomy; BMI≤25 (protective) Model 2 (based on stratification of composite risk scores from Risk Factor Model): Risk Assessment Tool Evaluation Lymphedema, RATE-L • 2 point factors: invasive cancer, post-mastectomy radiation, age >65 • 1 point factors: axillary dissection, BMI>35, neoadjuvant chemotherapy, bilateral mastectomy • -1 point factor: BMI≤25 Composite score 0-2=low risk, 3-4=moderate risk, 5-6=high risk, 7+=extreme risk, each corresponding to % risk of lymphedema	No	C-index=0.77–0.78. Plot of martingale hazard residuals against Cox-Snell generalized residuals for goodness-of-fit.

Source	Definition of Lymphedema	Cohort	Predictive Model	Nomogram	Accuracy/Validation
Gross et al. 2019	NCI of Canada Common Toxicity Criterion Version 2.0 grade 2 ("moderate lymphedema requiring compression") or higher	1,832 women with breast cancer (node-positive or high-risk node negative) who underwent BCS, radiation, adjuvant chemo and/or hormone therapy, and SLNB and/or ALND (3.7% with SLNB alone). Median 8.2 (IQR 5.1-10.1) year follow-up.	Model derived from odds ratios (logistic regression) including factors: • BMI • Extent of axillary surgery (number of nodes removed) • Extent of nodal radiation (RNI field group)	Yes	Internal: C-index=0.69 Calibration plot External: C-index=0.71 Calibration plot
Kwan et al. 2020	Limb volume calculated from circumferential measurements (mild >200ml, severe >500 ml)	373 women who completed breast cancer treatment, with median follow-up of 1.1 (IQR 0.6-2.5) years since cancer diagnosis, divided into training (n=247) and validation (n-126) cohorts. ALND in 54.3% of training cohort and 46.0% of validation cohort, no report of SLNB.	5-factor model based on linear regression to predict lymphedema risk: • Age • BMI • Mammographic breast density • Number of pathologic lymph nodes • ALND Factors also used to predict volume of lymphedema based on equation: lymphedema volume = -329 + [4 x Age] + [10 x BMI] – [37 x Mammographic breast density] + [13 x No. pathologic lymph nodes] + [99 x ALND]	No	AUC=0.72–0.83
Liu et al. 2021	Sequential circumferential arm measurements; difference of $\geq$ 2cm	533 women who underwent surgery for breast cancer including SLNB (19.3%) and/or ALND (80.7%); 355 for model establishment (28.7% with lymphedema) and 178 for validation (30.3% with lymphedema) with unspecified follow-up time.	Additive scoring system (6-22 points) based on odds ratios (logistic regression). Model factors: • Medical: surgery type (lumpectomy vs. mastectomy), type of axillary surgery (SLNB vs. ALND), early edema, neoadjuvant chemotherapy, radiotherapy • Behavioral: "use of the affected arm to lift or carry heavy objects suddenly"	No	AUC=0.74 Hosmer-Lemeshow test p=0.274

Source	Definition of Lymphedema	Cohort	Predictive Model	Nomogram	Accuracy/Validation
Byun et al. 2021	Subjective patient report of arm swelling, heaviness, tightness, or numbness, and/or difference in arm circumference ≥ 2cm at >1 location	5,549 women with breast cancer who underwent lumpectomy or mastectomy. 639 developed BCRL at median follow-up of 60.1 months (range 12-140.2). SLNB/ALND not reported.	Model derived from hazard ratios (Cox regression) to predict 2-, 3-, and 5-year probability. Factors in model: • BMI • Total vs. partial mastectomy • Taxane-based chemotherapy • Radiation field/fractionation type • Number of dissected nodes	Yes	Internal: C-index = 0.77 iAUC = 0.75 Calibration plots External: C-index = 0.82-0.83, iAUC = 0.78-0.80 Calibration plots External (Byun et al 2022): C-index = 0.79 iAUC = 0.76 Calibration plots
Wei et al. 2021	Sequential circumferential measurements; difference of ≥ 1cm for early detection or ≥ 2cm for late detection	553 breast cancer survivors who had completed surgery including SLNB (19.3%), ALND (44.3%), or both (36.4%), split into training and validation groups.	Symptom-warning model derived from logistic regression using 17 symptom features for early detection and 12 symptoms for late detection	No	Early detection: (internal validation) AUC=0.89 (0.84-0.94) Sensitivity=0.77 Specificity=0.88 Accuracy=0.83 Brier score=0.14 Late detection: (internal validation) AUC=0.93 (0.88-0.97) Sensitivity=0.90 Specificity=0.85 Accuracy=0.86 Brier score=0.10

Source	Definition of Lymphedema	Cohort	Predictive Model	Nomogram	Accuracy/Validation
Yuan et al. 2021	Volumetric arm measurements (water displacement); >10% difference defined as lymphedema	320 women with node-positive breast cancer who underwent BCS or mastectomy, and ALND; 60 (18.7%) with BCRL at median 29 months (range 20-34). Excluded if neoadjuvant chemotherapy.	Arm Lymphatics Distribution (ALD) model for intraoperative risk prediction of lymphedema development based on odds ratios (logistic regression). Factors in model: • BMI • Taxane-based chemotherapy • Radiotherapy • Proportion of arm lymph flow above the level of the axillary vein (protective)	Yes	Internal: AUC=0.83 Hosmer-Lemeshow test p=0.721 Calibration plot External: AUC=0.80 Hosmer-Lemeshow test p=0.804 Calibration plot
Martinez-Jaimez et al. 2022	Recorded diagnosis of lymphedema, and medical/ physiotherapist report indicating ≥ 2cm difference in arm circumference	504 women who underwent breast cancer surgery (BCS or mastectomy) including ALND. 156 (31%) developed lymphedema within 2 years.	Logistic regression to model and identify significant risk factors: • Level of ALND • Lymph node status • Postoperative complications • BMI • Number of nodes extracted	No	AUC=0.68
Konishi et al. 2022	Diagnosis of lymphedema based on record of treatment associated with postoperative lymphedema, as documented in nationwide claims database	84,022 women who underwent breast cancer surgery; 1,547 (1.8%) received treatment for lymphedema during median follow up of 119 weeks (IQR 59-187). SLNB in 63.4%, ALND in 24.7%.	Identified prognostic factors based on multivariable survival analysis • Baseline factors: young age, BMI, smoking history, collagen diseases, advanced cancer stage, total mastectomy, ALND • Postoperative factors: bleeding, chemotherapy, radiotherapy	No	N/A

ALND, axillary lymph node dissection. AUC, area under curve. BCS, breast-conserving surgery. IQR, interquartile range. N/A, not available. NCI, National Cancer Institute. RNI, regional nodal irradiation. SLNB, sentinel lymph node biopsy. WBI, whole breast irradiation.