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Dose to the axillary-lateral thoracic vessel junction predicts breast cancer-related lymphedema after postmastectomy radiotherapy: development and temporal validation of NTCP and Nomogram models

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Abstract

Background

Breast cancer-related lymphedema (BCRL) is a disabling late complication after postmastectomy radiotherapy (PMRT). This study evaluated the axillary-lateral thoracic vessel junction (ALTJ) as a functional organ-at-risk (OAR), established its dose-response relationship with BCRL, and developed validated predictive models to guide individualized risk mitigation.

Methods

271 patients treated with PMRT from 2019 to 2022 constituted the development cohort, and 45 independent patients treated in 2023 formed the temporal validation cohort. All patients underwent modified radical mastectomy. The ALTJ was contoured on planning CT according to Gross et al. Candidate clinical factors and ALTJ dose–volume histogram (DVH) parameters were analyzed. A normal tissue complication probability (NTCP) model was developed using LASSO-based screening followed by multivariable logistic regression, and a Cox regression–based nomogram was built using multi-method consensus feature selection. Both models were evaluated and validated without refitting in the temporal cohort.

Results

The 2-year cumulative BCRL incidence was 25.1% in the development and 22.2% in the validation cohort. Multivariable analysis identified the number of dissected lymph nodes (LNDno) and ALTJ V30 as the strongest predictors. The final NTCP model achieved an AUC of 0.816 in the development cohort and 0.860 in the validation cohort, with Brier scores of 0.135 and 0.111, respectively. A clinically actionable risk stratification system was derived using thresholds of LNDno > 13 and ALTJ V30 > 51.75%, identifying high-, moderate-, and low-risk groups with 2-year BCRL rates of 58.8%/54.5%, 26.4%/18.2%, and 5.3%/0% in the development and validation cohorts, respectively. A nomogram, integrating LNDno with ALTJ V25, V30, V35, and Dmean, achieved C-indices of 0.948 and 0.894 in the two cohorts, respectively.

Conclusions

This study identifies ALTJ V30 and surgical extent as important predictors of BCRL in postmastectomy patients receiving radiotherapy. The findings support the consideration of ALTJ as a quantifiable OAR and provide an evidence-based dose–volume constraint (V30 < 51.75%). The validated NTCP model and nomogram offer practical tools for individualized risk estimation and may inform targeted surveillance and preventive strategies.

1 Background

Long-term survival rate among patients with breast cancer has improved substantially in recent decades[1]. As survivorship has increased, greater emphasis has shifted toward preventing treatment-related chronic morbidity. Breast cancer-related lymphedema (BCRL) remains a major, often irreversible complication, causing chronic swelling, pain, functional limitation, and psychological distress[2]. Reported incidence ranges from 10% to 30% in general survivor populations and may exceed 50% in high-risk subgroups[3, 4].

Axillary lymph node dissection (ALND) is a well-established primary risk factor, directly damaging the axillary lymphatic network and associates with a BCRL incidence as high as 28.5%[5]. Postoperative radiotherapy can further amplify risk through microvascular endothelial injury and progressive fibrosis, thereby compromising residual lymphatic channels and soft-tissue compliance[6]. Historically, radiotherapy planning and research have focused on dosage of broad anatomical regions, lacking precision in delineating and sparing specific functional substructures within the complex axillary anatomy[7]. Furthermore, existing predictive models for BCRL rely predominantly on clinical parameters such as age, body mass index (BMI), and nodal status[8, 9], largely omitting critical dosimetric information. Even radiotherapy-specific nomograms rarely incorporate detailed dose-volume data from key axillary substructures[10, 11], limiting their utility for personalized, dosimetry-driven risk assessment.

Recent anatomical investigation has highlighted the axillary-lateral thoracic vessel junction (ALTJ) as a critical lymphatic confluence, serving as the principal hub for drainage from axillary Level I to central lymphatics[12]. This functional role supports the ALTJ as a novel, potential organ-at-risk (OAR) for BCRL. Preliminary studies have suggested a correlation between radiation dose to this area and lymphedema risk[13, 14]; however, these studies are limited by heterogeneous patient cohorts that include both breast-conserving surgery and mastectomy patients, obscuring the risk profile for the most vulnerable population.

Accordingly, this study aimed to: 1) definitively establish the dose-response relationship between ALTJ dose-volume histogram (DVH) parameters and BCRL risk in a homogeneous cohort of post-mastectomy patients; 2) develop and independently validate integrative normal tissue complication probability (NTCP) and nomogram models that synergize ALTJ dosimetry with established clinical features; and 3) propose an optimized, evidence-based dose constraint for the ALTJ as a functional OAR to guide precision radiotherapy planning.

2 Materials and Methods

2.1 Study design and population

This retrospective, single-center cohort study was approved by the Ethics Committee of Changshu No.1 People's Hospital, and the requirement for informed consent was waived due to the retrospective design.

Consecutive patients treated with postoperative radiotherapy after modified radical mastectomy between January 2019 and December 2022 were included as the development cohort (n = 271) for model building. An independent temporal validation cohort consisted of consecutive patients treated between January and December 2023 (n = 45) were included to assess model generalizability without refitting.

Eligibility criteria were: (1) female, age < 80 years; (2) Karnofsky performance status (KPS) > 80; (3) status post modified radical mastectomy; (4) pathologically confirmed invasive breast carcinoma; (5) indication for postoperative radiotherapy defined as tumor size > 5 cm or ≥ 4 positive axillary lymph nodes, or T1–2 disease with 1–3 positive axillary lymph nodes plus high-risk features (fewer than 10 axillary lymph nodes retrieved, lymphovascular tumor emboli, triple-negative breast cancer, or age < 35 years); (6) no contraindications to radiotherapy; and (7) no evidence of upper limb lymphedema prior to radiotherapy.

2.2 Radiotherapy technique and ALTJ delineation

All patients underwent CT simulation in the supine position using a dedicated breast board with the affected arm abducted and externally rotated. Radiotherapy plans were generated using either three-dimensional conformal radiotherapy (3D-CRT) or intensity-modulated radiotherapy (IMRT) techniques. The clinical target volumes (CTVs) were delineated according to European Society for Radiotherapy and Oncology (ESTRO) recommendations[15] and Radiation Therapy Oncology Group (RTOG) consensus guidelines[16]. Target volumes included the ipsilateral chest wall and supra-/infraclavicular regions; inclusion of the internal mammary drainage region was performed when clinically indicated. A conventional fractionation schedule of 50 Gy delivered in 25 fractions was prescribed.

The ALTJ was retrospectively delineated on the original planning CT images by two radiation oncologists, each with more than 10 years of subspecialty experience, in accordance with the definition and contouring guidance proposed by Gross et al.[12]. The ALTJ was defined as the anatomical confluence where the lateral thoracic vein and subscapular vein drain into the axillary vein, located superior to axillary Level I and inferior to the humeral head. All contours underwent blinded review by a senior radiation oncologist with over 15 years of experience, and discrepancies were resolved by consensus.

2.3 Lymphedema assessment and follow-up

The primary endpoint was the development of clinically significant upper limb BCRL. Diagnosis was based on serial circumferential measurements, defined as a persistent difference of ≥ 2 cm between the affected and contralateral limbs at any of the standard measurement points: 5 cm and 15 cm proximal to the olecranon process, or 10 cm distal to it[17]. Assessments were performed at the completion of radiotherapy and subsequently at each 3-month follow-up visit. The maximum follow-up was 28 months after radiotherapy. Patients without lymphedema were censored at the date of last follow-up.

2.4 Clinical and dosimetric variables

Based on prior literature[8–11], four clinical covariates were prespecified as candidate predictors: body mass index (BMI), number of dissected lymph nodes (LNDno), number of pathologically positive lymph nodes, and receipt of chemotherapy.

ALTJ dosimetric parameters were extracted from the treatment planning system and included maximum dose (Dmax), minimum dose (Dmin), mean dose (Dmean), and Vx parameters (V5, V10, V15, V20, V25, V30, V35, V40, V45, and V50), where Vx denotes the percentage volume of ALTJ receiving ≥ x Gy.

2.5 Statistical analysis

Patient, tumor and treatment characteristics were summarized using descriptive statistics. Continuous variables were reported as median with interquartile range (IQR) or mean ± standard deviation (SD) as appropriate, and categorical variables were reported as frequencies and percentages. Differences in baseline characteristics between the development and validation cohorts were compared using the Pearson's χ^2 test or Fisher's exact test for categorical variables, and the Mann-Whitney U test for continuous variables.

Predictive performance for binary outcomes (lymphedema vs. no lymphedema) was evaluated using the area under the receiver operating characteristic (ROC) curve (AUC). For time-to-event outcomes, Harrell's C-index was used. Calibration was assessed with the Hosmer-Lemeshow goodness-of-fit test ($P > 0.05$ indicating good fit). Kaplan–Meier methods were used to estimate cumulative BCRL incidence across risk strata, with comparisons by log-rank test. Statistical analyses were performed using SPSS (version 27.0.1.0) and R (version 4.5.1), with a two-sided $P < 0.05$ considered statistically significant.

2.6 Model development and validation

In accordance with TRIPOD principles[18], two distinct prediction models were developed using the development cohort and subsequently validated in the independent temporal validation cohort.

2.6.1 NTCP model

Least absolute shrinkage and selection operator (LASSO) regression was used for initial variable screening among candidate clinical and dosimetric predictors. Variables meeting prespecified significance criteria were entered into a multivariable logistic regression framework. Forward stepwise selection guided by the Akaike information criterion (AIC) was then performed: the subset with the lowest AIC was selected as the final NTCP model estimating probability of BCRL.

2.6.2 Nomogram Model

For time-to-event prediction, candidate predictors were screened using a consensus strategy comprising three approaches to ensure robustness: (1) variables with $P < 0.05$ in univariable Cox regression; (2) significant factors identified by the LASSO regression; and (3) features identified as important by the Boruta algorithm, a wrapper method built around a random forest classifier. Variables confirmed by all

three approaches were included in the final multivariable Cox model. A nomogram was constructed based on this final model to predict the 2-year cumulative lymphedema incidence rate.

3 Results

2.7 Patient characteristics

A total of 316 patients were included (development cohort, n = 271; independent validation cohort, n = 45). Baseline characteristics were generally balanced between cohorts (Table 1). In the development and validation cohorts, mean age was 56.63 ± 9.64 years and 56.58 ± 10.31 years, respectively. Mean BMI was 23.97 ± 3.27 kg/m² and 24.53 ± 3.12 kg/m², respectively. Mean LNDno was 13.50 ± 4.68 and 13.78 ± 2.63, and mean number of positive lymph nodes was 4.22 ± 5.04 and 4.84 ± 4.94, respectively. No significant differences were observed in tumor laterality, T/N stage, hormone receptor status, or other key variables.

Table 1
Baseline patient, tumor, and treatment characteristics of the patient cohorts

	Development Cohort **N = 271[1]**	**Validation Cohort** **N = 45[1]**	**P-value[2]**
Age	56.63(9.64)	56.58 (10.31)	0.967
Location			0.138
Left	145 (53.5%)	30 (66.7%)	
Right	126 (46.5%)	15 (33.3%)	
T Stage			0.154
1	104 (38.4%)	11 (24.4%)	
2	141 (52.0%)	27 (60.0%)	
3	24 (8.9%)	6 (13.3%)	
4	2 (0.7%)	1 (2.2%)	
N Stage			0.679
0	21 (7.7%)	2 (4.4%)	
1	153 (56.5%)	23 (51.1%)	
2	65 (24.0%)	13 (28.9%)	
3	32 (11.8%)	7 (15.6%)	
Stage			0.337
1	3 (1.1%)	0 (0%)	
2	160 (59.0%)	22 (48.9%)	
3	108 (39.9%)	23 (51.1%)	
Number of Dissected Lymph Nodes	13.50 (4.68)	13.78 (2.63)	0.565
Number of Pathologically Positive Lymph Nodes	4.22 (5.04)	4.84 (4.94)	0.438
Chemotherapy	262(96.7%)	43(95.6%)	0.824
ER			0.636
Negative	95 (35.1%)	18 (40.0%)	
Positive	176 (64.9%)	27 (60.0%)	

Abbreviations: BMI=body mass index; SD= standard deviation.

	Development Cohort N = 271[1]	Validation Cohort N = 45[1]	P-value[2]
PR			> 0.9
Negative	133 (49.1%)	22 (48.9%)	
Positive	138 (50.9%)	23 (51.1%)	
Her2			0.743
Negative	173 (63.8%)	27 (60.0%)	
Positive	98 (36.2%)	18 (40.0%)	
Ki-67			> 0.9
≤ 5	20 (7.4%)	3 (6.7%)	
5 ~ 30	111 (41.0%)	18 (40.0%)	
>30	140 (51.6%)	24 (53.3%)	
BMI(kg/m^2)	23.97 (3.27)	24.53 (3.12)	0.271
BMI Group			0.232
≥ 23.9	133 (49.1%)	27 (60.0%)	
≤ 23.9	138 (50.9%)	18 (40.0%)	
Lymphedema Event	68 (25.1%)	10 (22.2%)	0.821
[1]Mean (SD); n (%).[2]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test			
Abbreviations: BMI=body mass index; SD= standard deviation.			

2.8 Lymphedema incidence

In the development cohort, 68 patients (25.1%) developed BCRL during follow-up, with a median time to onset of 13.5 months. The cumulative incidence rates at 12 and 24 months were 11.4% and 25.1%, respectively. In the validation cohort, 10 patients (22.2%) developed BCRL (median time: 10.5 months), with 12- and 24-month cumulative incidences of 13.3% and 22.2%. The difference in 24-month incidence between the two cohorts was not statistically significant (P = 0.821).

2.9 ALTJ dosimetric parameters

Dosimetric parameters for ALTJ are detailed in Table 2. In the development cohort, the median ALTJ volume was 14.9 cm³ (IQR: 13.3–17.7). Median Dmax, Dmean, and Dmin were 49.0 Gy (46.2–52.1), 26.8 Gy (19.6–33.6), and 2.6 Gy (1.7–8.6), respectively. Median ALTJ V30 was 41.4% (26.2–60.0). In the

validation cohort, the corresponding values were 12.2 cm³ (9.8–15.1), 49.6 Gy (48.2–50.6), 30.1 Gy (26.7–33.1), 10.2 Gy (6.0–17.9), and 49.2% (41.5–54.6), respectively. Overall distributions of ALTJ DVH metrics were broadly similar between cohorts, although selected metrics (including ALTJ volume and Dmin) differed.

Table 2
ALTJ dosimetric parameters in the development and validation cohorts

	Development Cohort N = 271[1]	**Validation Cohort N = 45[1]**	**P-value[2]**
ALTJ volume(cm^3)	14.9 (13.3, 17.7)	12.2 (9.8, 15.1)	< 0.001
ALTJ Dmax(Gy)	49.0 (46.2, 52.1)	49.6 (48.2, 50.6)	0.595
ALTJ Dmean(Gy)	26.8 (19.6, 33.6)	30.1 (26.7, 33.1)	0.052
ALTJ Dmin(Gy)	2.6 (1.7, 8.6)	10.2 (6.0, 17.9)	< 0.001
ALTJ V5(%)	79.9 (69.3, 95.9)	84.5 (81.9, 90.0)	0.051
ALTJ V10(%)	73.6 (57.4, 91.5)	78.4 (74.7, 79.8)	0.076
ALTJ V15(%)	68.8 (52.4, 86.8)	71.9 (69.9, 75.3)	0.124
ALTJ V20(%)	62.7 (46.9, 81.3)	67.2 (64.1, 70.0)	0.105
ALTJ V25(%)	52.1 (35.6, 68.5)	56.2 (51.4, 61.2)	0.126
ALTJ V30(%)	41.4 (26.2, 60.0)	49.2 (41.5, 54.6)	0.111
ALTJ V35(%)	43.4 (26.6, 57.3)	44.4 (40.5, 50.3)	0.613
ALTJ V40(%)	34.2 (17.3, 45.4)	36.2 (28.7, 45.7)	0.294
ALTJ V45(%)	21.2 (4.0, 29.4)	21.5 (13.8, 30.4)	0.231
ALTJ V50(%)	10.6 (1.5, 15.4)	5.5 (2.4, 11.2)	0.031

[1]Median (IQR); [2]Wilcoxon rank sum test

Abbreviations: ALTJ= axillary-lateral thoracic vessel junction; Dmax= maximum dose; Dmin=minimum dose; Dmean=mean dose; Vx denotes the percentage volume of ALTJ receiving ≥ x Gy; IQR= interquartile range.

2.10 Model performance

2.10.1 NTCP model

Univariable analysis followed by LASSO regression identified LNDno, ALTJ V30, ALTJ Dmean, and ALTJ V25 as significant predictors. In multivariable logistic regression, ALTJ V30 (OR = 3.47, 95% CI: 2.00–6.00, P < 0.001), LNDno (OR = 1.55, 95% CI: 1.13–2.21, P < 0.001) and ALTJ V25 (OR = 0.322, 95% CI: 0.194–0.532, P < 0.001) were significantly associated with BCRL and remained independent predictors

(**Fig. 1**). LNDno (OR = 1.30, 95% CI: 1.19–1.43, P < 0.001) and ALTJ V30 (OR = 1.03, 95% CI: 1.02–1.05, P < 0.001) were used as 2 highly predictive variable to develop the NTCP model. The final NTCP model was:

$$NTCP_{Logit} = \frac{1}{1 + e^{-Logit(P)}}$$

Logit(P) = 1.03×ALTJ V30 + 1.30×LNDno − 6.53

Figure 1. LASSO regression multi-factor importance analysis

The model demonstrated robust performance with an AUC of 0.816 and a Brier score of 0.135 in the development cohort. In the independent validation cohort, the model maintained high predictive accuracy with an AUC of 0.860 and a Brier score of 0.111, supporting its external validity (Fig. 2).

For clinical implementation, the optimal cut-off was determined by the Youden index. Patients were stratified into three risk groups based on LNDno and ALTJ V30: (1) High risk: LNDno > 13 and ALTJ V30 > 51.75%; (2) Moderate risk: one of the two factors present; (3) Low risk: neither factor present.

In the development cohort, the 2-year BCRL incidence was 58.8% in the high-risk group, 26.4% in the moderate-risk group, and 5.3% in the low-risk group. The corresponding rates in the validation cohort were 54.5%, 18.2%, and 0%, respectively. Kaplan–Meier curves confirmed a significantly different cumulative incidence of lymphedema among these groups. (log-rank P < 0.001, Fig. 3).

2.10.2 Nomogram model

After consensus feature selection (including LASSO and Boruta), LNDno and multiple ALTJ DVH parameters (including Dmean, V25, V30, V35, and V50) were evaluated in multivariable Cox regression (Fig. 4). The final predictors used to construct the nomogram for estimating 2-year BCRL risk were LNDno (HR = 0.99, 95%CI: 0.95–1.04), ALTJ Dmean (HR = 1.13, 95%CI: 1.03–1.23), ALTJ V25 (HR = 0.75, 95%CI: 0.69–0.81), ALTJ V30 (HR = 1.54, 95%CI: 1.41–1.68), and ALTJ V35 (HR = 0.85, 95%CI: 0.81–0.89) (Fig. 5).

The nomogram demonstrated excellent discrimination, with a C-index of 0.948 in the development cohort and 0.894 in the validation cohort. Moreover, decision curve analysis indicated a favorable net benefit, and the calibration plots showed good agreement between predicted and observed risk (Fig. 6).

4 Discussion

In this homogeneous cohort of patients treated with modified radical mastectomy and followed by postoperative radiotherapy, we identified a synergistic relationship between surgical extent and functionally targeted axillary dosimetry in predicting BCRL. Specifically, the number of dissected lymph nodes (LNDno) and ALTJ V30 emerged as independent, dominant predictors and formed the basis of a parsimonious, clinically interpretable NTCP model that retained strong performance in an independent

temporal validation cohort. We further developed a clinical–dosimetric nomogram integrating LNDno with multiple ALTJ intermediate-dose metrics (Dmean, V25, V30, V35), achieving high discrimination and demonstrable clinical utility. Importantly, risk stratification based on two readily accessible thresholds (ALTJ V30 > 51.75% and LNDno > 13) delineated a marked gradient in 2-year BCRL risk. This approach identifies a patient subgroup for whom targeted preventive strategies and ALTJ-focused plan optimization may be particularly impactful.

A key strength of the present study is its exclusive focus on patients treated with modified radical mastectomy. Prior ALTJ-related studies often included heterogeneous cohorts combining breast-conserving surgery and mastectomy[12–14]. Because breast-conserving surgery typically preserves more axillary lymphatic architecture, baseline lymphatic reserve—and therefore BCRL susceptibility—differs substantially from that of patients undergoing more extensive axillary surgery[19–21]. By restricting the cohort to modified radical mastectomy, our analysis targets a clinically relevant setting of substantial baseline lymphatic disruption. Within this context, the ALTJ—conceptualized as a critical lymphatic confluence for axillary Level I drainage[12]—may represent a disproportionately important residual pathway. Radiation-related endothelial injury and fibrosis at this junction, even at the intermediate-dose range, could plausibly impair lymphatic decompensation. Our findings support the "dual-hit" pathophysiological model, where the initial surgical insult is critically exacerbated by subsequent radiation injury to this pivotal structure[22, 23]. The stability and interpretability of the combined LNDno–ALTJ V30 signal in our models may reflect this biologically and anatomically constrained vulnerability.

Our findings also refine that how radiotherapy dose should be conceptualized in relation to BCRL. Historically, many studies have focused on dose to broad axillary anatomical regions (Levels I–III)[24]. This approach, by averaging dose over large volumes, may mask clinically significant heterogeneity within functionally critical substructures. By delineating the ALTJ as a distinct OAR and evaluating its DVH identified, we identified ALTJ V30 as a robust, clinically relevant predictor in the NTCP model. While prior studies by Park et al.[14] and Kim et al.[13] identified correlations with parameters like V35 or Dmax, we identify V30 as the dominant factor, particularly in a mastectomy-only cohort, thereby refining the understanding of the dose-risk relationship.

The clinical impact of this work is twofold. First, the two-parameter stratification (LNDno and ALTJ V30) provides an immediately implementable approach to identify patients at high risk (2-year risk > 54%), in whom early physiotherapy referral, structured surveillance, and preventive counseling could be prioritized. Second, the proposed dose constraint—maintaining ALTJ V30 below 51.75%—provides a clear, quantitative objective for the radiotherapy planner. Using techniques such as IMRT or proton therapy to achieve this constraint while preserving target coverage provides a tangible strategy for reducing the risk of BCRL.

Furthermore, the nomogram provides additional nuance by incorporating multiple intermediate-dose metrics (V25, V30, V35) and Dmean, which collectively suggest a continuous dose–response relationship across approximately 25–35 Gy rather than an exclusively threshold-driven phenomenon.

This continuous-risk profile likely explains why the multivariable nomogram provides better discrimination than the simpler, clinical-only tools reported in prior studies[25]. Methodologically, we strengthened predictor identification by combining conventional regression screening with LASSO and Boruta selection. This multi-method consensus strategy was designed to improve feature stability in the presence of collinearity among DVH parameters and to limit overfitting when evaluating high-dimensional dosimetric feature sets[18, 26]. The maintenance of performance in an independent temporally cohort, without refitting, supports the transportability of these models within comparable PMRT practice settings.

Several limitations should be acknowledged. Firstly, the retrospective, single-center design limits causal inference and introduces potential selection bias. Although the use of a temporally independent validation cohort is valuable, it cannot fully address the fundamental constraints of the retrospective approach. Secondly, the sample size—particularly in the validation cohort—was modest; therefore, multicenter validation across institutions and involving patient populations with diverse racial backgrounds will be essential to establish broader generalizability. Thirdly, BCRL was defined using circumferential measurements, a clinically standard method[17], which may be less sensitive than bioimpedance spectroscopy (BIS) for detecting subclinical lymphedema[27]. Future studies incorporating BIS-based endpoints, together with emerging strategies such as radiomics[28] and circulating biomarkers[29], may enable earlier risk identification and facilitate further refinement of ALTJ constraints and risk-adapted preventive interventions.

5 Conclusions

In conclusion, this study establishes the ALTJ as a pivotal functional OAR, whose radiation dose, specifically the V30, interacts synergistically with surgical extent to determine BCRL risk following mastectomy. We developed and validated an NTCP model and a Cox-based nomogram in an independent temporal cohort, providing clinically implementable tools that translating ALTJ dosimetry into individualized risk estimates. This evidence translates into a specific planning constraint: limiting ALTJ V30 to < 51.75%. Collectively, these findings represent a pivotal advancement towards function-preserving breast cancer radiotherapy. Prospective trials are warranted to confirm that adherence to these dosimetric principles yield measurable improvements in patient-reported lymphedema outcomes without compromising oncologic efficacy.

Abbreviations

BCRL
breast cancer-related lymphedema
PMRT
postmastectomy radiotherapy
ALND

axillary lymph node dissection
BMI
body mass index
ALTJ
axillary-lateral thoracic vessel junction
OAR
organ at risk
DVH
dose-volume histogram
NTCP
normal tissue complication probability
KPS
Karnofsky performance status
3D-CRT
three-dimensional conformal radiotherapy
IMRT
intensity-modulated radiotherapy
CTV
clinical target volume
ESTRO
European Society for Radiotherapy and Oncology
RTOG
Radiation Therapy Oncology Group
LNDno
number of dissected lymph nodes
Dmax
maximum dose
Dmin
minimum dose
Dmean
mean dose
IQR
interquartile range
SD
standard deviation
ROC
receiver operating characteristic
AUC
area under the ROC curve
LASSO

least absolute shrinkage and selection operator
AIC
Akaike information criterion
BIS
bioimpedance spectroscopy

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Changshu No.1 People's Hospital, and the requirement for informed consent was waived due to the retrospective design. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and the principles of the Declaration of Helsinki.

Consent for publication

Not applicable.

Availability of data and materials

The data are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

N.X and C.Y. performed data statistics and drafted the main manuscript. F.W., C.Z. and H.G. were involved in data collection and data statistics. Z.J. reviewed the target regions, and participated in the revision and review of the manuscript.

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Figures

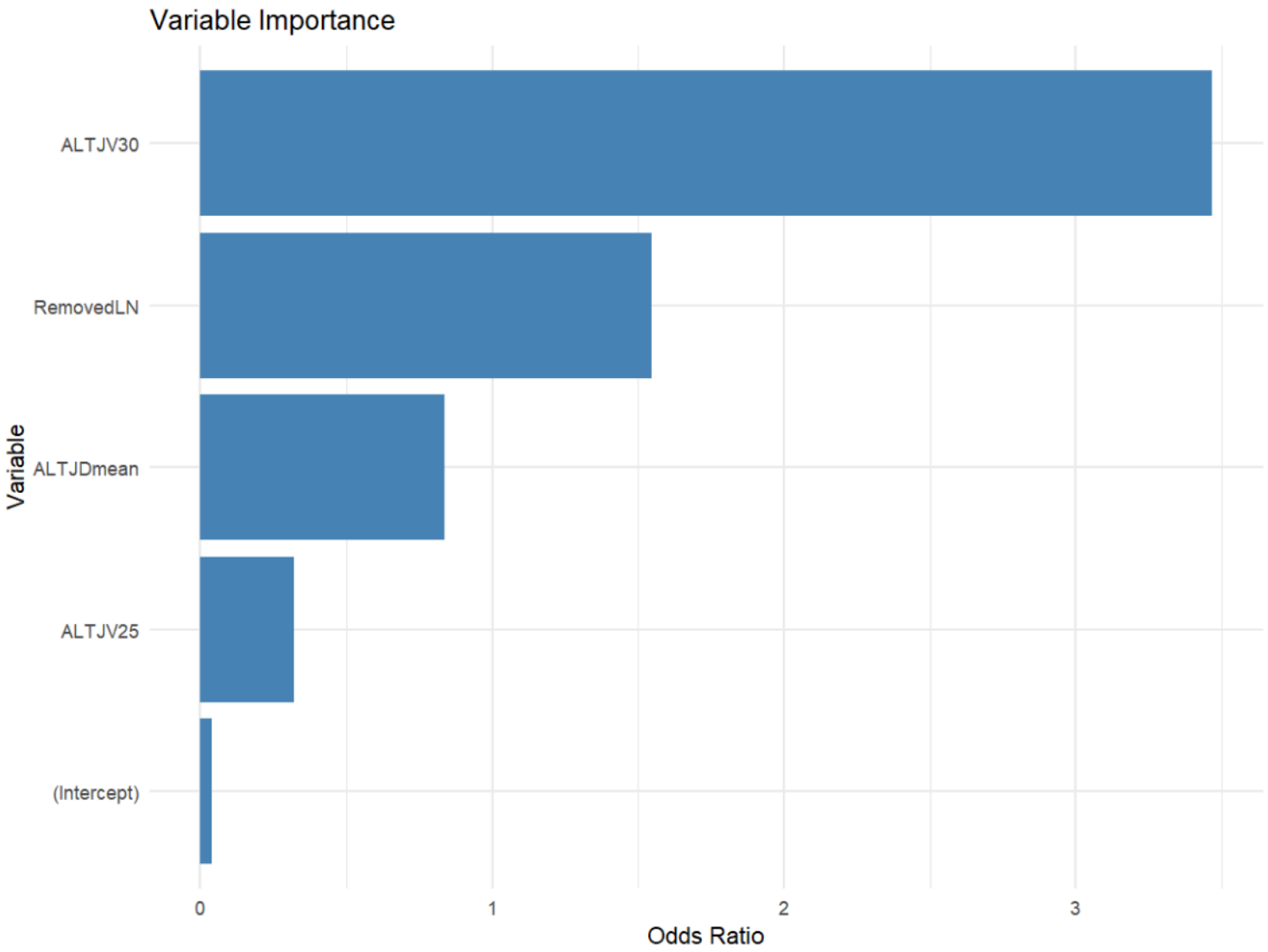


Figure 1

LASSO regression multi-factor importance analysis

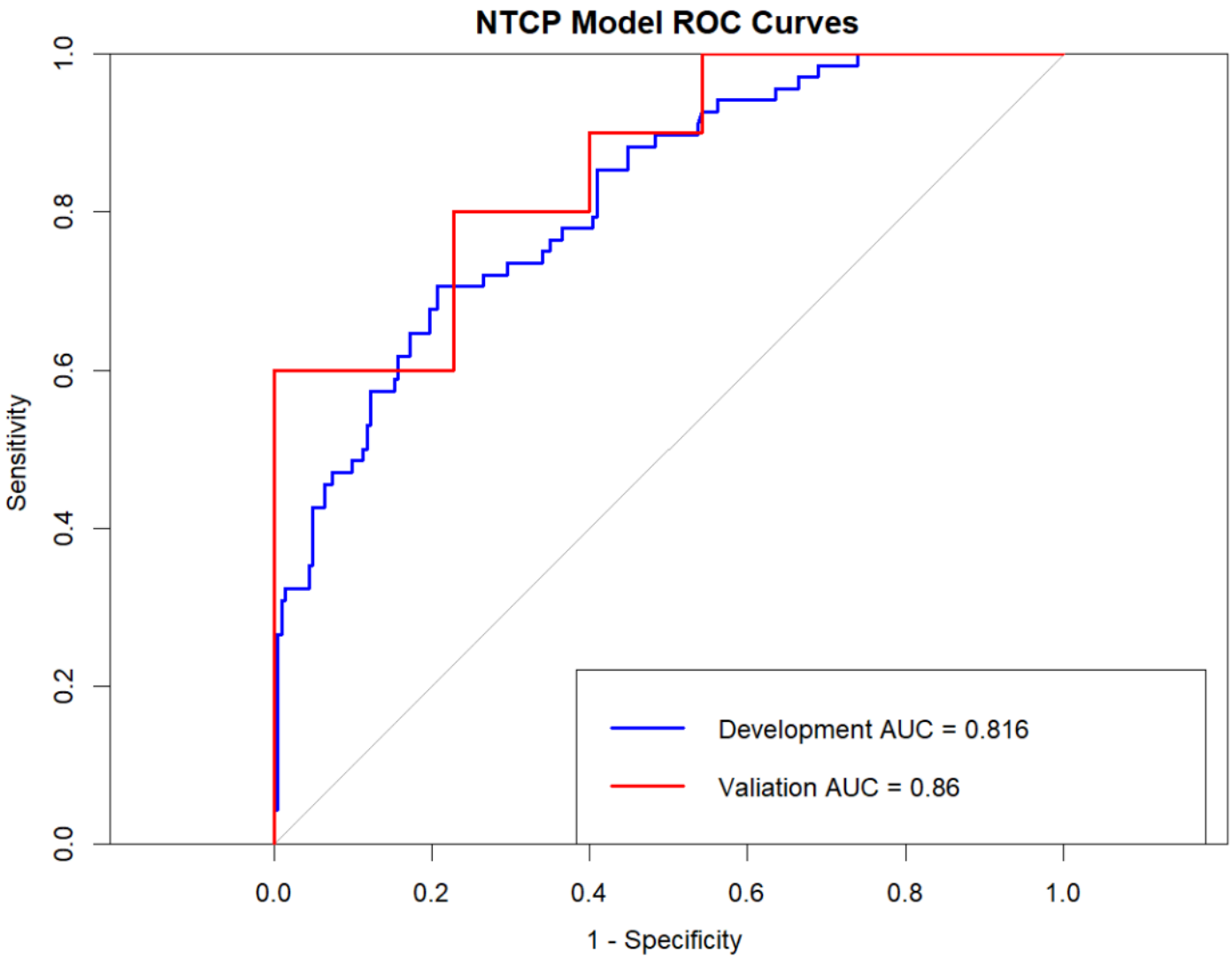


Figure 2

ROC curves of NTCP model in development and validation cohorts

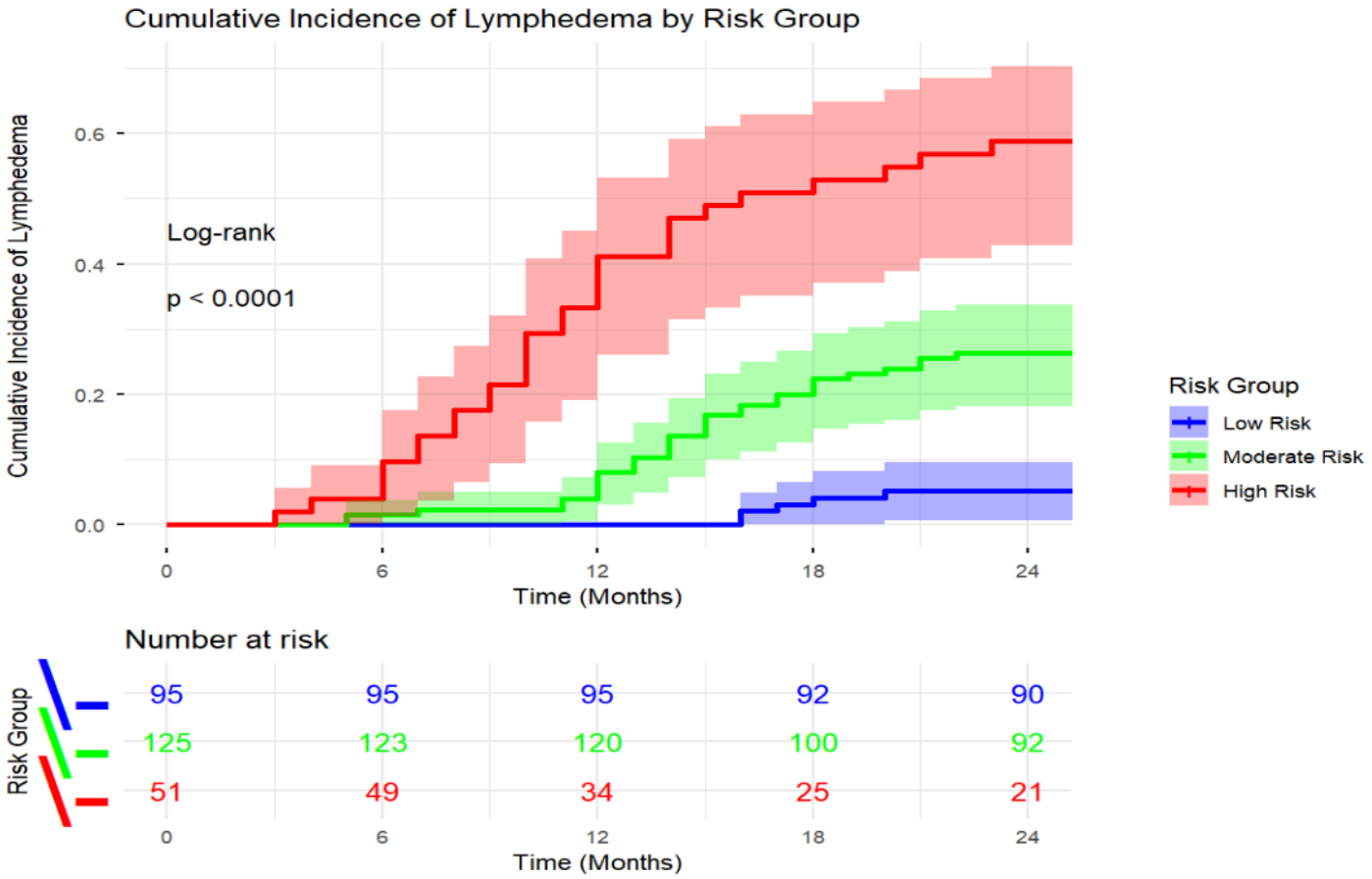


Figure 3

Cumulative incidence of lymphedema stratified by clinical and dosimetric risk factors. High risk: LNDno > 13 and ALTJ V30 > 51.75%, Moderate risk: LNDno > 13, ALTJ V30 ≤ 51.75% or LNDno ≤ 13, ALTJ V30 > 51.75%, Low risk: LNDno ≤ 13, ALTJ V30 ≤ 51.75%. ALTJ= axillary-lateral thoracic vessel junction, ALTJ V30= percentage volume of ALTJ receiving ≥ 30 Gy.

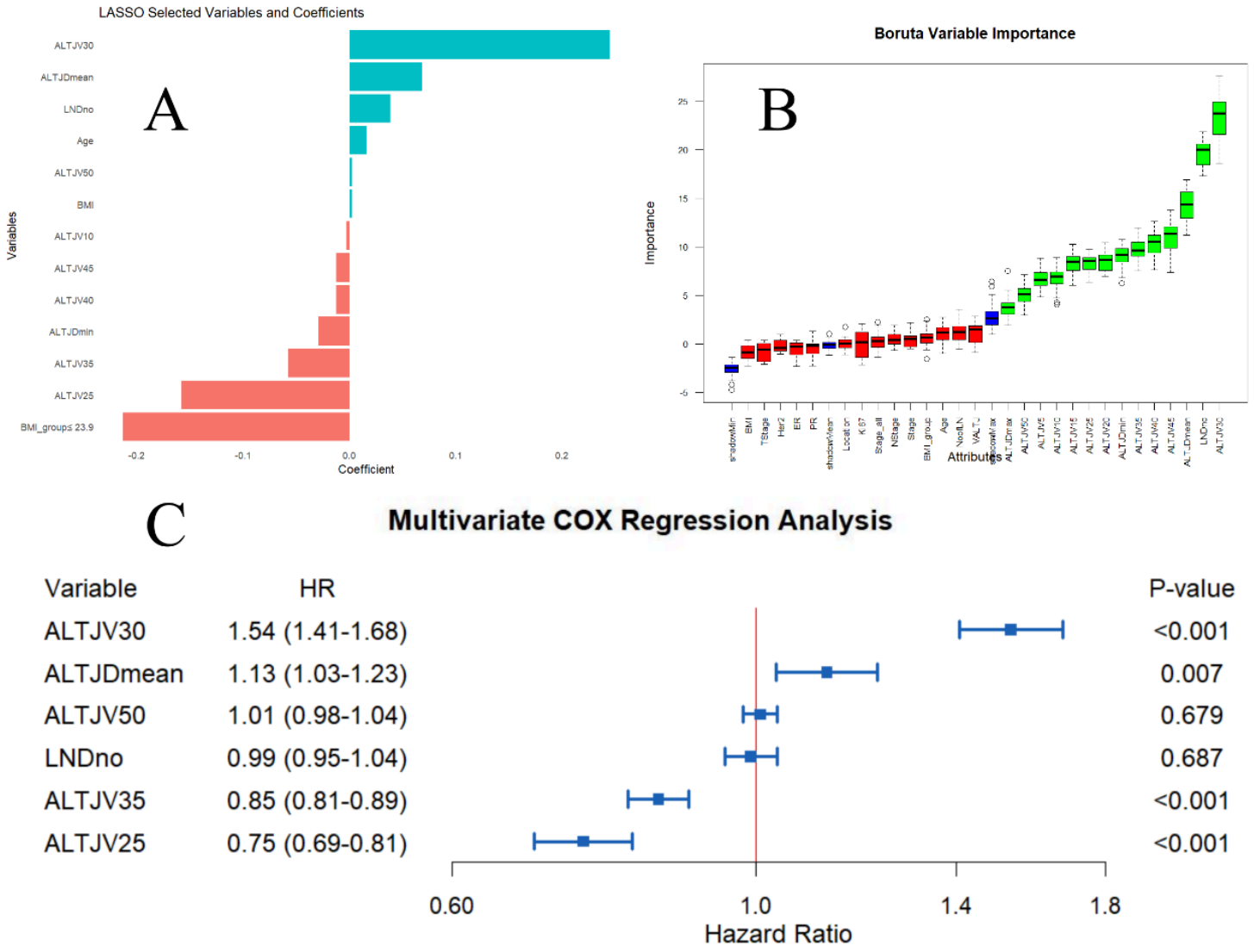


Figure 4

A: Factors selected by LASSO regression. B: Importance distribution of factors identified by the Boruta algorithm. C: Results of the multivariate Cox regression model.

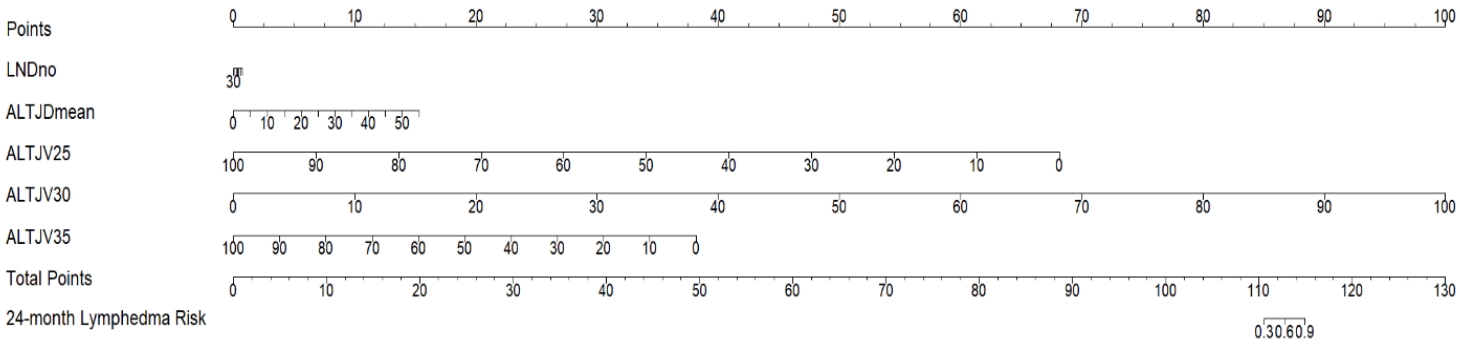


Figure 5

Nomogram model

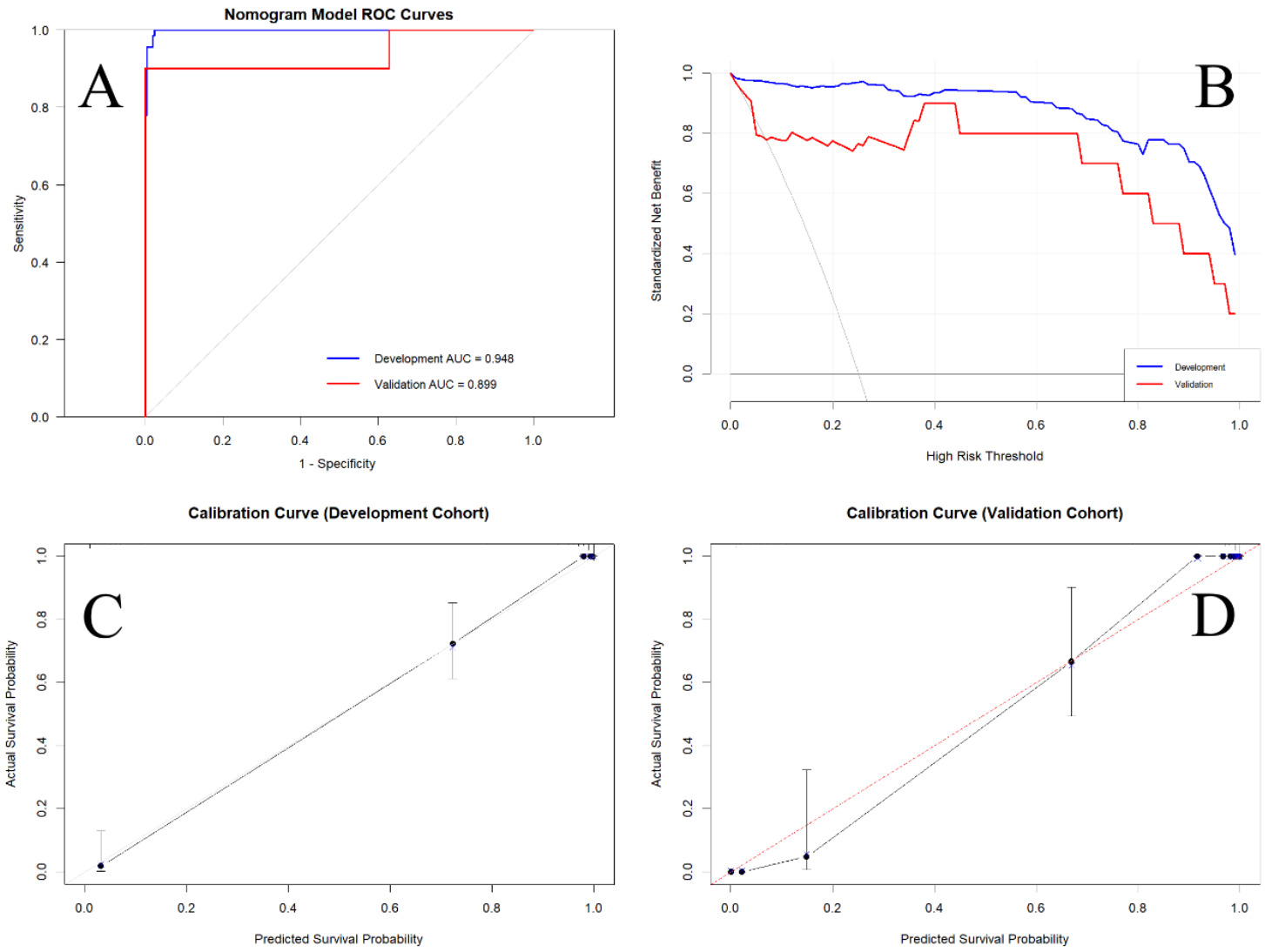


Figure 6

A: ROC curve of the nomogram model. B: Decision curve analysis (DCA) curve. C: Calibration curve in the development cohort. D: Calibration curve in the validation cohort.