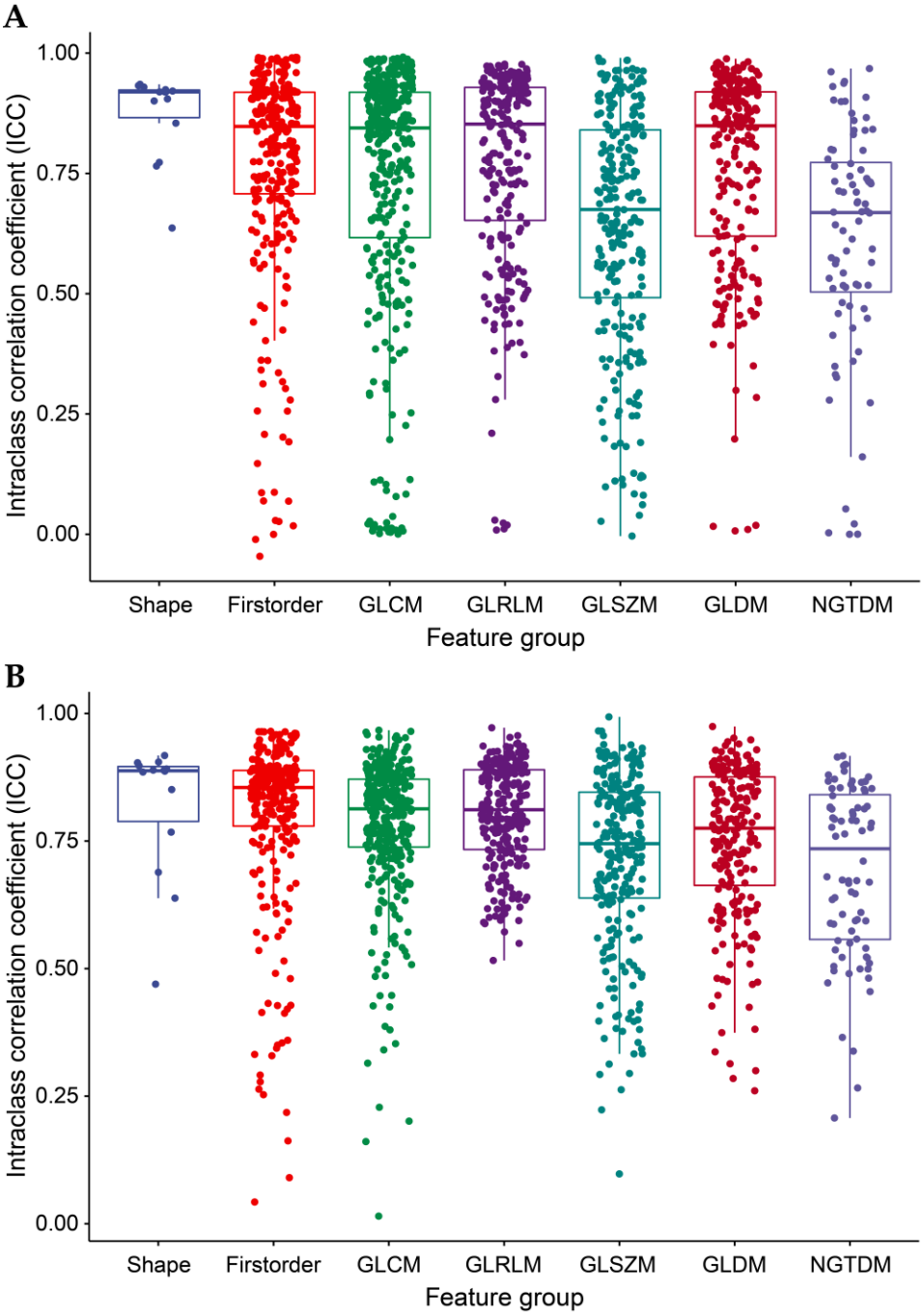
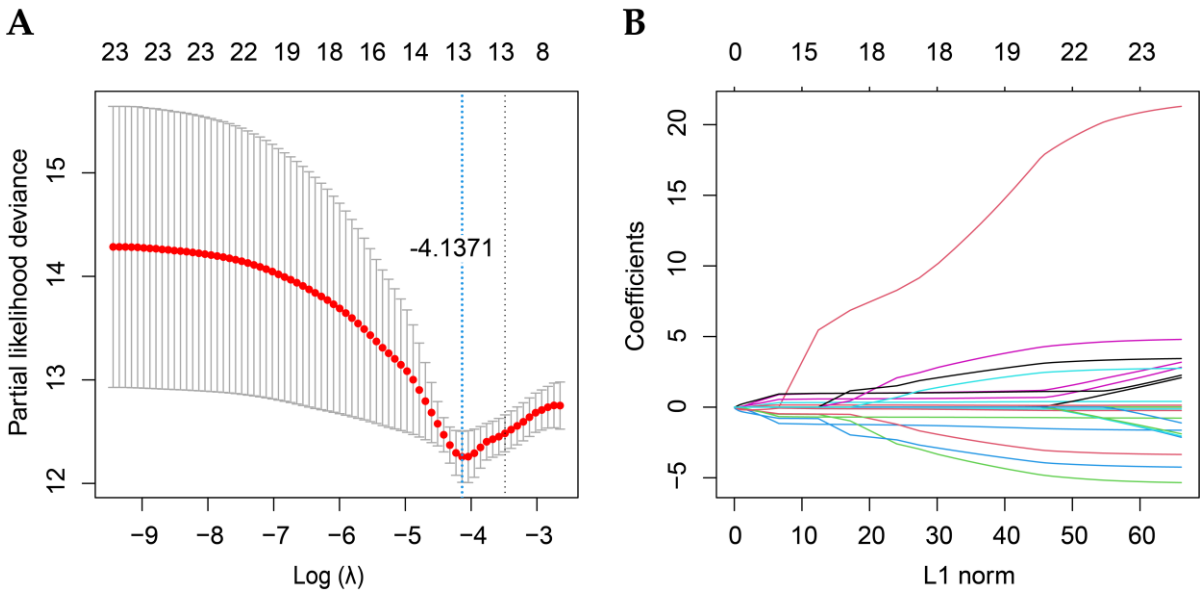
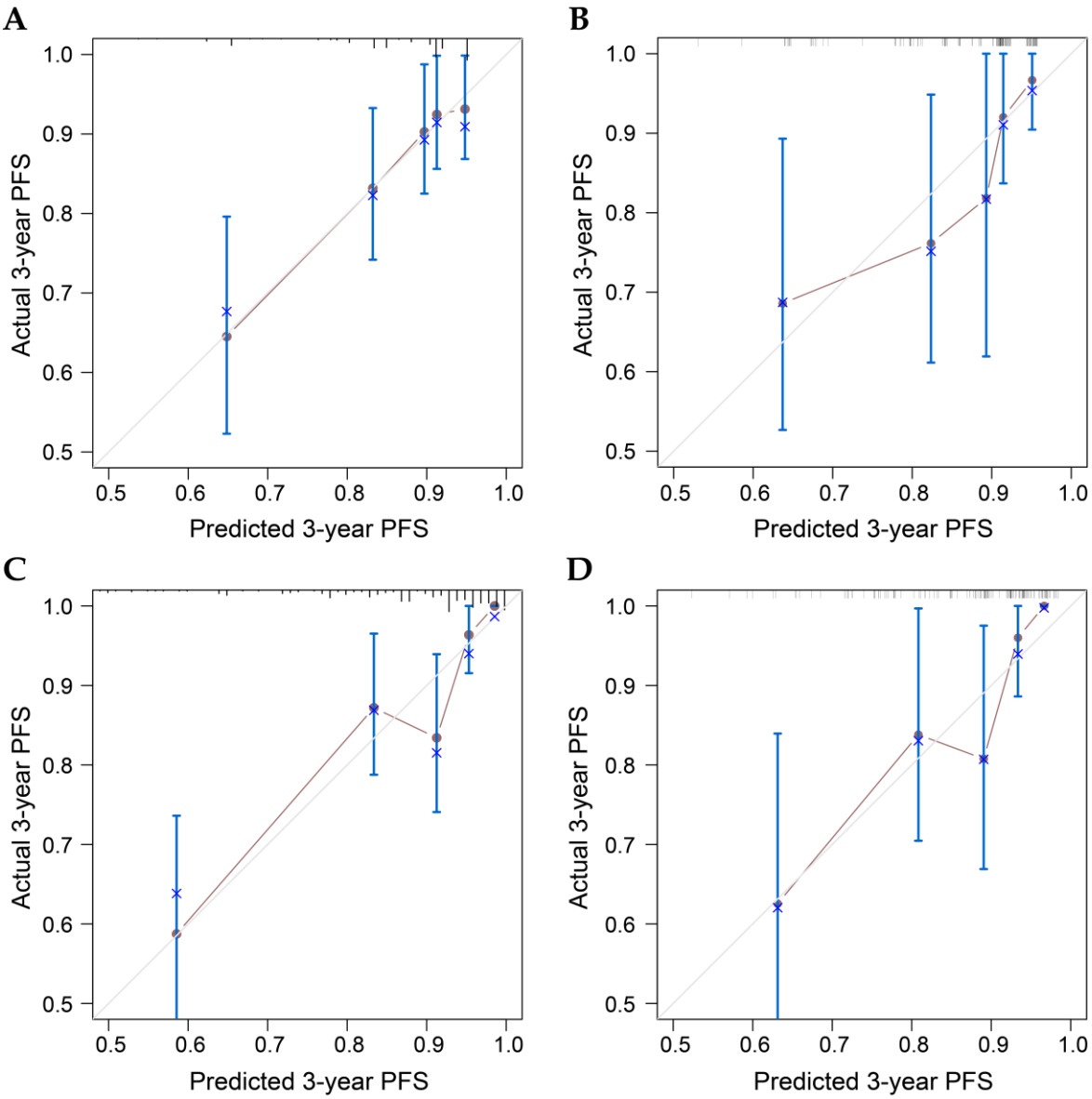
Supplementary Figures



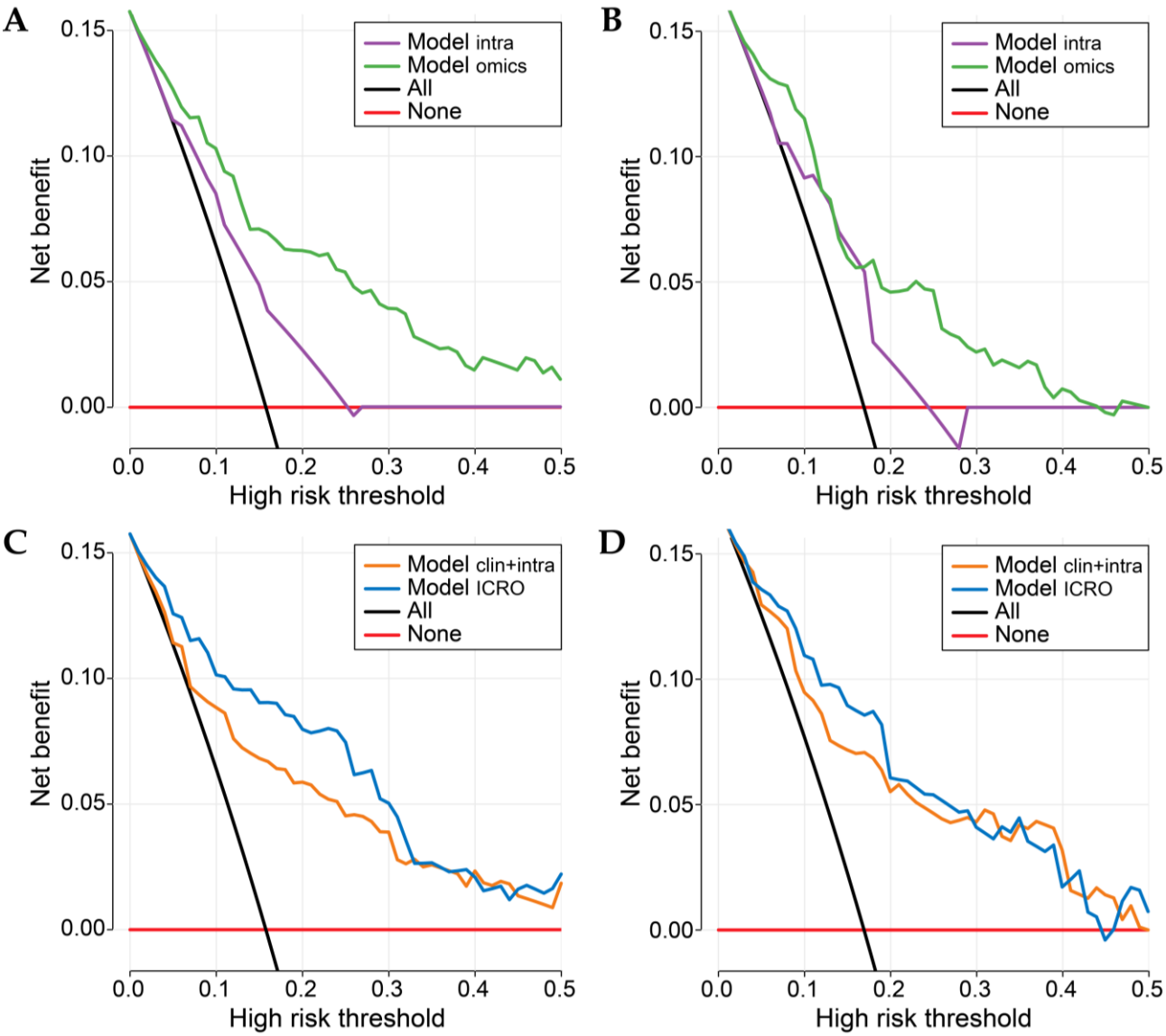
Supplementary Figure 1 Distribution of intraclass correlation coefficien for different radiomic feature groups. A: Intratumoral features; B: Peritumoral features across various radiomic feature categories, including Shape, Firstorder, GLCM, GLRLM, GLSZM, GLDM, and NGTDM. ICC: Intraclass correlation coefficient; GLCM: Gray level co-occurrence matrix; GLRLM: Gray level run length matrix; GLSZM: Gray level size zone matrix; GLDM: Gray level dependence matrix; NGTDM: Neighborhood gray tone difference matrix.



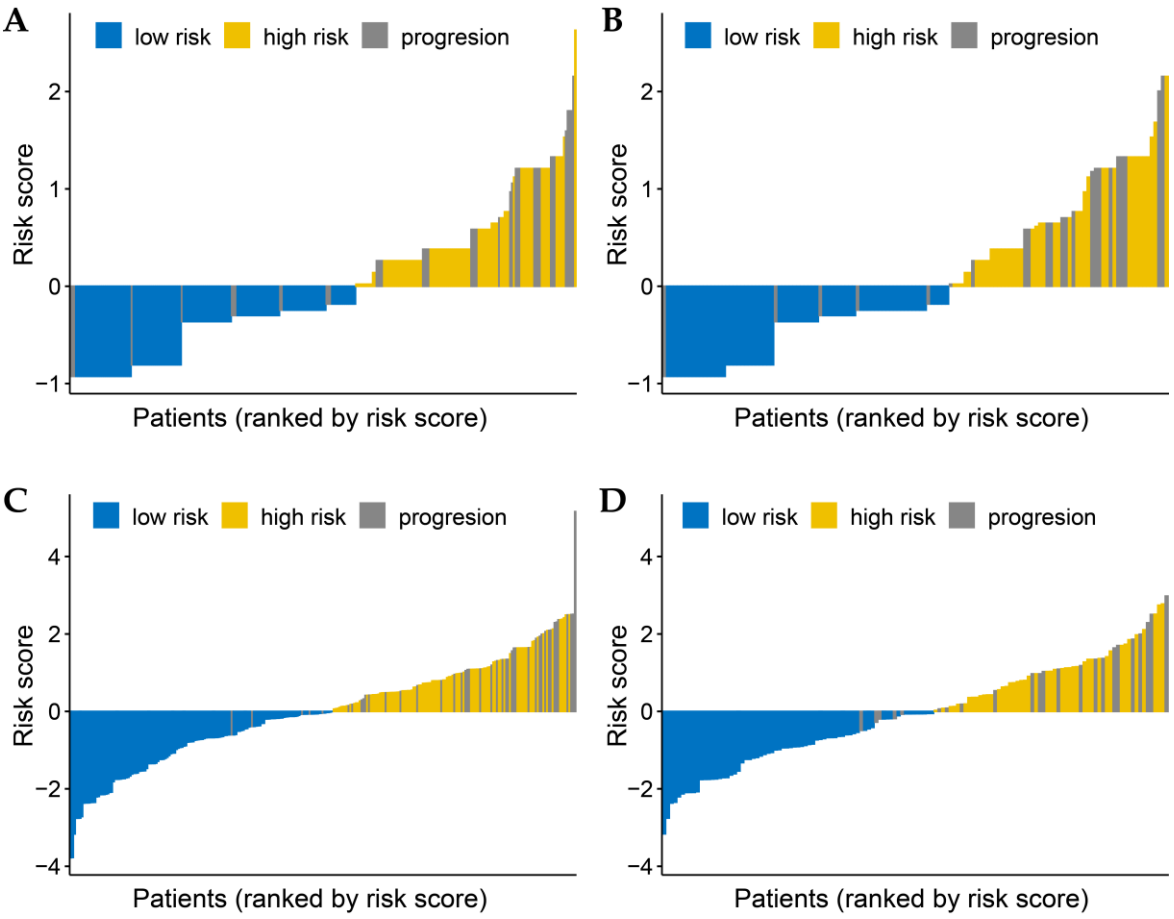
Supplementary Figure 2 Radiomics feature selection using least absolute shrinkage and selection operator. LASSO regression was employed for feature selection within a Cox proportional hazards model framework. The tuning parameter (λ) was determined through 10-fold cross-validation. A: The deviance curve illustrates the partial likelihood of the Cox model plotted against log(λ). The vertical dotted lines indicate the optimal values based on the minimum criterion (blue line) and the 1-standard-error criterion (grey line). The minimum criterion yielded an optimal λ value of 0.0160 (log(λ) = -4.1371), resulting in the identification of 13 features with nonzero coefficients; B: Coefficient profiles of the radiomics features in the LASSO-Cox regression model are displayed. Further bidirectional stepwise selection of the LASSO-Cox model retained three intratumoral and seven peritumoral features. LASSO: Least absolute shrinkage and selection operator.



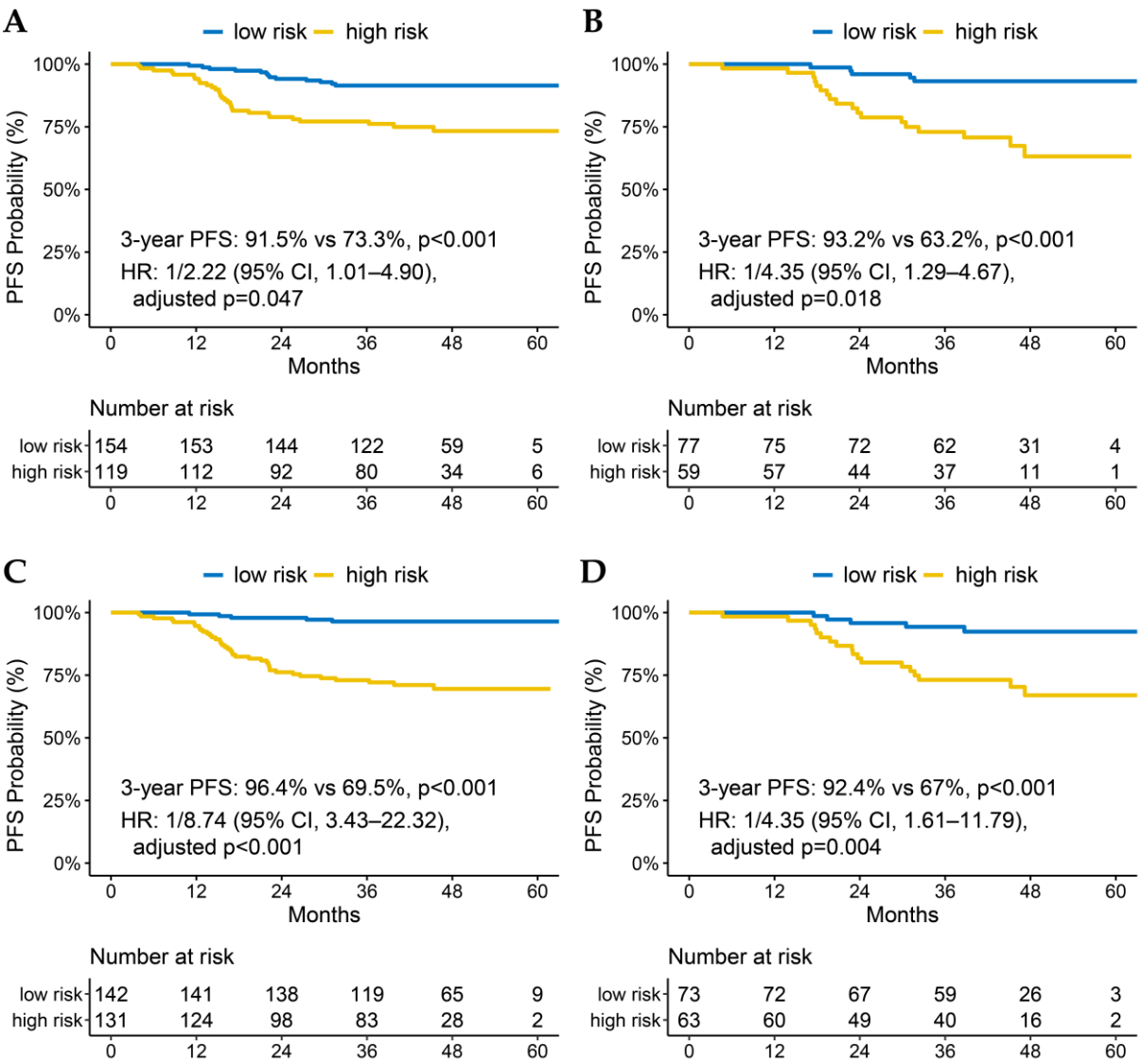
Supplementary Figure 3 Calibration curves of $Model_{clin}$ and $Model_{omics}$. A and B: Calibration curves of $Model_{clin}$; Cand D: $Model_{omics}$ for 3-year PFS prediction in the training and validation sets. The model predicted 3-year PFS is shown on the X-axis and the actual 3-year PFS on the Y-axis. clin: clinicoradiological; omics: radiomics including intratumoral and peritumoral; PFS: Progression-free survival.



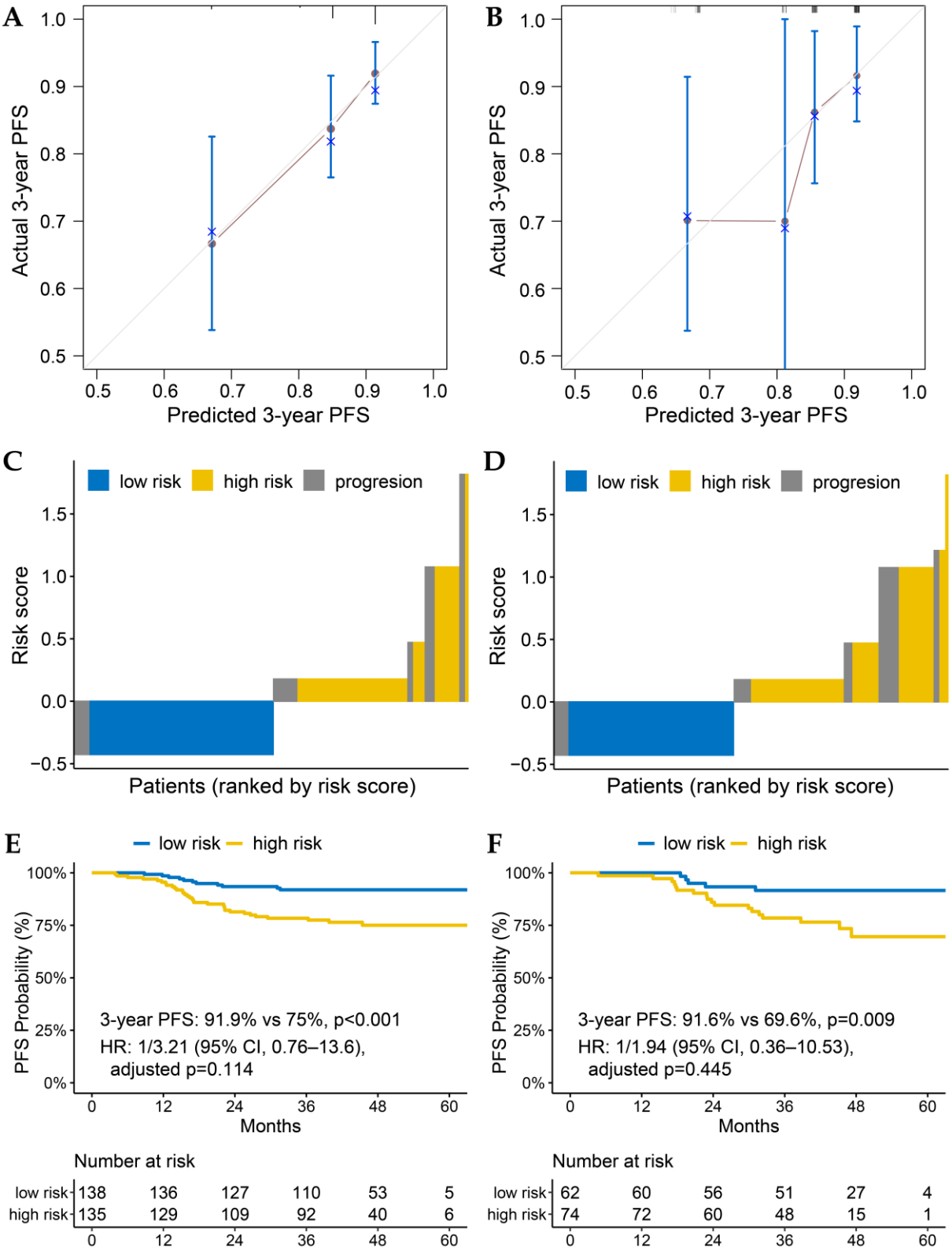
Supplementary Figure 4 Decision curves of the prognostic models with and without peritumoral features. The curves show the added value of peritumoral radiomics in net benefit across a range of threshold probabilities. When incorporating peritumoral features to $Model_{intra}$ (purple line) and $Model_{clin+intra}$ (orange line), $Model_{omics}$ (green line) and $Model_{ICRO}$ (blue line) exhibit increased net benefit in the A and C: Training; B and D: Validation sets. clin: Clinicoradiological; intra: Intratumoral; omics: Radiomics including intratumoral and peritumoral; ICRO: Integrated clinical-radiological-omics.



Supplementary Figure 5 Risk score and risk stratification using $Model_{clin}$ and $Model_{omics}$. Progression status, risk scores and risk stratification for each patient using: A and B: $Model_{clin}$; Cand D: $Model_{omics}$ in the training and validation sets. clin: Clinicoradiological; omics: Radiomics including intratumoral and peritumoral.



Supplementary Figure 6 Survival analysis for risk-stratified patients. Kaplan-Meier survival curves for PFS for patients in the high- and low-risk groups stratified by risk scores according to: A and B: $Model_{clin}$; C and D: $Model_{omics}$ in the training and validation sets. PFS: Progression-free survival; CI: Confidence interval; HR: Hazard ratio; clin: Clinicoradiological; omics: Radiomics including intratumoral and peritumoral.



Supplementary Figure 7 Calibration curves, risk score, and survival analysis using Model$_{ypTN}$. Calibration curves of Model$_{ypTN}$ for 3-year PFS prediction in the A: Training; B: Validation sets. The predicted 3-year PFS is shown on the X-axis and the actual 3-year PFS on the Y-axis. Progression status, risk scores, and risk stratification for each patient in the C:

Training; D: Validation sets. Kaplan-Meier survival curves for PFS for patients in the high- and low-risk groups in the E: Training; F: Validation sets. HR: Hazard ratio; CI: Confidence interval; PFS: Progression-free survival; ypTN: Pathological T and N stages after neoadjuvant chemoradiotherapy.

Supplementary Table 1 magnetic resonance imaging sequence protocols

Sequence	FOV (cm)	Slice thickness (mm)	Slice gap (mm)
Sagittal T2WI sFOV	20	3	0.5
Axial T2WI sFOV (Matrix ≥ 320 × 256)	20	3	0.5
Coronal T2WI sFOV (Matrix ≥ 320 × 256)	20	3	0.5
Axial T2WI	30–40	5	1
Axial T1WI	30–40	5	1
Axial DWI FS/b=800	30–40	1	1
Sagittal contrast-enhanced LAVA	20–26	4	−2
Axial contrast-enhanced LAVA	30–40	4	−2
Coronal contrast-enhanced LAVA	30–40	4	−2

DWI: diffusion-weighted imaging; FOV: field-of-view; FS: fat-suppressed; LAVA: liver acquisition with volume acceleration; MRI: magnetic resonance imaging; sFOV: small field-of-view; T1WI: T1-weighted imaging; T2WI: T2-weighted imaging.

Supplementary Table 2 Comparisons of C-indices between prognostic models for progression-free survival prediction in both training and validation sets

Patient set	Model	ypTN	clin	intra	peri	omics	Clin + intra	Clin + peri	ICRO
Training set	ypTN		0.003	0.389	0.001	<0.001	<0.001	<0.001	<0.001
	clin	0.003		0.297	0.194	<0.001	<0.001	<0.001	<0.001

	intra	0.389	0.297		0.015	<0.001	<0.001	<0.001	<0.001
	peri	0.001	0.194	0.015		<0.001	0.644	<0.001	<0.001
	omics	<0.001	<0.001	<0.001	<0.001		0.025	0.683	<0.001
	clin+intra	<0.001	<0.001	<0.001	0.644	0.025		0.044	<0.001
	clin+peri	<0.001	<0.001	<0.001	<0.001	0.683	0.044		<0.001
	ICRO	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	
Validation set	ypTN		0.009	0.561	0.151	<0.001	<0.001	<0.001	<0.001
	clin	0.009		0.310	0.839	0.101	0.030	0.010	<0.001
	intra	0.561	0.310		0.316	<0.001	<0.001	0.002	<0.001
	peri	0.151	0.839	0.316		<0.001	0.128	<0.001	<0.001
	omics	<0.001	0.101	<0.001	<0.001		0.569	0.974	0.001
	clin+intra	<0.001	0.030	<0.001	0.128	0.569		0.432	0.001
	clin+peri	<0.001	0.010	0.002	<0.001	0.974	0.432		<0.001
	ICRO	<0.001	<0.001	<0.001	<0.001	0.001	0.001	<0.001	

The *P* value of C-indices between models calculated using the DeLong test. Eight prognostic models were constructed, integrating different types of features as follows: (1) $Model_{ypTN}$ based on ypT and ypN stages; (2) $Model_{clin}$ based on clinicoradiological features, including body mass index, mesorectal fascia status, ypN stage, and tumor regression grade; (3) $Model_{intra}$ based on intratumoral radiomic features; (4) $Model_{peri}$ based on peritumoral radiomic features; (5) $Model_{omics}$ based on intratumoral–peritumoral radiomic features; (6) $Model_{clin+intra}$ based on clinicoradiological–intratumoral features; (7) $Model_{clin+peri}$ based on clinicoradiological–peritumoral features; and (8) $Model_{ICRO}$ based on clinicoradiological–intratumoral–peritumoral features.

C-index: concordance index; clin: clinicoradiological; PFS: progression-free survival; intra: intratumoral; peri: peritumoral; ypN stage, pathological N stage after neoadjuvant chemoradiotherapy; ypT stage, pathological T stage after neoadjuvant chemoradiotherapy; ypTN, pathological T and N stages after neoadjuvant chemoradiotherapy; omics: radiomics including intratumoral and peritumoral; ICRO: integrated clinical-radiological-omics.

Supplementary Table 3 Multivariate Cox regression parameters of prognostic models

Model	Variable	β	HR (95% CI)	*P*
ypTN	ypT stage			
	ypT0–2		1 (Reference)	
	ypT3–4	0.604	1.83 (0.94–3.56)	0.075
	ypN stage			
	ypN0		1 (Reference)	
	ypN1	0.897	2.45 (1.19–5.04)	0.015
	ypN2	1.639	5.15 (1.72–15.38)	0.003
clin	BMI			
	<18.5		1 (Reference)	
	18.5–24	−0.828	0.44 (0.20–0.97)	0.041
	>24	−0.947	0.39 (0.17–0.88)	0.024
	MRF status			

	Negative		1 (Reference)	
	Positive	0.562	1.75 (0.88–3.49)	0.109
	ypN stage			
	ypN0		1 (Reference)	
	ypN1	0.947	2.58 (1.27–5.23)	0.009
	ypN2	1.421	4.14 (1.39–12.37)	0.011
	TRG			
	1–2		1 (Reference)	
	3–5	0.625	1.87 (0.96–3.62)	0.064
intra	Log.sigma.5.0.mm.3D_GLDM_DependenceVariance	−1.267	0.28 (0.10–0.79)	0.016
	Wavelet.HHL_firstorder_RootMeanSquared	0.621	1.86 (0.95–3.64)	0.069
	Wavelet.LHL_GLSZM_LargeAreaLowGrayLevelEmphasis	−1.024	0.36 (0.12–1.04)	0.059
peri	Wavelet.LLH_GLCM_ClusterShade	0.007	1.01 (1.00–1.01)	0.008
	Wavelet.LLL_GLSZM_LargeAreaLowGrayLevelEmphasis	0.016	1.02 (1.01–1.03)	0.002
	Log.sigma.3.0.mm.3D_firstorder_90Percentile	0.654	1.92 (0.93–3.99)	0.080
	Wavelet.LHL_GLCM_Correlation	−0.878	0.42 (0.22–0.78)	0.007
	Wavelet.HLH_firstorder_Kurtosis	−0.889	0.41 (0.22–0.77)	0.005
	Wavelet.HHH_NGTDM_Contrast	0.774	2.17 (1.02–4.62)	0.045
	Square_GLDM_DependenceVariance	0.865	2.37 (1.21–4.65)	0.012

omics	Intratumoral radiomic score[1]	0.944	2.57 (1.46–4.51)	0.001
	Peritumoral radiomic score[1]	0.993	2.70 (2.00–3.64)	<0.001
Clin + intra	Intratumoral radiomic score[1]	0.879	2.41 (1.41–4.11)	0.001
	BMI			
	<18.5		1 (Reference)	
	18.5–24	−0.577	0.56 (0.25–1.26)	0.162
	>24	−0.734	0.48 (0.21–1.11)	0.085
	MRF status			
	Negative		1 (Reference)	
	Positive	0.498	1.65 (0.82–3.31)	0.162
	ypN stage			
	ypN0		1 (Reference)	
	ypN1	0.894	2.44 (1.19–5.01)	0.015
	ypN2	1.095	2.99 (1.00–8.98)	0.051
	TRG			
	1–2		1 (Reference)	
	3–5	0.664	1.94 (1.00–3.77)	0.050
Clin + peri	Peritumoral radiomic score[1]	0.900	2.46 (1.84–3.28)	<0.001
	BMI			

<18.5		1 (Reference)	
18.5–24	−0.463	0.63 (0.28–1.44)	0.271
>24	−0.726	0.48 (0.21–1.11)	0.087
MRF status			
Negative		1 (Reference)	
Positive	0.299	1.35 (0.67–2.71)	0.402
ypN stage			
ypN0		1 (Reference)	
ypN1	1.006	2.73 (1.33–5.61)	0.006
ypN2	1.160	3.19 (1.03–9.85)	0.044
TRG			
1–2		1 (Reference)	
3–5	0.606	1.83 (0.95–3.55)	0.073

The β, HR, and *P* value were calculated using multivariable Cox regression analysis.

[1]Intratumoral and peritumoral radiomic scores calculated by combining radiomic feature values weighted by their coefficient β values (radiomic features are listed in the present table).

BMI: body mass index; CI: confidence interval; clin: clinicoradiological; omics: radiomics including intratumoral and peritumoral; GLCM: grey level co-occurrence matrix; GLDM: grey level dependence matrix; GLSZM: grey level size zone matrix; HHH: high-high-high; HHL: high-high-low; HLH: high-low-high; HR: hazard ratio; intra: intratumoral; LHL: low-high-low; LLH: low-low-high; LLL: low-low-low; MRF: mesorectal fascia; NGTDM: neighboring grey tone difference matrix; peri: peritumoral; ROC: receiver operating characteristic; TRG:

tumor regression grade; ypN: pathological N stage after neoadjuvant chemoradiotherapy; ypT: pathological T stage after neoadjuvant chemoradiotherapy; ypTN: pathological T and N stages after neoadjuvant chemoradiotherapy.

Supplementary Table 4 Distribution differences in groups of the most important peritumoral feature, *n* (%)

Variable	Value	Square_GLDM_DependenceVariance < cutoff[a]	Square_GLDM_DependenceVariance ≥ cutoff[1]	[2]*P* value
Patients with immune response evaluation on HE-stained sections of the biopsy sample (*n* = 178)				
Number of patients	178 (100)	95 (53.4)	83 (46.6)	
Immune response[3]				0.001
Low	81 (45.5)	32 (33.7)	49 (59.0)	
High	97 (54.5)	63 (66.3)	34 (41.0)	
Lymphocyte count (IQR)	1.80 (1.50–2.20)	1.90 (1.60–2.35)	1.60 (1.40–2.00)	0.002
Lymphocyte percentage (IQR)	0.29 (0.25–0.34)	0.30 (0.25–0.36)	0.28 (0.23–0.33)	0.007
Lymphocyte percentage				0.033
<20%	20 (11.2)	7 (7.4)	13 (15.7)	
20%-40%	146 (82.0)	78 (82.1)	68 (81.9)	
>40%	12 (6.7)	10 (10.5)	2 (2.4)	

All patients (*n* = 409)				
Number of patients	409 (100)	234 (57.2)	175 (42.8)	
Lymphocyte count (IQR)	1.80 (1.50–2.20)	1.90 (1.60–2.30)	1.70 (1.40–2.10)	0.001
Lymphocyte percentage (IQR)	0.29 (0.24–0.34)	0.30 (0.25–0.36)	0.28 (0.23–0.33)	0.008
Lymphocyte percentage				0.008
<20%	48 (11.7)	25 (10.7)	23 (13.1)	
20%-40%	324 (79.2)	179 (76.5)	145 (82.9)	
>40%	37 (9)	30 (12.8)	7 (4)	

[1]Cutoff value for this peritumoral radiomic feature was 36.278.

[2]Comparison of training and validation sets using the chi-square test for categorical variables or the Mann–Whitney U test for continuous variables.

[3]Immune response assessment involved quantifying the tumor-associated immune cell count on HE-stained sections of the biopsy sample. Cases where the immune cell count is less than half tumor cell count are classified low, whereas all other cases are classified high.

GLDM: grey level dependence matrix; HE: hematoxylin–eosin; IQR: interquartile range.