

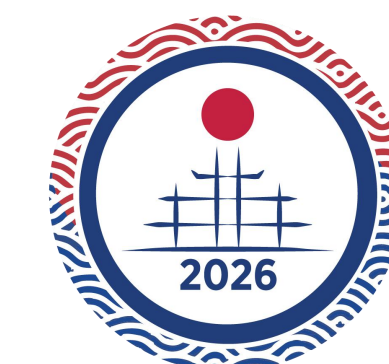


P1.053: A Multimodal Radio-Pathomics Model for Predicting Immunotherapy Response and Prognosis in Advanced Non-Small Cell Lung Cancer: A Multicenter Retrospective Study

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INTRODUCTION

•Lung cancer is the leading cause of cancer-related mortality; NSCLC accounts for ~85% of cases, and over two-thirds present with advanced disease.¹

•Immune checkpoint inhibitors (ICIs) have reshaped advanced NSCLC management, yet only 20%–50% of patients achieve durable clinical benefit (DCB); others may even develop hyperprogression.^{2,3}

•Current biomarkers are imperfect: some PD-L1–negative patients benefit while PD-L1–high tumours can resist; TMB/MSI testing is costly and lacks harmonised thresholds.^{4,5}

•CT radiomics captures whole-tumour heterogeneity, while H&E whole-slide image (WSI) pathomics resolves tumour micro-architecture — cross-scale fusion may leverage complementary information.^{6–8}

•Whether pretreatment CT–WSI fusion can anticipate immunotherapy benefit and prognosis in advanced NSCLC remains unclear.^{9,10}

Objective: To develop and validate a cascaded radio-pathomics framework (CT radiomics + H&E WSI pathomics) for predicting DCB and OS in advanced NSCLC.

METHODS

Design: Multicentre retrospective study at three academic centres in China; IRB approvals 2025(I)-229-01 / 2508051124371 / 2025-11-02; informed consent waived.

Patients: 344 patients with advanced NSCLC treated with ICIs — Centre A (n = 224) split into training (n = 156) and internal validation (n = 68); external validation cohort 1 (Centre B, n = 66); external validation cohort 2 (Centre C, n = 54).

CT radiomics: Contrast-enhanced chest CT (unenhanced, arterial, venous) within 4 weeks before ICI; nnU-Net¹¹ segmentation with manual quality check; 3,111 radiomic features.

Pathomics: H&E WSIs tiled at 20× into 512 × 512 patches; ImageNet-pretrained Vision Transformer [CLS] → 768-d patch features; KNN graph + PatchGCN¹² → 768-d patient-level vector.

Feature selection: Z-score → t test (458 radiomic, 296 pathomic) → Pearson $r > 0.90$ (89, 136) → LASSO (13 radiomic, 10 pathomic).

Modelling: SVM (5-fold CV, Bayesian optimisation) predicted DCB; LASSO-Cox derived the radiopathomics score (RPS; maximally selected log-rank cut-off); Kaplan–Meier, multivariable Cox and nomogram (1/2/3-year OS); SHAP; DeLong test.

Statistics: Python 3.9 (lifelines, scikit-learn); two-sided $P < 0.05$.

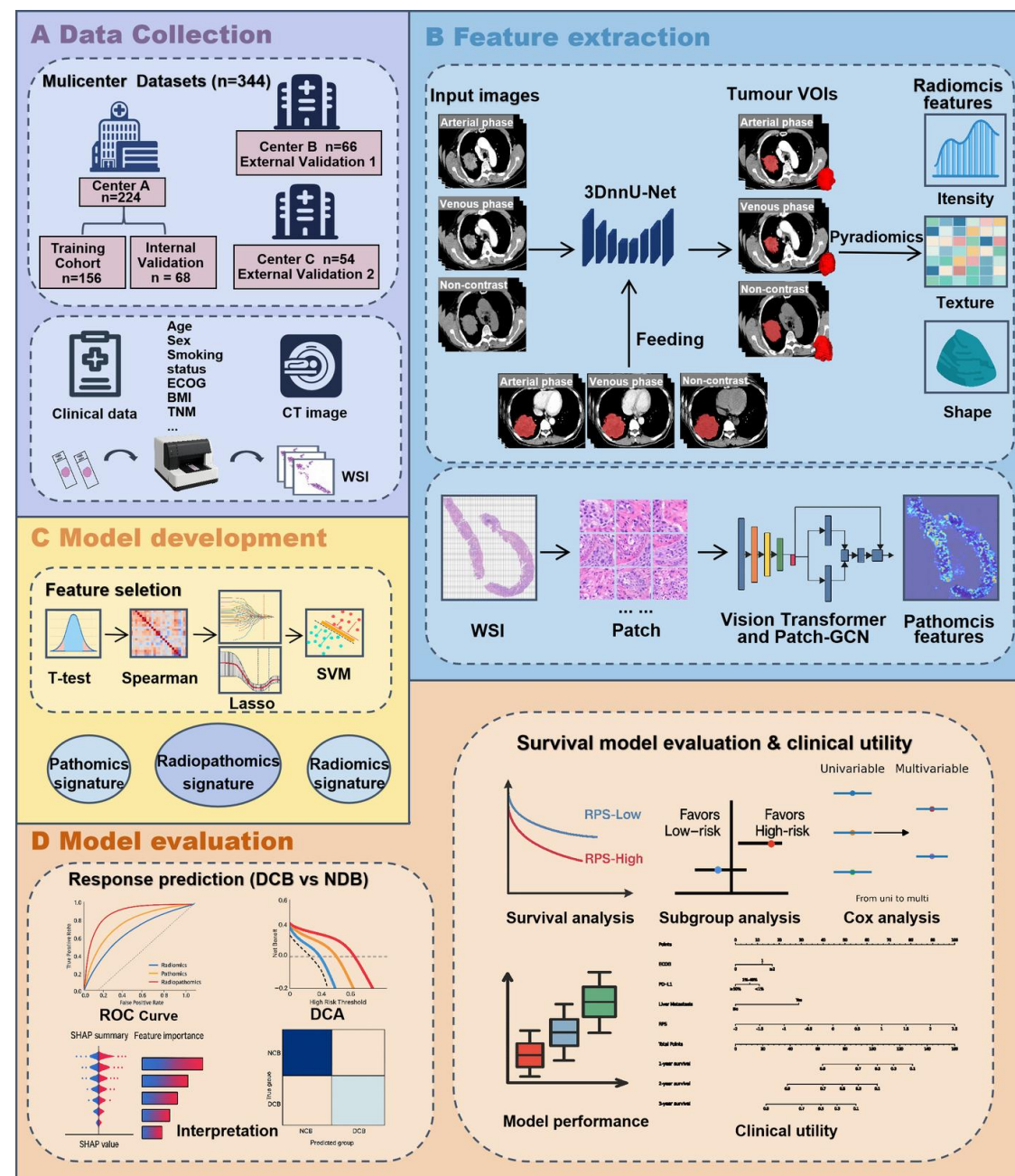


Figure 2. Flowchart of the study steps: data collection, feature extraction, feature selection and model construction, and model evaluation.

DISCUSSION AND CONCLUSION

Actionable Take Away Message

- A cascaded framework fusing CT radiomics with H&E WSI deep pathomics predicted durable clinical benefit from ICIs — training AUC **0.972**, external AUCs **0.908 / 0.898** — outperforming unimodal signatures.
- The radiopathomics score (RPS) gave reproducible OS stratification across three centres (pooled HR **5.18**, $P < 0.0001$) and stayed independently prognostic after clinical adjustment (HR 9.72).
- RPS refined risk within PD-L1 strata — flagging high-risk patients despite PD-L1 $\geq 50\%$ (HR 22.09) and low-risk PD-L1–negative patients with prolonged survival.
- SHAP analyses showed complementary contributions of deep pathomic features and multi-phase CT texture/shape features.

Limitations

- Retrospective, single-country sampling — prospective multi-regional validation required.
- Depends on quality of both CT and WSI; semi-automatic segmentation is labour-intensive; missing-modality robustness untested.

Future Direction for Research

- Prospective validation, fully automated segmentation, and missing-modality learning for real-world deployment.

Conclusion

- Integrating routinely acquired CT radiomics and digital pathomics enables pre-treatment prediction of ICI benefit and refined survival risk estimation in advanced NSCLC, within standard diagnostic pathways.

REFERENCES & ACKNOWLEDGEMENTS

1. Bray F, et al. Global cancer statistics 2022: GLOBOCAN incidence and mortality worldwide. CA Cancer J Clin. 2024;74(3):229-63.
2. Zhao X, et al. A decision model for durable clinical benefit from immune checkpoint inhibitors in advanced NSCLC. Med (N Y). 2024;5:100762.
3. Park HJ, et al. Hyperprogressive disease during treatment with immune checkpoint inhibitors. JAMA Netw Open. 2021;4:e211136.
4. Yamaguchi O, et al. Biomarkers for immune checkpoint inhibitors in NSCLC. Cell Rep Med. 2024;5:101348.
5. Budczies J, et al. Tumour mutational burden: clinical utility, challenges and opportunities. Nat Rev Clin Oncol. 2024;21:123-141.
6. Zheng J, et al. CT-based radiomics for predicting immune checkpoint inhibitor responses in NSCLC. Front Immunol. 2024;15:1434171.
7. Wang S, et al. Pathomics from whole-slide images for cancer prognosis and treatment response prediction. Lung Cancer. 2023;176:89-101.
8. Aerts HJWL. The potential of radiomic-based phenotyping in precision medicine. Nat Rev Clin Oncol. 2022;19:341-353.
9. Liu X, et al. Radiopathomics for predicting immunotherapy efficacy in lung adenocarcinoma. Lung Cancer. 2025;188:45-55.
10. van der Velden BHM, et al. Development and validation of a radiopathomics model to predict response to treatment. Lancet Digit Health. 2021;3:e554-e563.
11. Isensee F, et al. nnU-Net: a self-configuring method for deep learning-based biomedical image segmentation. Nat Methods. 2021;18:203-211.
12. Chen RJ, et al. Whole slide images are 2D point clouds: context-aware survival prediction using PatchGCN. Proc MICCAI. 2021:339-349.

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RESULTS

344 patients with advanced NSCLC treated with ICIs across four cohorts (training n = 156; internal validation n = 68; external validation n = 66 and n = 54); DCB rates **43.9%–66.7%**; median OS 14.6–20.9 months.

Table 1. Baseline characteristics and outcomes across cohorts

Characteristic	Training (n=156)	Internal val. (n=68)	External val. 1 (n=66)	External val. 2 (n=54)
Age, years, mean $\pm$ SD	64.8 $\pm$ 8.6	66.5 $\pm$ 8.9	68.6 $\pm$ 8.0	68.7 $\pm$ 7.4
Male, n (%)	143 (91.7)	59 (86.8)	60 (90.9)	47 (87.0)
ECOG 0–1, n (%)	149 (95.5)	62 (91.2)	58 (87.9)	47 (87.0)
Squamous cell carcinoma, n (%)	108 (69.2)	49 (72.1)	48 (72.7)	31 (57.4)
Stage IV, n (%)	86 (55.1)	40 (58.8)	39 (59.1)	33 (61.1)
PD-L1 TPS $\geq 50\%$, n (%)	34 (21.8)	11 (16.2)	21 (31.8)	22 (40.7)
First-line ICI, n (%)	124 (79.5)	50 (73.5)	63 (95.5)	53 (98.1)
DCB, n (%)	104 (66.7)	35 (51.5)	29 (43.9)	36 (66.7)
Median OS, months [IQR]	19.1 [12.7–29.3]	14.6 [8.2–24.8]	20.9 [9.4–33.9]	20.7 [12.8–29.3]

Table 2. AUC (95% CI) of the three signatures for predicting DCB

Signature	Training	Internal val.	External val. 1	External val. 2
Radiomics (RS)	0.825 (0.786–0.864)	0.745 (0.682–0.809)	0.749 (0.712–0.787)	0.762 (0.703–0.822)
Pathomics (PS)	0.936 (0.882–0.991)	0.832 (0.745–0.918)	0.859 (0.755–0.962)	0.828 (0.722–0.934)
Radio-pathomics (RPS)	0.972 (0.916–1.000)	0.882 (0.795–0.970)	0.908 (0.799–1.000)	0.898 (0.801–0.995)

RPS stratified OS (high- vs low-risk): training HR **7.09** (4.21–11.93); internal validation HR **3.79** (1.87–7.66); external validation HRs **3.09** (1.51–6.35) and **5.15** (1.93–13.77); pooled HR **5.18** (3.70–7.26). Nomogram C-index **0.824** vs 0.676 (clinical-only) and 0.804 (RPS-only).

Figure 3. ROC curves of the radiomics, pathomics and radio-pathomics signatures for predicting DCB in the four cohorts.

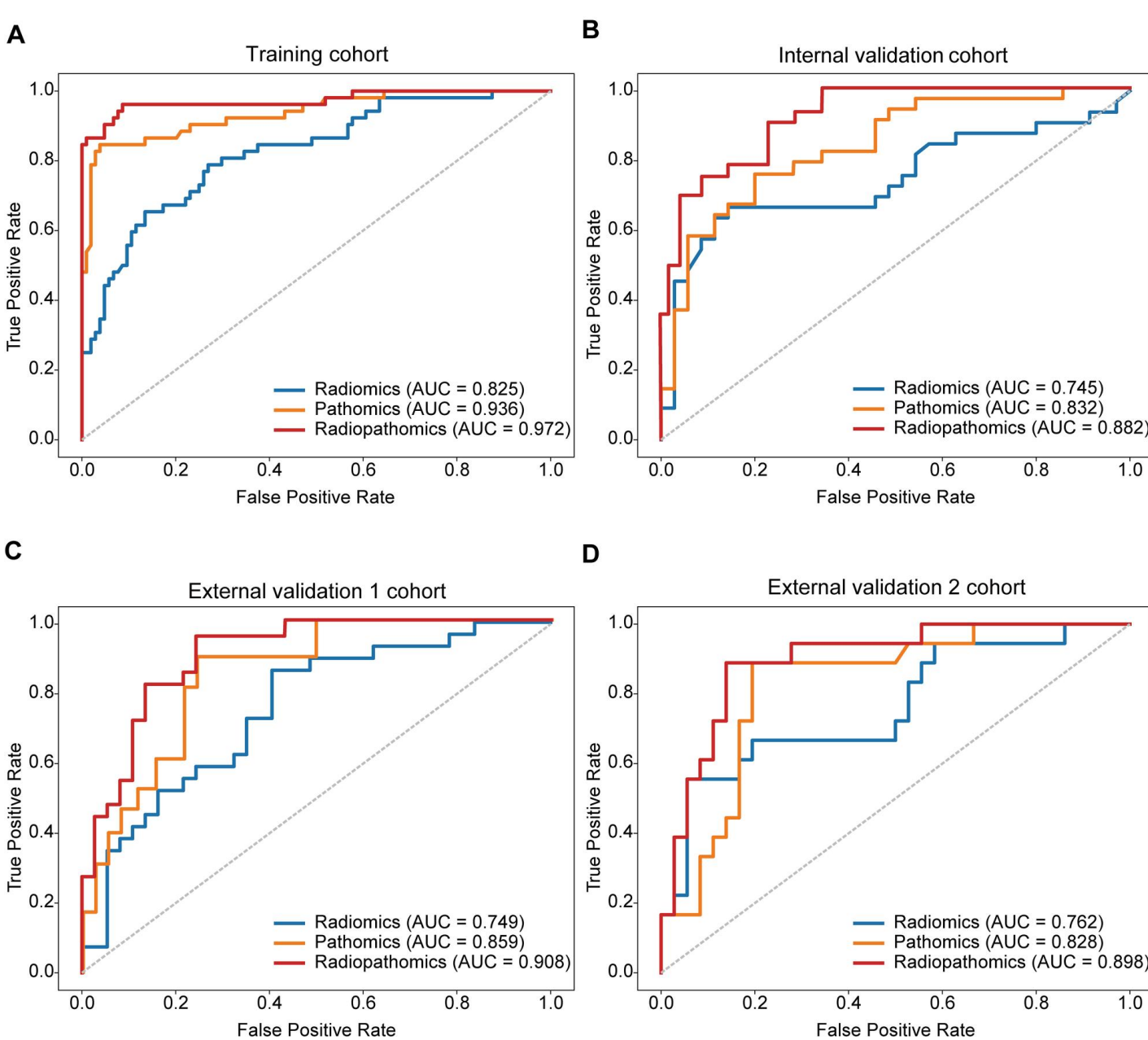


Figure 9. Nomogram integrating RPS, ECOG score, PD-L1 expression and liver metastasis for predicting 1-, 2- and 3-year OS.

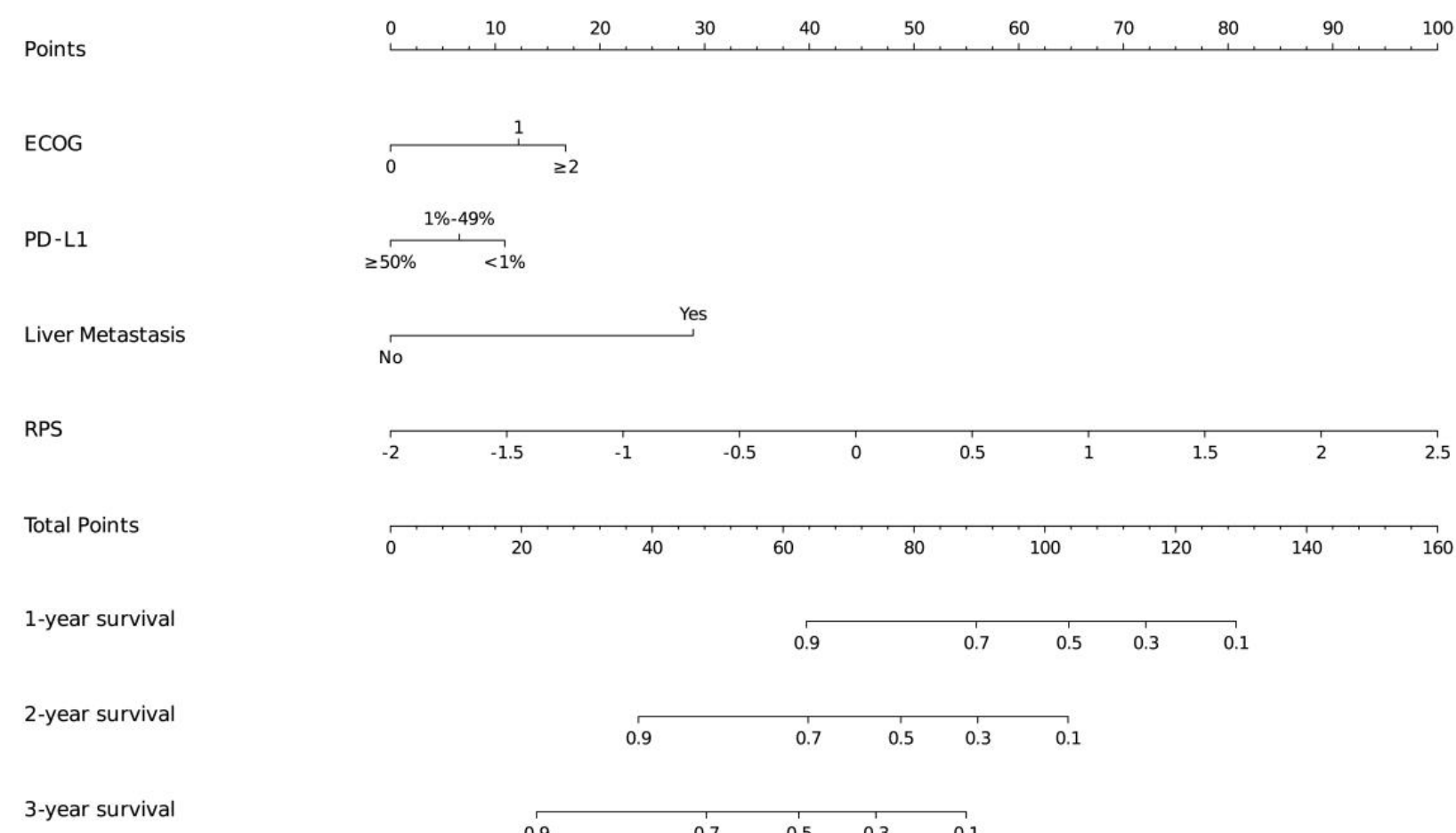


Figure 5. Kaplan–Meier OS curves by RPS risk group (RPS-L vs RPS-H) in the training, internal validation and two external validation cohorts.

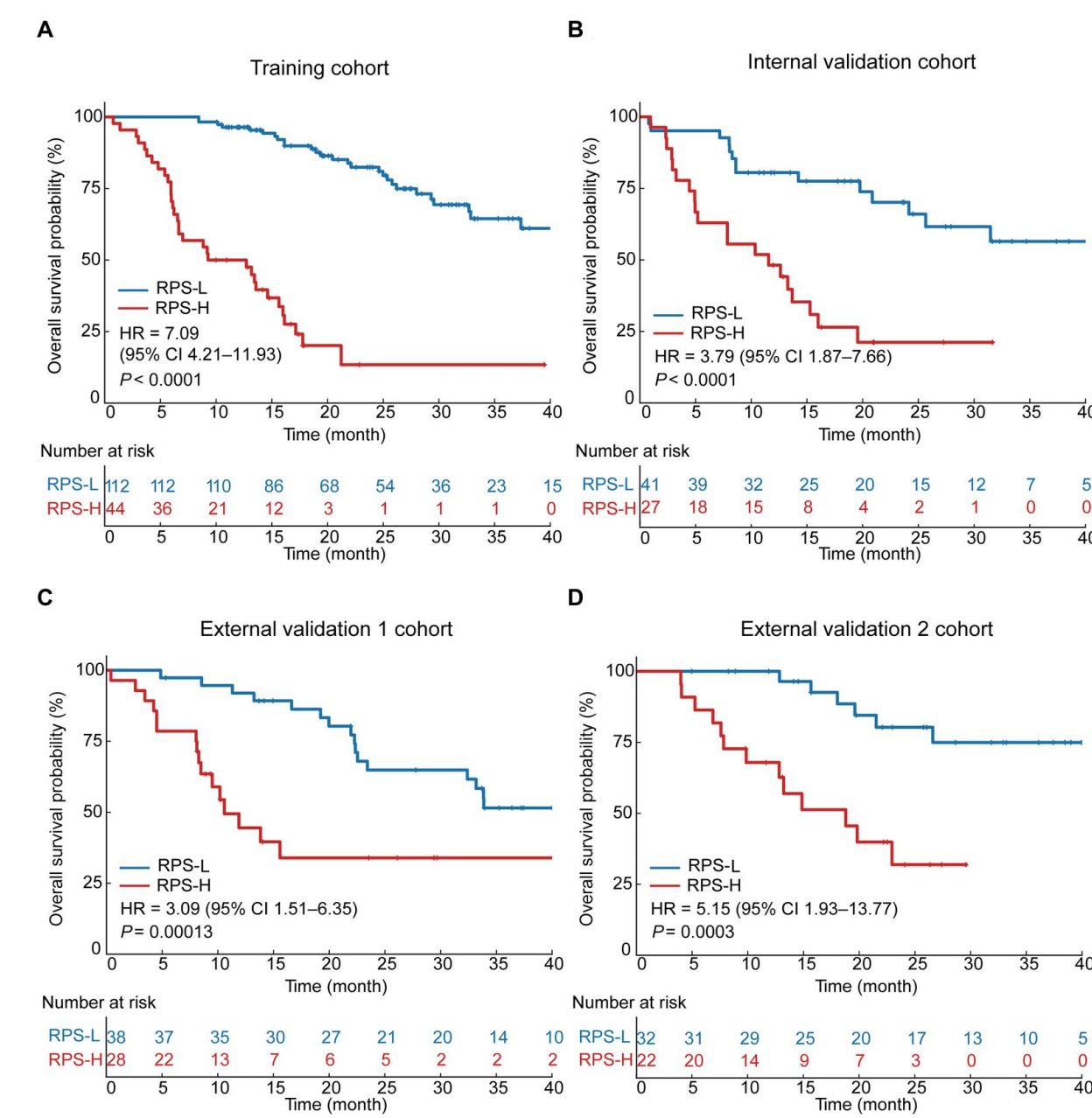


Figure 10. Concordance index (C-index) of the clinical, RPS and nomogram models across cohorts (bootstrap resampling).

