

AI-Driven Deep Learning Model for Predicting Immunotherapy Maintenance Benefit in Advanced Esophageal Squamous Cell Carcinoma: A Multicenter Precision Oncology Study

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Abstract

Objective: Identifying which patients with advanced esophageal squamous cell carcinoma (ESCC) benefit from immunotherapy maintenance following first-line chemoimmunotherapy and radiotherapy remains a critical challenge in precision oncology. This study leverages artificial intelligence (AI)-driven deep learning to establish a predictive model for optimizing immunotherapy maintenance strategies in advanced ESCC.

Methods: This multicenter study collected CT images and clinical data from 362 patients with advanced ESCC across three centers. An AI-powered segmentation framework (VISTA3D) was employed for automated tumor delineation, integrating point-prompt enhanced segmentation with deep learning-based feature extraction. A ResNet18-based multiple instance learning (MIL) model combining CT habitat features and clinical variables was developed to predict overall survival and identify patients likely to benefit from immunotherapy maintenance.

Results: The study included a total of 362 patients. When performing automatic segmentation based on the VISTA3D segmentation model, the model achieved a Dice coefficient of 0.87 on the external validation cohort, with a C-index reaching 0.86 (95% CI: 0.73–0.94). In analyses of PFS and OS, patients classified as low risk by the model demonstrated significantly better outcomes than those classified as high risk (HR: 0.61, 95% CI: 0.46–0.79, $P < 0.001$; HR: 0.55, 95% CI: 0.39–0.77, $P < 0.001$). Among high-risk patients, those receiving immunotherapy maintenance demonstrated significantly improved PFS and OS (HR: 0.39, 95% CI: 0.26–0.75, $P < 0.001$; HR: 0.57, 95% CI: 0.31–0.89, $P = 0.023$).

Conclusion: This AI-driven deep learning model, based on automated segmentation, effectively identifies advanced ESCC patients who are most likely to benefit from immunotherapy maintenance, enabling precision treatment optimization. The model achieves robust predictive performance, offering a clinically translatable tool for AI-guided immunotherapy decision-making in precision oncology.

Introduction

Esophageal cancer represents the 11th most common cancer globally and the 7th leading cause of cancer-related deaths [1]. China accounts for nearly half of all new cases worldwide annually, with esophageal squamous cell carcinoma (ESCC) constituting the overwhelming majority [2, 3]. In recent years, immunotherapy has emerged as a highly regarded key strategy in cancer treatment. Its mechanism of action involves blocking immune checkpoint pathways, thereby enabling the patient's immune system to recognize and attack cancer cells [4–5]. Among these, programmed death-1/programmed death-ligand-1 (PD-1/PD-L1) inhibitors have demonstrated promising antitumor activity in patients with advanced ESCC [6]. Furthermore, multiple clinical studies have demonstrated that PD-1 inhibitors combined with chemotherapy as a first-line treatment regimen for advanced ESCC significantly improve survival outcomes: median overall survival (OS) reaches 13 to 17 months, and median progression-free survival (PFS) reaches 6 to 7 months [7–14].

Currently, chemotherapy combined with immunotherapy is widely recognized as the standard first-line treatment regimen for advanced ESCC. However, not all patients benefit from this treatment regimen. In the KEYNOTE-590 study, patients with PD-L1 CPS ≥ 10 demonstrated more significant clinical benefits following immunotherapy, achieving a 5-year survival rate of 13.8%—3.7 times higher than that of the chemotherapy-only group [8]. Despite this, the overall long-term survival rate for patients with advanced ESCC remains low, and most patients still face the risk of disease progression or recurrence. Therefore, actively exploring new therapeutic strategies to improve treatment efficacy and survival outcomes remains of significant importance.

Radiotherapy is one of the key local treatment modalities for esophageal cancer, effectively alleviating local compression symptoms and improving quality of life. Previous studies have demonstrated that chemoradiotherapy, compared to chemotherapy alone, enhances the objective response rate and improves patient prognosis [15–16]. Some studies indicate that for patients with ESCC who experience local recurrence and/or distant metastasis after first-line treatment failure, continued combination radiotherapy following chemotherapy plus immunotherapy may yield clinical benefits with favorable safety profiles [17–18]. The ESO-Shanghai 13 study, a phase II clinical trial, demonstrated that radiotherapy targeting oligometastatic lesions delays disease progression and improves survival rates in patients with ESCC [19]. A single-arm clinical trial demonstrated that adding radiotherapy to chemotherapy combined with immunotherapy achieved a median PFS of 9.8 months [20]. All these findings confirm the feasibility of this combined treatment strategy.

However, it remains unclear which patients may benefit from immunotherapy maintenance following radiotherapy. Therefore, this study leverages AI-driven deep learning to propose a two-stage automated prediction framework for overall survival based on VISTA3D automated segmentation combined with point-prompt enhancement. This AI-powered approach aims to advance precision oncology by enabling data-driven identification of patients who benefit from immunotherapy maintenance, ultimately guiding personalized drug treatment strategies for advanced ESCC.

Methods and materials

Patients

This study retrospectively analyzed advanced ESCC patients receiving immunotherapy and radiotherapy between Jan 1, 2019, and Jun 30, 2024, from three centers: Center A (274 patients), Center B (51 patients), and Center C (37 patients). The patients did not participate in clinical trials investigating the addition of radiotherapy to improve outcomes in advanced ECSS patients. Center A served as the training cohort, while Center B and Center C functioned as the external validation cohort. Inclusion criteria for the study were: age ≥ 18 years; pathologically confirmed ESCC; TNM stage IVB; and received immunotherapy combined with radiotherapy. Patients who have received other systemic therapies (e.g., targeted therapy), those with concomitant other malignancies, patients with incomplete information, or

those lost to follow-up will be excluded. Figure 1 presents the study design flowchart. Detailed treatment regimens for all patients are provided in Appendix 1.

CT Image Acquisition and Preprocessing

All patients underwent CT screening prior to systemic therapy. Acquired CT images were uploaded to the Picture Archiving and Communication System (PACS) and exported in DICOM format. Where multiple CT scans existed, the scan closest to the treatment date was utilized. All CT images underwent standardized preprocessing to ensure data consistency. To mitigate the impact of variations in voxel spacing, spatial normalization is commonly employed. To address such issues, this study applied fixed-resolution resampling techniques. All images were resampled to a voxel size of 1 mm × 1 mm × 1 mm to achieve spacing normalization. Two senior radiation oncologists with ten years of experience manually delineated the primary tumor regions on CT scan images using ITK-SNAP 4.4.0 software (<https://www.itksnap.org/>).

VISTA3D Segmentation DL Model

This study employs VISTA3D—a unified segmentation framework for 3D medical images (Fig. 2)—based on the SegResNet backbone and sliding-window inference. By integrating 3D super-voxel distillation knowledge and a four-stage training process, it achieves automatic segmentation of 127 structural classes, 3D interactive refinement, and zero-shot segmentation. This study's reliability analysis focuses on the results of three core segmentation methods supported by VISTA3D compared against manually annotated gold standards on an external test dataset. The specific sources are as follows: First, automatic segmentation, which leverages the shared SegResNet backbone and auto-branching to perform end-to-end segmentation of target structures without additional manual intervention. Second, point-prompt segmentation (interactive segmentation). Third, automatic segmentation combined with point-prompt segmentation. This study selected four widely recognized quantitative metrics in medical image segmentation: Dice similarity coefficient, 95% Hausdorff distance, mean surface distance, and volume similarity. These metrics were used to calculate the consistency between the three segmentation results and manual segmentation. Detailed protocols are provided in Appendix 1.

Automated tumor habitat segmentation on CT

In this study, we constructed a 3mm peritumoral ring based on the primary lesion and subdivided the tumor and peritumoral ring into multiple subregions. To capture intratumoral heterogeneity, we employed unsupervised clustering algorithms to partition voxels within each tumor. First, principal component analysis was used to reduce the dimensionality of high-dimensional features, thereby eliminating redundancy and accelerating computation. Subsequently, the K-means clustering algorithm was employed to partition all voxels within the tumor into K different clusters. Each cluster represents a “habitat” with a unique radiological phenotype. The optimal number of clusters was determined using a

combined approach of the elbow rule and contour coefficient. Figure 2 illustrates the expanded peritumoral region and its subdivided subregions.

Multiple Instance Learning (MIL) Based on ImageNet

The pydicom library was used to read DICOM slice sequences from each patient's folder. All slices were numerically sorted to accurately reconstruct anatomically continuous 3D CT volumes. This study employs ResNet18 (an 18-layer residual network pre-trained on ImageNet) as the feature extraction backbone [21]. To balance the retention of pre-trained knowledge with adaptation to CT image features, a hierarchical freezing strategy is adopted. In the final configuration, the shallow stagelayers of the model are frozen, while only the two deeper stagelayers are unfrozen to participate in gradient updates. We implemented an aggregator based on AttentionMIL. This module consists of a two-layer Multi-Layer Perceptron (MLP) and a Softmax activation function.

This study employs the Cox Proportional Hazards Loss Function (CoxPHLoss) to evaluate the predictive capability of the model [22]. This study employed 5-fold cross-validation to evaluate model performance. During data fold partitioning, stratification was performed based on the "death" event indicator to ensure that the ratio of events to censored cases in each fold remained consistent with the overall dataset. The primary evaluation metric was Harrell's C-index, which quantifies the concordance between the model's predicted risk rankings and the actual observed survival time rankings (Fig. 1). The study also evaluated the predictive performance of the model using Negative Predictive Value (NPV), Positive Predictive Value (PPV), Accuracy (ACC), Sensitivity (SEN), and Specificity (SPE). Detailed protocols are provided in Appendix 1.

Identify patients who may benefit from subsequent radiotherapy

The model ultimately outputs a DL score for each individual. By combining this score with the patient's OS, a cutoff value is derived. Based on this cutoff, patients are categorized into low-risk (favorable prognosis) and high-risk (poor prognosis) groups. Kaplan-Meier survival analysis is then employed to evaluate the prognosis of both groups, followed by subgroup analysis. Patients were grouped based on whether they received immunotherapy maintenance in low-risk and high-risk cohorts, respectively. Kaplan-Meier survival analysis was conducted to evaluate the benefit of immunotherapy maintenance. Finally, a clinical decision pathway for advanced ESCC patients undergoing immunotherapy and radiotherapy was established in this study.

Statistical analysis

For statistical analysis, the Python statsmodels (version 3.7.12) module was utilized, and a P value < 0.05 was deemed statistically significant. We analyzed the differences between groups using the

Student’s t-test or Mann–Whitney U test for continuous variables and the chi-square test or Fisher’s exact test for categorical variables. Kaplan–Meier analysis was used to evaluate OS and PFS.

Results

Patient characteristics

The study ultimately included 362 patients, comprising 274 (75.69%) in the training cohort and 88 (24.31%) in the external validation cohort. By the end of follow-up, 244 (67.40%) patients experienced disease progression, and 156 (43.09%) patients experienced death. Among the two patient cohorts, 136 (49.64%) and 43 (48.86%) patients were aged > 60 years, respectively; 246 (89.78%) and 76 (86.36%) patients were male, respectively. The majority of patients in both groups were stage T3, comprising 207 (75.55%) and 62 (70.45%) patients, respectively (Table 1).

Table 1
Patient baseline information.

Variables	Total (n = 362)	Center A (n = 274)	Center B (n = 51)	Center C (n = 37)	P
Gender, n(%)					0.519
Female	40 (11.05)	28 (10.22)	8 (15.69)	4 (10.81)	
Man	322 (88.95)	246 (89.78)	43 (84.31)	33 (89.19)	
Age, n(%)					0.917
>60	179 (49.45)	136 (49.64)	24 (47.06)	19 (51.35)	
≤60	183 (50.55)	138 (50.36)	27 (52.94)	18 (48.65)	
Smoking, n(%)					0.721
No	144 (39.78)	107 (39.05)	20 (39.22)	17 (45.95)	
Yes	218 (60.22)	167 (60.95)	31 (60.78)	20 (54.05)	
ECOG, n(%)					0.812
0	171 (47.24)	131 (47.81)	24 (47.06)	16 (43.24)	
1	191 (52.76)	143 (52.19)	27 (52.94)	21 (56.76)	
T, n(%)					0.465
1	8 (2.21)	6 (2.19)	1 (1.96)	1 (2.70)	
2	31 (8.56)	25 (9.12)	4 (7.84)	2 (5.41)	
3	269 (74.31)	207 (75.55)	38 (74.51)	24 (64.86)	
4	54 (14.92)	36 (13.14)	8 (15.69)	10 (27.03)	
N, n(%)					0.817
0	7 (1.93)	6 (2.19)	0 (0.00)	1 (2.70)	
1	90 (24.86)	68 (24.82)	13 (25.49)	9 (24.32)	

Variables	Total (n = 362)	Center A (n = 274)	Center B (n = 51)	Center C (n = 37)	P
2	180 (49.72)	132 (48.18)	27 (52.94)	21 (56.76)	
3	85 (23.48)	68 (24.82)	11 (21.57)	6 (16.22)	
Location of the metastases, n(%)					0.839
DM	141 (38.95)	108 (39.42)	18 (35.29)	15 (40.54)	
LRR	221 (61.05)	166 (60.58)	33 (64.71)	22 (59.46)	

Performance of the 3D Automated Segmentation

The segmentation performance of three core segmentation methods was evaluated through an external validation cohort. Comparative results demonstrate that the point-prompt automated segmentation method effectively resolves misclassification issues inherent in standalone automated segmentation while maintaining automated segmentation efficiency. The Dice similarity coefficient for this method is 0.87 ± 0.22 , representing a 18% and 15% improvement over independent automatic segmentation and point-prompt segmentation, respectively. It also achieves significant enhancements in 95% Hausdorff distance, average surface distance, and volume similarity metrics (Fig. 3A). Furthermore, this method substantially reduces manual interaction costs compared to independent point-prompt segmentation, making it the chosen implementation for subsequent PFS prediction tasks based on automatic segmentation.

Model performance

The DL model achieved a C-index of 0.86 (95% confidence interval [CI]: 0.73–0.94), an ACC of 0.83 (95% CI: 0.70–0.88), an NPV of 0.84 (95% CI: 0.71–0.90), PPV was 0.76 (95% CI: 0.67–0.84), SEN was 0.74 (95% CI: 0.68–0.83), and SPE was 0.81 (95% CI: 0.73–0.92) (Fig. 3B). This study output DL model scores for all patients. Based on these scores and OS outcomes, a cutoff score of 0.48 was determined, dividing the entire cohort into high-risk (199 cases) and low-risk (163 cases) groups. Significant differences in scores were observed between the two groups (Fig. 3C). Multivariate Cox regression analysis confirmed that the DL model is an independent predictor of OS (Fig. 3D).

This study also conducted interpretability analysis on the DL model. By extracting the attention weights of the global representation cls_token across all image patches from the attention heatmap, we validated the model's decision logic from multiple dimensions: In the slice heatmaps across X, Y, and Z orthogonal planes for each sample, high-attention regions (with normalized weights approaching 1) precisely anchor tumor cores or pathologically specific tissue areas, while background tissues

predominantly exhibit low weights (approaching 0). Moreover, high-weight regions across samples and dimensions highly overlap with clinically relevant observation areas, confirming the model's reliance on task-specific core features and providing direct visual support for the interpretability of prediction results. (Fig. 4).

In the overall population survival analysis, PFS analysis demonstrated significantly better outcomes for low-risk patients compared to high-risk patients (hazard ratio [HR]: 0.61, 95% CI: 0.46–0.79, $P < 0.001$) (Fig. 5A). The OS analysis similarly demonstrated a significantly better prognosis for low-risk patients compared to high-risk patients (HR: 0.55, 95% CI: 0.39–0.77, $P < 0.001$) (Fig. 5B). Forest plots from subgroup analyses reveal that results across subgroups align with the primary analysis, consistently showing a significant advantage for low-risk patients (Fig. 5C and D).

Screening of patients who could benefit from radiotherapy

High-risk patients

Among the 199 patients assessed as high-risk by the DL model, 100 (50.25%) received immunotherapy maintenance, while 99 (49.75%) did not. Analysis of PFS revealed that patients who underwent radiotherapy demonstrated significantly superior median PFS compared to those who did not (14.9 [95% CI: 11.4–22.9] vs. 8.1 [95% CI: 6.4–15.4], HR: 0.39 [95% CI: 0.26–0.75], $P < 0.001$). Similar results were observed in the OS analysis (27.0 [95% CI: 18.6–35.7] vs. 19.2 [95% CI: 11.7–26.9], HR: 0.57 [95% CI: 0.31–0.59], $P = 0.023$) (Figs. 6A and B).

Low-risk patients

Among the 163 patients assessed as low risk by the DL model, 74 (45.40%) received radiotherapy, while 89 (54.60%) did not. Analysis of PFS revealed no significant benefit in median PFS between patients who received radiotherapy and those who did not (16.1 [95% CI: 8.4–23.4] vs. 17.9 [95% CI: 11.4–22.9], HR: 1.04 [95% CI: 0.87–1.33], $P = 0.711$). Similar results were observed in the OS analysis (24.4 [95% CI: 16.3–31.5] vs. NA [95% CI: 35.4–NA], HR: 1.12 [95% CI: 0.87–1.29], $P = 0.435$) (Figs. 6C and D). The clinical decision pathway established based on this study is detailed in Fig. 7.

Discussion

Patients with advanced ESCC remain at risk of disease progression or recurrence following first-line immunotherapy combined with radiotherapy. Predicting which patients may benefit from immunotherapy maintenance is crucial, not only to improve patient prognosis but also to reduce overtreatment. Therefore, this study was the first to achieve automated tumor identification in ESCC patients through automated segmentation combined with point-prompt segmentation technology, establishing a DL model for predicting prognosis. The study also found that patients identified as high-risk by the model could benefit from immunotherapy maintenance.

In advanced ESCC, multiple Phase III clinical trials—including KEYNOTE-590[6], JUPITER-06[7], ESCORT-1ST[8], RATIONALE-306[9], and ORIENT-15[10]—have reported survival data for immunotherapy as first-line treatment. Median PFS ranged from 5.8 to 7.2 months, while median OS ranged from 12.6 to 17.2 months. The PFS and OS observed in this study were slightly higher than those reported in previous studies. This may be attributed to the fact that all advanced ESCC patients enrolled in this study had not received prior treatment, whereas some patients in previous studies had experienced recurrence or metastasis following curative therapy, presenting risks of drug resistance or relatively poorer physical condition. Survival data for advanced ESCC patients receiving immunotherapy combined with radiotherapy remain limited at present. Large-scale phase III clinical trials (such as KEYNOTE-975[19] and RATIONALE-311[20]) are currently underway.

In a controlled study of locally advanced or metastatic ESCC, combined radiotherapy significantly improved PFS (16.00 months vs 12.00 months, $P = 0.008$) and OS (34.00 months vs 20.00 months, $P = 0.015$) [23]. In another retrospective controlled study comparing immunotherapy with or without radiotherapy in advanced ESCC patients, Li et al. found radiotherapy improved OS but not PFS. The investigators suggested this discrepancy might be related to the delayed response to immunotherapy [24]. Conversely, Chen et al. reported that combined radiotherapy not only prolonged OS (24.9 vs 14.6 months, $P = 0.003$) but also extended PFS (14.2 vs 10.6 months, $P = 0.002$) [25]. Therefore, radiotherapy can significantly improve the prognosis of advanced ESCC patients who have undergone immunotherapy. However, it remains unclear which patients may benefit from subsequent immunotherapy maintenance. Accurately predicting which patients will benefit and which will not can provide valuable guidance for clinicians' decision-making.

Previous studies have explored DL models based on CT radiomics to predict treatment efficacy [26–28]. However, such models are difficult to implement in busy clinical settings. With the rapid advancement of artificial intelligence (AI), replacing manual segmentation with automated AI segmentation will significantly enhance clinical applicability. In this study, when trained with the VISTA3D segmentation model, a C-index of 0.86 was achieved on an external validation cohort. The Dice similarity coefficient reached 0.87 ± 0.22 , indicating that models based on automated segmentation can effectively replace manual segmentation tasks.

This study employs VISTA3D's “point-prompt enhanced automatic segmentation” method to achieve target segmentation—a technique crucial for interactive segmentation—whose feasibility is supported across three dimensions: technical design, experimental validation, and clinical adaptability. Technically, VISTA3D's dual-branch collaborative architecture and fusion algorithm form the core foundation: the automated branch (sharing the SegResNet backbone network) rapidly completes automatic segmentation of 127 structures but may misclassify in complex scenarios (e.g., blurred boundaries). The interactive branch serves as an indispensable supplement, using 3D point-prompting to localize misclassified regions. The proprietary fusion algorithm exclusively refines regions associated with point-prompt pairs while preserving accurate segmentation results. This design leverages the necessity of

interactive segmentation to effectively address the shortcomings of standalone automatic segmentation, establishing a balanced architecture that achieves synergistic efficiency + precision.

Clinically, this method strikes a balance between efficiency and cost: automatic segmentation inference runs 3–4 times faster than TotalSegmentator, making it suitable for large-scale cohort batch processing; corrections require only 1–2 3D point-prompts, reducing manual intervention by approximately 50% compared to independent point-prompt segmentation. Its 3D super-pixel technology can also adapt to unlabeled rare lesions, meeting clinical demands. In conclusion, this composite method is technically robust and reliable, demonstrating excellent performance across multiple datasets while maintaining clinical adaptability. This fully validates its feasibility for supporting segmentation tasks in this study.

Furthermore, this model demonstrates robust clinical applicability, achieving an accuracy of 0.83 on automatically segmented data. This eliminates reliance on manual segmentation entirely, significantly reducing clinical costs. In summary, through its efficient core predictive capabilities, stable generalization performance, and outstanding clinical adaptability, this model provides reliable technical support for predicting the efficacy of immunotherapy + radiotherapy in advanced ESCC patients, highlighting its significant clinical translational value.

The DL model based on ResNet18 established in this study categorizes patients into low-risk and high-risk groups. Among patients in the high-risk group, this study identifies those with poorer prognosis following immunotherapy and radiotherapy, and who could benefit from immunotherapy maintenance. Therefore, this study recommends that patients identified as high-risk by this model should receive immunotherapy maintenance. In the low-risk group, this study identifies patients with favorable prognosis following immunotherapy and radiotherapy, and who cannot benefit from immunotherapy maintenance. Therefore, this study recommends that patients classified as low-risk by this model should carefully consider whether to undergo immunotherapy maintenance to avoid overtreatment. This study provides precise, personalized decision-making guidance for subsequent treatment in advanced ESCC patients who have received immunotherapy and radiotherapy, holding significant clinical importance.

The current study has several notable limitations. First, since the results are based on retrospective research, the necessity for prospective validation represents an area requiring future investigation. Second, the limited sample size in this study is a constraint, highlighting the need for larger datasets to confirm these findings. Furthermore, we have not yet explored the biological connections of radiomics features, which will be further investigated in subsequent research.

Conclusion

The AI-driven deep learning model developed in this study, based on automated segmentation combined with point-prompt segmentation, can replace prediction models relying on manual segmentation. This model effectively identifies advanced ESCC patients benefiting from immunotherapy maintenance, supporting precision oncology decision-making. By integrating deep learning-based image analysis with

clinical features, this approach demonstrates the potential of AI to optimize immunotherapy strategies, paving the way for computationally guided drug treatment selection in precision oncology.

Declarations

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Data Availability Statement

The datasets analyzed in this study are available from the corresponding author upon request.

Ethics Statement

This study was approved by the Ethics Committee of Shandong First Medical University Cancer Hospital(No.SDTHC202509088), the Ethics Committee of Zibo Fourth People's Hospital(EC-SOP-005-AF03), and the Ethics Committee of Xiaogan Central Hospital(XGSZYLL-EC-20251103). We declare that the patients' information will be kept confidential and that we have adhered to the principles of the Declaration of Helsinki. Because this study was a retrospective clinical study, the Ethics Committees of Shandong First Medical University Cancer Hospital, Zibo Fourth People's Hospital and Xiaogan Central Hospital have

waived the required informed participant consent for this study.

Author Contributions

Junfeng Zhao, Zongqian Yuan and Ying Li were responsible for data curation, formal analysis, investigation, methodology, and writing (original draft). Haoyu Liu, Haining Luo were responsible for Data curation, formal analysis, and writing (original draft). Ben Yang and Chengxin Liu were responsible for conceptualization, funding acquisition, and writing (review and editing).

Patient Consent for Publication

Not applicable.

Conflict of Interest Statement

The authors declare that they have no competing interests.

Clinical trial number

Not applicable.

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Figures

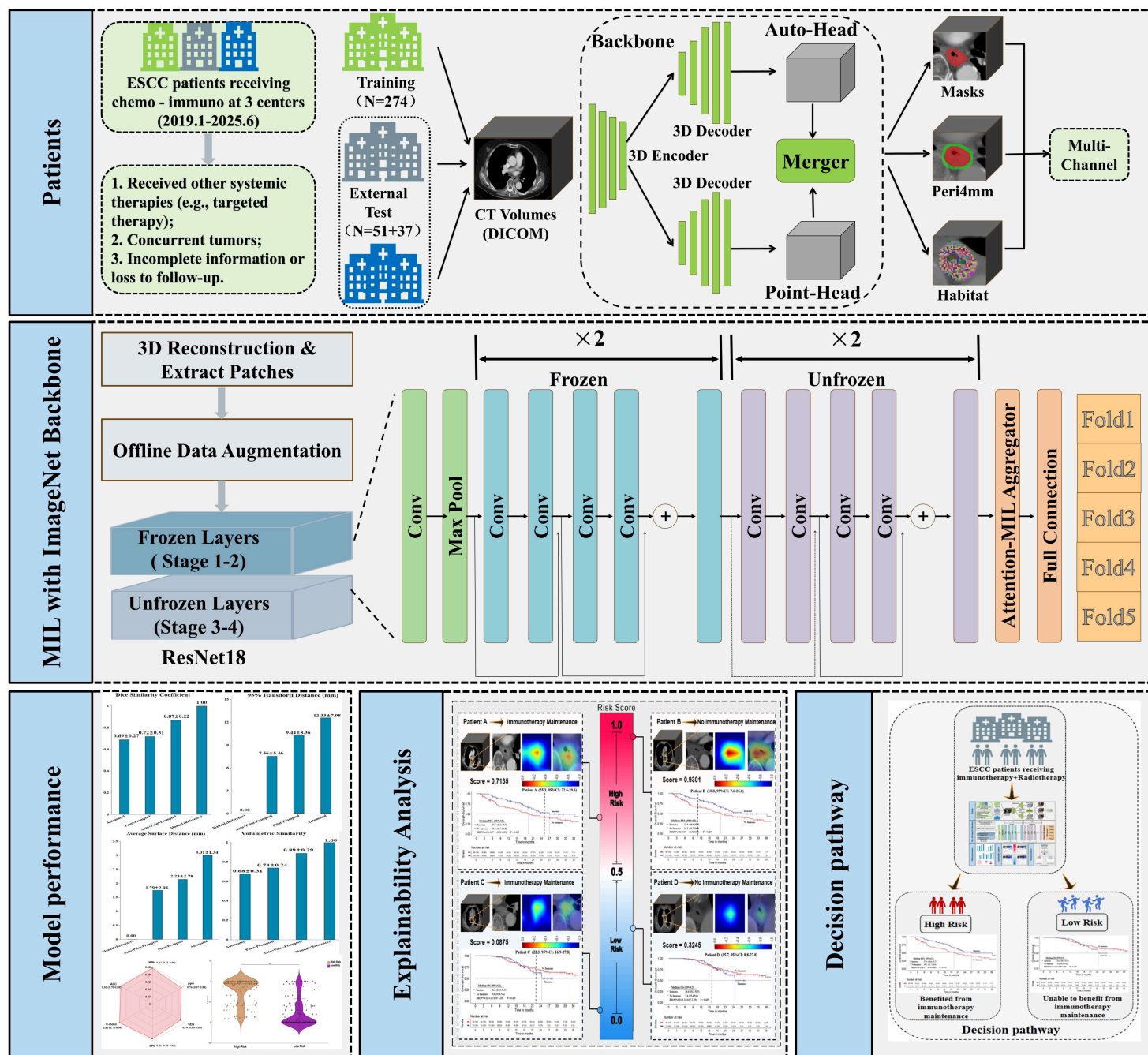


Figure 1

Overview of the study design and analytical workflow.

The study included data from three different centers. The automatic segmentation model was implemented using the VISTA3D architecture. The deep learning model was based on ResNet18 (an 18-layer residual network pre-trained on ImageNet).

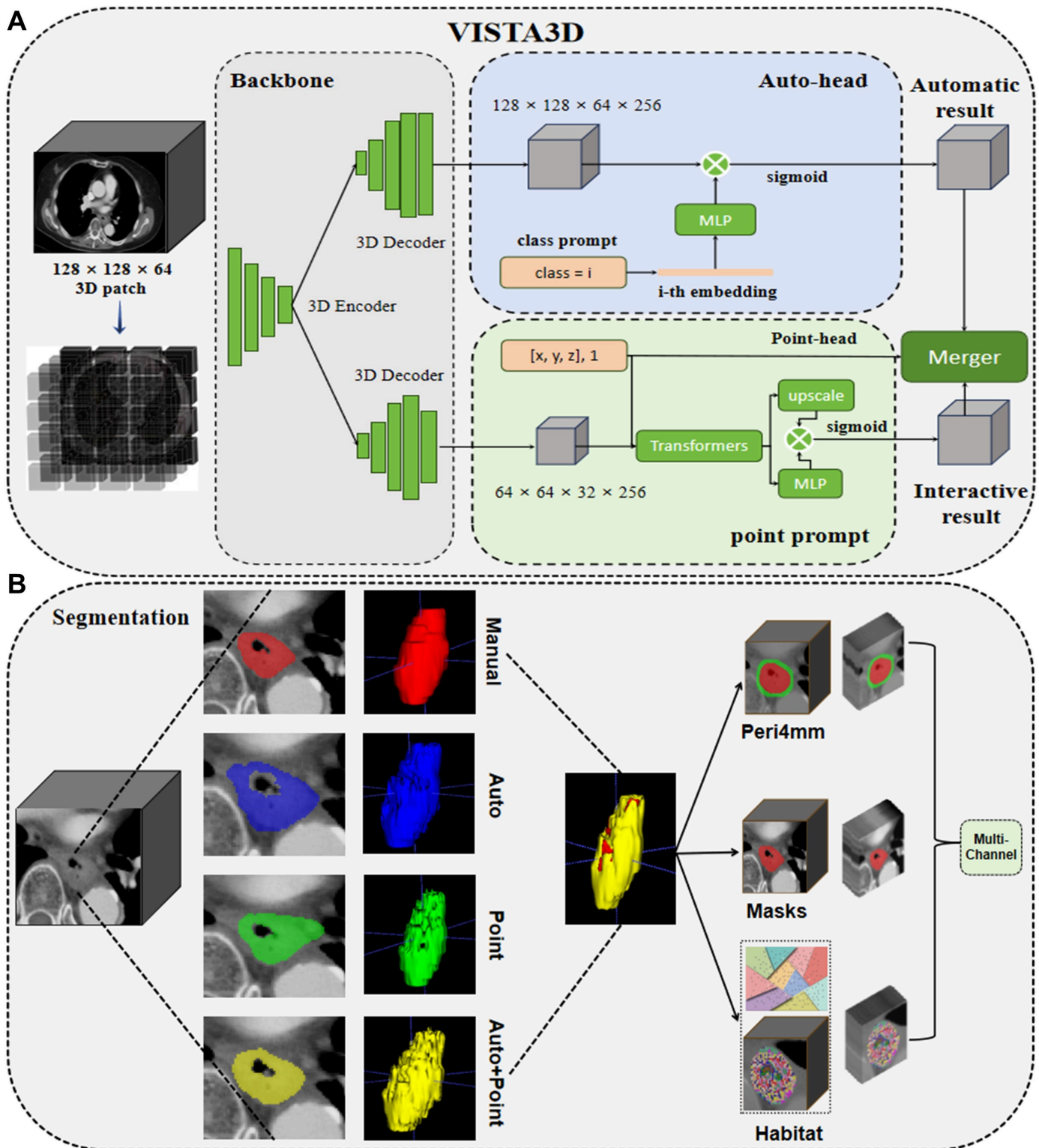


Figure 2

Automatic segmentation and habitat analysis.

(A) VISTA3D Architecture. It comprises two branches sharing the same image encoder. If the user provides a class prompt within the 127 supported classes, the top automatic branch activates pre-trained automatic segmentation. If the user provides a 3D point prompt, the bottom interactive branch

activates interactive segmentation. If both branches are activated, the fusion module uses the interactive results to edit the automatic results. (B) The VISTA3D-based automated segmentation architecture not only segments the tumor lesion itself but also constructs a 3mm peritumoral ring, dividing both the tumor and peritumoral ring into multiple subregions. The K-means clustering algorithm is employed to partition all voxels within the tumor into K distinct clusters.

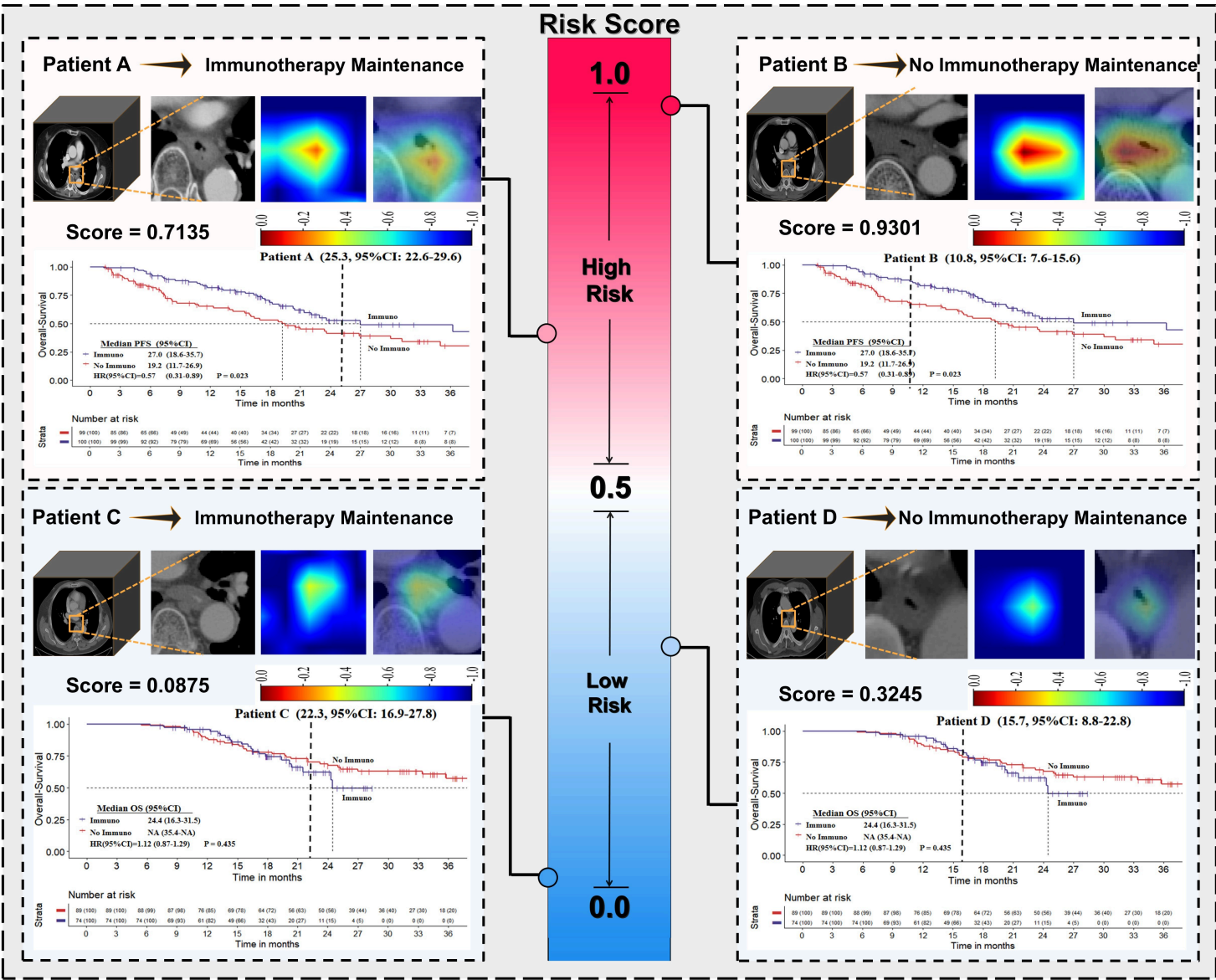


Figure 3

Evaluation of Model Performance.

(A) Comparison of segmentation performance among three segmentation models. (B) Radar chart of deep learning model prediction performance. (C) Violin plot of deep learning score distribution for low-risk and high-risk patients.(D) Forest plot of COX regression analysis.

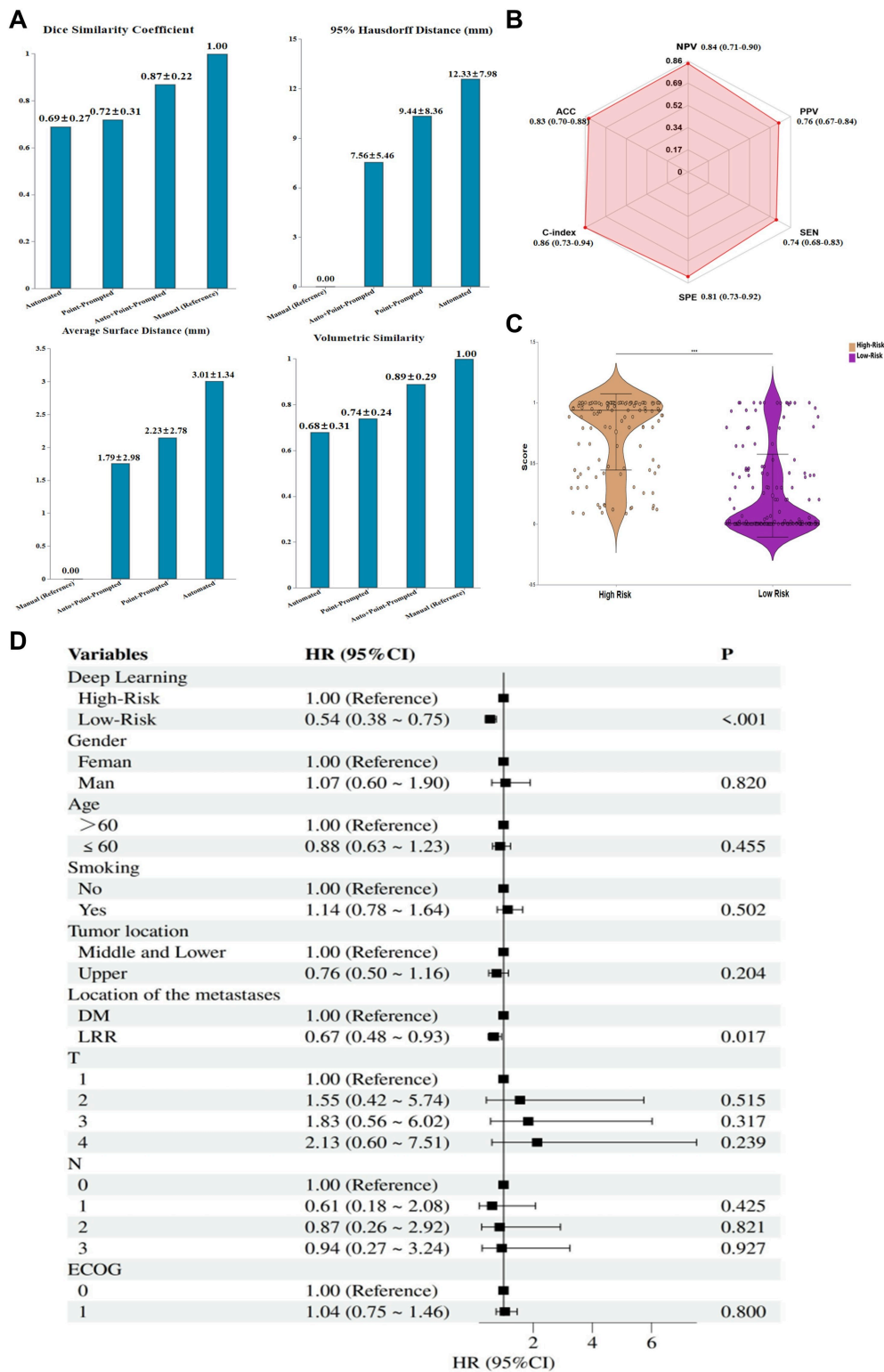


Figure 4

Model interpretability analysis.

Patients A and B were classified as high-risk by the model; Patients C and D were classified as low-risk. The attention weight heatmap visually represents the model's focus on lesions.

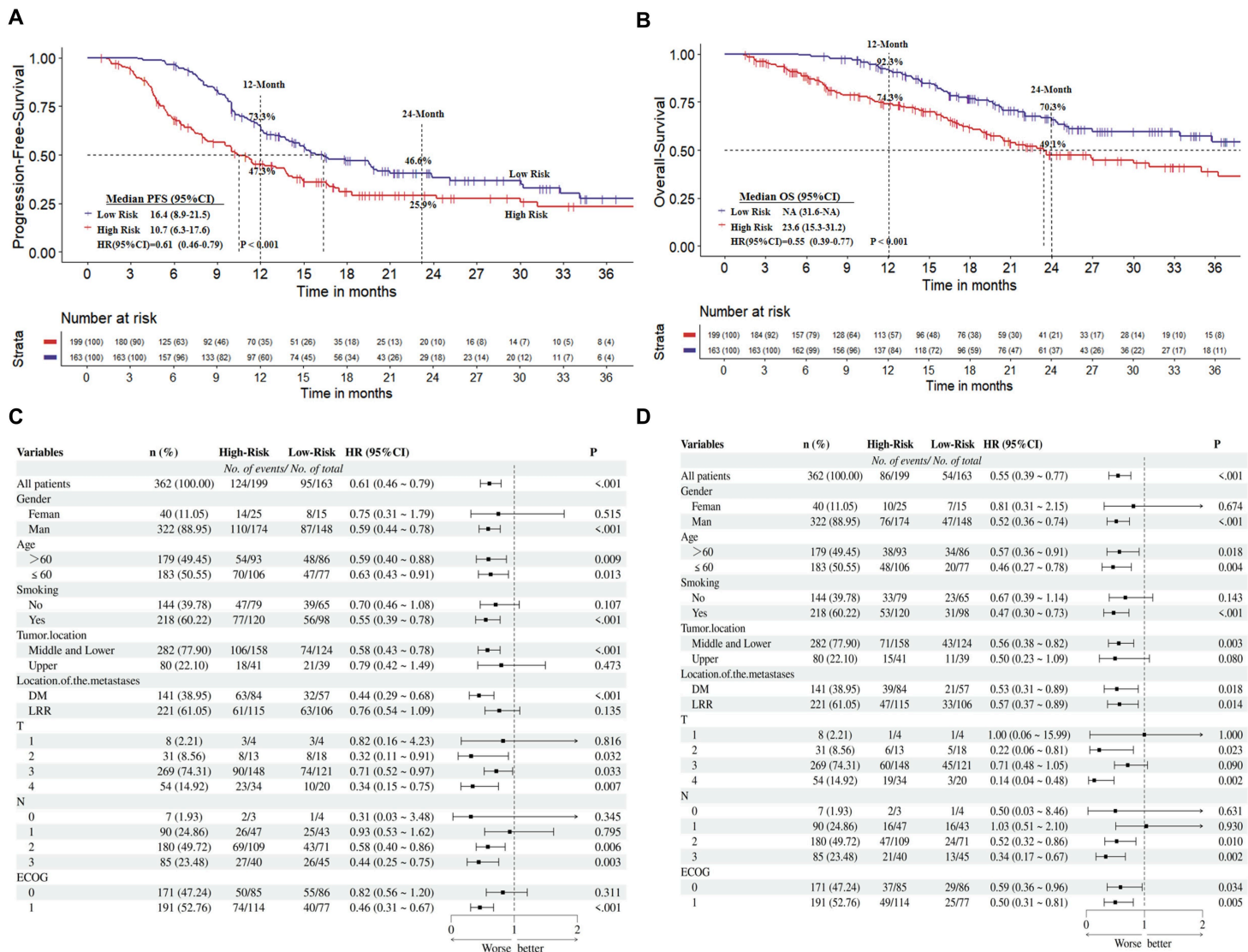


Figure 5

Kaplan–Meier survival analysis for low-risk and high-risk patients.

(A) Kaplan–Meier survival analysis of PFS in low-risk and high-risk cohorts. (B) Kaplan–Meier survival analysis of OS in low-risk and high-risk cohorts. (C) Subgroup analysis of PFS. (D) Subgroup analysis of OS.

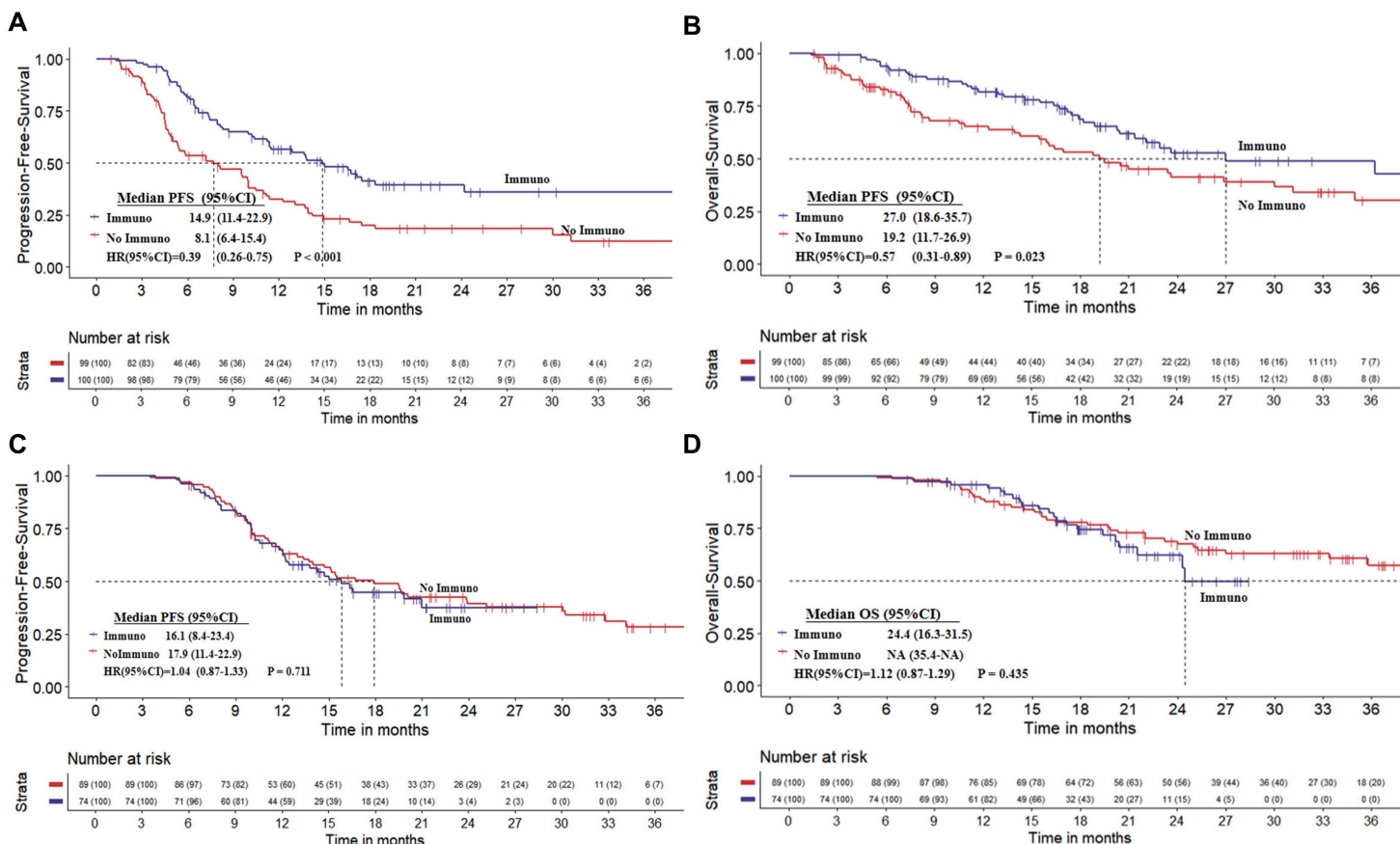


Figure 6

Kaplan–Meier survival analysis for whether to receive immunotherapy maintenance.

(A) Kaplan–Meier survival analysis of PFS in high-risk patients according to whether to receive immunotherapy maintenance. (B) Kaplan–Meier survival analysis of OS in high-risk patients according to whether to receive immunotherapy maintenance. (C) Kaplan–Meier survival analysis of PFS in low-risk patients according to whether to receive immunotherapy maintenance. (D) Kaplan–Meier survival analysis of OS in low-risk patients according to whether to receive immunotherapy maintenance.

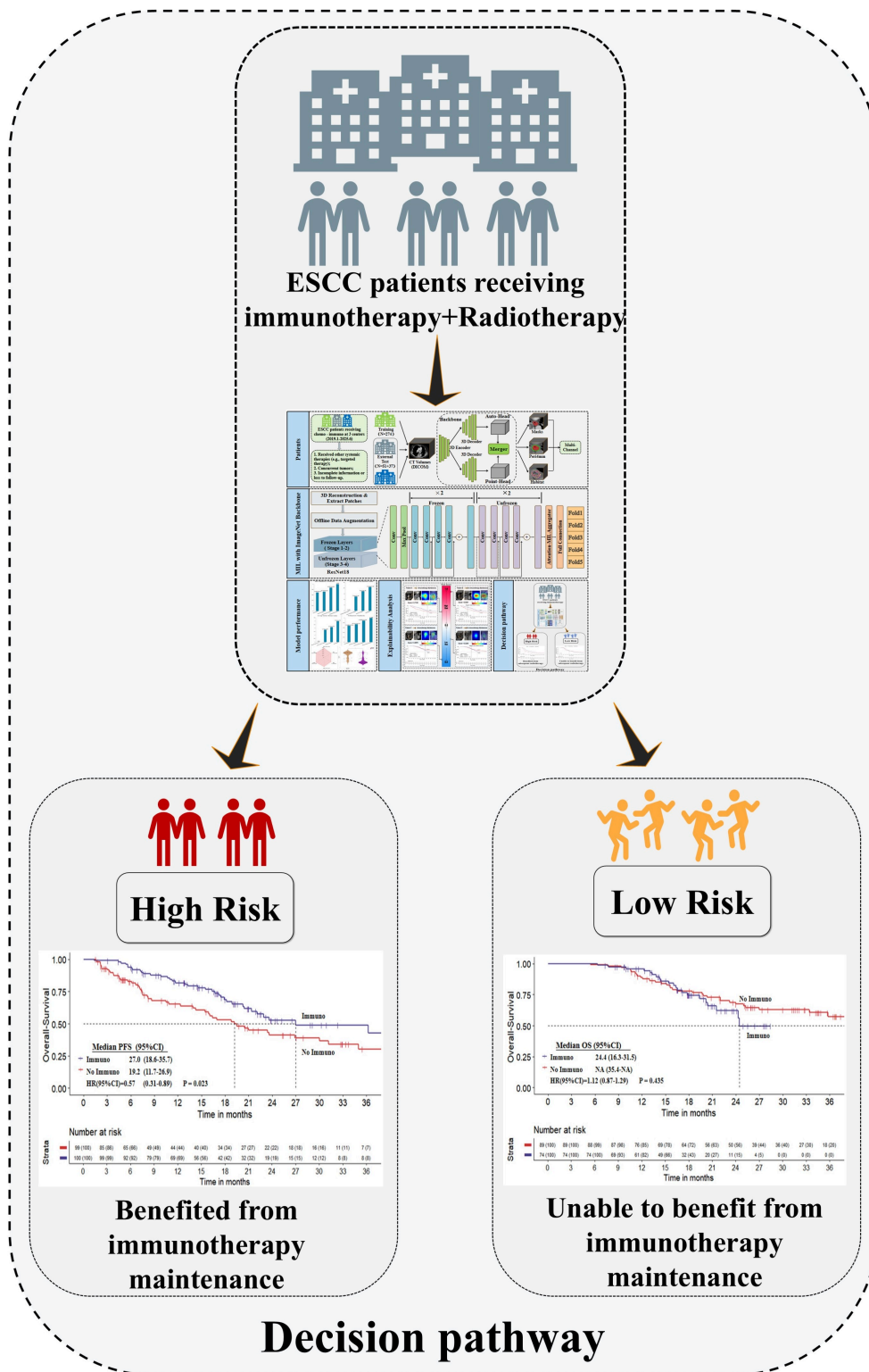


Figure 7

Clinical Decision Pathway.

The deep learning model based on ResNet18 established in this study categorizes patients into low-risk and high-risk groups. Among patients in the high-risk group, this study identifies those with poorer prognosis following immunotherapy and radiotherapy, and who could benefit from immunotherapy

maintenance. Therefore, this study recommends that patients identified as high-risk by this model should receive immunotherapy maintenance. In the low-risk group, this study identifies patients with favorable prognosis following immunotherapy and radiotherapy , and who cannot benefit from immunotherapy maintenance. Therefore, this study recommends that patients classified as low-risk by this model should carefully consider whether to undergo immunotherapy maintenance to avoid overtreatment.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Appendix1.docx](#)