## Supplementary Materials for

# Comprehensive Assessment of Immune Context and Immunotherapy Response via Noninvasive Imaging in Gastric Cancer

Zepang Sun, Taojun Zhang, M. Usman Ahmad, Zixia Zhou, Liang Qiu, Kangneng Zhou, Wenjun Xiong, Jingjing Xie, Zhicheng Zhang, Chuanli Chen, Qingyu Yuan, Yan Chen, Wanying Feng, Yikai Xu, Lequan Yu, Wei Wang, Jiang Yu, Guoxin Li, and Yuming Jiang

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## Supplementary Methods

### 1. Patients

The overall study design is shown in Figure 1. We retrospectively reviewed data for 2600 patients with gastric cancer in four medical centers. The patient inclusion criteria for patients without immunotherapy were: histologically confirmed gastric adenocarcinoma; standard unenhanced and contrast-enhanced abdominal CT imaging performed <30 days before surgical resection; lymphadenectomy performed and >15 lymph nodes harvested; no preoperative chemotherapy; complete information about clinicopathological characteristics; available follow-up data. We excluded those patients who had other synchronous malignant neoplasms or had received previous anticancer treatment; or if the tumor lesions could not be identified on CT images. For patients received immunotherapy, we included those with histologically confirmed gastric adenocarcinoma, standard unenhanced and contrast-enhanced abdominal CT imaging performed before immunotherapy, complete information about clinicopathological characteristics; available follow-up data. We excluded those patients who had other synchronous malignant neoplasms, or if the tumor lesions could not be identified on CT images.

### 2. Immunohistochemistry (IHC) staining

In the present study, lymphocytes and myelocytes at the center and invasive margin of tumor were stained and calculated. Formalin-fixed paraffin-embedded (FFPE) human samples were processed for IHC staining as previously described [1-3]. Following incubation with an antibody against human CD3 (pan T lymphocytes;

NeoMarker, clone SP7), CD8 (cytotoxic T lymphocytes; NeoMarker, clone SP16), and CD66b (myelocytes; BD Pharmingen), the paraffin sections were stained in an EnVision System (Dako). The antibody dilutions and antigen retrieval are shown in Supplementary Table 28. Every staining run contained a slide treated with phosphate buffer saline (PBS) buffer in place of the primary antibody as a negative control. Every staining run contained a slide of positive control. Prior to staining, sections were blocked with endogenous peroxidase (prepared in 1% $H_2O_2$/methanol solution) for 10 minutes and then microwaved for 30 minutes in 10 mM citrate buffer, pH 6.0. The sections were blocked using 10% normal rabbit serum for 30 minutes. Furthermore, all slides were stained with the same concentrations of primary antibody for each antibody and incubated with monoclonal primary antibody overnight at 4 ℃, followed by incubation with an amplification system with a labeled polymer/HRP (EnVision™, DakoCytomation, Denmark) at 37℃ for 30 minutes. The sections were developed with 0.05% 3, 3′-diaminobenzidine tetrahydrochloride (DAB) and counterstained with modified Harris hematoxylin. And all slides were stained with DAB dyeing for the same time for each antibody (Supplementary Table 28). Two pathologists who were blinded to clinical outcomes independently scored all samples. A third pathologist was consulted when a difference of opinion arose between the 2 primary pathologists. At low power (100), the tissue sections were screened using an inverted research microscope (model DM IRB; Leica, Germeny), and the 5 most representative fields were selected. Thereafter, to evaluate the density of stained immune cells, the 2 respective areas of invasive margin and center of tumor were measured at 200

magnification. The nucleated stained cells in each area were quantified and expressed as the number of cells per field.

We then calculated the lymphocytes (pan T lymphocytes and cytotoxic T lymphocytes) and myelocytes within the tumor and adjacent tissues. The median count was chosen for qualitative analysis of these immune cells at intratumor and peritumor in the training cohort (record 0 score when < the median or 1 score when ≥ the median), followed by application into the validation cohorts. Then, for each patient, the lymphoid immune context (also called lymphoid immune score, range: 0-4 score) and myeloid immune context (also called myeloid immune score, range: 0-2 score) were determined by adding the qualitative scores of the corresponding immune cells in the intratumor and peritumor. Next the lymphoid immune score (LIS) status was divided into two groups-LIS low (a total of 0-1 score in the intratumor and peritumor) and LIS high (a total of 2-4 score in the intratumor and peritumor). Also, the myeloid immune score (MIS) status was divided into two groups-MIS low (a total of 0 score in the intratumor and peritumor) and MIS high (a total of 1-2 score in the intratumor and peritumor).

Because IHC data was not available for patients in internal validation cohort 2, external validation cohort 2, and the prospective validation cohort, these datasets were used to validate the radiomics image biomarkers for the prognostic value, and were not used to evaluate the radiomics image biomarkers for prediction of lymphoid and myeloid immune context.

**3. CT Acquisition and Image Processing**

**3.1 CT acquisition**

All patients underwent contrast-enhanced abdominal CT scans prior to surgery or immunotherapy. All patients underwent contrast-enhanced abdominal CT using the multidetector row CT (MDCT) systems (GE Lightspeed 16, GE Healthcare Milwaukee, WI; 64-section LightSpeed VCT, GE Medical Systems, Milwaukee, WI; USA). Following intravenous contrast administration, arterial and portal venous-phase contrast-enhanced CT scans were performed after delays of 28 s and 60 s, respectively. Iodinated contrast material in the amount of 90 - 100 ml (Ultravist 370, Bayer Schering Pharma, Berlin, Germany) was injected at a rate of 3.0 or 3.5 ml/s with a pump injector (Ulrich CT Plus 150, Ulrich Medical, Ulm, Germany). The CT acquisition protocols were as follows: 120 kV; 150-190 mAs; 0.5- or 0.4-second rotation time. Contrast-enhanced CT was reconstructed with a field of view, 350×350 mm; data matrix, 512×512; in-plane spatial resolution 0.607-0.751 mm; axial slice thickness 5.0 mm for 98% patients with a range of 1.25-7.5 mm. For prospective data collection, a same CT machine and procedure (256-MDCT scanner Brilliance iCT, Philips Healthcare, Cleveland, OH, USA, Procedure sequence number: 16GSI Abdome-YAN) were selected to ensure the consistency of CT imaging, as well as in the charge of the same radiologist.

**3.2 Image processing**

We analyzed the portal venous-phase CT images because of well differentiation between the tumor tissue and adjacent normal bowel wall. The relatively coarse and heterogeneous resolution in z-axis compared with in-plane resolution would not allow a meaningful and reliable 3D analysis of the image. Therefore, we focused on the most

representative 2D slice, i.e., largest tumor section in the axial plane. Two radiologists C.C. and Q.Y. (with 13 and 12 years of clinical experience in abdominal CT interpretation, respectively) manually delineated the primary tumor on the CT images by using the ITK-SNAP (http://www.itksnap.org) [4, 5]. Both radiologists were present in the same room and reached visual consensus regarding tumor delineation. Both radiologists were blinded to the clinical and histopathological data but were aware that the patients had gastric cancer. All tumor contours were delineated by the two radiologists in consensus, and any discrepancy was resolved by a third radiologist (Y.X. with 33 years of experience in abdominal CT interpretation).

We extracted 584 quantitative features (292 in the intratumoral area and 292 in the peritumoral area) from the region of interest on each patient's CT imaging. The image features included 8 shape features, 14 first-order intensity features, and 270 second- and higher-order textural features. In this work, we investigated four types of texture features on the basis of gray-level co-occurrence matrices (GLCM), gray-level run length matrix (GLRLM), gray-level size zone matrix (GLSZM), and neighborhood gray-tone difference matrix wavelet decompositions (NGTDM). A Laplacian of Gaussian spatial band-pass filter ($\nabla^2 G$) was used to derive image features at different spatial scales by turning the filter parameter between 1.0 and 2.5 (1.0, 1.5, 2.0, 2.5). All the image features were implemented and computed using an open-source radiomics analysis package in the MATLAB platform (https://github.com/mvallieres/radiomics). The study design followed the Image Biomarker Standardization Initiative (IBSI) guidelines, and the software used was IBSI-compliant (Supplementary Table 29).

### 3.3 Inter-observer and intra-observer agreements of CT image feature extraction

The inter-observer and intra-observer reproducibility were initially analyzed with 100 randomly chosen images for ROI-based texture feature extraction by two experienced radiologists (readers 1 and 2, with 13 and 12 years of clinical experience in abdominal CT study interpretation, respectively). To assess the intra-observer reproducibility, reader 1 repeated the generation of texture features twice in a 4-week period following the same procedure. The workflow for the remaining images was completed by the first radiologist.

An independent samples t-test or Kruskal-Wallis H test, where appropriate, was used to assess the differences between the features generated by reader 1 (first time) and those by reader 2 as well as between the twice-generated features by reader 1. Inter- and intra-class correlation coefficients (ICCs) were used to evaluate the intra- and inter-observer agreement of features extraction. An ICC greater than 0.75 presents good agreement.

Satisfactory inter- and intra-observer reproducibility of the texture feature extraction was achieved. There was no statistically significant difference between the features of the two readers “i.e.” between reader 1’s first-extracted features and those of the reader 2, with *P* values ranging from 0.53 to 0.91. The inter-observer ICCs of all metrics calculated on the basis of the “two” reader’s measurements were good, ranging from 0.79 to 0.94. The intra-observer ICCs calculated based on reader 1’s twice feature extraction ranged from 0.81 to 0.89. Therefore, given the relatively heavy workload,

only the first radiologist drew all the patients' CT images, and all outcomes were based on the measurement of the first reader.

**4. Treatment regimens and patterns for immunotherapy cohorts**

The ICIs drugs, including Nivolumab, Pembrolizumab, Sintilimab, or Toripalimab, were used in combination with chemotherapy for patients in the immunotherapy cohorts. Chemotherapy regimens involved XELOX (capecitabine plus oxaliplatin), SOX (S-1 plus oxaliplatin), FOLFOX (leucovorin, fluorouracil, and oxaliplatin), FLOT (fluorouracil, leucovorin, oxaliplatin, and docetaxel), DCF (docetaxel plus fluorouracil), and other combinations. The treatment patterns included neoadjuvant therapy, adjuvant therapy or for advanced disease. The therapeutic regimens and strategies were based on the patient's condition and preference.

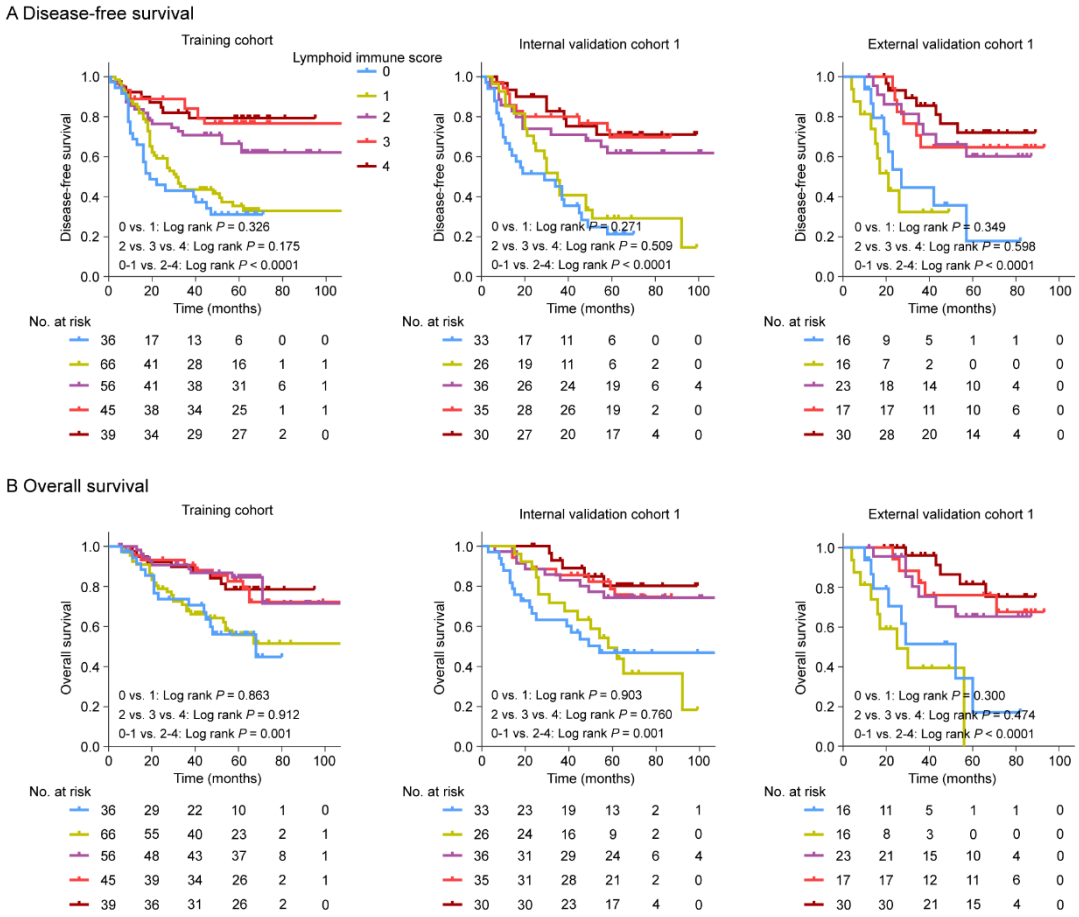
**5. Testing cut-off value for LRS and MRS**

We compared the performance of the optimal cut-off value from Youden's index, the median, upper quartile, and lower quartile in our study. Although the determination of a cutoff for the CT biomarkers was not the aim of this study, comparative data of these cut-off values based on different methods (Youden's index, median, upper quartile, or lower quartile) are presented in the Supplementary Table 16. Firstly, the optimal cut-off value for LRS and MRS was determined by the Youden's index. This strategy maximized the sum of sensitivity and specificity, which minimized identification errors. Secondly, we found that the binary variable derived from Youden's index had a slight improvement in prognosis prediction, compared with the median, upper quartile, and lower quartile in the aspects of risk evaluation and C-index.

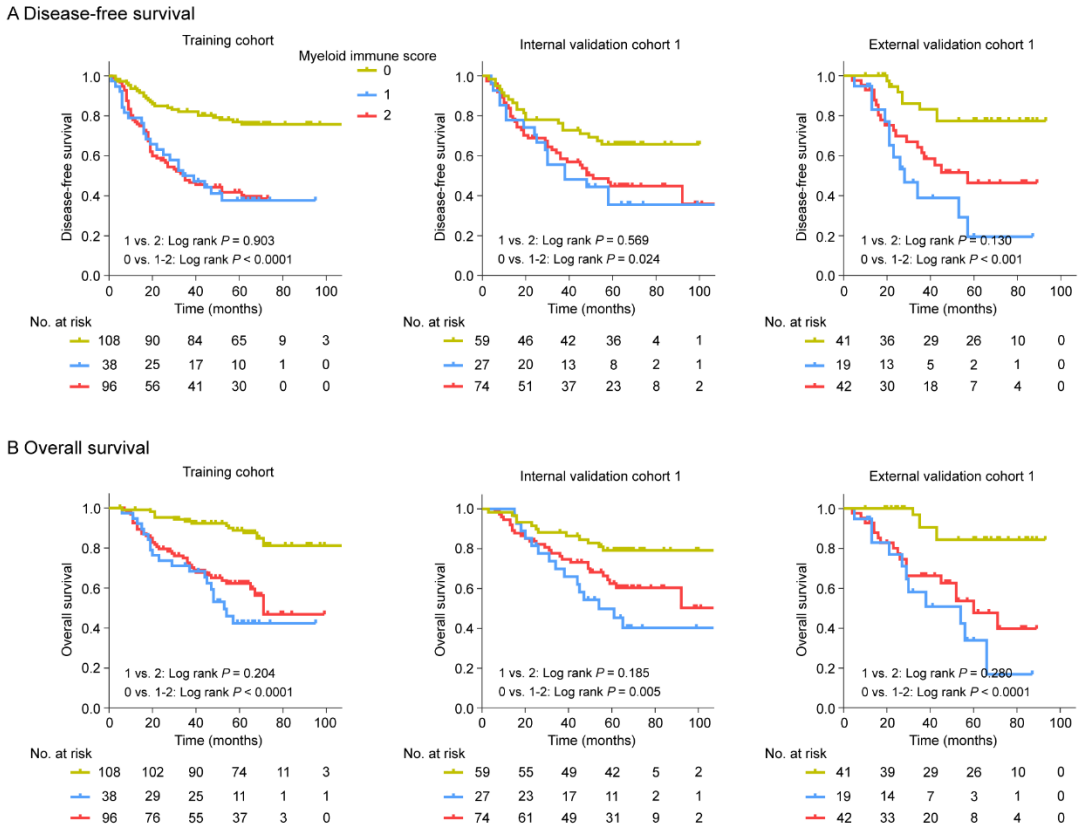
Thirdly, we found that the optimal cut-off value for LRS and MRS developed from Youden's index had more effective and reasonable guiding value for immunotherapy prediction. The difference in immunotherapy response was more obvious between the high and low groups derived from Youden's index, compared with that in the median, upper quartile, and lower quartile. Moreover, the highest AUC value in predicting immunotherapy response was observed in the binary variable of LRS and MRS derived from Youden's index. Finally, when combining LRS and MRS to predict the immunotherapy response, we also found that the four radiomics subtypes from the Youden's index are more valuable. Therefore, the optimal cut-off value for LRS and MRS was determined by the Youden's index, which was used for subsequent analysis.

**6. Statistical analysis**

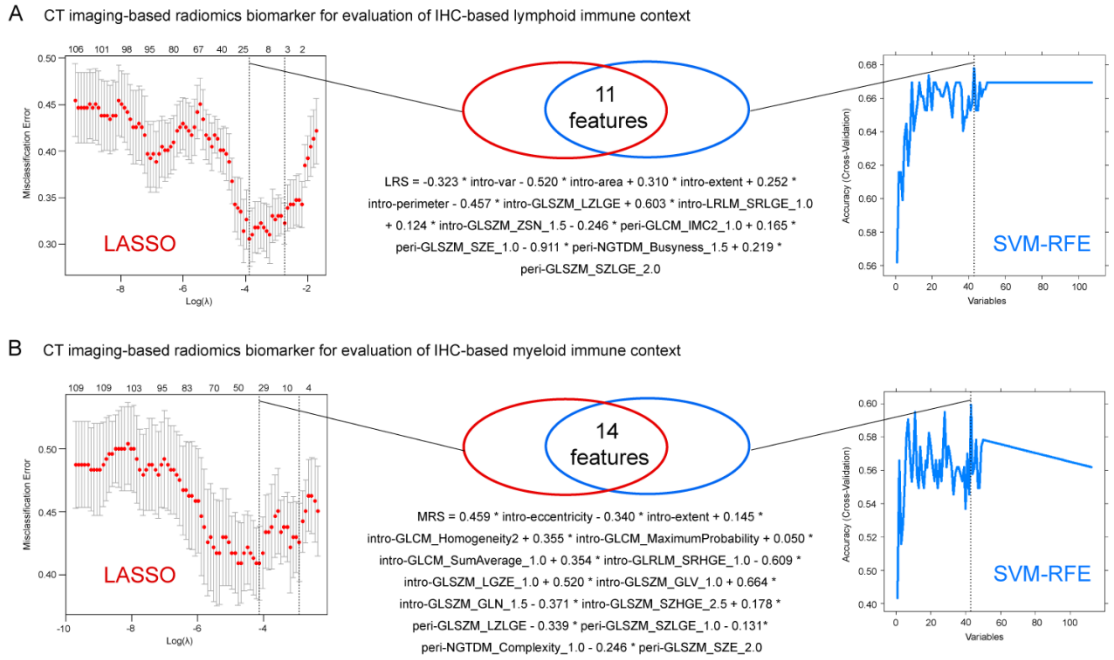
Redundant features elimination was performed using the Max-Relevance and Min-Redundancy (mRMR) algorithm in "mRMRe" package; Predictive features were selected using the Least Absolute Shrinkage and Selector Operation (LASSO) logistic regression algorithm by "glmnet" package and the Support Vector Machine-Recursive Feature Elimination (SVM-RFE) algorithm by the "e1071" package with 5-fold cross-validation; ROC curves were plotted by using the "pROC" packages; Nomogram were constructed by using the "rms" package.



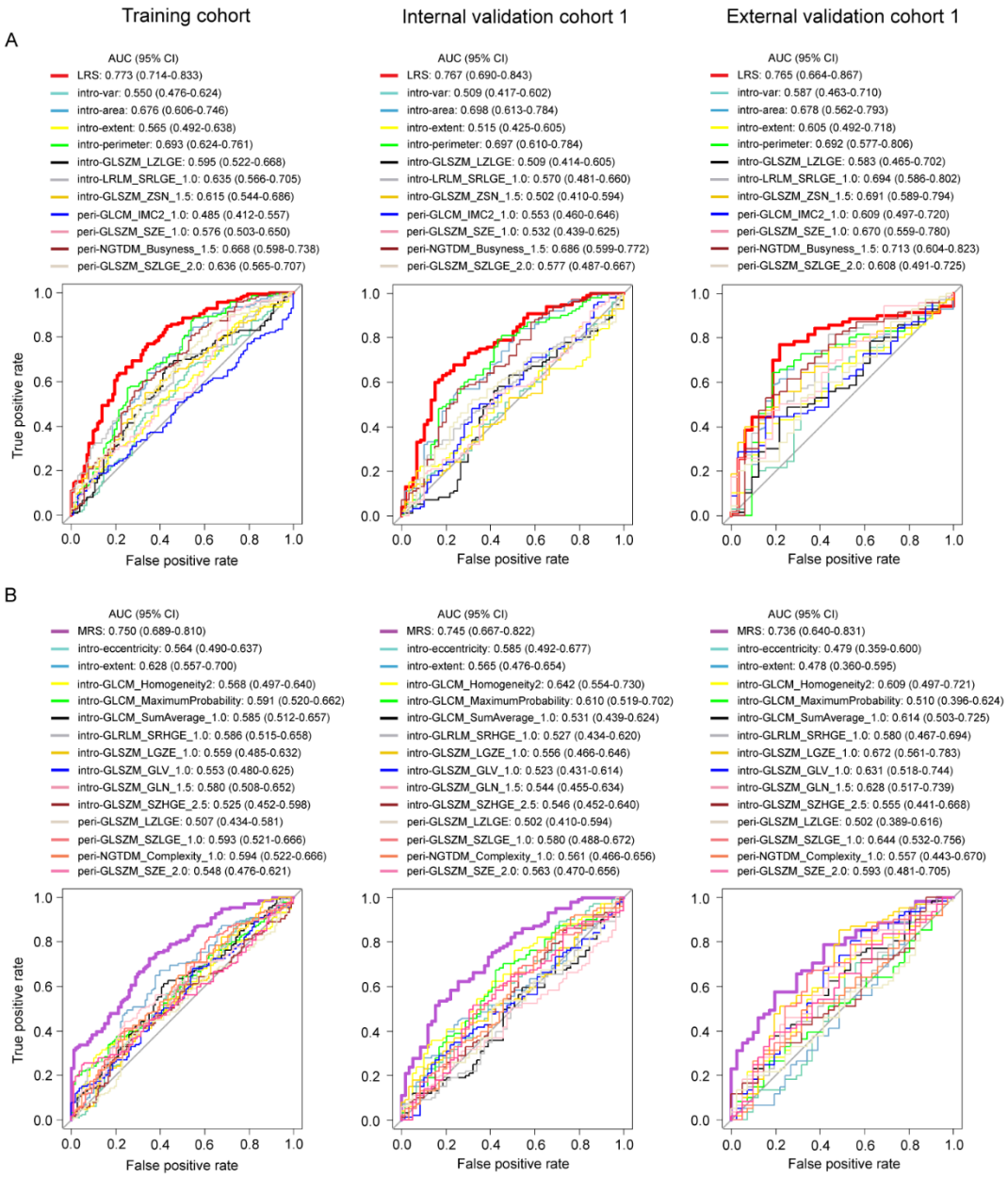

**Supplementary Figure 1. Kaplan-Meier analyses of disease-free survival (DFS) and overall survival (OS) according to each score of the LIS in patients with gastric cancer.** (A) Disease-free survival in the training cohort, internal validation cohort one, and external validation cohort one; (B) Overall survival in the training cohort, internal validation cohort one, and external validation cohort one. Comparisons of the above survival curves were performed with a two-sided log-rank test. LIS, lymphoid immune score.



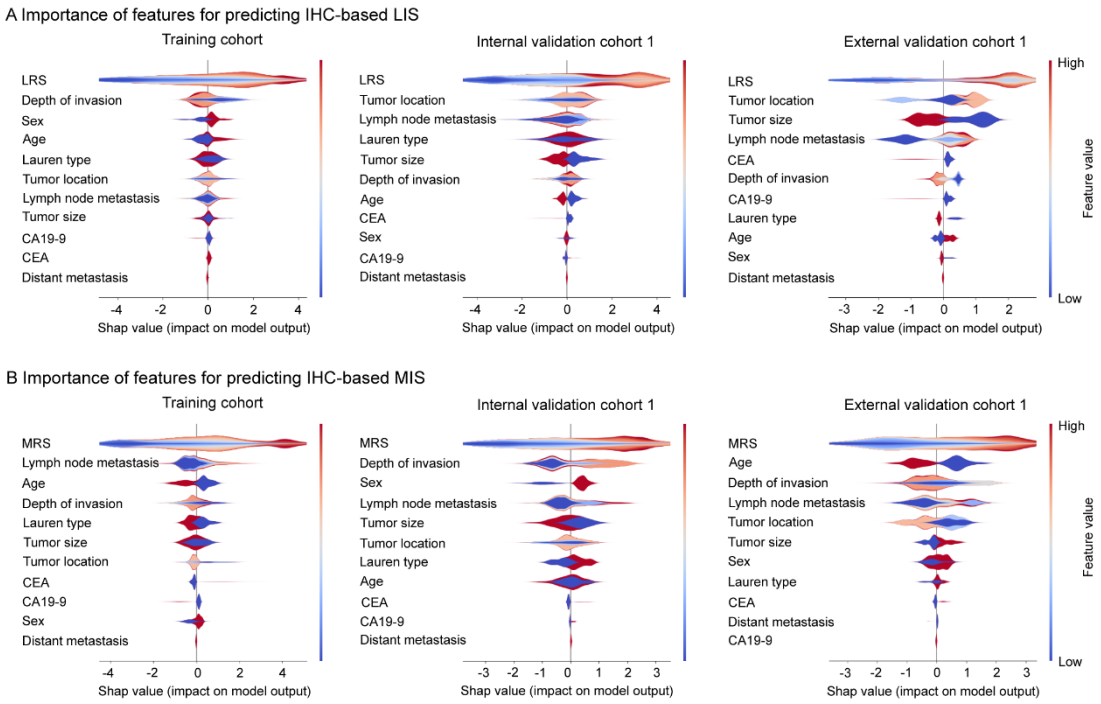

**Supplementary Figure 2. Kaplan-Meier analyses of disease-free survival (DFS) and overall survival (OS) according to each score of the MIS in patients with gastric cancer.** (A) Disease-free survival in the training cohort, internal validation cohort one, and external validation cohort one; (B). Overall survival in the training cohort, internal validation cohort one, and external validation cohort one. Comparisons of the above survival curves were performed with a two-sided log-rank test. MIS, myeloid immune score.



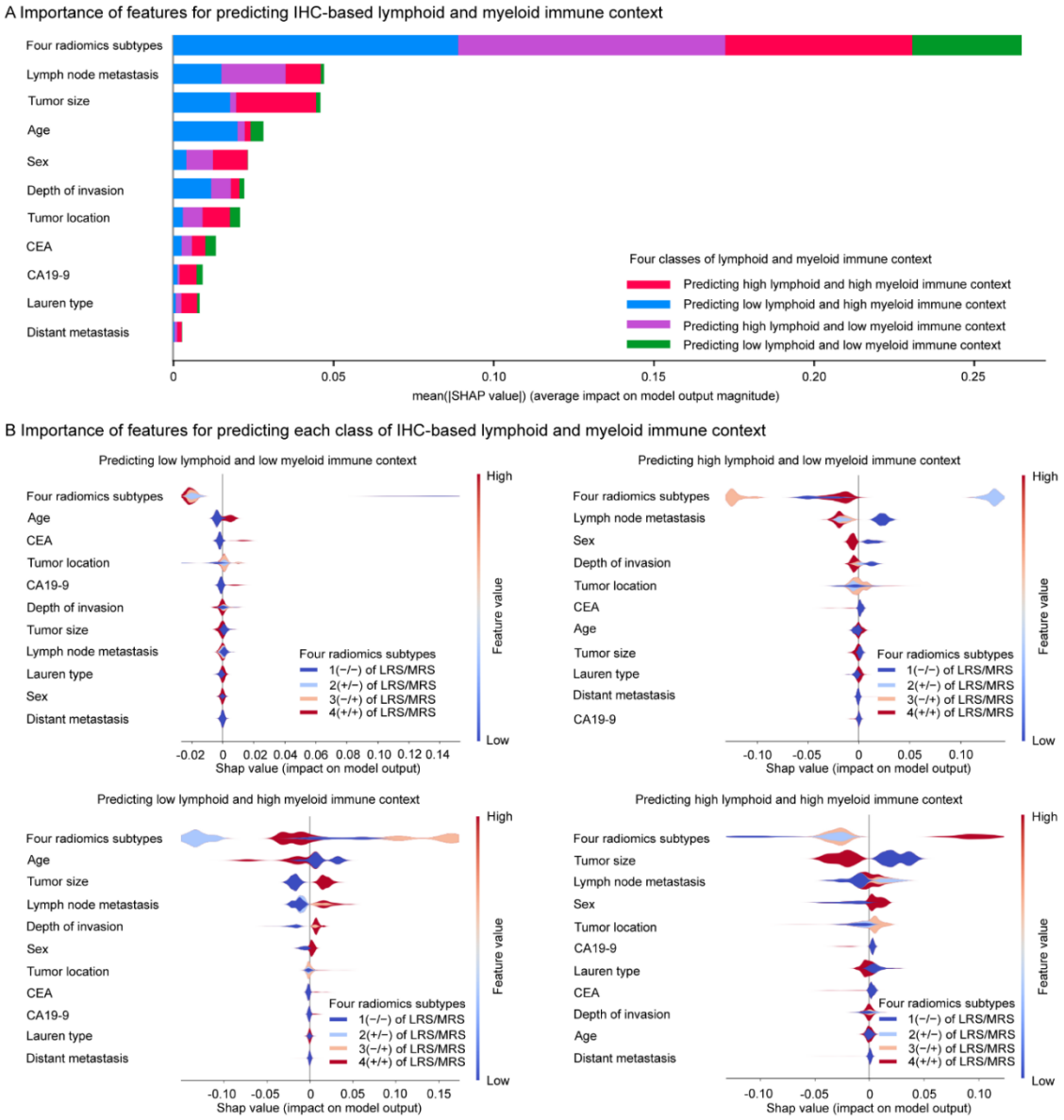

**Supplementary Figure 3. Development of two radiomics imaging biomarkers (LRS and MRS) for respective evaluation of IHC-based lymphoid and myeloid immune context.** (A) The overlapping features chosen by the Least Absolute Shrinkage and Selector Operation (LASSO) logistic regression and the Support Vector Machine-Recursive Feature Elimination (SVM-RFE) algorithms, and then assigned a coefficient for each radiomics features with the multivariate logistic regression (MLR) method to construct the LRS radiomics imaging biomarkers (n=242); (B) The overlapping features chosen by the LASSO logistic regression and SVM-RFE algorithms, and then assigned a coefficient for each radiomics features with the MLR method to construct the MRS radiomics imaging biomarkers (n=242). LRS, lymphoid radiomics score; MRS, myeloid radiomics score.




**Supplementary Figure 4. ROC curves of the radiomics imaging biomarkers (LRS and MRS) and radiomics features (11 of LRS and 14 of MRS) for the lymphoid and myeloid immune context in the training cohort (n=242), internal validation cohort one (n=160), and external validation cohort one (n=102).** (A) ROC curves of LRS and its 11 features for predicting the lymphoid immune context; (B) ROC curves of MRS and its 14 features for predicting the myeloid immune context. LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

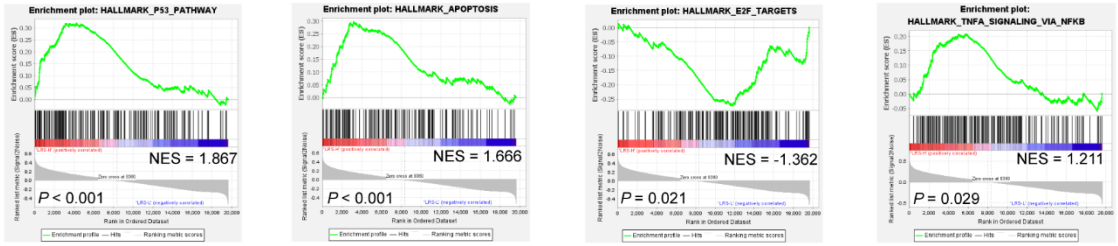



**Supplementary Figure 5. The radiomics imaging biomarkers (LRS and MRS) and clinicopathologic features to predict the lymphoid and myeloid immune context in the training cohort (n=242), internal validation cohort one (n=160), and external validation cohort one (n=102) by SHAP interpretations**. On the X-axis, the contribution of each feature is shown. The Shapley values is positively correlated with the importance. Moreover, a feature with a positive Shapley value will favorably impact the prediction (increase the possibility of LRS high or MRS high). The influence of the value of the feature itself is shown on the Y-axis, for example, for radiomics signature, a high value (in red) is associated with a positive Shapley value that will increase the possible of LRS high or MRS high, while a low value (in blue) will decrease the Shapley value and the possible of LRS high or MRS high. (A) SHAP plots of LRS and clinicopathologic features for predicting the lymphoid immune context; (B) SHAP plots of MRS and clinicopathologic features for predicting the myeloid immune context. LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

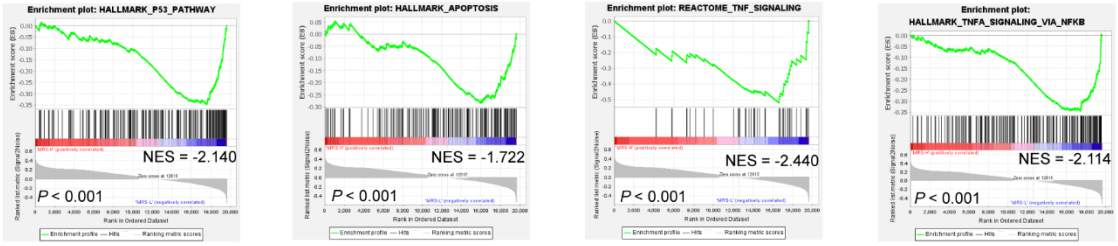



**Supplementary Figure 6. The radiomics imaging subtypes [1(−/−), 2(+/−), 3(−/+), and 4(+/+)] and clinicopathologic features to predict the lymphoid and myeloid immune context by SHAP interpretations (n=504).** (A) The radiomics imaging subtypes were the most important features for the prediction of the lymphoid and myeloid immune context, compared with other clinicopathological variables. (B) The imaging subtype 1(−/−) was characterized by low infiltration of lymphoid cells and myeloid cells; the imaging subtype 2(+/−) was characterized by high infiltration of lymphoid cells and low infiltration of myeloid cells; the imaging subtype 3(−/+) was characterized by low infiltration of lymphoid cells and high infiltration of myeloid cells; the imaging subtype 4(+/+) was characterized by high infiltration of lymphoid cells and myeloid cells.

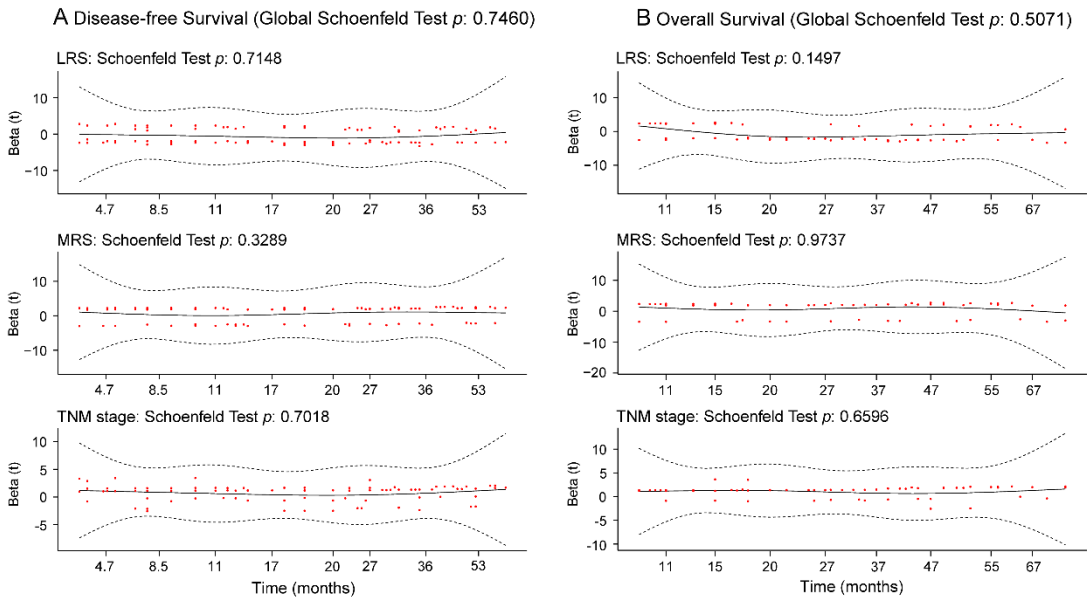
A Molecular signaling associated with LRS (LRS high vs. LRS low)



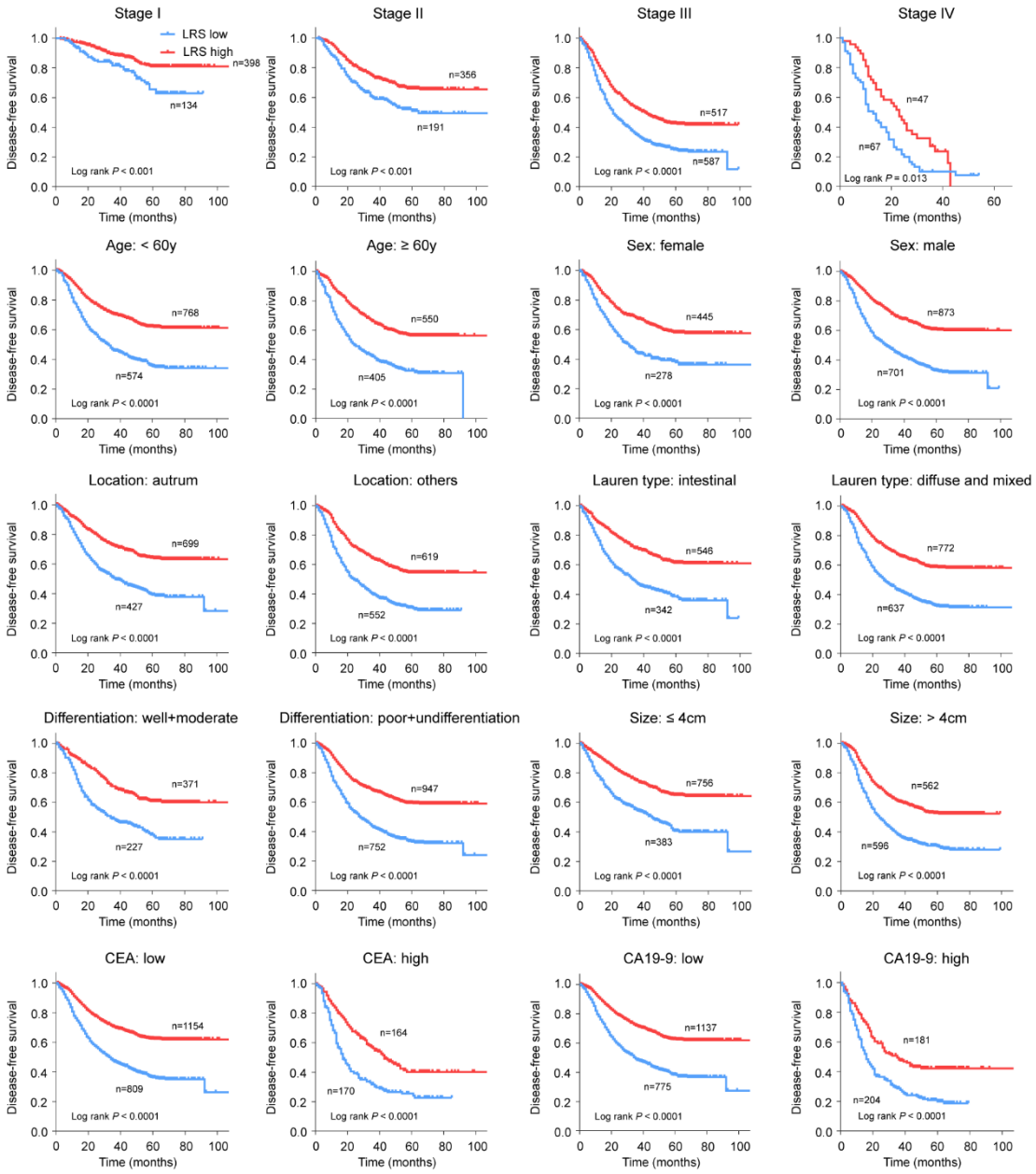

B Molecular signaling associated with MRS (MRS high vs. MRS low)



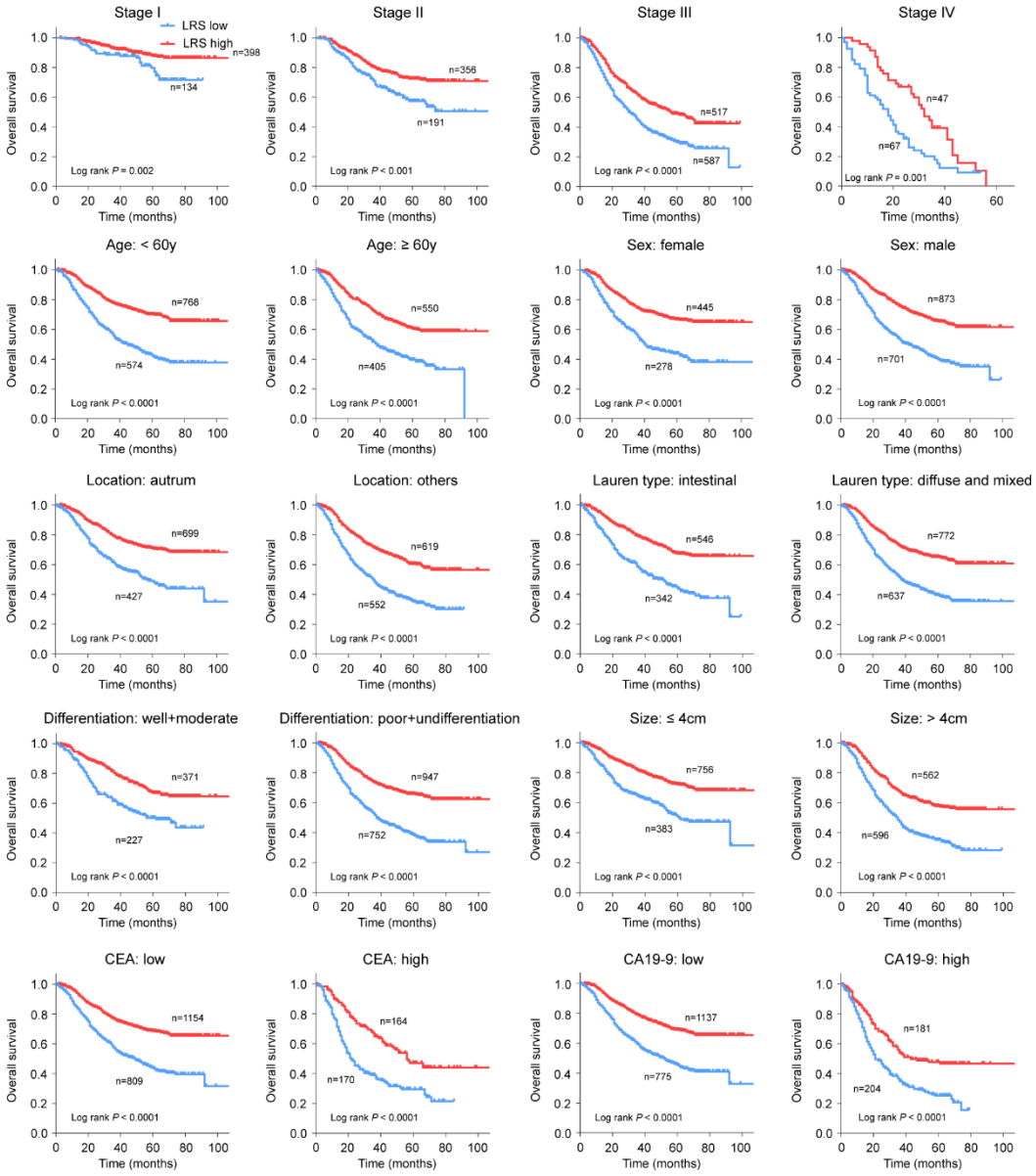

**Supplementary Figure 7. GSEA and KEGG examples on the molecular signaling pathways associated with the imaging biomarkers.** (A) Molecular signaling pathways associated with LRS, such as P53 pathway, apoptosis pathway, E2F targets signaling, and TNF signaling (n=42). The P value was calculated using permutation test, adjusted for multiple hypothesis testing; (B) Molecular signaling pathways associated with MRS, such as P53 pathway, apoptosis pathway, TNF signaling, and NFKB signaling (n=42). The P value was calculated using permutation test, adjusted for multiple hypothesis testing. LRS, lymphoid radiomics score; MRS, myeloid radiomics score.



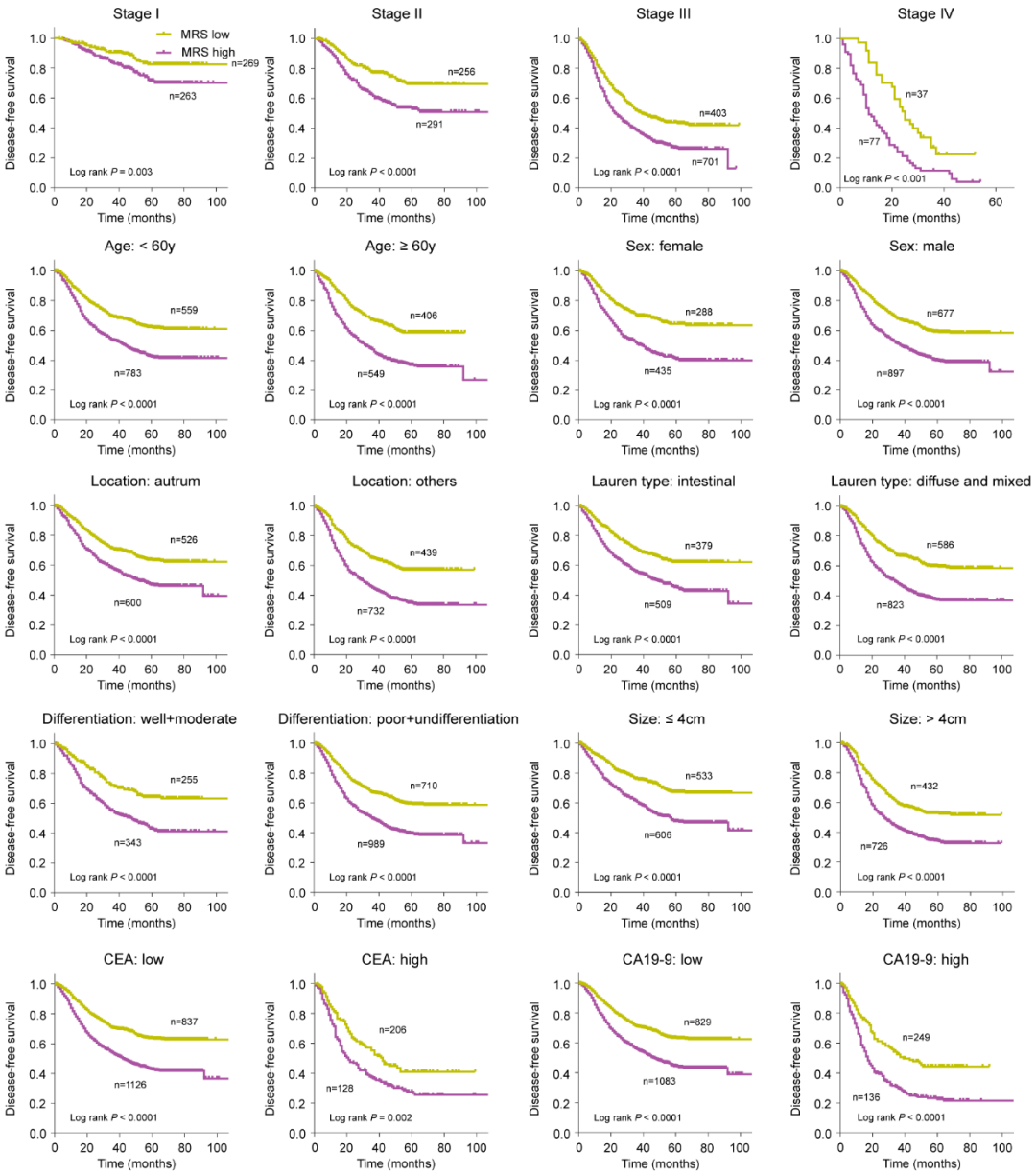

**Supplementary Figure 8. The PH assumption test of the multivariate Cox regression model (n=242).** (A) The PH assumption test for DFS; (B) The PH assumption test for OS. The PH assumption was checked by constructing test statistics based on Schoenfeld residual. PH, proportional hazards; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.



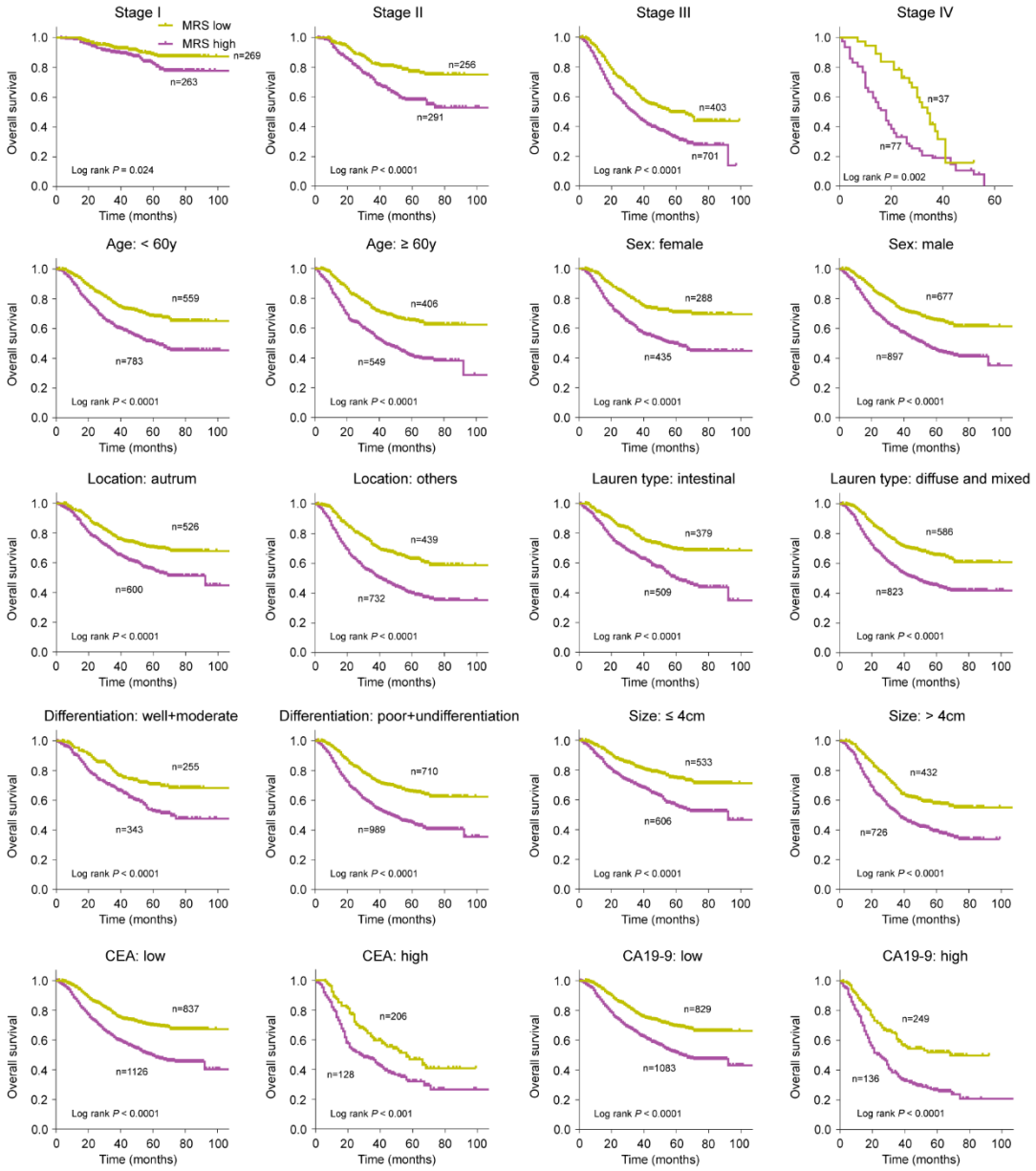

**Supplementary Figure 9. Kaplan-Meier analyses of disease-free survival (DFS) according to dichotomized LRS stratified by clinicopathological risk factors in 2297 patients with gastric cancer from the training cohort, two internal validation cohort; two external validation cohort, and the prospective validation cohort.** LRS, lymphoid radiomics score; *P*-values were calculated by log-rank test.



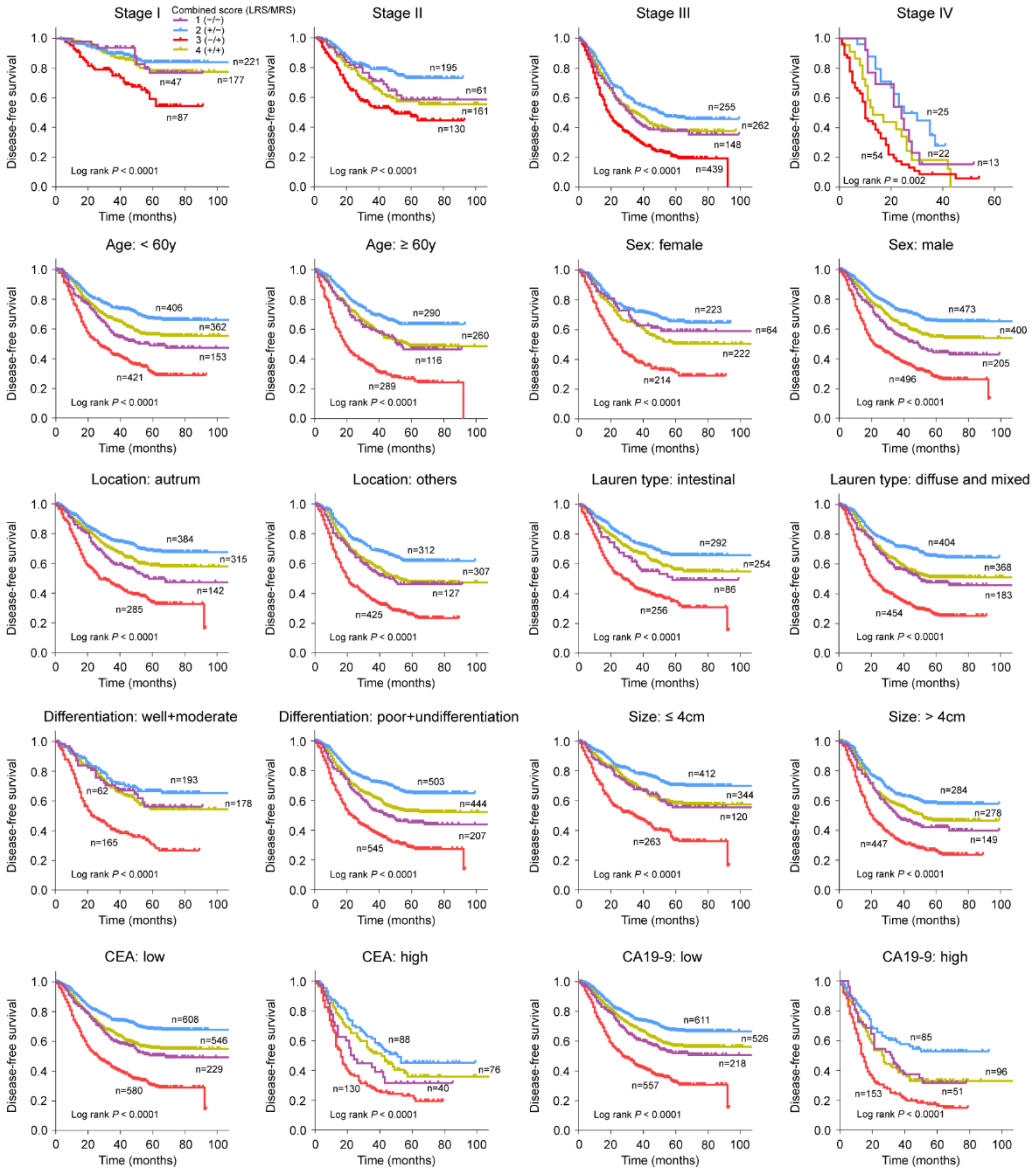

**Supplementary Figure 10. Kaplan-Meier analyses of overall survival (OS) according to dichotomized LRS stratified by clinicopathological risk factors in 2297 patients with gastric cancer from the training cohort, two internal validation cohort; two external validation cohort, and the prospective validation cohort.** LRS, lymphoid radiomics score; *P*-values were calculated by log-rank test.



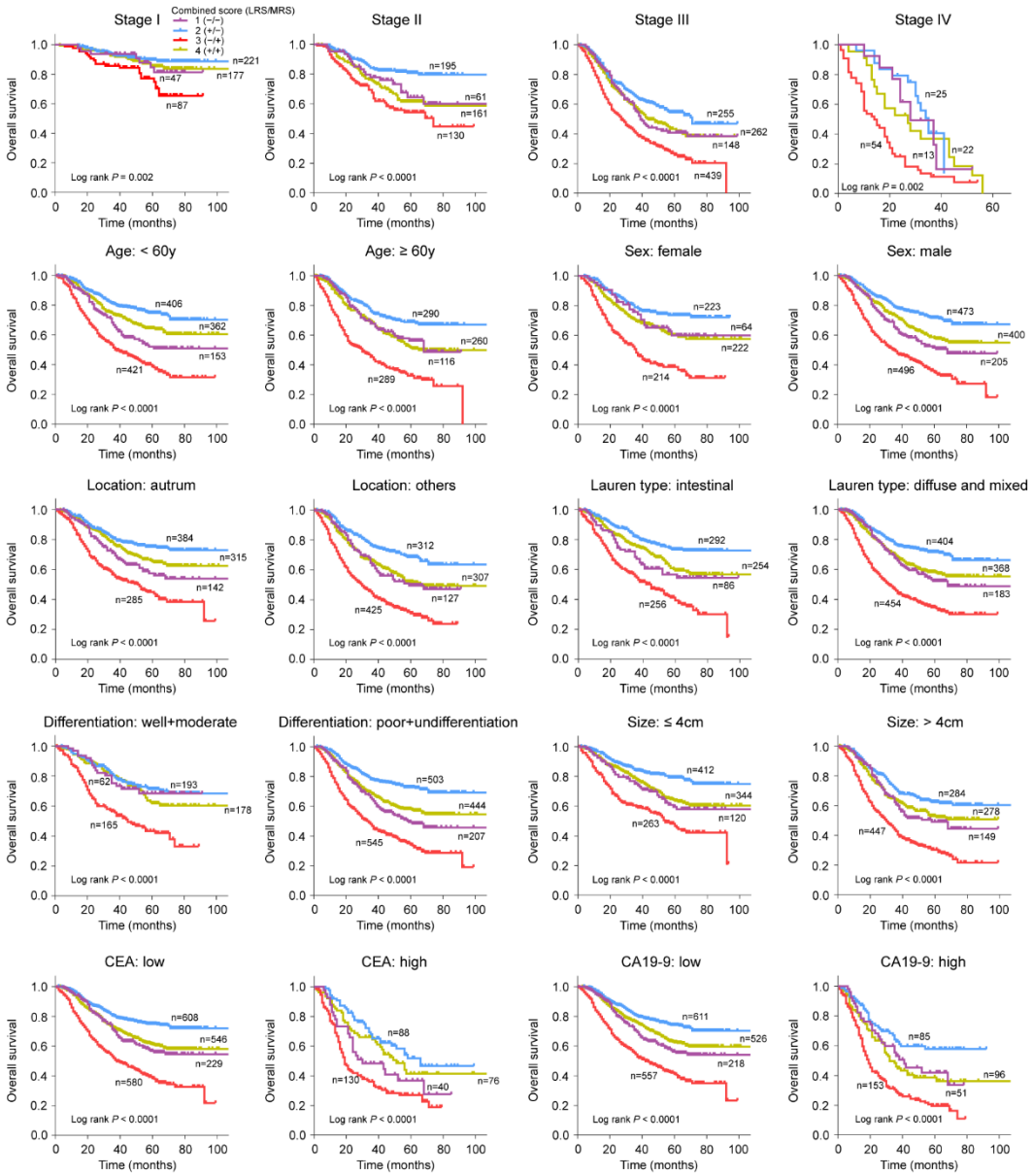

**Supplementary Figure 11. Kaplan-Meier analyses of disease-free survival (DFS) according to dichotomized MRS stratified by clinicopathological risk factors in 2297 patients with gastric cancer from the training cohort, two internal validation cohort; two external validation cohort, and the prospective validation cohort.** MRS, myeloid radiomics score; *P*-values were calculated by log-rank test.



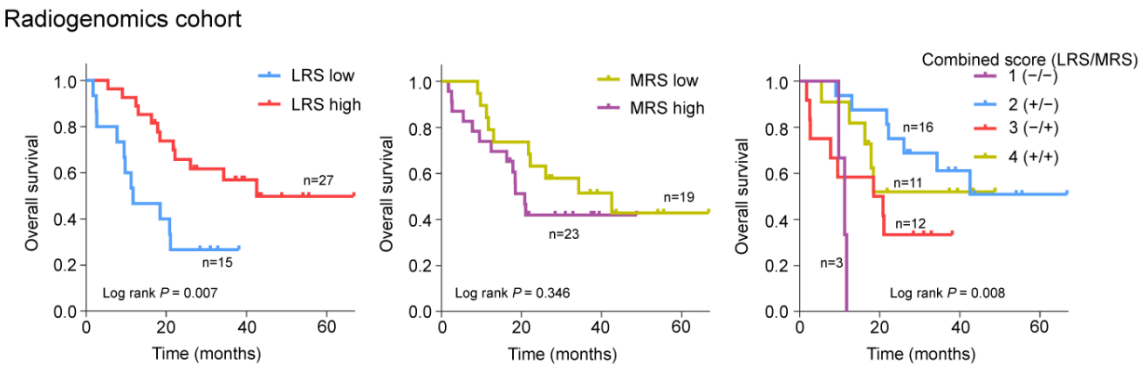

**Supplementary Figure 12. Kaplan-Meier analyses of overall survival (OS) according to dichotomized MRS stratified by clinicopathological risk factors in 2297 patients with gastric cancer from the training cohort, two internal validation cohort; two external validation cohort, and the prospective validation cohort.** MRS, myeloid radiomics score; *P*-values were calculated by log-rank test.



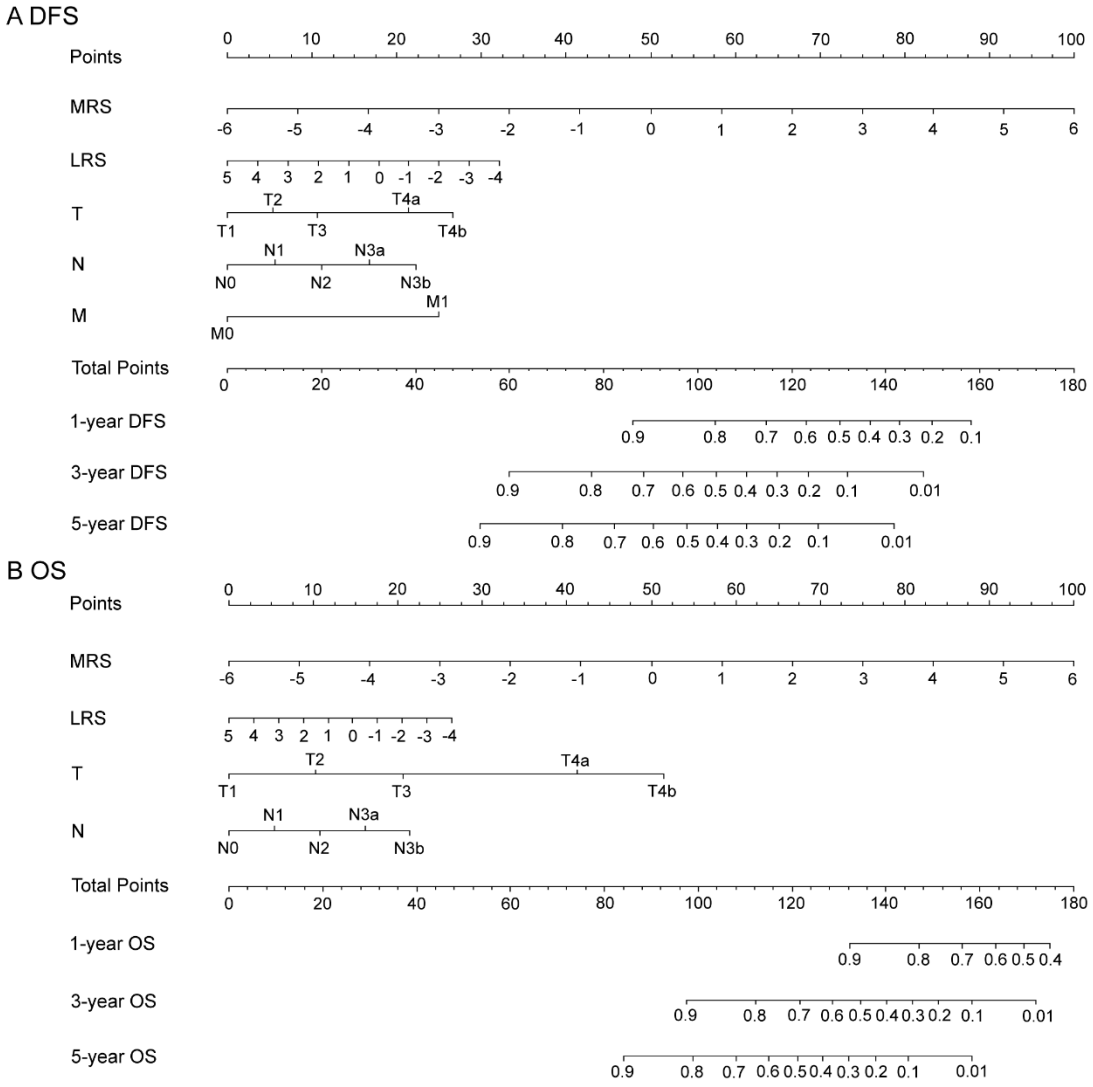

**Supplementary Figure 13. Kaplan-Meier analyses of disease-free survival (DFS) according to the combined imaging biomarker (LRS/MRS) with four subtypes stratified by clinicopathological risk factors in 2297 patients with gastric cancer from the training cohort, two internal validation cohort; two external validation cohort, and the prospective validation cohort.** The combined imaging biomarker (LRS/MRS): 1(-/-), 2(+/-), 3(-/+), and 4(+/+); *P*-values were calculated by log-rank test.




**Supplementary Figure 14. Kaplan-Meier analyses of overall survival (OS) according to the combined imaging biomarker (LRS/MRS) with four subtypes stratified by clinicopathological risk factors in 2297 patients with gastric cancer from the training cohort, two internal validation cohort; two external validation cohort, and the prospective validation cohort.** The combined imaging biomarker (LRS/MRS): 1(-/-), 2(+/-), 3(-/+), and 4(+/+); *P*-values were calculated by log-rank test.




**Supplementary Figure 15. Prognostic value of the radiomics imaging biomarkers for disease-free survival (DFS) and overall survival (OS) in the radiogenomics cohort.** According to LRS, MRS, and the combined imaging biomarker (LRS/MRS). *P*-values were calculated by log-rank test.




**Supplementary Figure 16. Integrated nomograms to predict 1-, 3-, 5- year disease free survival (DFS) and overall survival (OS) for patients with gastric cancer (n=242).** To determine how many points toward the probability of DFS and OS the patient receives for his or her LRS or MRS, locate the patient's LRS or MRS on their axis, draw a line straight upward to the point axis, repeat this process for each variable, sum the points achieved for each of the risk factors, locate the final sum on the Total Point axis, and draw a line straight down to find the patient's probability of DFS and OS. LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

A First line treatment


Immunotherapy response of radiomics subtypes in the first line anti-PD-1 treatment.

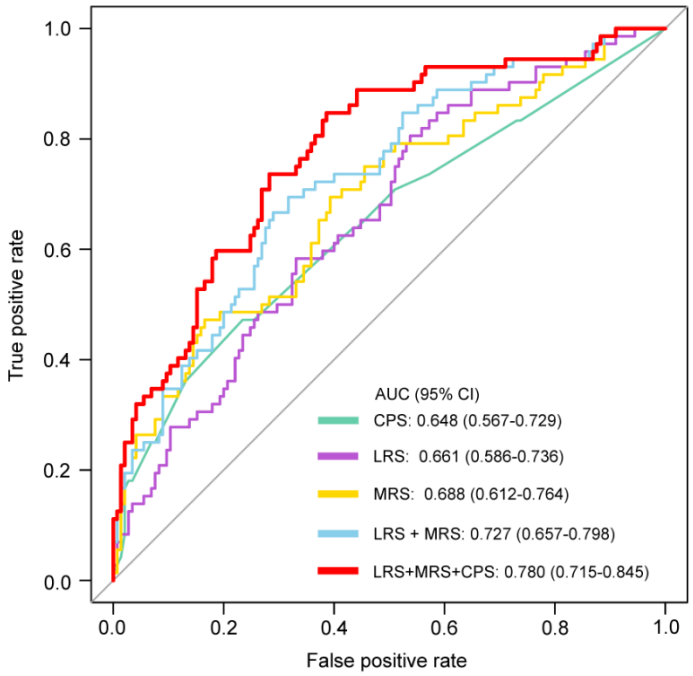
| Response | LRS | | *P* | MRS | | *P* | Combined score (LRS/MRS) | | | | *P* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Low | High | <0.001 | Low | High | 0.024 | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | 0.003 |
| CR (%) | 4.7% | 20.5% | | 20.4% | 10.2% | | 13.3% | 23.5% | 2.0% | 18.4% | |
| PR (%) | 15.6% | 33.7% | | 34.7% | 21.4% | | 26.7% | 38.2% | 12.2% | 30.6% | |
| SD (%) | 29.7% | 16.9% | | 22.4% | 22.4% | | 33.3% | 17.6% | 28.6% | 16.3% | |
| PD (%) | 50.0% | 28.9% | | 22.4% | 45.9% | | 26.7% | 20.6% | 57.1% | 34.7% | |

B Second and third line treatment

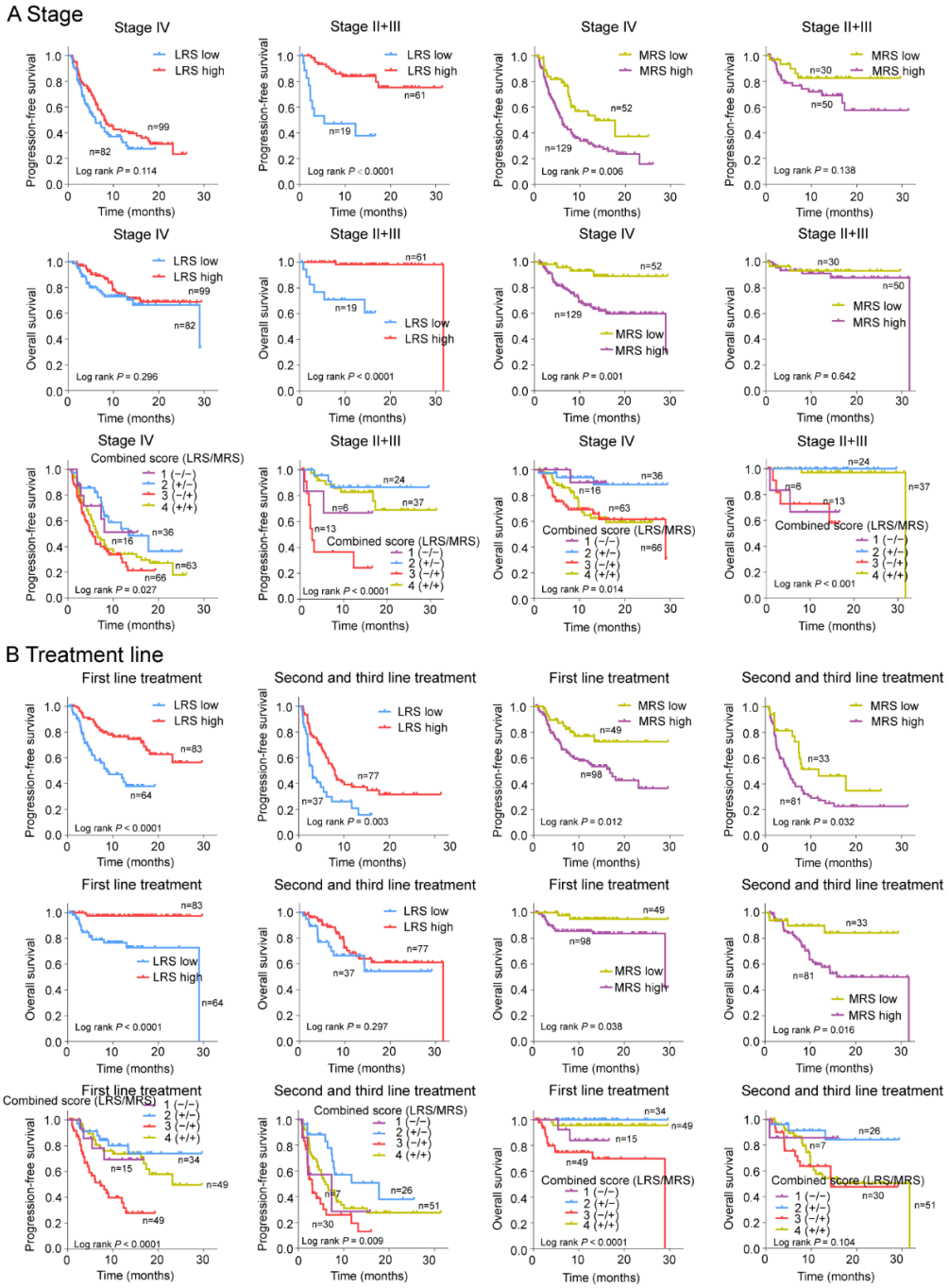

Immunotherapy response of radiomics subtypes in the second and third line anti-PD-1 treatment.

| Response | LRS | | *P* | MRS | | *P* | Combined score (LRS/MRS) | | | | *P* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Low | High | 0.066 | Low | High | 0.006 | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | 0.008 |
| CR (%) | 0.0% | 6.5% | | 12.1% | 1.2% | | 0.0% | 15.4% | 0.0% | 2.0% | |
| PR (%) | 2.7% | 15.6% | | 21.2% | 7.4% | | 0.0% | 26.9% | 3.3% | 9.8% | |
| SD (%) | 24.3% | 20.8% | | 21.2% | 22.2% | | 42.9% | 15.4% | 20.0% | 23.5% | |
| PD (%) | 73.0% | 57.1% | | 45.5% | 69.1% | | 57.1% | 42.3% | 76.7% | 64.7% | |

**Supplementary Figure 17. Predictive value of the radiomics imaging biomarkers for anti-PD-1 immunotherapy response according to the treatment line.** (A) The ratio of different immunotherapy responses from two radiomics imaging biomarkers (LRS and MRS) and their combined biomarker (LRS/MRS) in the first line treatment (n=147). Data was compared by the chi-squared test; (B) The ratio of different immunotherapy responses from two radiomics imaging biomarkers (LRS and MRS) and their combined biomarker (LRS/MRS) in the second-third line treatment (n=114). Data was compared by the chi-squared test. LRS, lymphoid radiomics score; MRS, myeloid radiomics score.




**Supplementary Figure 18. Receiver operator characteristic (ROC) curves of the CT imaging biomarkers (LRS and MRS), CPS and the integrated model combining CT imaging biomarkers and CPS for predicting immunotherapy response.** A significant improvement in the accuracy of immunotherapy response prediction was observed in the integrated model (available for n=217, $P < 0.001$). *P* value was calculated by Delong test. CPS, combined positive score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.




**Supplementary Figure 19. Kaplan-Meier analyses of progression-free survival (PFS) and overall survival (OS) according to two radiomics imaging biomarkers (LRS and MRS) and the combined imaging biomarker (LRS/MRS) with four subtypes stratified by clinicopathological risk factors in GC patients treated with anti-PD-1 immunotherapy.** (A) Stratified by stage; (B) Stratified by treatment line. Comparisons of the above survival curves were performed with a two-sided log-rank test. LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 1. Characteristics of patients with gastric cancer in two anti-PD-1 immunotherapy cohorts and the radiogenomics cohort.**

| Variables | Immunotherapy cohort 1, SMU cohort, n=198 | | Immunotherapy cohort 2, GPHCM cohort, n=63 | | Radiogenomics cohort, n=42 | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| **Median age (range)** | 55.0 (47.0-65.0) | | 60 (48-66) | | 67.0 (59.0-70.0) | |
| **Sex** | | | | | | |
| Female | 83 | 41.9 | 29 | 46.0 | 6 | 14.3 |
| Male | 115 | 58.1 | 34 | 54.0 | 36 | 85.7 |
| **Stage** | | | | | | |
| I | 0 | 0 | 0 | 0 | 1 | 2.4 |
| II | 17 | 8.6 | 0 | 0 | 7 | 16.7 |
| III | 47 | 23.7 | 16 | 25.4 | 31 | 73.8 |
| IV | 134 | 67.7 | 47 | 74.6 | 3 | 7.1 |
| **Immunotherapy response** | | | | | | |
| CR | 24 | 12.1 | 1 | 1.6 | - | - |
| PR | 40 | 20.2 | 11 | 17.5 | - | - |
| SD | 33 | 16.7 | 25 | 39.7 | - | - |
| PD | 101 | 51.0 | 26 | 41.3 | - | - |
| **Treatment line** | | | | | - | - |
| First line | 114 | 57.6 | 33 | 52.4 | - | - |
| Second line | 48 | 24.2 | 24 | 38.1 | - | - |
| Third line | 36 | 18.2 | 6 | 9.5 | - | - |
| **Treatment type** | | | | | | |
| Neoadjuvant therapy | 37 | 18.7 | 9 | 14.3 | - | - |
| Adjuvant therapy | 27 | 13.6 | 7 | 11.1 | - | - |
| For advanced disease | 134 | 67.7 | 47 | 74.6 | - | - |

CR: complete response, PR: partial response, SD: stable disease, PD: progressive disease.

**Supplementary Table 2. Clinical characteristics of patients according to the LIS in the training, internal, and external validation cohorts.**

| Variables | Training cohort, n = 242 | | | Internal validation cohort 1, n = 160 | | | External validation cohort 1, n = 102 | | |
|---|---|---|---|---|---|---|---|---|---|
| | low LIS | high LIS | *P* | low LIS | high LIS | *P* | low LIS | high LIS | *P* |
| **Median age (range)** | 58 (46-63) | 56 (48-64) | 0.643 | 59 (50-65) | 57 (49-65) | 0.824 | 55 (42-63) | 59 (50-66) | 0.177 |
| **Male (%)** | 67 (65.7%) | 92 (65.7%) | 0.552 | 45 (75.0%) | 69 (69.0%) | 0.417 | 26 (81.3%) | 47 (67.1%) | 0.143 |
| **Tumor size (%)** | | | 0.037 | | | 0.025 | | | 0.005 |
| ≤4cm | 43 (42.2%) | 78 (55.7%) | | 22 (36.7%) | 55 (55.0 %) | | 10 (31.3%) | 43 (61.4%) | |
| >4cm | 59 (57.8%) | 62 (44.3%) | | 38 (63.3%) | 45 (45.0%) | | 22 (68.8%) | 27 (38.6%) | |
| **Tumor location (%)** | | | 0.765 | | | 0.584 | | | 0.140 |
| Cardia | 18 (17.6%) | 28 (20.0%) | | 14 (23.3%) | 19 (19.0%) | | 12 (37.5%) | 21 (30.0%) | |
| Body | 18 (17.6%) | 28 (20.0%) | | 16 (26.7%) | 20 (20.0%) | | 9 (28.1%) | 13 (18.6%) | |
| Antrum | 58 (56.9%) | 81 (55.0%) | | 28 (46.7%) | 56 (56.0%) | | 9 (28.1%) | 35 (50.0%) | |
| Whole | 8 (7.8%) | 6 (5.0%) | | 2 (3.3%) | 5 (5.0%) | | 2 (6.3%) | 1 (1.4%) | |
| **Differentiation status (%)** | | | 0.277 | | | 0.218 | | | 0.687 |
| Well | 8 (7.8%) | 19 (13.6%) | | 5 (8.3%) | 14 (14.0%) | | 0 (0.0%) | 1 (1.4%) | |
| Moderate | 22 (21.6%) | 34 (24.3%) | | 20 (33.3%) | 22 (22.0%) | | 7 (21.9%) | 12 (17.1%) | |
| Poor and undifferentiated | 72 (70.6%) | 87 (62.1%) | | 35 (58.3%) | 64 (64.0%) | | 25 (78.1%) | 57 (81.4%) | |
| **Lauren type (%)** | | | 0.291 | | | 0.101 | | | 0.396 |
| Intestinal type | 44 (43.1%) | 70 (50.0%) | | 22 (36.7%) | 50 (50.0%) | | 10 (31.3%) | 28 (40.0%) | |
| Diffuse or mixed type | 58 (56.9%) | 70 (50.0%) | | 38 (63.3%) | 50 (50.0%) | | 22 (68.8%) | 42 (60.0%) | |
| **CEA (%)** | | | 0.320 | | | 0.459 | | | 0.188 |
| Normal | 91 (89.2%) | 130 (92.9%) | | 51 (85.0%) | 89 (89.0%) | | 24 (75.0%) | 60 (85.7%) | |
| Elevated | 11 (10.8%) | 10 (7.1%) | | 9 (15.0%) | 11 (11.0%) | | 8 (25.0%) | 10 (14.3%) | |
| **CA19-9 (%)** | | | 0.229 | | | 0.147 | | | 0.106 |
| Normal | 84 (82.4%) | 123 (87.9%) | | 50 (83.3%) | 91 (91.0%) | | 25 (78.1%) | 63 (90.0%) | |
| Elevated | 18 (17.6%) | 17 (12.1%) | | 10 (16.7%) | 9 (9.0%) | | 7 (21.9%) | 7 (10.0%) | |
| **Depth of invasion (%)** | | | 0.071 | | | 0.101 | | | 0.452 |
| pT1 | 16 (15.7%) | 37 (26.4%) | | 7 (11.7%) | 30 (30.0%) | | 3 (9.4%) | 15 (21.4%) | |
| pT2 | 9 (8.8%) | 20 (14.3%) | | 5 (8.3%) | 9 (9.0%) | | 3 (9.4%) | 11 (15.7%) | |
| pT3 | 9 (8.8%) | 14 (10.0%) | | 12 (20.0%) | 13 (13.0%) | | 8 (25.0%) | 12 (17.1%) | |
| pT4a | 52 (51.0%) | 57 (40.7%) | | 26 (43.3%) | 36 (36.0%) | | 15 (46.9%) | 26 (37.1%) | |
| pT4b | 16 (15.7%) | 12 (8.6%) | | 10 (16.7%) | 12 (12.0%) | | 3 (9.4%) | 6 (8.6%) | |
| **Lymph node metastasis (%)** | | | 0.053 | | | 0.164 | | | 0.834 |
| pN0 | 37 (36.3%) | 74 (52.9%) | | 21 (35.0%) | 50 (50.0%) | | 9 (28.1%) | 26 (37.1%) | |
| pN1 | 18 (17.6%) | 24 (17.1%) | | 11 (18.3%) | 17 (17.0%) | | 4 (12.5%) | 10 (14.3%) | |
| pN2 | 11 (10.8%) | 15 (10.7%) | | 7 (11.7%) | 11 (11.0%) | | 10 (31.3%) | 15 (21.4%) | |
| pN3a | 19 (18.6%) | 14 (10.0%) | | 15 (25.0%) | 11 (11.0%) | | 5 (15.6%) | 11 (15.7%) | |
| pN3b | 17 (16.7%) | 13 (9.3%) | | 6 (10.0%) | 11 (11.0%) | | 4 (12.5%) | 8 (11.4%) | |
| **Distant metastasis (%)** | | | 0.693 | | | 0.601 | | | 0.128 |
| pM0 | 99 (97.1%) | 137 (97.9%) | | 59 (98.3%) | 97 (97.0%) | | 28 (87.5%) | 67 (95.7%) | |
| pM1 | 3 (2.9%) | 3 (2.1%) | | 1 (1.7%) | 3 (3.0%) | | 4 (12.5%) | 3 (4.3%) | |
| **Stage (%)** | | | 0.034 | | | 0.057 | | | 0.205 |
| I | 21 (20.6%) | 52 (37.1%) | | 10 (16.7%) | 31 (31.0%) | | 6 (18.8%) | 22 (31.4%) | |
| II | 21 (20.6%) | 29 (20.7%) | | 14 (23.3%) | 29 (29.0%) | | 3 (9.4%) | 11 (15.7%) | |
| III | 57 (55.9%) | 56 (40.0%) | | 35 (58.3%) | 37 (37.0%) | | 19 (59.4%) | 34 (48.6%) | |
| IV | 3 (2.9%) | 3 (2.1%) | | 1 (1.7%) | 3 (3.0%) | | 4 (12.5%) | 3 (4.3%) | |
| **Chemotherapy (%)** | 52 (51.0%) | 72 (51.4%) | 0.945 | 32 (53.3%) | 45 (45.0%) | 0.307 | 19 (59.4%) | 27 (38.6%) | 0.050 |

LIS, lymphoid immune score.

**Supplementary Table 3. Clinical characteristics of patients according to the MIS in the training, internal, and external validation cohorts.**

| Variables | Training cohort, n = 242 | | | Internal validation cohort 1, n = 160 | | | External validation cohort 1, n = 102 | | |
|---|---|---|---|---|---|---|---|---|---|
| | low MIS | high MIS | *P* | low MIS | high MIS | *P* | low MIS | high MIS | *P* |
| **Median age (range)** | 58 (48-65) | 56 (46-62) | 0.400 | 57 (50-66) | 57 (49-65) | 0.531 | 61 (55-68) | 54 (43-63) | 0.008 |
| **Male (%)** | 70 (64.8%) | 89 (66.4%) | 0.794 | 37 (62.7%) | 77 (76.2%) | 0.068 | 27 (65.9%) | 46 (75.4%) | 0.294 |
| **Tumor size (%)** | | | 0.796 | | | 0.842 | | | 0.058 |
| ≤4cm | 55 (50.9%) | 66 (49.3%) | | 29 (49.2%) | 48 (47.5%) | | 26 (63.4%) | 27 (44.3%) | |
| >4cm | 53 (49.1%) | 68 (50.7%) | | 30 (50.8%) | 53 (52.5%) | | 15 (36.6%) | 34 (55.7%) | |
| **Tumor location (%)** | | | 0.749 | | | 0.052 | | | 0.019 |
| Cardia | 18 (16.7%) | 28 (20.9%) | | 14 (23.7%) | 19 (18.8%) | | 10 (24.4%) | 23 (37.7%) | |
| Body | 19 (17.6%) | 27 (20.1%) | | 19 (32.2%) | 17 (16.8%) | | 6 (14.6%) | 16 (26.2%) | |
| Antrum | 64 (59.3%) | 71(53.0%) | | 25 (42.4%) | 59 (58.4%) | | 25 (61.0%) | 19 (31.1%) | |
| Whole | 7 (6.5%) | 8 (6.0%) | | 1 (1.7%) | 6 (5.9%) | | 0 (0.0%) | 3 (4.9%) | |
| **Differentiation status (%)** | | | 0.254 | | | 0.600 | | | 0.665 |
| Well | 16 (14.8%) | 11 (8.2%) | | 9 (15.3%) | 10 (9.9%) | | 0 (0.0%) | 1 (1.6%) | |
| Moderate | 25 (23.1%) | 31 (23.1%) | | 15 (25.4%) | 27 (26.7%) | | 7 (17.1%) | 12 (19.7%) | |
| Poor and undifferentiated | 67 (62.0%) | 92 (68.7%) | | 35 (59.3%) | 64 (63.4%) | | 34 (82.9%) | 48 (78.7%) | |
| **Lauren type (%)** | | | 0.041 | | | 0.143 | | | 0.762 |
| Intestinal type | 43 (39.8%) | 71 (53.0%) | | 31 (52.5%) | 41 (40.6%) | | 16 (39.0%) | 22 (36.1%) | |
| Diffuse or mixed type | 65 (60.2%) | 63 (47.0%) | | 28 (47.5%) | 60 (59.4%) | | 25 (61.0%) | 39 (63.9%) | |
| **CEA (%)** | | | 0.121 | | | 0.757 | | | 0.513 |
| Normal | 102 (94.4%) | 119 (88.8%) | | 51 (86.4%) | 89 (88.1%) | | 35 (85.4%) | 49 (80.3%) | |
| Elevated | 6 (5.6%) | 15 (11.2%) | | 8 (13.6%) | 12 (11.9%) | | 6 (14.6%) | 12 (19.7%) | |
| **CA19-9 (%)** | | | 0.214 | | | 0.610 | | | 0.713 |
| Normal | 89 (82.4%) | 118 (88.1%) | | 53 (89.8%) | 88 (87.1%) | | 36 (87.8%) | 52 (85.2%) | |
| Elevated | 19 (17.6%) | 16 (11.9%) | | 6 (10.2%) | 13 (12.9%) | | 5 (12.2%) | 9 (14.8%) | |
| **Depth of invasion (%)** | | | 0.713 | | | 0.049 | | | 0.023 |
| pT1 | 25 (23.1%) | 28 (20.9%) | | 18 (30.5%) | 19 (18.8%) | | 12 (29.3%) | 6 (9.8%) | |
| pT2 | 13 (12.0%) | 16 (11.9%) | | 4 (6.8%) | 10 (9.9%) | | 7 (17.1%) | 7 (11.5%) | |
| pT3 | 10 (9.3%) | 13 (9.7%) | | 13 (22.0%) | 12 (11.9%) | | 3 (7.3%) | 17 (27.9%) | |
| pT4a | 51 (47.2%) | 58 (43.3%) | | 15 (25.4%) | 47 (46.5%) | | 15 (36.6%) | 26 (42.6%) | |
| pT4b | 9 (8.3%) | 19 (14.2%) | | 9 (15.3%) | 13 (12.9%) | | 4 (9.8%) | 5 (8.2%) | |
| **Lymph node metastasis (%)** | | | 0.320 | | | 0.076 | | | 0.054 |
| pN0 | 56 (51.9%) | 55 (41.0%) | | 31 (52.5%) | 40 (39.6%) | | 20 (48.8%) | 15 (24.6%) | |
| pN1 | 20 (18.5%) | 22 (16.4%) | | 7 (11.9%) | 21 (20.8%) | | 2 (4.9%) | 12 (19.7%) | |
| pN2 | 9 (8.3%) | 17 (12.7%) | | 8 (13.6%) | 10 (9.9%) | | 10 (24.4%) | 15 (24.6%) | |
| pN3a | 11 (10.2%) | 22 (16.4%) | | 11 (18.6%) | 15 (14.9%) | | 6 (14.6%) | 10 (16.4%) | |
| pN3b | 12 (11.1%) | 18 (13.4%) | | 2 (3.4%) | 15 (14.9%) | | 3 (7.3%) | 9 (14.8%) | |
| **Distant metastasis (%)** | | | 0.789 | | | 0.618 | | | 0.343 |
| pM0 | 105 (97.2%) | 131 (97.8%) | | 58 (98.3%) | 98 (97.0%) | | 37 (90.2%) | 58 (95.1%) | |
| pM1 | 3 (2.8%) | 3 (2.2%) | | 1 (1.7%) | 3 (3.0%) | | 4 (9.8%) | 3 (4.9%) | |
| **Stage (%)** | | | 0.189 | | | 0.268 | | | 0.005 |
| I | 34 (31.5%) | 39 (29.1%) | | 18 (30.5%) | 23 (22.8%) | | 18 (43.9%) | 10 (16.4%) | |
| II | 28 (25.9%) | 22 (16.4%) | | 19 (32.2%) | 24 (23.8%) | | 2 (4.9%) | 12 (19.7%) | |
| III | 43 (39.8%) | 70 (52.2%) | | 21 (35.6%) | 51 (50.5%) | | 17 (41.5%) | 36 (59.0%) | |
| IV | 3 (2.8%) | 3 (2.2%) | | 1 (1.7%) | 3 (3.0%) | | 4 (9.8%) | 3 (4.9%) | |
| **Chemotherapy (%)** | 58 (53.7%) | 66 (49.3%) | 0.491 | 30 (50.8%) | 47 (46.5%) | 0.598 | 14 (34.1%) | 32 (52.5%) | 0.068 |

MIS, myeloid immune score.

**Supplementary Table 4. Univariate association of IS, clinicopathological characteristics with disease-free and overall survival in the training cohort.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LIS (high vs. low) | 0.315 (0.210-0.471) | <0.0001 | 0.362 (0.223-0.587) | <0.0001 |
| MIS (high vs. low) | 3.396 (2.162-5.336) | <0.0001 | 4.399 (2.438-7.935) | <0.0001 |
| Age (years) (≥60 vs. <60) | 0.937 (0.631-1.391) | 0.748 | 0.757 (0.462-1.240) | 0.269 |
| Sex (male vs. female) | 1.043 (0.694-1.566) | 0.841 | 1.334 (0.798-2.229) | 0.271 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.831 (1.235-2.715) | 0.003 | 2.153 (1.324-3.503) | 0.002 |
| Tumor location | 1.053 (0.838-1.324) | 0.656 | 0.944 (0.719-1.240) | 0.680 |
| Differentiation | 1.379 (1.011-1.881) | 0.042 | 1.504 (1.022-2.214) | 0.039 |
| Lauren type | 1.005 (0.684-1.477) | 0.980 | 0.980 (0.613-1.567) | 0.933 |
| CEA (elevated vs. normal) | 2.033 (1.176-3.515) | 0.011 | 2.212 (1.162-4.213) | 0.016 |
| CA19-9 (elevated vs. normal) | 1.477 (0.878-2.485) | 0.142 | 1.001 (1.000-1.003) | 0.081 |
| Stage (IV vs. III vs. II vs. I) | 2.123 (1.645-2.739) | <0.0001 | 2.954 (2.095-4.144) | <0.0001 |
| Chemotherapy (yes vs. no) | 0.686 (0.466-1.010) | 0.056 | 0.489 (0.302-0.792) | 0.004 |

IS, immune score; LIS, lymphoid immune score; MIS, myeloid immune score.

**Supplementary Table 5. Univariate association of IS, clinicopathological characteristics with disease-free and overall survival in the internal validation cohort 1.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LIS (high vs. low) | 0.290 (0.183-0.461) | <0.0001 | 0.303 (0.175-0.525) | <0.0001 |
| MIS (high vs. low) | 1.971 (1.181-3.291) | 0.009 | 2.484 (1.305-4.726) | 0.006 |
| Age (years) (≥60 vs. <60) | 1.053 (0.669-1.655) | 0.824 | 0.890 (0.517-1.532) | 0.674 |
| Sex (male vs. female) | 1.366 (0.812-2.297) | 0.240 | 1.739 (0.896-3.374) | 0.102 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.867 (1.173-2.971) | 0.008 | 1.819 (1.046-3.163) | 0.034 |
| Tumor location | 0.950 (0.730-1.236) | 0.702 | 0.963 (0.703-1.319) | 0.814 |
| Differentiation | 0.966 (0.708-1.317) | 0.826 | 1.035 (0.711-1.507) | 0.856 |
| Lauren type | 0.913 (0.581-1.434) | 0.692 | 1.197 (0.692-2.069) | 0.521 |
| CEA (elevated vs. normal) | 1.365 (0.718-2.593) | 0.343 | 1.461 (0.687-3.105) | 0.324 |
| CA19-9 (elevated vs. normal) | 1.003 (0.998-1.009) | 0.220 | 1.185 (0.535-2.624) | 0.676 |
| Stage (IV vs. III vs. II vs. I) | 2.065 (1.520-2.804) | <0.0001 | 2.826 (1.894-4.216) | <0.0001 |
| Chemotherapy (yes vs. no) | 0.876 (0.558-1.376) | 0.567 | 1.169 (0.684-1.997) | 0.568 |

IS, immune score; LIS, lymphoid immune score; MIS, myeloid immune score.

**Supplementary Table 6. Univariate association of IS, clinicopathological characteristics with disease-free and overall survival in the external validation cohort 1.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LIS (high vs. low) | 0.231 (0.121-0.442) | <0.0001 | 0.183 (0.090-0.368) | <0.0001 |
| MIS (high vs. low) | 3.831 (1.751-8.384) | 0.001 | 6.014 (2.307-15.674) | <0.001 |
| Age (years) (≥60 vs. <60) | 0.752 (0.394-1.435) | 0.388 | 0.736 (0.368-1.472) | 0.377 |
| Sex (male vs. female) | 1.742 (0.799-3.794) | 0.163 | 2.081 (0.860-5.040) | 0.104 |
| Tumor size (>4 cm vs. ≤4 cm) | 2.748 (1.442-5.237) | 0.002 | 3.049 (1.518-6.128) | 0.002 |
| Tumor location | 0.760 (0.538-1.073) | 0.119 | 0.748 (0.517-1.081) | 0.123 |
| Differentiation | 1.473 (0.646-3.359) | 0.357 | 1.358 (0.592-3.114) | 0.470 |
| Lauren type | 1.234 (0.634-2.402) | 0.536 | 1.169 (0.578-2.363) | 0.664 |
| CEA (elevated vs. normal) | 1.091 (0.482-2.473) | 0.834 | 1.250 (0.544-2.875) | 0.599 |
| CA19-9 (elevated vs. normal) | 4.564 (2.287-9.108) | <0.0001 | 4.086 (1.922-8.687) | <0.0001 |
| Stage (IV vs. III vs. II vs. I) | 2.499 (1.616-3.865) | <0.0001 | 2.318 (1.485-3.617) | <0.0001 |
| Chemotherapy (yes vs. no) | 1.902 (1.009-3.584) | 0.047 | 2.004 (1.012-3.969) | 0.046 |

IS, immune score; LIS, lymphoid immune score; MIS, myeloid immune score.

**Supplementary Table 7. Multivariate cox regression analyses for disease-free survival and overall survival in patients with gastric cancer.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | **HR (95%CI)** | ***p*** | **HR (95%CI)** | ***p*** |
| **Training cohort** | | | | |
| LIS (high vs. low) | 0.395 (0.261-0.599) | <0.0001 | 0.479 (0.290-0.791) | 0.004 |
| MIS (high vs. low) | 3.193 (2.011-5.069) | <0.0001 | 4.113 (2.261-7.479) | <0.0001 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.090 (0.708-1.677) | 0.696 | 1.140 (0.675-1.923) | 0.624 |
| Differentiation (poor vs. moderate vs. well) | 0.968 (0.683-1.373) | 0.857 | 0.865 (0.558-1.340) | 0.516 |
| CEA (elevated vs. normal) | 0.962 (0.537-1.723) | 0.895 | 0.884 (0.440-1.778) | 0.730 |
| Stage (IV vs. III vs. II vs. I) | 1.990 (1.480-2.676) | <0.0001 | 2.793 (1.913-4.076) | <0.0001 |
| Chemotherapy (yes vs. no) | — | — | 0.436 (0.2688-0.710) | 0.001 |
| **Internal validation cohort 1** | | | | |
| LIS (high vs. low) | 0.344 (0.214-0.554) | <0.0001 | 0.375 (0.215-0.654) | 0.001 |
| MIS (high vs. low) | 1.933 (1.149-3.252) | 0.013 | 2.220 (1.162-4.243) | 0.016 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.346 (0.836-2.165) | 0.221 | 1.260 (0.719-2.210) | 0.419 |
| Stage (IV vs. III vs. II vs. I) | 1.740 (1.275-2.374) | <0.0001 | 2.516 (1.651-3.835) | <0.0001 |
| **External validation cohort 1** | | | | |
| LIS (high vs. low) | 0.431 (0.205-0.902) | 0.026 | 0.440 (0.203-0.953) | 0.037 |
| MIS (high vs. low) | 3.887 (1.502-10.058) | 0.005 | 5.372 (1.774-16.264) | 0.003 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.491 (0.758-2.934) | 0.247 | 1.464 (0.692-3.096) | 0.319 |
| CA19-9 (elevated vs. normal) | 3.962 (1.816-8.642) | 0.001 | 3.617 (1.560-8.385) | 0.003 |
| Stage (IV vs. III vs. II vs. I) | 2.200 (1.356-3.569) | 0.001 | 1.973 (1.203-3.238) | 0.007 |
| Chemotherapy (yes vs. no) | 1.342 (0.703-2.562) | 0.372 | 1.690 (0.819-3.485) | 0.156 |

LIS, lymphoid immune score; MIS, myeloid immune score.

**Supplementary Table 8. The optimal cut-off value for RS was determined using Youden's index in the training cohort.**

| | Cutoff | AUC (95%CI) | Sensitivity (95%CI) | Specificity (95%CI) | Accuracy | PPV | NPV |
|---|---|---|---|---|---|---|---|
| LRS | -0.1293 | 0.773 (0.714-0.833) | 0.771 (0.693-0.838) | 0.657 (0.556-0.748) | 0.719 | 0.755 (0.676-0.823) | 0.677 (0.575-0.767) |
| MRS | -0.2604 | 0.750 (0.689-0.810) | 0.724 (0.640-0.798) | 0.648 (0.550-0.738) | 0.682 | 0.719 (0.635-0.792) | 0.654 (0.556-0.744) |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score; AUC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value; RS, radiomics score.

**Supplementary Table 9. Clinical characteristics of patients according to the LRS in the training and internal validation cohorts.**

| Variables | Training cohort, n = 242 | | | Internal validation cohort 1, n = 160 | | | Internal validation cohort 2, n = 512 | | |
|---|---|---|---|---|---|---|---|---|---|
| | low LRS | high LRS | *P* | low LRS | high LRS | *P* | low LRS | high LRS | *P* |
| **Median age (range)** | 58 (49-64) | 55 (47-64) | 0.627 | 60 (49-65) | 56 (50-65) | 0.797 | 56 (47-64) | 57 (49-63) | 0.541 |
| **Male (%)** | 70 (70.7%) | 89 (62.2%) | 0.172 | 54 (77.1%) | 60 (66.7%) | 0.146 | 147 (71.0%) | 204 (66.9%) | 0.323 |
| **Tumor size (%)** | | | <0.001 | | | 0.033 | | | 0.038 |
| ≤4cm | 36 (36.4%) | 85 (59.4%) | | 27 (38.6%) | 50 (55.6%) | | 127 (61.4%) | 214 (70.2%) | |
| >4cm | 63 (63.6%) | 58 (40.6%) | | 43 (61.4%) | 40 (44.4%) | | 80 (38.6%) | 91 (29.8%) | |
| **Tumor location (%)** | | | 0.055 | | | 0.296 | | | 0.001 |
| Cardia | 25 (25.3%) | 21 (14.7%) | | 17 (24.3%) | 16 (17.8%) | | 24 (11.6%) | 42 (13.8%) | |
| Body | 13 (13.1%) | 33 (23.1%) | | 14 (20.0%) | 22 (24.4%) | | 40 (19.3%) | 50 (16.4%) | |
| Antrum | 53 (53.5%) | 82 (57.3%) | | 34 (48.6%) | 50 (55.6%) | | 114 (55.1%) | 199 (65.2%) | |
| Whole | 8 (8.1%) | 7 (4.9%) | | 5 (7.1%) | 2 (2.2%) | | 29 (14.0%) | 14 (4.6%) | |
| **Differentiation status (%)** | | | 0.439 | | | 0.180 | | | 0.213 |
| Well | 8 (8.1%) | 19 (13.3%) | | 5 (7.1%) | 14 (15.6%) | | 30 (14.5%) | 56 (18.4%) | |
| Moderate | 23 (23.2%) | 33 (23.1%) | | 17 (24.3%) | 25 (27.8%) | | 41 (19.8%) | 72 (23.6%) | |
| Poor and undifferentiated | 68 (68.7%) | 91 (63.6%) | | 48 (68.6%) | 51 (56.7%) | | 136 (65.7%) | 177 (58.0%) | |
| **Lauren type (%)** | | | 0.082 | | | 0.078 | | | 0.219 |
| Intestinal type | 40 (40.4%) | 74 (51.7%) | | 26 (37.1%) | 46 (51.1%) | | 87 (42.0%) | 145 (47.5%) | |
| Diffuse or mixed type | 59 (59.6%) | 69 (48.3%) | | 44 (62.9%) | 44 (48.9%) | | 120 (58.0%) | 160 (52.5%) | |
| **CEA (%)** | | | 0.263 | | | 0.718 | | | 0.049 |
| Normal | 88 (88.9%) | 133 (93.0%) | | 62 (88.6%) | 78 (86.7%) | | 178 (86.0%) | 279 (91.5%) | |
| Elevated | 11 (11.1%) | 10 (7.0%) | | 8 (11.4%) | 12 (13.3%) | | 29 (14.0%) | 26 (8.5%) | |
| **CA19-9 (%)** | | | 0.319 | | | 0.069 | | | 0.414 |
| Normal | 82 (82.8%) | 125 (87.4%) | | 58 (82.9%) | 83 (92.2%) | | 168 (81.2%) | 256 (83.9%) | |
| Elevated | 17 (17.2%) | 18 (12.6%) | | 12 (17.1%) | 7 (7.8%) | | 39 (18.8%) | 49 (16.1%) | |
| **Depth of invasion (%)** | | | 0.003 | | | 0.022 | | | <0.001 |
| pT1 | 11 (11.1%) | 42 (29.4%) | | 10 (14.3%) | 27 (30.0%) | | 43 (20.8%) | 98 (32.1%) | |
| pT2 | 11 (11.1%) | 18 (12.6%) | | 5 (7.1%) | 9 (10.0%) | | 24 (11.6%) | 52 (17.0%) | |
| pT3 | 10 (10.1%) | 13 (9.1%) | | 8 (11.4%) | 17 (18.9%) | | 4 (1.9%) | 10 (3.3%) | |
| pT4a | 49 (49.5%) | 60 (42.0%) | | 36 (51.4%) | 26 (28.9%) | | 64 (30.9%) | 100 (32.8%) | |
| pT4b | 18 (18.2%) | 10 (7.0%) | | 11(15.7%) | 11 (12.2%) | | 72 (34.8%) | 45 (14.8%) | |
| **Lymph node metastasis (%)** | | | 0.002 | | | 0.002 | | | 0.108 |
| pN0 | 31 (31.3%) | 80 (55.9%) | | 19 (27.1%) | 52 (57.8%) | | 87 (42.0%) | 153 (50.2%) | |
| pN1 | 20 (20.2%) | 22 (15.4%) | | 16 (22.9%) | 12 (13.3%) | | 51 (24.6%) | 62 (20.3%) | |
| pN2 | 15 (15.2%) | 11 (7.7%) | | 8 (11.4%) | 10 (11.1%) | | 21 (10.1%) | 41 (13.4%) | |
| pN3a | 20 (20.2%) | 13 (9.1%) | | 15 (21.4%) | 11 (12.2%) | | 36 (17.4%) | 34 (11.1%) | |
| pN3b | 13 (13.1%) | 17 (11.9%) | | 12 (17.1%) | 5 (5.6%) | | 12 (5.8%) | 15 (4.9%) | |
| **Distant metastasis (%)** | | | 0.702 | | | 0.202 | | | - |
| pM0 | 97 (98.0%) | 139 (97.2%) | | 67 (95.7%) | 89 (98.9%) | | 207 (100%) | 305 (100%) | |
| pM1 | 2 (2.0%) | 4 (2.8%) | | 3 (4.3%) | 1 (1.1%) | | 0 (0.0%) | 0 (0.0%) | |
| **Stage (%)** | | | 0.001 | | | 0.002 | | | 0.001 |
| I | 19 (19.2%) | 54 (37.8%) | | 11 (15.7%) | 30 (33.3%) | | 35 (16.9%) | 94 (30.8%) | |
| II | 17 (17.2%) | 33 (23.1%) | | 14 (20.0%) | 29 (32.2%) | | 52 (25.1%) | 71 (23.3%) | |
| III | 61 (61.6%) | 52 (36.4%) | | 42 (60.0%) | 30 (33.3%) | | 120 (58.0%) | 140 (45.9%) | |
| IV | 2 (2.0%) | 4 (2.8%) | | 3 (4.3%) | 1 (1.1%) | | 0 (0.0%) | 0 (0.0%) | |
| **Chemotherapy (%)** | 53 (53.5%) | 71 (49.7%) | 0.552 | 39 (55.7%) | 38 (42.2%) | 0.090 | 93 (44.9%) | 137 (44.9%) | 0.998 |

LRS, lymphoid radiomics score.

**Supplementary Table 10. Clinical characteristics of patients according to the MRS in the training and internal validation cohorts.**

| Variables | Training cohort, n = 242 | | | Internal validation cohort 1, n = 160 | | | Internal validation cohort 2, n = 512 | | |
|---|---|---|---|---|---|---|---|---|---|
| | low MRS | high MRS | *P* | low MRS | high MRS | *P* | low MRS | high MRS | *P* |
| **Median age (range)** | 55 (48-64) | 57 (47-64) | 0.771 | 58 (50-65) | 57 (48-66) | 0.889 | 57 (49-64) | 56 (48-63) | 0.845 |
| **Male (%)** | 76 (71.7%) | 83 (61.0%) | 0.083 | 41 (70.7%) | 73 (71.6%) | 0.906 | 151 (74.0%) | 200 (64.9%) | 0.030 |
| **Tumor size (%)** | | | 1.000 | | | 0.764 | | | 0.828 |
| ≤4cm | 53 (50.0%) | 68 (50.0%) | | 27 (46.6%) | 50 (49.0%) | | 137 (67.2%) | 204 (66.2%) | |
| >4cm | 53 (50.0%) | 68 (50.0%) | | 31 (53.4%) | 52 (51.0%) | | 67 (32.8%) | 104 (33.8%) | |
| **Tumor location (%)** | | | 0.206 | | | 0.911 | | | 0.018 |
| Cardia | 24 (22.6%) | 22 (16.2%) | | 13 (22.4%) | 20 (19.6%) | | 32 (15.7%) | 34 (11.0%) | |
| Body | 15 (14.2%) | 31 (22.8%) | | 14 (24.1%) | 22 (21.6%) | | 29 (14.2%) | 61 (19.8%) | |
| Antrum | 62 (58.5%) | 73 (53.7%) | | 29 (50.0%) | 55 (53.9%) | | 133 (65.2%) | 180 (58.4%) | |
| Whole | 5 (4.7%) | 10 (7.4%) | | 2 (3.4%) | 5 (4.9%) | | 10 (4.9%) | 33 (10.7%) | |
| **Differentiation status (%)** | | | 0.372 | | | 0.112 | | | 0.647 |
| Well | 12 (11.3%) | 15 (11.0%) | | 11 (19.0%) | 8 (7.8%) | | 32 (15.7%) | 54 (17.5%) | |
| Moderate | 20 (18.9%) | 36 (26.5%) | | 14 (24.1%) | 28 (27.5%) | | 49 (24.0%) | 64 (20.8%) | |
| Poor and undifferentiated | 74 (69.8%) | 85 (62.5%) | | 33 (56.9%) | 66 (64.7%) | | 123 (60.3%) | 190 (61.7%) | |
| **Lauren type (%)** | | | 0.039 | | | 0.197 | | | 0.937 |
| Intestinal type | 42 (39.6%) | 72 (52.9%) | | 30 (51.7%) | 42 (41.2%) | | 92 (45.1%) | 140 (45.5%) | |
| Diffuse or mixed type | 64 (60.4%) | 64 (47.1%) | | 28 (48.3%) | 60 (58.8%) | | 112 (54.9%) | 168 (54.5%) | |
| **CEA (%)** | | | 0.712 | | | 0.263 | | | 0.543 |
| Normal | 96 (90.6%) | 125 (91.9%) | | 53 (91.4%) | 87 (85.3%) | | 180 (88.2%) | 277 (89.9%) | |
| Elevated | 10 (9.4%) | 11 (8.1%) | | 5 (8.6%) | 15 (14.7%) | | 24 (11.8%) | 31 (10.1%) | |
| **CA19-9 (%)** | | | 0.037 | | | 0.572 | | | 0.622 |
| Normal | 85 (80.2%) | 122 (89.7%) | | 50 (86.2%) | 91 (89.2%) | | 171 (83.8%) | 253 (82.1%) | |
| Elevated | 21 (19.8%) | 14 (10.3%) | | 8 (13.8%) | 11 (10.8%) | | 33 (16.2%) | 55 (17.9%) | |
| **Depth of invasion (%)** | | | 0.344 | | | 0.677 | | | 0.251 |
| pT1 | 24 (22.6%) | 29 (21.3%) | | 16 (27.6%) | 21 (20.6%) | | 64 (31.4%) | 77 (25.0%) | |
| pT2 | 13 (12.3%) | 16 (11.8%) | | 3 (5.2%) | 11 (10.8%) | | 32 (15.7%) | 44 (14.3%) | |
| pT3 | 8 (7.5%) | 15 (11.0%) | | 9 (15.5%) | 16 (15.7%) | | 4 (2.0%) | 10 (3.2%) | |
| pT4a | 53 (50.0%) | 56 (41.2%) | | 23 (39.7%) | 39 (38.2%) | | 66 (32.4%) | 98 (31.8%) | |
| pT4b | 8 (7.5%) | 20 (14.7%) | | 7 (12.1%) | 15 (14.7%) | | 38 (18.6%) | 79 (25.6%) | |
| **Lymph node metastasis (%)** | | | 0.636 | | | 0.384 | | | 0.119 |
| pN0 | 51 (48.1%) | 60 (44.1%) | | 26 (44.8%) | 45 (44.1%) | | 95 (46.6%) | 145 (47.1%) | |
| pN1 | 17 (16.0%) | 25 (18.4%) | | 11 (19.0%) | 17 (16.7%) | | 40 (19.6%) | 73 (23.7%) | |
| pN2 | 10 (9.4%) | 16 (11.8%) | | 9 (15.5%) | 9 (8.8%) | | 34 (16.7%) | 28 (9.1%) | |
| pN3a | 12 (11.3%) | 21 (15.4%) | | 9 (15.5%) | 17 (16.7%) | | 25 (12.3%) | 45 (14.6%) | |
| pN3b | 16 (15.1%) | 14 (10.3%) | | 3 (5.2%) | 14 (13.7%) | | 10 (4.9%) | 17 (5.5%) | |
| **Distant metastasis (%)** | | | 0.601 | | | 0.635 | | | - |
| pM0 | 104 (98.1%) | 132 (97.1%) | | 57 (98.3%) | 99 (97.1%) | | 204 (100%) | 308 (100%) | |
| pM1 | 2 (1.9%) | 4 (2.9%) | | 1 (1.7%) | 3 (2.9%) | | 0(0.0%) | 0(0.0%) | |
| **Stage (%)** | | | 0.824 | | | 0.812 | | | 0.590 |
| I | 33 (31.1%) | 40 (29.4%) | | 14 (24.1%) | 27 (26.5%) | | 55 (27.0%) | 74 (24.0%) | |
| II | 24 (22.6%) | 26 (19.1%) | | 18 (31.0%) | 25 (24.5%) | | 51 (25.0%) | 72 (23.4%) | |
| III | 47 (44.3%) | 66 (48.5%) | | 25 (43.1%) | 47 (46.1%) | | 98 (48.0%) | 162 (52.6%) | |
| IV | 2 (1.9%) | 4 (2.9%) | | 1 (1.7%) | 3 (2.9%) | | 0 (0.0%) | 0 (0.0%) | |
| **Chemotherapy (%)** | 54 (50.9%) | 70 (51.5) | 0.935 | 26 (44.8%) | 51 (50.0%) | 0.529 | 92 (45.1%) | 138 (44.8%) | 0.948 |

MRS, myeloid radiomics score.

**Supplementary Table 11. Clinical characteristics of patients according to the LRS in the external validation cohorts and prospective validation cohort.**

| Variables | External validation cohort 1, n =160 | | | External validation cohort 2, n = 1123 | | | Prospective validation cohort, n = 158 | | |
|---|---|---|---|---|---|---|---|---|---|
| | low LRS | high LRS | *P* | low LRS | high LRS | *P* | low LRS | high LRS | *P* |
| **Median age (range)** | 53 (42-60) | 61 (53-66) | 0.005 | 57 (50-65) | 58 (49-65) | 0.967 | 60 (48-66) | 56 (50-64) | 0.785 |
| **Male (%)** | 32 (86.5%) | 41 (63.1%) | 0.012 | 351 (71.1%) | 422 (67.1%) | 0.155 | 47 (65.3%) | 57 (66.3%) | 0.895 |
| **Tumor size (%)** | | | 0.613 | | | <0.001 | | | <0.001 |
| ≤4cm | 18 (48.6%) | 35 (53.8%) | | 139 (28.1%) | 301 (47.9%) | | 36 (50.0%) | 71 (82.6%) | |
| >4cm | 19 (51.4%) | 30 (46.2%) | | 355 (71.9%) | 328 (52.1%) | | 36 (50.0%) | 15 (17.4%) | |
| **Tumor location (%)** | | | 0.457 | | | <0.001 | | | 0.681 |
| Cardia | 14 (37.8%) | 19 (29.2%) | | 174 (35.2%) | 200 (31.8%) | | 15 (20.8%) | 18 (20.9%) | |
| Body | 8 (21.6%) | 14 (21.5%) | | 109 (22.1%) | 127 (20.2%) | | 16 (22.2%) | 14 (16.3%) | |
| Antrum | 13 (35.1%) | 31 (47.7%) | | 173 (35.0%) | 286 (45.5%) | | 40 (55.6%) | 51 (59.3%) | |
| Whole | 2 (5.4%) | 1 (1.5%) | | 38 (7.7%) | 16 (2.5%) | | 1 (1.4%) | 3 (3.5%) | |
| **Differentiation status (%)** | | | 0.220 | | | 0.439 | | | 0.220 |
| Well | 0 (0.0%) | 1 (1.5%) | | 6 (1.2%) | 14 (2.2%) | | 6 (8.3%) | 6 (7.0%) | |
| Moderate | 4 (10.8%) | 15 (23.1%) | | 78 (15.8%) | 96 (15.3%) | | 9 (12.5%) | 20 (23.3%) | |
| Poor and undifferentiated | 33 (89.2%) | 49 (75.4%) | | 410 (83.0%) | 519 (82.5%) | | 57 (79.2%) | 60 (69.8%) | |
| **Lauren type (%)** | | | 0.236 | | | 0.122 | | | 0.813 |
| Intestinal type | 11 (29.7%) | 27 (41.5%) | | 155 (31.4%) | 225 (35.8%) | | 23 (31.9%) | 29 (33.7%) | |
| Diffuse or mixed type | 26 (70.3%) | 38 (58.5%) | | 339 (68.6%) | 404 (64.2%) | | 49 (68.1%) | 57 (66.3%) | |
| **CEA (%)** | | | 0.409 | | | 0.003 | | | 0.529 |
| Normal | 32 (86.5%) | 52 (80.0%) | | 381 (77.1%) | 529 (84.1%) | | 68 (94.4%) | 83 (96.5%) | |
| Elevated | 5 (13.5%) | 13 (20.0%) | | 113 (22.9%) | 100 (15.9%) | | 4 (5.6%) | 3 (3.5%) | |
| **CA19-9 (%)** | | | 0.581 | | | <0.001 | | | 0.362 |
| Normal | 31 (83.8%) | 57 (87.7%) | | 372 (75.3%) | 536 (85.2%) | | 64 (88.9%) | 80 (93.0%) | |
| Elevated | 6 (16.2%) | 8 (12.3%) | | 122 (24.7%) | 93 (14.8%) | | 8 (11.1%) | 6 (7.0%) | |
| **Depth of invasion (%)** | | | 0.623 | | | <0.001 | | | <0.001 |
| pT1 | 4 (10.8%) | 14 (21.5%) | | 32 (6.5%) | 116 (18.4%) | | 8 (11.1%) | 41 (47.7%) | |
| pT2 | 5 (13.5%) | 9 (13.8%) | | 36 (7.3%) | 94 (14.9%) | | 9 (12.5%) | 16 (18.6%) | |
| pT3 | 7 (18.9%) | 13 (20.0%) | | 92 (18.6%) | 147 (23.4%) | | 25 (34.7%) | 16 (18.6%) | |
| pT4a | 18 (48.6%) | 23 (35.4%) | | 272 (55.1%) | 244 (38.8%) | | 22 (30.6%) | 10 (11.6%) | |
| pT4b | 3 (8.1%) | 6 (9.2%) | | 62 (12.6%) | 28 (4.5%) | | 8 (11.1%) | 3 (3.5%) | |
| **Lymph node metastasis (%)** | | | 0.384 | | | <0.001 | | | 0.002 |
| pN0 | 10 (27.0%) | 25 (38.5%) | | 112 (22.7%) | 257 (40.9%) | | 22 (30.6%) | 50 (58.1%) | |
| pN1 | 6 (16.2%) | 8 (12.3%) | | 73 (14.8%) | 104 (16.5%) | | 10 (13.9%) | 12 (14.0%) | |
| pN2 | 8 (21.6%) | 17 (26.2%) | | 94 (19.0%) | 105 (16.7%) | | 13 (18.1%) | 13 (15.1%) | |
| pN3a | 9 (24.3%) | 7 (10.8%) | | 129 (26.1%) | 117 (18.6%) | | 15 (20.8%) | 7 (8.1%) | |
| pN3b | 4 (10.8%) | 8 (12.3%) | | 86 (17.4%) | 46 (7.3%) | | 12 (16.7%) | 4 (4.7%) | |
| **Distant metastasis (%)** | | | 0.234 | | | 0.001 | | | 0.667 |
| pM0 | 33 (89.2%) | 62 (95.4%) | | 437 (88.5%) | 592 (94.1%) | | 71 (98.6%) | 84 (97.7%) | |
| pM1 | 4 (10.8%) | 3 (4.6%) | | 57 (11.5%) | 37 (5.9%) | | 1 (1.4%) | 2 (2.3%) | |
| **Stage (%)** | | | 0.448 | | | <0.001 | | | <0.001 |
| I | 8 (21.6%) | 20 (30.8%) | | 49 (9.9%) | 155 (24.6%) | | 12 (16.7%) | 45 (52.3%) | |
| II | 4 (10.8%) | 10 (15.4%) | | 84 (17.0%) | 193 (30.7%) | | 20 (27.8%) | 20 (23.3%) | |
| III | 21 (56.8%) | 32 (49.2%) | | 304 (61.5%) | 244 (38.8%) | | 39 (54.2%) | 19 (22.1%) | |
| IV | 4 (10.8%) | 3 (4.6%) | | 57 (11.5%) | 37 (5.9%) | | 1 (1.4%) | 2 (2.3%) | |
| **Chemotherapy (%)** | 21 (56.8%) | 25 (38.5%) | 0.074 | 228 (46.2%) | 309 (49.1%) | 0.322 | 49 (68.1%) | 39 (45.3%) | 0.004 |

LRS, lymphoid radiomics score.

**Supplementary Table 12. Clinical characteristics of patients according to the MRS in the external validation cohorts and prospective validation cohort.**

| Variables | External validation cohort 1, n =160 | | | External validation cohort 2, n = 1123 | | | Prospective validation cohort, n = 158 | | |
|---|---|---|---|---|---|---|---|---|---|
| | low MRS | high MRS | *P* | low MRS | high MRS | *P* | low MRS | high MRS | *P* |
| **Median age (range)** | 60 (51-66) | 55 (45-64) | 0.263 | 57 (48-64) | 57 (49-65) | 0.527 | 58 (50-66) | 56 (48-65) | 0.546 |
| **Male (%)** | 28 (62.2%) | 45 (78.9%) | 0.063 | 329 (69.1%) | 444 (68.6%) | 0.860 | 52 (68.4%) | 52 (63.4%) | 0.507 |
| **Tumor size (%)** | | | 0.065 | | | <0.001 | | | 0.026 |
| ≤4cm | 28 (62.2%) | 25 (43.9%) | | 230 (48.3%) | 210 (32.5%) | | 58 (76.3%) | 49 (59.8%) | |
| >4cm | 17 (37.8%) | 32 (56.1%) | | 246 (51.7%) | 437 (67.5%) | | 18 (23.7%) | 33 (40.2%) | |
| **Tumor location (%)** | | | 0.159 | | | <0.001 | | | 0.436 |
| Cardia | 12 (26.7%) | 21 (36.8%) | | 145 (30.5%) | 229 (35.4%) | | 20 (26.3%) | 13 (15.9%) | |
| Body | 7 (15.6%) | 15 (26.3%) | | 83 (17.4%) | 153 (23.6%) | | 14 (18.4%) | 16 (19.5%) | |
| Antrum | 25 (55.6%) | 19 (33.3%) | | 237 (49.8%) | 222 (34.3%) | | 40 (52.6%) | 51 (62.2%) | |
| Whole | 1 (2.2%) | 2 (3.5%) | | 11 (2.3%) | 43 (6.6%) | | 2 (2.6%) | 2 (2.4%) | |
| **Differentiation status (%)** | | | 0.492 | | | 0.112 | | | 0.337 |
| Well | 1 (2.2%) | 0 (0.0%) | | 13 (2.7%) | 7 (1.1%) | | 8 (10.5%) | 4 (4.9%) | |
| Moderate | 9 (20.0%) | 10 (17.5%) | | 71 (14.9%) | 103 (15.9%) | | 15 (19.7%) | 14 (17.1%) | |
| Poor and undifferentiated | 35 (77.8%) | 47 (82.5%) | | 392 (82.4%) | 537 (83.0%) | | 53 (69.7%) | 64 (78.0%) | |
| **Lauren type (%)** | | | 0.610 | | | 0.254 | | | 0.501 |
| Intestinal type | 18 (40.0%) | 20 (35.1%) | | 170 (35.7%) | 210 (32.5%) | | 27 (35.5%) | 25 (30.5%) | |
| Diffuse or mixed type | 27 (60.0%) | 37 (64.9%) | | 306 (64.3%) | 437 (67.5%) | | 49 (64.5%) | 57 (69.5%) | |
| **CEA (%)** | | | 0.580 | | | 0.041 | | | 0.776 |
| Normal | 36 (80.0%) | 48 (84.2%) | | 399 (83.8%) | 511 (79.0%) | | 73 (96.1%) | 78 (95.1%) | |
| Elevated | 9 (20.0%) | 9 (15.8%) | | 167 (16.2%) | 136 (21.0%) | | 3 (3.9%) | 4 (4.9%) | |
| **CA19-9 (%)** | | | 0.066 | | | <0.001 | | | 0.331 |
| Normal | 42 (93.3%) | 46 (80.7%) | | 410 (86.1%) | 498 (77.0%) | | 71 (93.4%) | 73 (89.0%) | |
| Elevated | 3 (6.7%) | 11 (19.3%) | | 66 (13.9%) | 149 (23.0%) | | 5 (6.6%) | 9 (11.0%) | |
| **Depth of invasion (%)** | | | 0.755 | | | <0.001 | | | 0.029 |
| pT1 | 9 (20.0%) | 9 (15.8%) | | 87 (18.3%) | 61 (9.4%) | | 29 (38.2%) | 20 (24.4%) | |
| pT2 | 8 (17.8%) | 6 (10.5%) | | 68 (14.3%) | 62 (9.6%) | | 16 (21.1%) | 9 (11.0%) | |
| pT3 | 8 (17.8%) | 12 (21.1%) | | 105 (22.1%) | 134 (20.7%) | | 18 (23.7%) | 23 (28.0%) | |
| pT4a | 17 (37.8%) | 24 (42.1%) | | 187 (39.3%) | 329 (50.9%) | | 10 (13.2%) | 22 (26.8%) | |
| pT4b | 3 (6.7%) | 6 (10.5%) | | 29 (6.1%) | 61 (9.4%) | | 3 (3.9%) | 8 (9.8%) | |
| **Lymph node metastasis (%)** | | | 0.512 | | | 0.001 | | | 0.002 |
| pN0 | 19 (42.2%) | 16 (28.1%) | | 188 (39.5%) | 181 (28.0%) | | 46 (60.5%) | 26 (31.7%) | |
| pN1 | 5 (11.1%) | 9 (15.8%) | | 75 (15.8%) | 102 (15.8%) | | 10 (13.2%) | 12 (14.6%) | |
| pN2 | 10 (22.2%) | 15 (26.3%) | | 77 (16.2%) | 122 (18.9%) | | 11 (14.5%) | 15 (18.3%) | |
| pN3a | 5 (11.1%) | 11 (19.3%) | | 90 (18.9%) | 156 (24.1%) | | 5 (6.6%) | 17 (20.7%) | |
| pN3b | 6 (13.3%) | 6 (10.5%) | | 46 (9.7%) | 86 (13.3%) | | 4 (5.3%) | 12 (14.6%) | |
| **Distant metastasis (%)** | | | 0.100 | | | 0.087 | | | 0.605 |
| pM0 | 44 (97.8%) | 51 (89.5%) | | 444 (93.3%) | 585 (90.4%) | | 75 (98.7%) | 80 (97.6%) | |
| pM1 | 1 (2.2%) | 6 (10.5%) | | 32 (6.7%) | 62 (9.6%) | | 1 (1.3%) | 2 (2.4%) | |
| **Stage (%)** | | | 0.182 | | | <0.001 | | | 0.001 |
| I | 16 (35.6%) | 12 (21.1%) | | 114 (23.9%) | 90 (13.9%) | | 37 (48.7%) | 20 (24.4%) | |
| II | 5 (11.1%) | 9 (15.8%) | | 136 (28.6%) | 141 (21.8%) | | 22 (28.9%) | 18 (22.0%) | |
| III | 23 (51.1%) | 30 (52.6%) | | 194 (40.8%) | 354 (54.7%) | | 16 (21.1%) | 42 (51.2%) | |
| IV | 1 (2.2%) | 6 (10.5%) | | 32 (6.7%) | 62 (9.6%) | | 1 (1.3%) | 2 (2.4%) | |
| **Chemotherapy (%)** | 15 (33.3%) | 31 (54.4%) | 0.034 | 226 (47.5%) | 311 (48.1%) | 0.845 | 34 (44.7%) | 54 (65.9%) | 0.008 |

MRS, myeloid radiomics score.

**Supplementary Table 13. Clinical characteristics of patients according to the combined score in the training cohort and internal validation cohort 1.**

| Variables | Training cohort, n =242 | | | | | Internal validation cohort 1, n = 160 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Combined score (LRS/MRS) | | | | | Combined score (LRS/MRS) | | | | |
| | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Median age (range)** | 60 (49-66) | 55 (47-61) | 58 (48-62) | 56 (47-65) | 0.860 | 63 (53-65) | 56 (50-63) | 59 (45-65) | 56 (50-66) | 0.799 |
| **Male** | 27 (73.0%) | 49 (71.0%) | 43 (69.4%) | 40 (54.1%) | 0.088 | 11 (64.7%) | 30 (73.2%) | 43 (81.1%) | 30 (61.2%) | 0.147 |
| **Tumor size** | | | | | 0.003 | | | | | 0.033 |
| ≤4cm | 15 (40.5%) | 38 (55.1%) | 21 (33.9%) | 47 (63.5%) | | 3 (17.6%) | 24 (58.5%) | 24 (45.3%) | 26 (53.1%) | |
| >4cm | 22 (59.5%) | 31 (44.9%) | 41 (66.1%) | 27 (36.5%) | | 14 (82.4%) | 17 (41.5%) | 29 (54.7%) | 23 (46.9%) | |
| **Tumor location** | | | | | 0.130 | | | | | 0.859 |
| Cardia | 12 (32.4%) | 12 (17.4%) | 13 (21.0%) | 9 (12.2%) | | 5 (29.4%) | 8 (19.5%) | 12 (22.6%) | 8 (16.3%) | |
| Body | 2 (5.4%) | 13 (18.8%) | 11 (17.7%) | 20 (27.0%) | | 3 (17.6%) | 11 (26.8%) | 11 (20.8%) | 11 (22.4%) | |
| Antrum | 21 (56.8%) | 41 (59.4%) | 32 (51.6%) | 41 (55.4%) | | 8 (47.1%) | 21 (51.2%) | 26 (49.1%) | 29 (59.2%) | |
| Whole | 2 (5.4%) | 3 (4.3%) | 6 (9.7%) | 4 (5.4%) | | 1 (5.9%) | 1 (2.4%) | 4 (7.5%) | 1 (2.0%) | |
| **Differentiation status** | | | | | 0.323 | | | | | 0.076 |
| Well | 3 (8.1%) | 9 (13.0%) | 5 (8.1%) | 10 (13.5%) | | 3 (17.6%) | 8 (19.5%) | 2 (3.8%) | 6 (12.2%) | |
| Moderate | 4 (10.8%) | 16 (23.2%) | 19 (30.6%) | 17 (23.0%) | | 6 (35.3%) | 8 (19.5%) | 11 (20.8%) | 17 (34.7%) | |
| Poor and undifferentiated | 30 (81.1%) | 44 (63.8%) | 38 (61.3%) | 47 (63.5%) | | 8 (47.1%) | 25 (61.0%) | 40 (75.5%) | 26 (53.1%) | |
| **Lauren type** | | | | | 0.019 | | | | | 0.241 |
| Intestinal type | 9 (24.3%) | 33 (47.8%) | 31 (50.0%) | 41 (55.4%) | | 8 (47.1%) | 22 (53.7%) | 18 (34.0%) | 24 (49.0%) | |
| Diffuse or mixed type | 28 (75.7%) | 36 (52.2%) | 31 (50.0%) | 33 (44.6%) | | 9 (52.9%) | 19 (46.3%) | 35 (66.0%) | 25 (51.0%) | |
| **CEA** | | | | | 0.627 | | | | | 0.453 |
| Normal | 33 (89.2%) | 63 (91.3%) | 55 (88.7%) | 70 (94.6%) | | 15 (88.2%) | 38 (92.7%) | 47 (88.7%) | 40 (81.6%) | |
| Elevated | 4 (10.8%) | 6 (8.7%) | 7 (11.3%) | 4 (5.4%) | | 2 (11.8%) | 3 (7.3%) | 6 (11.3%) | 9 (18.4%) | |
| **CA19-9** | | | | | 0.030 | | | | | 0.088 |
| Normal | 26 (70.3%) | 59 (85.5%) | 56 (90.3%) | 66 (89.2%) | | 12 (70.6%) | 38 (92.7%) | 46 (86.8%) | 45 (91.8%) | |
| Elevated | 11 (29.7%) | 10 (14.5%) | 6 (9.7%) | 8 (10.8%) | | 5 (29.4%) | 3 (7.3%) | 7 (13.2%) | 4 (8.2%) | |
| **Depth of invasion** | | | | | 0.008 | | | | | 0.068 |
| pT1 | 4 (10.8%) | 20 (29.0%) | 7 (11.3%) | 22 (29.7%) | | 1 (5.9%) | 15 (36.6%) | 9 (17.0%) | 12 (24.5%) | |
| pT2 | 6 (16.2%) | 7 (10.1%) | 5 (8.1%) | 11 (14.9%) | | 2 (11.8%) | 1 (2.4%) | 3 (5.7%) | 8 (16.3%) | |
| pT3 | 1 (2.7%) | 7 (10.1%) | 9 (14.5%) | 6 (8.1%) | | 2 (11.8%) | 7 (17.1%) | 6 (11.3%) | 10 (20.4%) | |
| pT4a | 19 (51.4%) | 34 (49.3%) | 30 (48.4%) | 26 (35.1%) | | 10 (58.8%) | 13 (31.7%) | 26 (49.1%) | 13 (26.5%) | |
| pT4b | 7 (18.9%) | 1 (1.4%) | 11 (17.7%) | 9 (12.2%) | | 2 (11.8%) | 5 (12.2%) | 9 (17.0%) | 6 (12.2%) | |
| **Lymph node metastasis** | | | | | 0.004 | | | | | 0.009 |
| pN0 | 7 (18.9%) | 44 (63.8%) | 24 (38.7%) | 36 (48.6%) | | 4 (23.5%) | 22 (53.7%) | 15 (28.3%) | 30 (61.2%) | |
| pN1 | 10 (27.0%) | 7 (10.1%) | 10 (16.1%) | 15 (20.3%) | | 3 (17.6%) | 8 (19.5%) | 13 (24.5%) | 4 (8.2%) | |
| pN2 | 6 (16.2%) | 4 (5.8%) | 9 (14.5%) | 7 (9.5%) | | 4 (23.5%) | 5 (12.2%) | 4 (7.5%) | 5 (10.2%) | |
| pN3a | 6 (16.2%) | 6 (8.7%) | 14 (22.6%) | 7 (9.5%) | | 5 (29.4%) | 4 (9.8%) | 10 (18.9%) | 7 (14.3%) | |
| pN3b | 8 (21.6%) | 8 (11.6%) | 5 (8.1%) | 9 (12.2%) | | 1 (5.9%) | 2 (4.9%) | 11 (20.8%) | 3 (6.1%) | |
| **Distant metastasis** | | | | | 0.765 | | | | | 0.523 |
| pM0 | 37 (100%) | 67 (97.1%) | 60 (96.8%) | 72 (97.3%) | | 16 (94.1%) | 41 (100%) | 51 (96.2%) | 48 (98.0%) | |
| pM1 | 0 (0.0%) | 2 (2.9%) | 2 (3.2%) | 2 (2.7%) | | 1 (5.9%) | 0 (0.0%) | 2 (3.8%) | 1 (2.0%) | |
| **Stage** | | | | | 0.001 | | | | | 0.055 |
| I | 8 (21.6%) | 25 (36.2%) | 11 (17.7%) | 29 (39.2%) | | 1 (5.9%) | 13 (31.7%) | 10 (18.9%) | 17 (34.7%) | |
| II | 2 (5.4%) | 22 (31.9%) | 15 (24.2%) | 11 (14.9%) | | 4 (23.5%) | 14 (34.1%) | 10 (18.9%) | 15 (30.6%) | |
| III | 27 (73.0%) | 20 (29.0%) | 34 (54.8%) | 32 (43.2%) | | 11 (64.7%) | 14 (34.1%) | 31 (58.5%) | 16 (32.7%) | |
| IV | 0 (0.0%) | 2 (2.9%) | 2 (3.2%) | 2 (2.7%) | | 1 (5.9%) | 0 (0.0%) | 2 (3.8%) | 1 (2.0%) | |
| **Chemotherapy** | 19 (51.4%) | 36 (52.2%) | 35 (56.5%) | 35 (47.3%) | 0.739 | 12 (70.6%) | 14 (34.1%) | 27 (50.9%) | 24 (49.0%) | 0.078 |

LRS, lymphoid radiomics score; MRS, myeloid radiomics score. 1, L-LRS and L-MRS; 2, H-LRS and L-MRS; 3, L-LRS and H-MRS; 4, H-LRS and H-MRS.

**Supplementary Table 14. Clinical characteristics of patients according to the combined score in the internal validation cohort 2 and prospective validation cohort.**

| Variables | Internal validation cohort 2, n = 512 | | | | | Prospective validation cohort, n = 158 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Combined score (LRS/MRS) | | | | | Combined score (LRS/MRS) | | | | |
| | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Median age (range)** | 57 (48-64) | 57 (49-64) | 55 (47-65) | 56 (48-62) | 0.829 | 61 (50-67) | 55 (50-64) | 55 (46-65) | 57 (50-63) | 0.593 |
| **Male** | 46 (82.1%) | 105 (70.9%) | 101 (66.9%) | 99 (63.1%) | 0.055 | 20 (76.9%) | 32 (64.0%) | 27 (58.7%) | 25 (69.4%) | 0.432 |
| **Tumor size** | | | | | 0.212 | | | | | <0.001 |
| ≤4cm | 33 (58.9%) | 104 (70.3%) | 94 (62.3%) | 110 (70.1%) | | 15 (57.7%) | 43 (86.0%) | 21 (45.7%) | 28 (77.8%) | |
| >4cm | 23 (41.1%) | 44 (29.7%) | 57 (37.7%) | 47 (29.9%) | | 11 (42.3%) | 7 (14.0%) | 25 (54.3%) | 8 (22.2%) | |
| **Tumor location** | | | | | 0.006 | | | | | 0.781 |
| Cardia | 7 (12.5%) | 25 (16.9%) | 17 (11.3%) | 17 (10.8%) | | 8 (30.8%) | 12 (24.0%) | 7 (15.2%) | 6 (16.7%) | |
| Body | 8 (14.3%) | 21 (14.2%) | 32 (21.2%) | 29 (18.5%) | | 5 (19.2%) | 9 (18.0%) | 11 (23.9%) | 5 (13.9%) | |
| Antrum | 35 (62.5%) | 98 (66.2%) | 79 (52.3%) | 101 (64.3%) | | 13 (50.0%) | 27 (54.0%) | 27 (58.7%) | 24 (66.7%) | |
| Whole | 6 (10.7%) | 4 (2.7%) | 23 (15.2%) | 10 (6.4%) | | 0 (0.0%) | 2 (4.0%) | 1 (2.2%) | 1 (2.8%) | |
| **Differentiation status** | | | | | 0.639 | | | | | 0.108 |
| Well | 7 (12.5%) | 25 (16.9%) | 23 (15.2%) | 31 (19.7%) | | 3 (11.5%) | 5 (10.0%) | 3 (6.5%) | 1 (2.8%) | |
| Moderate | 11 (19.6%) | 38 (25.7%) | 30 (19.9%) | 34 (21.7%) | | 6 (23.1%) | 9 (18.0%) | 3 (6.5%) | 11 (30.6%) | |
| Poor and undifferentiated | 38 (67.9%) | 85 (57.4%) | 98 (64.9%) | 92 (58.6%) | | 17 (65.4%) | 36 (72.0%) | 40 (87.0%) | 24 (66.7%) | |
| **Lauren type** | | | | | 0.538 | | | | | 0.533 |
| Intestinal type | 21 (37.5%) | 71 (48.0%) | 66 (43.7%) | 74 (47.1%) | | 11 (42.3%) | 16 (32.0%) | 12 (26.1%) | 13 (36.1%) | |
| Diffuse or mixed type | 35 (62.5%) | 77 (52.0%) | 85 (56.3%) | 83 (52.9%) | | 15 (57.7%) | 34 (68.0%) | 34 (73.9%) | 23 (63.9%) | |
| **CEA** | | | | | 0.092 | | | | | 0.861 |
| Normal | 45 (80.4%) | 135 (91.2%) | 133 (88.1%) | 144 (91.7%) | | 25 (96.2%) | 48 (96.0%) | 43 (93.5%) | 35 (97.2%) | |
| Elevated | 11 (19.6%) | 13 (8.8%) | 18 (11.9%) | 13 (8.3%) | | 1 (3.8%) | 2 (4.0%) | 3 (6.5%) | 1 (2.8%) | |
| **CA19-9** | | | | | 0.855 | | | | | 0.669 |
| Normal | 46 (82.1%) | 125 (84.5%) | 122 (80.8%) | 131 (83.4%) | | 24 (92.3%) | 47 (94.0%) | 40 (87.0%) | 33 (91.7%) | |
| Elevated | 10 (17.9%) | 23 (15.5%) | 29 (19.2%) | 26 (16.6%) | | 2 (7.7%) | 3 (6.0%) | 6 (13.0%) | 3 (8.3%) | |
| **Depth of invasion** | | | | | <0.001 | | | | | <0.001 |
| pT1 | 17 (30.4%) | 47 (31.8%) | 26 (17.2%) | 51 (32.5%) | | 3 (11.5%) | 26 (52.0%) | 5 (10.9%) | 15 (41.7%) | |
| pT2 | 8 (14.3%) | 24 (16.2%) | 16 (10.6%) | 28 (17.8%) | | 6 (23.1%) | 10 (20.0%) | 3 (6.5%) | 6 (16.7%) | |
| pT3 | 1 (1.8%) | 3 (2.0%) | 3 (2.0%) | 7 (4.5%) | | 7 (26.9%) | 11 (22.0%) | 18 (39.1%) | 5 (13.9%) | |
| pT4a | 17 (30.4%) | 49 (33.1%) | 47 (31.1%) | 51 (32.5%) | | 7 (26.9%) | 3 (6.0%) | 15 (32.6%) | 7 (19.4%) | |
| pT4b | 13 (23.2%) | 25 (16.9%) | 59 (39.1%) | 20 (12.7%) | | 3 (11.5%) | 0 (0.0%) | 5 (10.9%) | 3 (8.3%) | |
| **Lymph node metastasis** | | | | | 0.250 | | | | | 0.001 |
| pN0 | 22 (39.3%) | 73 (49.3%) | 65 (43.0%) | 80 (51.0%) | | 13 (50.0%) | 33 (66.0%) | 9 (19.6%) | 17 (47.2%) | |
| pN1 | 14 (25.0%) | 26 (17.6%) | 37 (24.5%) | 36 (22.9%) | | 5 (19.2%) | 5 (10.0%) | 5 (10.9%) | 7 (19.4%) | |
| pN2 | 7 (12.5%) | 27 (18.2%) | 14 (9.3%) | 14 (8.9%) | | 3 (11.5%) | 8 (16.0%) | 10 (21.7%) | 5 (13.9%) | |
| pN3a | 10 (17.9%) | 15 (10.1%) | 26 (17.2%) | 19 (12.1%) | | 3 (11.5%) | 2 (4.0%) | 12 (26.1%) | 5 (13.9%) | |
| pN3b | 3 (5.4%) | 7 (4.7%) | 9 (6.0%) | 8 (5.1%) | | 2 (7.7%) | 2 (4.0%) | 10 (21.7%) | 2 (5.6%) | |
| **Distant metastasis** | | | | | - | | | | | 0.879 |
| pM0 | 56 (100%) | 148 (100%) | 151 (100%) | 157 (100%) | | 26 (100%) | 49 (98.0%) | 45 (97.8%) | 35 (97.2%) | |
| pM1 | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | 0 (0.0%) | 1 (2.0%) | 1 (2.2%) | 1 (2.8%) | |
| **Stage** | | | | | 0.006 | | | | | <0.001 |
| I | 14 (25.0%) | 41 (27.7%) | 21 (13.9%) | 53 (33.8%) | | 6 (23.1%) | 31 (62.0%) | 6 (13.0%) | 14 (38.9%) | |
| II | 15 (26.8%) | 36 (24.3%) | 37 (24.5%) | 35 (22.3%) | | 12 (46.2%) | 10 (20.0%) | 8 (17.4%) | 10 (27.8%) | |
| III | 27 (48.2%) | 71 (48.0%) | 93 (61.6%) | 69 (43.9%) | | 8 (30.8%) | 8 (16.0%) | 31 (67.4%) | 11 (30.6%) | |
| IV | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | 0 (0.0%) | | 0 (0.0%) | 1 (2.0%) | 1 (2.2%) | 1 (2.8%) | |
| **Chemotherapy** | 26 (46.4%) | 66 (44.6%) | 67 (44.4%) | 71 (45.2%) | 0.994 | 15 (57.7%) | 19 (38.0%) | 34 (73.9%) | 20 (55.6%) | 0.006 |

LRS, lymphoid radiomics score; MRS, myeloid radiomics score. 1, L-LRS and L-MRS; 2, H-LRS and L-MRS; 3, L-LRS and H-MRS; 4, H-LRS and H-MRS.

**Supplementary Table 15. Clinical characteristics of patients according to the combined score in the external validation cohort 1 and external validation cohort 2.**

| Variables | External validation cohort 1, n = 102 | | | | | External validation cohort 2, n = 1123 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Combined score (LRS/MRS) | | | | | Combined score (LRS/MRS) | | | | |
| | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Median age (range)** | 58 (44-61) | 61 (51-67) | 51 (42-60) | 60 (55-66) | 0.039 | 57 (48-64) | 58 (49-65) | 57 (50-65) | 57 (48-65) | 0.874 |
| **Male** | 7 (100%) | 22 (57.9%) | 25 (83.3%) | 19 (70.4%) | 0.040 | 94 (74.6%) | 235 (67.1%) | 257 (69.8%) | 187 (67.0%) | 0.389 |
| **Tumor size** | | | | | 0.544 | | | | | <0.001 |
| ≤4cm | 4 (57.1%) | 23 (60.5%) | 14 (46.7%) | 12 (44.4%) | | 50 (39.7%) | 180 (51.4%) | 89 (24.2%) | 121 (43.4%) | |
| >4cm | 3 (42.9%) | 15 (39.5%) | 16 (53.3%) | 15 (55.6%) | | 76 (60.3%) | 170 (48.6%) | 279 (75.8%) | 158 (56.6%) | |
| **Tumor location** | | | | | 0.344 | | | | | <0.001 |
| Cardia | 1 (14.3%) | 11 (28.9%) | 13 (43.3%) | 8 (29.6%) | | 39 (31.0%) | 106 (30.3%) | 135 (36.7%) | 94 (33.7%) | |
| Body | 1 (14.3%) | 6 (15.8%) | 7 (23.3%) | 8 (29.6%) | | 23 (18.3%) | 60 (17.1%) | 86 (23.4%) | 67 (24.0%) | |
| Antrum | 5 (71.4%) | 20 (52.6%) | 8 (26.7%) | 11 (40.7%) | | 60 (47.6%) | 177 (50.6%) | 113 (30.7%) | 109 (39.1%) | |
| Whole | 0 (0.0%) | 1 (2.6%) | 2 (6.7%) | 0 (0.0%) | | 4 (3.2%) | 7 (2.0%) | 34 (9.2%) | 9 (3.2%) | |
| **Differentiation status** | | | | | 0.561 | | | | | 0.392 |
| Well | 0 (0.0%) | 1 (2.6%) | 0 (0.0%) | 0 (0.0%) | | 2 (1.6%) | 11 (3.1%) | 4 (1.1%) | 3 (1.1%) | |
| Moderate | 0 (0.0%) | 9 (23.7%) | 4 (13.3%) | 6 (22.2%) | | 17 (13.5%) | 54 (15.4%) | 61 (16.6%) | 42 (15.1%) | |
| Poor and undifferentiated | 7 (100%) | 28 (73.7%) | 26 (86.7%) | 21 (77.8%) | | 107 (84.9%) | 285 (81.4%) | 303 (82.3%) | 234 (83.9%) | |
| **Lauren type** | | | | | 0.167 | | | | | 0.217 |
| Intestinal type | 0 (0.0%) | 17 (44.7%) | 11 (36.7%) | 10 (37.0%) | | 37 (29.4%) | 133 (38.0%) | 118 (32.1%) | 92 (33.0%) | |
| Diffuse or mixed type | 7 (100%) | 21 (55.3%) | 19 (63.3%) | 17 (63.0%) | | 89 (70.6%) | 217 (62.0%) | 250 (67.9%) | 187 (67.0%) | |
| **CEA** | | | | | 0.454 | | | | | 0.007 |
| Normal | 7 (100%) | 29 (76.3%) | 25 (83.3%) | 23 (85.2%) | | 104 (82.5%) | 295 (84.3%) | 277 (75.3%) | 234 (83.9%) | |
| Elevated | 0 (0.0%) | 9 (23.7%) | 5 (16.7%) | 4 (14.8%) | | 22 (17.5%) | 55 (15.7%) | 91 (24.7%) | 45 (16.1%) | |
| **CA19-9** | | | | | 0.244 | | | | | <0.001 |
| Normal | 6 (85.7%) | 36 (94.7%) | 25 (83.3%) | 21 (77.8%) | | 104 (82.5%) | 306 (87.4%) | 268 (72.8%) | 230 (82.4%) | |
| Elevated | 1 (14.3%) | 2 (5.3%) | 5 (16.7%) | 6 (22.2%) | | 22 (17.5%) | 44 (12.6%) | 100 (27.2%) | 49 (17.6%) | |
| **Depth of invasion** | | | | | 0.934 | | | | | <0.001 |
| pT1 | 1 (14.3%) | 8 (21.1%) | 3 (10.0%) | 6 (22.2%) | | 14 (11.1%) | 73 (20.9%) | 18 (4.9%) | 43 (15.4%) | |
| pT2 | 1 (14.3%) | 6 (15.8%) | 4 (13.3%) | 3 (11.1%) | | 11 (8.7%) | 57 (16.3%) | 25 (6.8%) | 37 (13.3%) | |
| pT3 | 1 (14.3%) | 7 (18.4%) | 6 (20.0%) | 6 (22.2%) | | 24 (19.0%) | 81 (23.1%) | 68 (18.5%) | 66 (23.7%) | |
| pT4a | 3 (42.9%) | 15 (39.5%) | 15 (50.0%) | 8 (29.6%) | | 60 (47.6%) | 127 (36.3%) | 212 (57.6%) | 117 (41.9%) | |
| pT4b | 1 (14.3%) | 2 (5.3%) | 2 (6.7%) | 4 (14.8%) | | 17 (13.5%) | 12 (3.4%) | 45 (12.2%) | 16 (5.7%) | |
| **Lymph node metastasis** | | | | | 0.583 | | | | | <0.001 |
| pN0 | 3 (42.9%) | 16 (42.1%) | 7 (23.3%) | 9 (33.3%) | | 33 (26.2%) | 155 (44.3%) | 79 (21.5%) | 102 (36.6%) | |
| pN1 | 0 (0.0%) | 5 (13.2%) | 6 (20.0%) | 3 (11.1%) | | 15 (11.9%) | 60 (17.1%) | 58 (15.8%) | 44 (15.8%) | |
| pN2 | 2 (28.6%) | 8 (21.1%) | 6 (20.0%) | 9 (33.3%) | | 28 (22.2%) | 49 (14.0%) | 66 (17.9%) | 56 (20.1%) | |
| pN3a | 2 (28.6%) | 3 (7.9%) | 7 (23.3%) | 4 (14.8%) | | 30 (23.8%) | 60 (17.1%) | 99 (26.9%) | 57 (20.4%) | |
| pN3b | 0 (0.0%) | 6 (15.8%) | 4 (13.3%) | 2 (7.4%) | | 20 (15.9%) | 26 (7.4%) | 66 (17.9%) | 20 (7.2%) | |
| **Distant metastasis** | | | | | 0.543 | | | | | 0.004 |
| pM0 | 6 (85.7%) | 37 (97.4%) | 27 (90.0%) | 25 (92.6%) | | 115 (91.3%) | 329 (94.0%) | 322 (87.5%) | 263 (94.3%) | |
| pM1 | 1 (14.3%) | 1 (2.6%) | 3 (10.0%) | 2 (7.4%) | | 11 (8.7%) | 21 (6.0%) | 46 (12.5%) | 16 (5.7%) | |
| **Stage** | | | | | 0.735 | | | | | <0.001 |
| I | 2 (28.6%) | 13 (34.2%) | 6 (20.0%) | 7 (25.9%) | | 16 (12.7%) | 98 (28.0%) | 33 (9.0%) | 57 (20.4%) | |
| II | 1 (14.3%) | 4 (10.5%) | 3 (10.0%) | 6 (22.2%) | | 27 (21.4%) | 109 (31.1%) | 57 (15.5%) | 84 (30.1%) | |
| III | 3 (42.9%) | 20 (52.6%) | 18 (60.0%) | 12 (44.4%) | | 72 (57.1%) | 122 (34.9%) | 232 (63.0%) | 122 (43.7%) | |
| IV | 1 (14.3%) | 1 (2.6%) | 3 (10.0%) | 2 (7.4%) | | 11 (8.7%) | 21 (6.0%) | 46 (12.5%) | 16 (5.7%) | |
| **Chemotherapy** | 3 (42.9%) | 13 (34.2%) | 18 (60.0%) | 12 (44.4%) | 0.210 | 56 (44.4%) | 170 (48.6%) | 172 (46.7%) | 139 (49.8%) | 0.735 |

LRS, lymphoid radiomics score; MRS, myeloid radiomics score. 1, L-LRS and L-MRS; 2, H-LRS and L-MRS; 3, L-LRS and H-MRS; 4, H-LRS and H-MRS.

**Supplementary Table 16. The predictive value of radiomics signature is compared according to cut-off values determined by different methods.**

| Variables | Cut-off value from Youden's index | The median | The upper quartile | The lower quartile |
|---|---|---|---|---|
| **Cut-off value** | | | | |
| LRS | −0.1293 | 0.1463 | -0.6966 | 0.8603 |
| MRS | −0.2604 | -0.0659 | -0.7254 | 0.6153 |
| **Predictive value for DFS in patients with radical surgery, n=2,297, HR (P value)** | | | | |
| Patients (High vs Low) | 1317 vs 980 | 1115 vs 1182 | 1630 vs 667 | 669 vs 1628 |
| LRS (dichotomy) | 0.463 (<0.00001) | 0.472 (<0.00001) | 0.475 (<0.00001) | 0.511 (<0.00001) |
| Patients (High vs Low) | 1329 vs 968 | 1191 vs 1106 | 1647 vs 650 | 690 vs 1607 |
| MRS (dichotomy) | 1.857 (<0.00001) | 1.767 (<0.00001) | 1.769 (<0.00001) | 1.517 (<0.00001) |
| **Predictive value for DFS in patients with radical surgery, n=2,297, C-index** | | | | |
| LRS (dichotomy) | 0.599 | 0.595 | 0.585 | 0.568 |
| MRS (dichotomy) | 0.576 | 0.573 | 0.557 | 0.547 |
| **Predictive value for OS in patients with radical surgery, n=2,297, HR (P value)** | | | | |
| LRS (dichotomy) | 0.451 (<0.00001) | 0.452 (<0.00001) | 0.472 (<0.00001) | 0.518 (<0.00001) |
| MRS (dichotomy) | 1.939 (<0.00001) | 1.853 (<0.00001) | 1.772 (<0.00001) | 1.566 (<0.00001) |
| **Predictive value for OS in patients with radical surgery, n=2,297, C-index** | | | | |
| LRS (dichotomy) | 0.602 | 0.599 | 0.585 | 0.567 |
| MRS (dichotomy) | 0.581 | 0.578 | 0.557 | 0.548 |
| **Predictive value of LRS for immunotherapy, n=261, Low (%) vs High (%)** | | | | |
| Patients (High vs Low) | 160 vs 101 | 124 vs 137 | 66 vs 195 | 217 vs 44 |
| CR (%) | 3.0% vs 13.8% | 5.1% vs 14.5% | 1.5% vs 12.3% | 7.8% vs 18.2% |
| PR (%) | 10.9% vs 25.0% | 14.6% vs 25.0% | 10.6% vs 22.6% | 16.6% vs 34.1% |
| SD (%) | 27.7% vs 18.8% | 26.3% vs 17.7% | 31.8% vs 19.0% | 23.0% vs 18.2% |
| PD (%) | 58.4% vs 42.5% | 54.0% vs 42.7% | 56.1% vs 46.2% | 52.5% vs 29.5% |
| **Predictive value of MRS for immunotherapy, n=261, Low (%) vs High (%)** | | | | |
| Patients (High vs Low) | 179 vs 82 | 161 vs 100 | 206 vs 55 | 66 vs 195 |
| CR (%) | 17.1% vs 6.1% | 15.0% vs 6.2% | 14.5% vs 8.3% | 12.3% vs 1.5% |
| PR (%) | 29.3% vs 15.1% | 25.0% vs 16.1% | 34.5% vs 15.5% | 21.5% vs 13.6% |
| SD (%) | 22.0% vs 22.3% | 22.0% vs 22.4% | 25.5% vs 21.4% | 21.5% vs 24.2% |
| PD (%) | 31.7% vs 56.4% | 38.0% vs 55.3% | 25.5% vs 54.9% | 44.6% vs 60.6% |
| **AUC of immunotherapy response** | | | | |
| LRS (dichotomy) | 0.643 (0.572-0.714) | 0.620 (0.545-0.694) | 0.604 (0.533-0.676) | 0.595 (0.515-0.674) |
| MRS (dichotomy) | 0.631 (0.554-0.708) | 0.601 (0.524-0.678) | 0.602 (0.523-0.681) | 0.586 (0.513-0.658) |
| **Predictive value of LRS/MRS for immunotherapy, n=261, 1(%), 2(%) 3(%), or 4(%)** | | | | |
| Patients (1 vs 2 vs 3 vs 4) | 22 vs 60 vs 79 vs 100 | 42 vs 58 vs 95 vs 66 | 11 vs 44 vs 55 vs 151 | 161 vs 34 vs 56 vs 10 |
| CR (%) | 9.1 vs 20.0 vs 1.3 vs 10.0 | 4.8 vs 22.4 vs 5.3 vs 7.6 | 9.1 vs 15.9 vs 0 vs 11.3 | 9.9 vs 23.5 vs 1.8 vs 0 |
| PR (%) | 18.2 vs 33.3 vs 8.9 vs 20.0 | 23.8 vs 25.9 vs 10.5 vs 24.2 | 18.2 vs 38.6 vs 9.1 vs 17.9 | 19.3 vs 32.4 vs 8.9 vs 40.0 |
| SD (%) | 36.4 vs 16.7 vs 25.3 vs 20.0 | 31.0 vs 15.5 vs 24.2 vs 19.7 | 45.5 vs 20.5 vs 29.1 vs 18.5 | 22.4 vs 17.6 vs 25.0 vs 20.0 |
| PD (%) | 36.4 vs 30.0 vs 64.6 vs 50.0 | 40.5 vs 36.2 vs 60.0 vs 48.5 | 27.3 vs 25.0 vs 61.8 vs 52.3 | 48.4 vs 26.5 vs 64.3% vs 40.0 |

LRS, lymphoid radiomics score; MRS, myeloid radiomics score. 1, L-LRS and L-MRS; 2, H-LRS and L-MRS; 3, L-LRS and H-MRS; 4, H-LRS and H-MRS.

CR: complete response, PR: partial response, SD: stable disease, PD: progressive disease.

**Supplementary Table 17. Univariate association of RS, clinicopathological characteristics with disease-free and overall survival in the training cohort.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LRS (high vs. low) | 0.429 (0.291-0.633) | <0.0001 | 0.345 (0.212-0.561) | <0.0001 |
| MRS (high vs. low) | 2.022 (1.333-3.069) | 0.001 | 2.533 (1.482-4.331) | 0.001 |
| Age (years) (≥60 vs. <60) | 0.937 (0.631-1.391) | 0.748 | 0.757 (0.462-1.240) | 0.269 |
| Sex (male vs. female) | 1.043 (0.694-1.566) | 0.841 | 1.334 (0.798-2.229) | 0.271 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.831 (1.235-2.715) | 0.003 | 2.153 (1.324-3.503) | 0.002 |
| Tumor location | 1.053 (0.838-1.324) | 0.656 | 0.944 (0.719-1.240) | 0.680 |
| Differentiation | 1.379 (1.011-1.881) | 0.042 | 1.504 (1.022-2.214) | 0.039 |
| Lauren type | 1.005 (0.684-1.477) | 0.980 | 0.980 (0.613-1.567) | 0.933 |
| CEA (elevated vs. normal) | 2.033 (1.176-3.515) | 0.011 | 2.212 (1.162-4.213) | 0.016 |
| CA19-9 (elevated vs. normal) | 1.477 (0.878-2.485) | 0.142 | 1.001 (1.000-1.003) | 0.081 |
| Stage (IV vs. III vs. II vs. I) | 2.123 (1.645-2.739) | <0.0001 | 2.954 (2.095-4.144) | <0.0001 |
| Chemotherapy (yes vs. no) | 0.686 (0.466-1.010) | 0.056 | 0.489 (0.302-0.792) | 0.004 |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 18. Univariate association of RS, clinicopathological characteristics with disease-free and overall survival in the internal validation cohort 1.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LRS (high vs. low) | 0.330 (0.207-0.528) | <0.0001 | 0.322 (0.184-0.565) | <0.0001 |
| MRS (high vs. low) | 2.219 (1.305-3.772) | 0.003 | 3.034 (1.525-6.034) | 0.002 |
| Age (years) (≥60 vs. <60) | 1.053 (0.669-1.655) | 0.824 | 0.890 (0.517-1.532) | 0.674 |
| Sex (male vs. female) | 1.366 (0.812-2.297) | 0.240 | 1.739 (0.896-3.374) | 0.102 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.867 (1.173-2.971) | 0.008 | 1.819 (1.046-3.163) | 0.034 |
| Tumor location | 0.950 (0.730-1.236) | 0.702 | 0.963 (0.703-1.319) | 0.814 |
| Differentiation | 0.966 (0.708-1.317) | 0.826 | 1.035 (0.711-1.507) | 0.856 |
| Lauren type | 0.913 (0.581-1.434) | 0.692 | 1.197 (0.692-2.069) | 0.521 |
| CEA (elevated vs. normal) | 1.365 (0.718-2.593) | 0.343 | 1.461 (0.687-3.105) | 0.324 |
| CA19-9 (elevated vs. normal) | 1.003 (0.998-1.009) | 0.220 | 1.185 (0.535-2.624) | 0.676 |
| Stage (IV vs. III vs. II vs. I) | 2.065 (1.520-2.804) | <0.0001 | 2.826 (1.894-4.216) | <0.0001 |
| Chemotherapy (yes vs. no) | 0.876 (0.558-1.376) | 0.567 | 1.169 (0.684-1.997) | 0.568 |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 19. Univariate association of RS, clinicopathological characteristics with disease-free and overall survival in the internal validation cohort 2.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LRS (high vs. low) | 0.476 (0.378-0.600) | <0.0001 | 0.466 (0.359-0.603) | <0.0001 |
| MRS (high vs. low) | 1.640 (1.281-2.099) | <0.0001 | 1.652 (1.252-2.181) | <0.0001 |
| Age (years) (≥60 vs. <60) | 1.139 (0.901 -1.440) | 0.276 | 1.364 (1.053-1.767) | 0.019 |
| Sex (male vs. female) | 0.954 (0.746-1.219) | 0.705 | 0.978 (0.743-1.286) | 0.872 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.191 (0.937-1.514) | 0.152 | 1.257 (0.964-1.640) | 0.091 |
| Tumor location | 1.040 (0.893-1.211) | 0.617 | 1.039 (0.879-1.229) | 0.654 |
| Differentiation | 1.164 (0.997-1.359) | 0.055 | 1.292 (1.078-1.548) | 0.006 |
| Lauren type | 1.187 (0.940-1.499) | 0.149 | 1.085 (0.837-1.406) | 0.537 |
| CEA (elevated vs. normal) | 2.556 (1.859-3.515) | <0.0001 | 2.701 (1.900-3.841) | <0.0001 |
| CA19-9 (elevated vs. normal) | 2.742 (2.091-3.595) | <0.0001 | 2.643 (1.954-3.574) | <0.0001 |
| Stage (III vs. II vs. I) | 2.416 (2.037-2.865) | <0.0001 | 2.641 (2.157-3.242) | <0.0001 |
| Chemotherapy (yes vs. no) | 1.108 (0.880 -1.395) | 0.384 | 1.106 (0.854-1.432) | 0.444 |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 20. Univariate association of RS, clinicopathological characteristics with disease-free and overall survival in the external validation cohort 1.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LRS (high vs. low) | 0.310 (0.164-0.588) | <0.0001 | 0.274 (0.136-0.552) | <0.001 |
| MRS (high vs. low) | 3.772 (1.825-7.796) | <0.001 | 4.679 (2.089-10.480) | <0.001 |
| Age (years) (≥60 vs. <60) | 0.752 (0.394-1.435) | 0.388 | 0.736 (0.368-1.472) | 0.377 |
| Sex (male vs. female) | 1.742 (0.799-3.794) | 0.163 | 2.081 (0.860-5.040) | 0.104 |
| Tumor size (>4 cm vs. ≤4 cm) | 2.748 (1.442-5.237) | 0.002 | 3.049 (1.518-6.128) | 0.002 |
| Tumor location | 0.760 (0.538-1.073) | 0.119 | 0.748 (0.517-1.081) | 0.123 |
| Differentiation | 1.473 (0.646-3.359) | 0.357 | 1.358 (0.592-3.114) | 0.470 |
| Lauren type | 1.234 (0.634-2.402) | 0.536 | 1.169 (0.578-2.363) | 0.664 |
| CEA (elevated vs. normal) | 1.091 (0.482-2.473) | 0.834 | 1.250 (0.544-2.875) | 0.599 |
| CA19-9 (elevated vs. normal) | 4.564 (2.287-9.108) | <0.0001 | 4.086 (1.922-8.687) | <0.0001 |
| Stage (IV vs. III vs. II vs. I) | 2.499 (1.616-3.865) | <0.0001 | 2.318 (1.485-3.617) | <0.0001 |
| Chemotherapy (yes vs. no) | 1.902 (1.009-3.584) | 0.047 | 2.004 (1.012-3.969) | 0.046 |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 21. Univariate association of RS, clinicopathological characteristics with disease-free and overall survival in the external validation cohort 2.**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LRS (high vs. low) | 0.522 (0.441-0.619) | <0.0001 | 0.509 (0.428-0.604) | <0.0001 |
| MRS (high vs. low) | 1.662 (1.392-1.984) | <0.0001 | 1.738 (1.451-2.082) | <0.0001 |
| Age (years) (≥60 vs. <60) | 1.294 (1.092-1.533) | 0.003 | 1.305 (1.099-1.551) | 0.002 |
| Sex (male vs. female) | 1.023 (0.852-1.228) | 0.811 | 1.028 (0.854-1.238) | 0.772 |
| Tumor size (>4 cm vs. ≤4 cm) | 1.906 (1.583-2.294) | <0.0001 | 1.979 (1.637-2.392) | <0.0001 |
| Tumor location | 0.935 (0.853-1.024) | 0.149 | 0.933 (0.850-1.024) | 0.143 |
| Differentiation | 1.240 (1.009-1.524) | 0.041 | 1.228 (0.998-1.511) | 0.052 |
| Lauren type | 1.287 (1.070-1.549) | 0.007 | 1.289 (1.069-1.555) | 0.008 |
| CEA (elevated vs. normal) | 1.573 (1.290-1.917) | <0.0001 | 1.582 (1.294-1.933) | <0.0001 |
| CA19-9 (elevated vs. normal) | 1.873 (1.544-2.270) | <0.0001 | 1.908 (1.570-2.318) | <0.0001 |
| Stage (IV vs. III vs. II vs. I) | 2.244 (2.001-2.516) | <0.0001 | 2.253 (2.006-2.531) | <0.0001 |
| Chemotherapy (yes vs. no) | 0.990 (0.836 -1.174) | 0.911 | 1.020 (0.858-1.212) | 0.823 |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 22. Univariate association of RS, clinicopathological characteristics with disease-free and overall survival in the prospective validation cohort**

| Variables | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | HR (95%CI) | *p* | HR (95%CI) | *p* |
| LRS (high vs. low) | 0.218 (0.110-0.435) | <0.0001 | 0.180 (0.077-0.418) | <0.0001 |
| MRS (high vs. low) | 3.591 (1.796-7.178) | <0.001 | 4.249 (1.828-9.872) | 0.001 |
| Age (years) (≥60 vs. <60) | 1.742 (0.954-3.181) | 0.071 | 2.658 (1.281-5.515) | 0.009 |
| Sex (male vs. female) | 0.971 (0.59-1.819) | 0.927 | 1.015 (0.489-2.105) | 0.969 |
| Tumor size (>4 cm vs. ≤4 cm) | 3.785 (2.051-6.984) | <0.0001 | 4.066 (1.986-8.323) | <0.001 |
| Tumor location | 1.007 (0.708-1.431) | 0.971 | 0.886 (0.593-1.323) | 0.553 |
| Differentiation | 1.368 (0.784-2.390) | 0.270 | 1.000 (0.569-1.758) | 0.999 |
| Lauren type | 1.358 (0.697-2.646) | 0.368 | 0.976 (0.470-2.023) | 0.947 |
| CEA (elevated vs. normal) | 2.451 (0.874-6.870) | 0.088 | 2.331 (0.710-7.655) | 0.163 |
| CA19-9 (elevated vs. normal) | 2.590 (1.150-5.831) | 0.022 | 2.602 (1.070-6.327) | 0.035 |
| Stage (IV vs. III vs. II vs. I) | 3.232 (2.121-4.924) | <0.0001 | 2.813 (1.778-4.451) | <0.0001 |
| Chemotherapy | 2.822 (1.420-5.611) | 0.003 | 1.988 (0.940-4.206) | 0.072 |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 23. Clinical characteristics of patients according to the LRS, MRS, and combined score in the radiogenomics cohort.**

| Variables | LRS, n =42 | | | MRS, n = 42 | | | Combined score (LRS/MRS), n = 42 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | low LRS | high LRS | *P* | low MRS | high MRS | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Median age (range)** | 68 (63-74) | 67 (58-70) | 0.344 | 68 (63-72) | 67 (58-69) | 0.168 | 70 (67-/) | 68 (59-71) | 68 (61-74) | 59 (57-67) | 0.202 |
| **Male (%)** | 14 (93.3%) | 22 (81.5%) | 0.293 | 16 (84.2%) | 20 (87.0%) | 0.800 | 3 (100%) | 13 (81.3%) | 11 (91.7%) | 9 (81.8%) | 0.742 |
| **Stage (%)** | | | 0.840 | | | 0.278 | | | | | 0.565 |
| I | 0 (0.0%) | 1 (3.7%) | | 1 (5.3%) | 0 (0.0%) | | 0 (0.0%) | 1 (6.3%) | 0 (0.0%) | 0 (0.0%) | |
| II | 2 (13.3%) | 5 (18.5%) | | 5 (26.3%) | 2 (8.7%) | | 0 (0.0%) | 5 (31.3%) | 2 (16.7%) | 0 (0.0%) | |
| III | 12 (80.0%) | 19 (70.4%) | | 12 (63.2%) | 19 (82.6%) | | 3 (100%) | 9 (56.3%) | 9 (75.0%) | 10 (90.9%) | |
| IV | 1 (6.7%) | 2 (7.4%) | | 1 (5.3%) | 2 (8.7%) | | 0 (0.0%) | 1 (6.3%) | 1 (8.3%) | 1 (9.1%) | |

**Supplementary Table 24. Comparing the prediction accuracy of the integrated nomogram with RS and TNM stage in the training and validation cohorts.**

| Variable | Disease-free survival | | Overall survival | |
|---|---|---|---|---|
| | C-Index (95% CI) | *P* | C-Index (95% CI) | *P* |
| **Training cohort** | | <0.001 | | <0.001 |
| Nomogram | 0.735 (0.686-0.784) | | 0.816 (0.774-.858) | |
| LRS | 0.637 (0.581-0.693) | | 0.661 (0.598-0.724) | |
| MRS | 0.627 (0.571-0.683) | | 0.645 (0.580-0.710) | |
| Stage | 0.662 (0.613-0.711) | | 0.723 (0.679-0.767) | |
| **Internal validation cohort 1** | | <0.001 | | <0.001 |
| Nomogram | 0.726 (0.672-0.780) | | 0.766 (0.706-0.826) | |
| LRS | 0.633 (0.564-0.702) | | 0.621 (0.547-0.695) | |
| MRS | 0.577 (0.410-0.644) | | 0.615 (0.541-0.689) | |
| Stage | 0.656 (0.600-0.712) | | 0.699 (0.642-0.756) | |
| **Internal validation cohort 2** | | <0.001 | | <0.001 |
| Nomogram | 0.748 (0.722-0.774) | | 0.754 (0.724-0.784) | |
| LRS | 0.627 (0.592-0.662) | | 0.639 (0.600-0.678) | |
| MRS | 0.570 (0.534-0.606) | | 0.581 (0.541-0.621) | |
| Stage | 0.686 (0.661-0.711) | | 0.687 (0.658-0.716) | |
| **External validation cohort 1** | | <0.001 | | <0.001 |
| Nomogram | 0.767 (0.705-0.829) | | 0.779 (0.716-0.842) | |
| LRS | 0.698 (0.627-0.769) | | 0.699 (0.622-0.776) | |
| MRS | 0.653 (0.574-0.732) | | 0.662 (0.576-0.748) | |
| Stage | 0.692 (0.620-0.764) | | 0.684 (0.608-0.760) | |
| **External validation cohort 2** | | <0.001 | | <0.001 |
| Nomogram | 0.716 (0.695-0.737) | | 0.715 (0.693-0.737) | |
| LRS | 0.620 (0.596-0.644) | | 0.619 (0.594-0.644) | |
| MRS | 0.577 (0.552-0.602) | | 0.580 (0.555-0.605) | |
| Stage | 0.676 (0.656-0.696) | | 0.675 (0.654-0.696) | |
| **Prospective validation cohort** | | <0.001 | | <0.001 |
| Nomogram | 0.839 (0.779-0.899) | | 0.841 (0.782-0.900) | |
| LRS | 0.780 (0.707-0.853) | | 0.803 (0.730-0.876) | |
| MRS | 0.693 (0.621-0.765) | | 0.677 (0.600-0.754) | |
| Stage | 0.731 (0.658-0.804) | | 0.709 (0.628-0.790) | |

RS, radiomics score; LRS, lymphoid radiomics score; MRS, myeloid radiomics score.

**Supplementary Table 25. Clinical characteristics of patients according to the LRS, MRS, and combined score in the immunotherapy cohort 1 (SMU).**

| Variables | LRS, n =198 | | | MRS, n = 198 | | | Combined score (LRS/MRS), n = 198 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | low LRS | high LRS | *P* | low MRS | high MRS | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Median age (range)** | 54 (45-64) | 56 (48-66) | 0.301 | 57 (49-65) | 55 (46-65) | 0.393 | 58 (52-63) | 56 (49-67) | 54 (44-65) | 56 (48-66) | 0.496 |
| **Male (%)** | 40 (58.8%) | 75 (57.7%) | 0.879 | 36 (62.1%) | 79 (56.4%) | 0.467 | 7 (53.8%) | 29 (64.4%) | 33 (60.0%) | 46 (54.1%) | 0.693 |
| **Stage (%)** | | | 0.023 | | | 0.079 | | | | | 0.071 |
| II | 2 (2.9%) | 15 (11.5%) | | 8 (13.8%) | 9 (6.4%) | | 1 (7.7%) | 7 (15.6%) | 1 (1.8%) | 8 (9.4%) | |
| III | 12 (17.6%) | 35 (26.9%) | | 17 (29.3%) | 30 (21.4%) | | 2 (15.4%) | 15 (33.3%) | 10 (18.2%) | 20 (23.5%) | |
| IV | 54 (79.4%) | 80 (61.5%) | | 33 (56.9%) | 101 (72.1%) | | 10 (76.9%) | 23 (51.1%) | 44 (80.0%) | 57 (67.1%) | |
| **Response (%)** | | | 0.001 | | | <0.0001 | | | | | <0.0001 |
| CR | 3 (4.4%) | 21 (16.2%) | | 13 (22.4%) | 11 (7.9%) | | 2 (15.3%) | 11 (24.5%) | 1 (1.8%) | 10 (11.7%) | |
| PR | 8 (11.8%) | 32 (24.6%) | | 17 (29.3%) | 23 (16.5%) | | 3 (23.1%) | 14 (31.1%) | 5 (9.1%) | 18 (21.2%) | |
| SD | 14 (20.6%) | 19 (14.6%) | | 9 (15.5%) | 24 (17.1%) | | 3 (23.1%) | 6 (13.3%) | 11 (20.0%) | 13 (15.3%) | |
| PD | 43 (63.2%) | 58 (44.6%) | | 19 (32.8%) | 82 (58.5%) | | 5 (38.5%) | 14 (31.1%) | 38 (69.1%) | 44 (51.8%) | |
| **Treatment line (%)** | | | 0.538 | | | 0.014 | | | | | 0.071 |
| First line | 42 (61.8%) | 72 (55.4%) | | 39 (67.2%) | 75 (53.6%) | | 10 (76.9%) | 29 (64.4%) | 32 (58.2%) | 43 (50.6%) | |
| Second line | 14 (20.6%) | 34 (26.2%) | | 15 (25.9%) | 33 (23.6%) | | 2 (15.4%) | 13 (28.9%) | 12 (21.8%) | 21 (24.7%) | |
| Third line | 12 (17.6%) | 24 (18.5%) | | 4 (6.9%) | 32 (22.9%) | | 1 (7.7%) | 3 (6.7%) | 11 (20.0%) | 21 (24.7%) | |

LRS, lymphoid radiomics score; MRS, myeloid radiomics score. 1, L-LRS and L-MRS; 2, H-LRS and L-MRS; 3, L-LRS and H-MRS; 4, H-LRS and H-MRS.

**Supplementary Table 26. Clinical characteristics of patients according to the LRS, MRS, and combined score in the immunotherapy cohort 2 (GPHCM).**

| Variables | LRS, n =63 | | | MRS, n = 63 | | | Combined score (LRS/MRS), n = 63 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | low LRS | high LRS | *P* | low MRS | high MRS | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Median age (range)** | 58 (48-65) | 62 (48-66) | 0.343 | 64 (50-68) | 58 (48-64) | 0.384 | 68 (60-70) | 59 (47-66) | 55 (48-60) | 62 (50-71) | 0.078 |
| **Male (%)** | 20 (60.6%) | 14 (46.7%) | 0.268 | 15 (62.5%) | 19 (48.7%) | 0.287 | 8 (88.9%) | 7 (46.7%) | 12 (50.0%) | 7 (46.7%) | 0.157 |
| **Stage (%)** | | | 0.050 | | | 0.514 | | | | | 0.002 |
| III | 5 (15.2%) | 11 (36.7%) | | 5 (20.8%) | 11 (28.2%) | | 3 (33.3%) | 2 (13.3%) | 2 (8.3%) | 9 (60.0%) | |
| IV | 28 (84.8%) | 19 (63.3%) | | 19 (79.2%) | 28 (71.8%) | | 6 (66.7%) | 13 (86.7%) | 22 (91.7%) | 6 (40.0%) | |
| **Response (%)** | | | 0.180 | | | 0.107 | | | | | 0.193 |
| CR | 0 (0.0%) | 1 (3.3%) | | 1 (4.2%) | 0 (0.0%) | | 0 (0.0%) | 1 (6.7%) | 0 (0.0%) | 0 (0.0%) | |
| PR | 3 (9.1%) | 8 (26.7%) | | 7 (29.2%) | 4 (10.3%) | | 1 (11.1%) | 6 (40.0%) | 2 (8.3%) | 2 (13.3%) | |
| SD | 14 (42.4%) | 11 (36.7%) | | 9 (37.4%) | 16 (41.0%) | | 5 (55.6%) | 4 (26.7%) | 9 (37.5%) | 7 (46.7%) | |
| PD | 16 (48.5%) | 10 (33.3%) | | 7 (29.2%) | 19 (48.7%) | | 3 (33.3%) | 4 (26.7%) | 13 (54.2%) | 6 (40.0%) | |
| **Treatment line (%)** | | | 0.032 | | | 0.048 | | | | | 0.071 |
| First line | 22 (66.7%) | 11 (36.7%) | | 10 (41.7%) | 23 (59.0%) | | 5 (55.6%) | 5 (33.3%) | 17 (70.8%) | 6 (40.0%) | |
| Second line | 10 (30.3%) | 14 (46.7%) | | 9 (37.5%) | 15 (38.5%) | | 3 (33.3%) | 6 (40.0%) | 7 (29.2%) | 8 (53.3%) | |
| Third line | 1 (3.0%) | 5 (16.7%) | | 5 (20.8%) | 1 (2.6%) | | 1 (11.1%) | 4 (26.7%) | 0 (0.0%) | 1 (6.7%) | |

LRS, lymphoid radiomics score; MRS, myeloid radiomics score. 1, L-LRS and L-MRS; 2, H-LRS and L-MRS; 3, L-LRS and H-MRS; 4, H-LRS and H-MRS.

**Supplementary Table 27. Immunotherapy response of patients according to the LRS, MRS, and combined score in different treatment types.**

| Variables | LRS, n =261 | | | MRS, n = 261 | | | Combined score (LRS/MRS), n = 261 | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | low LRS | high LRS | *P* | low MRS | high MRS | *P* | 1 (−/−) | 2 (+/−) | 3 (−/+) | 4 (+/+) | *P* |
| **Neoadjuvant therapy** | | | 0.250 | | | 0.061 | | | | | 0.169 |
| CR | 2 (18.2%) | 10 (28.6%) | | 7 (43.8%) | 5 (16.7%) | | 1 (33.3%) | 6 (46.2%) | 1 (12.5%) | 4 (18.2%) | |
| PR | 3 (27.3%) | 16 (45.7%) | | 7 (43.8%) | 12 (40.0%) | | 1 (33.3%) | 6 (46.2%) | 2 (25.0%) | 10 (45.5%) | |
| SD | 2 (18.2%) | 5 (14.3%) | | 2 (12.5%) | 5 (16.7%) | | 1 (33.3%) | 1 (7.7%) | 1 (12.5%) | 4 (18.2%) | |
| PD | 4 (36.4%) | 4 (11.4%) | | 0 | 8 (26.7%) | | 0 | 0 | 4 (50.0%) | 4 (18.2%) | |
| **Adjuvant therapy** | | | 0.052 | | | 0.952 | | | | | 0.494 |
| CR | 0 | 8 (30.8%) | | 4 (28.6%) | 4 (20.0%) | | 0 | 4 (36.4%) | 0 | 4 (26.7%) | |
| PR | 0 | 5 (19.2%) | | 2 (14.3%) | 3 (15.0%) | | 0 | 2 (18.2%) | 0 | 3 (20.0%) | |
| SD | 2 (25.0%) | 6 (23.1%) | | 3 (21.4%) | 5 (25.0%) | | 1 (33.3%) | 2 (18.2%) | 1 (20.0%) | 4 (26.7%) | |
| PD | 6 (75.0%) | 7 (26.9%) | | 5 (35.7%) | 8 (40.0%) | | 2 (66.7%) | 3 (27.3%) | 4 (80.0%) | 4 (26.7%) | |
| **For advanced disease** | | | 0.115 | | | 0.001 | | | | | 0.010 |
| CR | 1 (1.2) | 4 (4.0%) | | 3 (5.8%) | 2 (1.6%) | | 1 (6.3) | 2 (5.6%) | 0 | 2 (3.2%) | |
| PR | 8 (9.8%) | 19 (19.2%) | | 15 (28.8%) | 12 (9.3%) | | 3 (18.8%) | 12 (33.3%) | 5 (7.6%) | 7 (11.1%) | |
| SD | 24 (29.3%) | 19 (19.2%) | | 13 (25.0%) | 30 (23.3%) | | 6 (37.5%) | 7 (19.4%) | 18 (27.3%) | 12 (19.0%) | |
| PD | 49 (59.8%) | 57 (57.6%) | | 21 (40.4%) | 85 (65.9%) | | 6 (37.5%) | 15 (41.7%) | 43 (65.2%) | 42 (66.7%) | |

CR: complete response, PR: partial response, SD: stable disease, PD: progressive disease.

**Supplementary Table 28. Antibody sources and staining conditions.**

| Markers | Main target | Antibody source | Species | Dilution | DAB dyeing time | Antigen Retrieval | Cellular localization |
|---|---|---|---|---|---|---|---|
| CD3 | Pan T lymphocyte | NeoMarker, clone SP7 | Rabbit monoclonal | 1:300 | 1.0 min | Citrate buffer (pH 6.0) microwave 20min | Membranous |
| CD8 | Cytotoxic T lymphocyte | NeoMarker, clone SP16 | Rabbit monoclonal | 1:200 | 1.5 min | Citrate buffer (pH 6.0) microwave 20min | Membranous |
| CD66b | Myelocyte | BD Pharmingen | Mouse monoclonal | 1:200 | 1.0 min | Citrate buffer (pH 6.0) microwave 20min | Membranous |

min: minute; sec: second. DAB: diaminobenzidine.

**Supplementary Table 29. Imaging Biomarker Standardization Initiative (IBSI) reporting structure of the study.**

| | |
|---|---|
| **Patients** | |
| Region of interest | CT positive lesion in stomach |
| Patient Preparation | Patients were required to drink enough water before CT examination to ensure sufficient distention of gastric cavity in CT images |
| Computed tomography (CT) developing agent | iodinated contrast material |
| **Acquisition and Reconstruction** | |
| Protocol | The acquisition parameters are as follows: 120 kV; 150-190 mAs; 0.5- or 0.4-second rotation time; detector collimation: 8×2.5 mm or 64×0.625 mm; field of view, 350×350 mm; matrix, 512×512. After routine non-enhanced CT, arterial and portal venous-phase contrast-enhanced CT were performed after delays of 28 s and 60 s following intravenous administration of 90 - 100 ml of iodinated contrast material (Ultravist 370, Bayer Schering Pharma, Berlin, Germany) at a rate of 3.0 or 3.5 ml/s with a pump injector (Ulrich CT Plus 150, Ulrich Medical, Ulm, Germany). Contrast-enhanced CT was reconstructed with a reconstruction thickness of 2.5 mm. Portal venous phase CT images (thickness: 2.5 mm) were retrieved from the picture archiving and communication system (PACS) (Carestream, Canada) for image feature extraction because of well differentiation of the tumor tissue from the adjacent tissue. |
| Scanner type | multidetector row CT systems |
| **Delineation** | |
| Software | ITK-SNAP software (version 3.6; www.itksnap.org). |
| ROI definition | Standard 2D ROI tools |
| Number of experts | 2 + 1 (2 experienced radiologists participated in independent delineations, followed by 1 senior radiologist cross-validation if necessary) |
| Reference image | CT |
| **Radiomics feature extraction** | |
| Software | Matlab R2016a (The MathWorks Inc.) |
| Package | radiomics analysis package (https://github.com/mvallieres/radiomics/) |
| Method | Reads the DICOM content of a single directory; Equal-probability quantization on the region of interest (ROI); computes Lloyd-Max quantization on the region of interest (ROI) of an input volume; computes uniform quantization on the region of interest (ROI) of an input volume; applies the intensity normalization scheme; Computation of the smallest box containing region of interest (ROI), if |

| | |
|---|---|
| | necessary (ROIbox); Wavelet band-pass filtering (WBPF); Isotropic resampling; Quantization of intensity dynamic range. |
| Discretization | Bin width and LoG filters |
| Bin width | 25 for CT |
| Kernels of the filter | Gaussian spatial band-pass filter (∇2G) |
| Biomarker set | intensity features, shape features, gray Level Co-occurrence Matrix-based (GLCM) features, gray Level Run Length Matrix-based (GLRLM) features, gray Level Size Zone Matrix-based (GLSZM) features and neighborhood Gray Tone Difference Matrix–based (NGTDM) features. |
| Exclusion criteria | ICC smaller than 0.75 |

## Supplementary References

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