SHORT COMMUNICATION

Comparison of malignancy-prediction efficiency between contrast and non-contract CT-based radiomics features in gastrointestinal stromal tumors: A multicenter study

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Abstract

This work seeks the development and validation of radiomics signatures from nonenhanced computed tomography (CT, NE-RS) to preoperatively predict the malignancy degree of gastrointestinal stromal tumors (GISTs) and the comparison of these signatures with those from contrast-enhanced CT. A dataset for 370 GIST patients was collected from four centers. This dataset was divided into cohorts for training, as well as internal and external validation. The minimum-redundancy maximum-relevance algorithm and the least absolute shrinkage and selection operator (LASSO) algorithm were used to filter unstable features. (a) NE-RS and radiomics signature from contrast-enhanced CT (CE-RS) were built and compared for the prediction of malignancy potential of GIST based on the area under the receiver operating characteristic curve (AUC). (b) The radiomics model was also developed with both the tumor size and NE-RS. The AUC values were comparable between NE-RS and CE-RS in the training (.965 vs .936; P = .251), internal validation (.967 vs .960; P = .801), and external validation (.941 vs .899; P = .173) cohorts in diagnosis of high malignancy potential of GISTs. We

Abbreviations: 2D, two-dimensional; AUC, area under the receiver operating characteristic curve; CE-CT, contrast-enhanced computed tomography; CE-RS, radiomics signature from contrast-enhanced CT; CT, computed tomography; GIST, gastrointestinal stromal tumors; ROI, region of interest

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Gastrointestinal stromal tumors (GISTs) are among the most common subepithelial tumors in the digestive system. Different treatment strategies have been applied to treat GIST, including close follow-up, submucosal endoscopic dissection, endoscopic full-thickness resection, and surgery.\(^1\)\(^2\)\(^3\) Although risk classifications were developed and validated in clinical practice,\(^4\)\(^5\) all of the proposed risk classifications were based on histological examination and were applied postoperatively. On the other hand, endoscopic performance, clinical symptoms, and findings from computed tomography (CT)\(^6\) are useful and typically combined in the GIST preoperative risk stratification for subsequent treatment decision. However, the assessments mentioned above are subjective based on the experience of observers.

Radiomics represents an emerging tool for extracting numerous numerical features from medical images and has gained popularity in cancer diagnosis.\(^7\)\(^8\) Previous studies have identified radiomics features from contrast-enhanced CT (CE-CT) as a superior tool for predicting the malignancy potential of GIST compared with clinical factors.\(^9\)\(^10\)\(^11\) However, whether radiomics features extracted from nonenhanced CT are useful for preoperative GIST malignancy assessment is still unknown. Therefore, we assessed whether radiomics signature from nonenhanced CT (NE-RS) is useful in predicting potentially malignant GIST compared to those from contrast-enhanced CT (CE-RS). We recruited 370 patients with GIST from four hospitals according to the following criteria: (a) patients who had surgeries or endoscopic resections; (b) both conventional CT and arterial phase CE-CT examinations were done within a 15-day period before treatment; (c) GIST diagnosis was carried out with histological and immunohistochemical tests; and (d) all reported clinical and pathological variables were available. Patients who received or were revived with imatinib preoperatively or those with multiple GIST detections were excluded. Ethical approvals were obtained for all four collaborating hospitals. The training cohort consisted of patients diagnosed consecutively between January 2011 and December 2016 in Renji Hospital. The internal validation cohort contained patients from January 2017 to June 2019 in Renji Hospital. The external validation cohort included patients from three hospitals diagnosed between January 2017 and June 2019 in Renji Hospital. We next focused on the NE-RS. With 0.185 selected as the cutoff of NE-RS for diagnosis of the malignancy potential of GISTs, accuracy, sensitivity, and specificity for diagnosis high-malignancy potential GIST was 90.0%, 88.2%, and 92.3%, respectively, in the training cohort. For the internal validation set, the corresponding metrics are 89.1%, 94.9%, and 80.0%, respectively. The corresponding metrics for the external cohort are 84.6%, 76.1%, and 91.0%, respectively. Compared with only NE-RS, the radiomics model increased the sensitivity in the diagnosis of GIST with high-malignancy potential by 5.9% \((P = .025)\), 2.5% \((P = .317)\), 10.5% \((P = .008)\) for the training set, internal validation set, and external validation set, respectively. The NE-RS had comparable prediction efficiency in the diagnosis of high-risk GISTs to CE-RS. The NE-RS and radiomics model both had excellent accuracy in predicting malignancy potential of GISTs.

**KEYWORDS**
gastrointestinal stromal tumor, malignant potential, prediction, radiomics signature

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Table 1

| Clinical characteristic | Training cohort | Internal validation cohort | External validation cohort |
|-------------------------|-----------------|---------------------------|---------------------------|
| Low-malignant            | High-malignant  | P-value                   | Low-malignant            | High-malignant  | P-value                   | Low-malignant            | High-malignant  | P-value                   |
| Age, mean ± SD (years)   | 61.43 ± 11.02   | .709                      | 60.87 ± 10.81            | .965                 | 61.64 ± 10.28            | .506                 | 60.22 ± 10.28            | .124                 | 49 (53.06%)               |
| Sex                      |                 |                           |                           |                      |                         |                      |                           |                       |                           |
| Female                   | 29 (44.62%)    | .798                      | 35 (41.18%)              | .124                 | 16 (88.00%)              | .006                 | 40 (64.49%)              | .006                 | 0 (0)                     |
| Male                     | 36 (55.38%)    | .798                      | 50 (58.82%)              | .124                 | 9 (12.00%)               | (0)                  | 19 (26.67%)              | (0)                  | 0 (0)                     |
| Location                 |                 |                           |                           |                      |                         |                      |                           |                       |                           |
| Stomach                  | 47 (72.31%)    | .002                      | 40 (47.06%)              | .002                 | 3 (12.00%)               | (0)                  | 27 (52.49%)              | (0)                  | 0 (0)                     |
| Nonstomach               | 18 (27.69%)    | <.001                     | 23 (46.23%)              | <.001                | 17 (28.00%)              | <.001                | 33 (58.02%)              | <.001                | 0 (0)                     |
| Size (cm)                | <5              | .002                      | 7 (17.95%)               | .002                 | 7 (17.95%)               | <.001                | 8 (14.10%)               | <.001                | 0 (0)                     |
| ≥5                       | 65 (100%)      | (0)                       | 26 (46.67%)              | (0)                  | 36 (53.75%)              | 31 (46.27%)          |                           |                       |                           |
| Mitotic count            | ≤5              | .002                      | 2 (100%)                 | <.001                | 26 (51.96%)              | <.001                | 2 (100%)                 | <.001                | 0 (0)                     |
|                        | >5              | .002                      | 2 (100%)                 | <.001                | 26 (46.67%)              | <.001                | 2 (100%)                 | <.001                | 0 (0)                     |
|                        | ≤5/50 HPF       | (0)                       | 2 (100%)                 | <.001                | 26 (46.67%)              | <.001                | 2 (100%)                 | <.001                | 0 (0)                     |
|                        | >5/50 HPF       | (0)                       | 2 (100%)                 | <.001                | 26 (46.67%)              | <.001                | 2 (100%)                 | <.001                | 0 (0)                     |

Abbreviations: HPF, high-power field; SD, standard deviation.
Table 2 Performance evaluation of the radiomics models

|                      | Internal validation cohort | External validation cohort |
|----------------------|----------------------------|----------------------------|
|                      | Radiomics signature        | Radiomics signature        |
|                      | Size                       | Size                       |
|                      | Combination                | Combination                |
| TP                   | 37                         | 51                         |
| TN                   | 20                         | 81                         |
| FN                   | 2                          | 16                         |
| FP                   | 5                          | 8                          |
| Recall               | 0.95 (0.81-0.99)            | 0.76 (0.64-0.85)            |
| Precision            | 0.88 (0.74-0.96)            | 0.86 (0.74-0.94)            |
| Accuracy             | 0.89 (0.80-0.96)            | 0.85 (0.78-0.90)            |
| Average precision recall | 0.98                        | 0.94                       |

Abbreviations: FN, false negative; FP, false positive; TN, true negative; TP, true positive.

Because nonenhanced CT is more commonly used for preoperative GIST diagnosis and is similar to CE-CT in prediction efficacy, we focused on the radiomics signature from nonenhanced CT. The optimal threshold of the radiomics signature for GIST malignancy diagnosis was set at the point of the ROC curve with the highest Youden index. Based on this thresholding method, NE-RS cutoff value was set to 0.185. GIST samples with NE-RS exceeding this value were identified as high-malignancy-potential GIST samples, whereas the other samples were identified as low-risk samples. Performance metrics of precision, recall, average precision recall, accuracy, and the confusion matrix were computed for the radiomics signature using this threshold. As shown in Table 2, the precision, recall, accuracy, and average precision recall of the diagnosis of high-malignancy-potential GIST were .88 (95% CI, .74-.96), .95 (95% CI, .81-.99), .89 (95% CI, .80-.96), and .98, respectively, for the internal validation cohort. The corresponding results for the external validation cohort are .76 (95% CI, .64-.85), .86 (95% CI, .74-.94), .85 (95% CI, .78-90), and .94, respectively.

Similar to other studies,


clinical setting, for example, different scanners, systems, or parameters, may explain it.

With the advancement in resection methods, multiple resection methods could be performed for the treatment of GIST, including submucosal endoscopic dissection, full-thickness endoscopic resection, and surgery. However, the choice of the resection method is based on preoperative evaluation of tumors, including evaluation of tumor size, growth pattern, and malignancy. It is recommended that endoscopic resection with choice of submucosal endoscopic dissection or endoscopic full-thickness resection based on the clinical decision should be performed for GIST sized ≤5 cm without high-malignant potential and that GIST sized >5 cm or with high-malignant potential should be resected by surgery. Using our proposed radiomics model, 92.1% of GIST with high malignancy potential and 89.9% of GIST with low malignancy potential were correctly diagnosed and recommended for endoscopic resection.

In this study, radiomics features were extracted for a single two-dimensional (2D) slice with the largest tumor area for each patient. No significant differences have been shown in the diagnostic efficacy between the texture analysis obtained from a single-slice 2D slice versus a three-dimensional volume. Segmentation of single-slice 2D images could also save time compared with volumetric segmentation. In our study, a high AUC of .94 or more
Figure 1  A, Schematic diagram of the proposed workflow. Based on the malignant potential profile, tumor area segmentation and feature extraction were performed. GIST patients were categorized into training, internal validation, and external validation cohorts. The training cohort data were subjected to further downstream processing and clinical tests. B, Receiver operating characteristic curves of the NE-RS in predicting malignancy potential of GIST for the cohorts of internal validation and external validation. C, ROC curves of the CE-RS in predicting malignancy potential of GIST for the cohorts of internal validation and external validation. Abbreviations: AUC, area under the receiver operating characteristic curve; CE-RS, radiomics signature from contrast-enhanced computed tomography; GIST, gastrointestinal stromal tumors; NE-RS, radiomics signature from nonenhanced computed tomography.
was found for the diagnosis of GIST with high-malignancy potential in all three independent cohorts. Also, radiomics scores built from single-slice 2D ROIs of CE-CT achieved similar predictive accuracy compared to those from volumetric ROI of CE-CT, in diagnosing GIST with high malignancy potential.\(^{10,11}\) It confirmed that the single-slice-based 2D radiomics model might be feasible for the diagnosis of cancer-related tumors.

The present work has some limitations. First of all, the dataset collection was done retrospectively. Thus, selective bias could not be eliminated. Nevertheless, patients were consecutively enrolled for bias reduction. Prospective studies are needed for the validation of our radiomics signature and model. Second, data heterogeneity bias resulted from CT parameter variations among the collaborating hospitals. Before the extraction of features, this bias was reduced through CT slice normalization and resampling. The z-score method was applied to standardize the training features by their respective means and standard deviations. The AUC of NE-RS did not vary among different hospitals. This demonstrated that our normalization method was reliable. Third, the predictive model did not account for gene mutations. Nevertheless, these variables could not be acquired by preoperative clinical tests and thus were not considered. Further investigations are needed to explore the relationship of gene mutation and radiomics features.

In summary, we have developed and validated the NE-RS with high performance in the diagnosis of GIST with high- and low-malignancy potential and was comparable to the CE-RS. Including tumour size and NE-RS further increased the diagnostic accuracy in predicting GIST with high-malignancy potential to make a preoperatively more precise clinical decision compared to only NE-RS used.

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

The study protocol was approved by the Ethics Committee of the Renji Hospital, Zhongshan Hospital, Sir Run Run Shaw Hospital, and First Affiliated Hospital, Wenzhou Medical University. Informed consent was obtained from each patient before performing CE-CT examination.

**AVAILABILITY OF DATA AND MATERIALS**

The datasets generated and/or analyzed during the current study are not publicly available due personal information involved but are available from the corresponding author on reasonable request.

**CONFLICT OF INTEREST**

The authors declare no conflict of interest.

**AUTHOR CONTRIBUTIONS**

Q-WZ, JL, J-RX, Y-JG, and Z-ZG conceptualized and designed the study. Q-WZ, X-XZ, R-YZ, S-LC, YZ, QL, and JW helped with generation, collection, assembly, analysis, and/or interpretation of the data. Q-WZ, X-XZ, R-YZ, and S-LC drafted and revised the manuscript. Q-WZ, JL, J-RX, Y-JG, and Z-ZG approved the final version of the manuscript.

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**SUPPORTING INFORMATION**

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