Original Article

Computed Tomography Scan and Clinical-based Complete Response Prediction in Locally Advanced Rectal Cancer after Neoadjuvant Chemoradiotherapy: A Machine Learning Approach

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Abstract

Background: Treatment of locally advanced rectal cancer (LARC) involves neoadjuvant chemoradiotherapy (nCRT), followed by total mesorectal excision. Examining the response to treatment is one of the most important factors in the follow-up of patients; therefore, in this study, radiomics patterns derived from pretreatment computed tomography images in rectal cancer and its relationship with treatment response measurement criteria have been investigated. **Methods:** Fifty patients with rectal adenocarcinoma who were candidates for nCRT and surgery were included. The information obtained from the tumor surgical pathology report, including pathological T and N, the degree of tumor differentiation, lymphovascular invasion, and perineural invasion along with radiomics characteristics to each patient, was assessed. Modeling with disturbed forest model was used for radiomics data. For other variables, Shapiro–Wilk, Chi-Square, and Pearson Chi-square tests were used. **Results:** The participants of this study were 50 patients (23 males [46%] and 27 females [54%]). There was no significant difference in the rate of response to neoadjuvant treatment in between age and gender groups. According to the modeling based on combined clinical and radiomics data together, area under the curves for the nonresponders and complete respond group (responder group) was 0.97 and 0.99, respectively. **Conclusion:** Random forests modeling based on combined radiomics and clinical characteristics of the pretreatment tumor images has the ability to predict the response or non-response to neoadjuvant treatment in LARC to an acceptable extent.

Keywords: *Computed tomography, neoadjuvant chemoradiation, radiomics feature, rectal cancer*

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Introduction

Colorectal cancers are of the most common cancers and of major causes of cancer death in developing countries. These cancers were the third most common malignancy diagnosed and the second cause of death due to cancer in 2020, as the incidence of approximately 1.9 million people and the death of 0.9 million people in that year were attributed to this cancer, globally.[1] Due to the known risk factors of these cancers, such as obesity, reduced activity, consumption of red meat, alcoholic beverages, and tobacco; its incidence has increased in recent years in developing countries, including Iran.[2] The main treatment of nonmetastatic rectal cancer is surgical resection.[3,4] This surgery should include a safe normal tissue margin of the primary tumor as well as regional lymph nodes. Treatment of locally advanced rectal cancer (LARC) is challenging due to necessity of invasive surgery which results in severe morbidity. Therefore, accurate clinical staging of the tumor before surgery and as well as performing other treatment modalities naming chemotherapy and radiotherapy, along with surgery leads to improvement of treatment results and reduction of complications. Based on the available evidence and studies, the accuracy of magnetic resonance imaging (MRI) and endoscopic ultrasonography (EUS) to determine T and N of the tumor is quite similar, but the less dependence of MRI on the operator, made it modality of choice for clinical staging of rectal cancer.[5-8] This study is based on the features of computed tomography (CT) because it is used for radiation therapy treatment planning. However, in this study, MRI imaging was

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also used to better determine the extension of the tumor. Although many more studies have used MR features, CT can still be used in artificial intelligence (AI) studies.

Evaluating the degree of response to neoadjuvant chemoradiotherapy (nCRT) preoperatively is one of the most important and challenging factors in the treatment of LARC patients. Researchers have not yet found an ideal method to predict pathologic complete response (pCR) following nCRT in the case of LARC in such a way that patient can be exempted from total mesorectal resection surgery by ensuring proper locoregional control.[9-15] In recent years, applying AI with radiomic features obtained from imaging of MRI or CT after nCRT, this approach has been shown to show superior prediction in terms of pCR.

At present omics studies or in general Medomics and specially radiomics, a very bright perspective is put in front of us. The process of radiomics analysis, after acquisition of the images of a sort of cross sectional modality; includes tumor segmentation, extraction of features, modeling and finally, validation. It has been widely reported that radiomics features extracted from CT, MRI, and ^{18}F-fluorodeoxyglucose-positron emission tomography/CT images has been used as potential imaging biomarkers to predict LARC response to nCRT.[16,17] While morphological features are based on tumor shape and size, voxel intensity distribution features are based on first-order statistics. Second-order texture features describe statistical inter-relationships between neighbor voxels and finally higher-order features are extracted after applying transformations on the basic images.[18]

Many machine learning (ML) algorithms can be applied to represent the extracted features for problem solving. Classification algorithms include, but are not limited to, logistic regression, support vector machines (SVMs), deep neural networks (DNNs), artificial neural network, k-nearest neighbor, and random forests (RF).[19,20] Since RF has been used in many studies to predict pCR after nCRT in rectal cancer patients.[21,22]

Despite many studies that have been conducted in the field of predicting the response to treatment in LARC, conducting investigation on predicting treatment output based on CT scan images, which are routinely performed prior to radiotherapy, can help in planning strategies. In one of the latest researches, it was shown that the best results are obtained from the segmentation of the tumor, especially the mesorectum.[23] In current study, we investigated radiomics patterns derived from CT scan images of LARC patients and their relationship with treatment response after nCRT by ML modeling.

Materials and Methods

Patient series

Sixty-eight patients aged 25–75 years, referred to the radiation oncology clinic, between 2019 and 2021 diagnosed with American joint committee for cancer stage II and III rectal adenocarcinoma based on colonoscopy and pathology findings were subscribed. Patients were then planned to receive nCRT followed by surgical resection. The nCRT includes radiation of gross tumor volume (GTV) as well as at risk regional lymph nodes including internal iliac, presacral and distal common iliac chain to total dose of 50.4 Gy, prescribed daily, 5 days of the week; 1.8 Gy/day. Concurrent chemotherapy prescribed to each patient contains capecitabine (825 mg/m^2) taken orally on days of radiation. After 6–8 weeks following nCRT termination, patients were referred for local resection. Because of the fact that elapsed time until surgery and its effect on the pathological response after nCRT treatment is still one of the challenges, controversial, and research topics in rectal cancer,[24-26] so a total of 18 patients were excluded from the study due to significant comorbidity, history of pelvic surgery or radiation, treatment interruption for more than 5 consecutive fractions or intolerability of at least 85% of a prescribed chemotherapy regimen. Among the remaining 50 patients who participated in this study, 23 patients (46%) and 27 patients (54%) were male and female, respectively.

Seven clinical data features included initial T and N of the tumor, sex, tumor grade, lymphovascular invasion, perineural invasion, and age of patients were chosen for ML. Table 1 shows the patient demographics which was used as clinical features in this study.

Image segmentation and feature extraction

On simulation CT images, the rectal GTV for each patient was manually delineated by MRI and EUS guidance by a

Table 1: Summary of patients characteristics

Variables	*n*=50, *n* (%)
Age, mean±SD	57.4±12.6
Female	27 (54)
Male	23 (46)
Clinical T stage	
T2	22 (44)
T3	22 (44)
T4	6 (12)
Clinical N stage	
N0	6 (12)
N1	17 (34)
N2	21 (42)
N3	6 (12)
LVI	0 (38)
	1 (62)
PNI	0 (56)
	1 (44)
Treatment response	
Partial	34 (68)
Complete	8 (16)
No response	8 (16)

SD – Standard deviation; LVI – Lymphovascular invasion; PNI – Perineural invasion

radiation oncologist. All the CT images were imported into open source 3D Slicer software version 4.8.0 (https://slicer.org). Feature selection process was performed yielding mineable data by 3D Slicer software. PyRadiomics toolbox, provided as an extension module in the 3D Slicer software, was utilized to extract the radiomics features (RFs) from the segmented region of interest in CT images. Herein, RFs were derived from original CT images (i.e. no filter applied) as well as after wavelet transform (all combinations of applying either a high-pass or low-pass filter in each of the x-, y-, and z-axis directions). Using the radiomics module, RFs were extracted from CT images, including shape, first-order, Gray-Level Co-occurrence Matrix, Gray-Level Dependence Matrix, Gray-Level Run-Length Matrix, Gray-Level Size-Zone Matrix, and Neighboring Gray-Tone Difference Matrix. A total of 851 RFs was extracted using the original CT images as well as after wavelet decomposition.

Feature selection and classifier model

Over-sampling method was used to duplicate the number of samples (patient). By using Python software (v. 3.9), three groups of data were used for modeling, which includes modeling based on clinical data alone, radiomics data alone, and all characteristics together. After standardization of feature values, the Maximum Relevance Minimum Redundancy (mRMR) algorithm was used as feature selection method.[24]

Finally, patients with complete, partial, and no response were compared using three-class (Multi class) classification and ML method. Random forest algorithm was applied for fitting into the training dataset. We implemented RF algorithm on the Python scikit-learn ML package (version 0.20.4). Seventy percentage of all patients were used for train phase, and 30% were used for test phase in ML modeling.

For the purpose of internal validation, the master training set randomly was split into a train set and a validation set in an 70/30 proportion. The model was trained on the train set, and its performance was assessed on the validation set, with accuracy measured and recorded. This process was repeated 100 times, selecting the model with the highest accuracy as the final model. The corresponding best features used in that model were also retained. Figure 1 shows the flowchart of the modeling for better understanding.

Performance evaluation

The performance of the proposed prediction models was assessed using the testing. The area under the receiver operating characteristic (ROC) curve area under the curve (AUC) was used to quantify the predictive values of the models. In addition, the performance of predictive models was also evaluated for each group of patients using sensitivity, specificity, negative predictive value, positive predictive value, and F1-measure based on the confusion matrices.

Results

Totally, 50 patients were selected to participate in this study. The average (standard deviation) age of the patients was 57.4 (12.6) with a range of 26–75 years [Table 1]. The results of the Shapiro–Wilk test showed that the age variable does not follow a normal distribution in the sample.

Radiomics and clinical data were examined based on the response rate to treatment. The heat map of the variables and their variations including initial T and N, sex, tumor grade, lympho-vascular invasion, peri-neural invasion, and age of patients are shown in Figure 2.

Following nCRT and surgical resection, 34 patients (68%) had a partial response and 8 patients (16%) had complete response. In 8 patients (16%), no response or disease progression occurred following nCRT.

Features selected with maximum relevance minimum redundancy feature selection method

The top 10 mRMR-ranked CT scan image features were selected to train random forest classifier, because using fewer features can efficiently prevent overfitting. Ten independent features which were selected among 851 radiomics features were included: "LargeDependenceEmphasis.3," "SizeZoneNonUniformityNormalized.5," "Median.5," "GrayLevelNonUniformity.26," "Mean.2," "Contrast.13," "SizeZoneNonUniformityNormalized," "10Percentile," "Run Variance.7" and "Interquartile Range.7." All seven clinical features were fed to the ML modeling.

Modeling based on clinical features alone

Clinical data features were analyzed by the modeling of the clinical characteristics based on rate of response to treatment. Figure 3 shows the ROC curve based on clinical feature modeling alone. As it could be figured out, the best prediction was found for the complete response group with the AUC = 0.8.

F1 scores in this model for nonresponders, partial responders, and complete responders were 0.52, 0.37, and 0, respectively. It is conclusive that modeling based on the clinical data alone cannot create a reliable model to predict response to nCRT.

Modeling based on radiomics features alone

In the next step, the above-mentioned 10 features of radiomics were investigated by modeling based on radiomics characteristics, according to the response rate to treatment. Figure 4 shows the ROC curve based on the radiomics feature modeling alone.

F1 scores in this model for none, partial, and complete responders were 0.82, 0.69, and 0.80, respectively. The relationship between the sensitivity and specificity of this model in predicting the response in the three categories

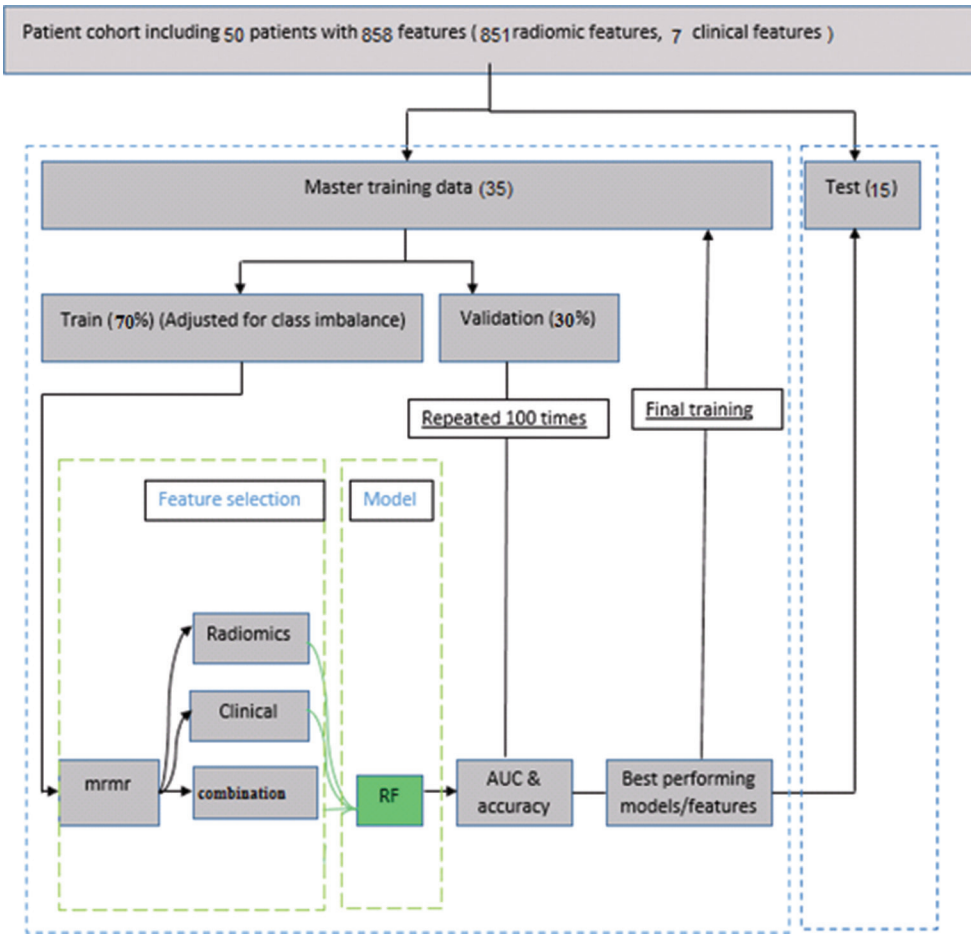

Figure 1: The flowchart of the machine learning modeling and validation process. AUC – Area under the curve; RF – Radiomics feature

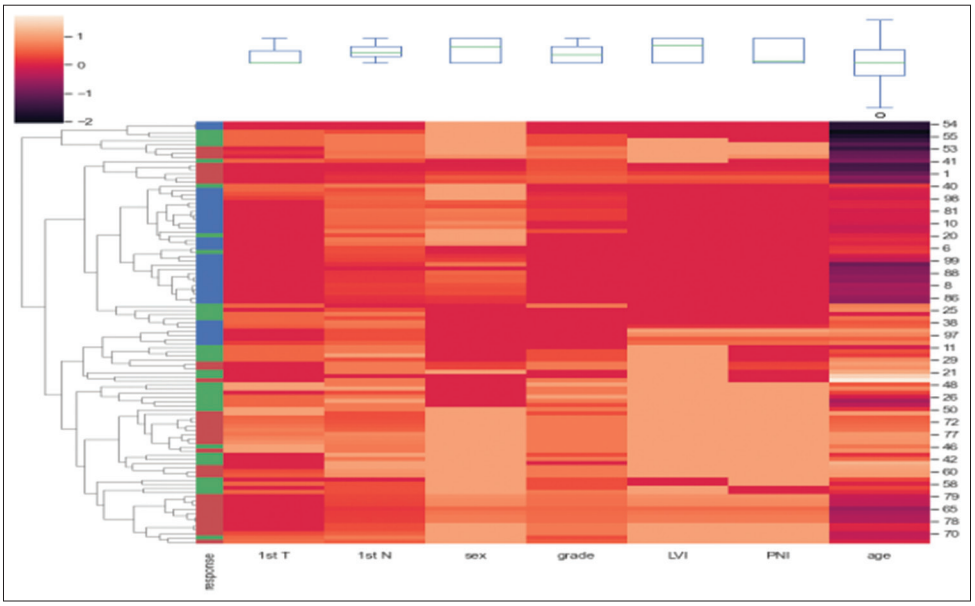

Figure 2: Heat map of radiomics and clinical features correlated to complete response. LVI – lymphovascular invasion; PNI – Perineural invasion

based on the response to treatment is shown in the ROC curve. According to the graph, AUCs related to no response, partial response, and complete response groups were 0.94, 0.83, and 0.99, respectively. In this way, it is concluded that modeling based on radiomics features alone can be reliably predicted only in the complete response group and partially in the group without response to nCRT.

Modeling based on the combination of all features

The last ML modeling was performed according to the all radiomics and clinical features together. Figure 5 shows ROC curves based on all features together. According to these results, it is obviously understandable that the combination of all radiomics and clinical features could yield better prediction of response in all three groups.

Table 2 briefly compares the different scores obtained from all features combination modeling. In this table, the result of three respond categories is shown.

By comparing the evaluation for all groups of different features, it could be found out that by using all feature together, the performance of ML prediction increases. Although because of the weakness of clinical features for prediction, the difference between radiomics features alone and all features is not significant.

Discussion

To preserve the organ in LARC and secure the patient's lifestyle, many studies have shown that using AI and computer models can accurately predict pCR following nCRT. In this study, we explored the feasibility of predicting pCR in LARC patients using radiomics modeling extracted from radiation therapy planning CT images. Based on the results obtained from the present study, modeling based on pretreatment CT radiomics and clinical features of the primary GTV has the ability to predict the presence or lack of response to nCRT in rectal cancer to an acceptable extent.

As shown in Figures 3-5, in modeling from clinical features only to radiomics features only, the statistical results of prediction, precision, and accuracy were greatly improved. Furthermore, by combining these two categories of features together, the findings have become completely more reliable. Eight patients out of 50 (16%) had pCR after resection following nCRT by the disturbed forest model with 80% accuracy. If it is shown that with clinical T stage combined with Laplacian of Gaussian (LoG) transformed intensity features of pretreatment CT and MRI, the best possible result can be obtained.[21] Furthermore, modeling based on radiomics data alone has the ability to predict response to treatment. In contrast, modeling solely based on tumor clinical data was not able to predict the response or lack of response to treatment. However, our finding is similar to Zheng-Yan Li's study, which showed that no differences were found in the clinical variables of sex, age, BMI, TNM stage, CEA, CA199, and lesion area between the responder and nonresponder groups.[22]

In the study of Bibault *et al*., 22 out of 95 rectal cancer patients (23%) had pCR following nCRT.[26] The DNN model predicted complete response with 80% accuracy, which was better than the linear regression model (69.5%) and the SVM model (71.58%). This situation in our study was such that 8 (16%) patients had complete response. An ensemble ML model was estimated to be more accurate

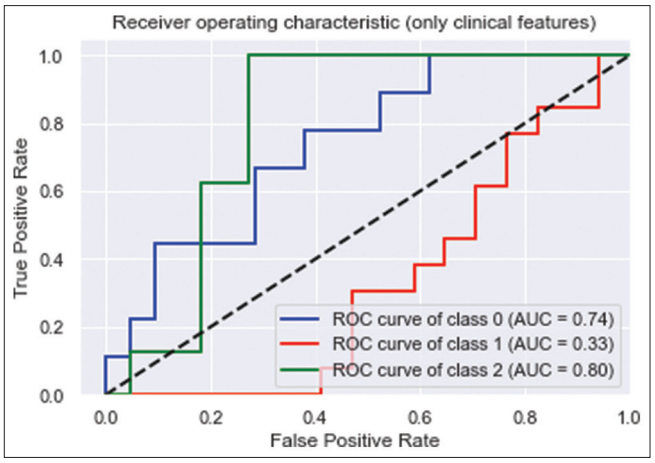

Figure 3: Receiver operating characteristic curve of sensitivity and specificity based on modeling clinical features alone. Blue – No response, Red – Partial response, Green – Complete response

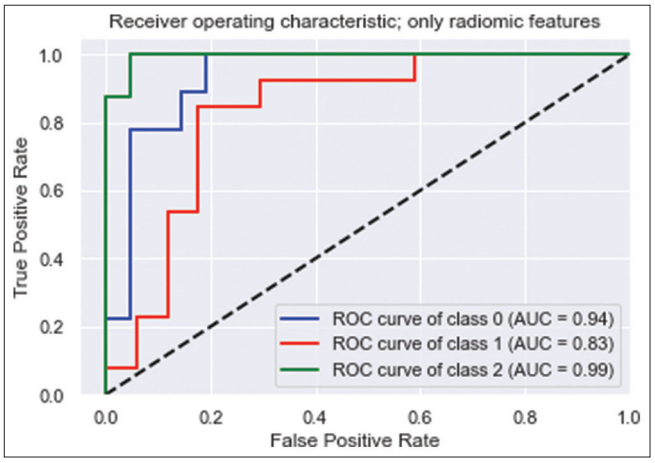

Figure 4: Receiver operating characteristic curve of sensitivity and specificity based on modeling radiomics features alone. Blue – No response, Red – Partial response, Green – Complete response

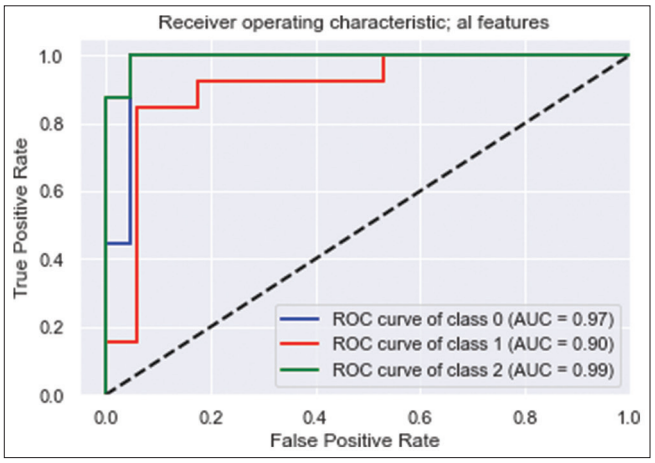

Figure 5: Receiver operating characteristic curve of sensitivity and specificity based on modeling clinical and radiomics features. Blue – No response, Red – Partial response, Green – Complete response

Table 2: Sensitivity, specificity, positive predictive value, negative predictive value, F1 score and area under the curve in modeling based on clinical data and radiomics features to predict treatment response rate

Groups	Response	Sensitivity	Specificity	PPV	NPV	F1 score	AUC
Clinical features alone	No	0.67	0.38	0.43	0.81	0.52	0.74
	Partial	0.38	0.94	0.36	0.5	0.37	0.33
	Complete	0.0	0.91	0.0	0.71	0.0	0.8
RFs alone	No	0.78	0.95	0.87	0.91	0.82	0.94
	Partial	0.61	0.88	0.8	0.75	0.69	0.83
	Complete	1	0.82	0.67	1	0.8	0.99
All features	No	1	0.95	0.9	1	0.94	0.97
	Partial	0.84	0.57	0.91	0.88	0.6	0.9
	Complete	0.87	0.95	0.87	1	0.87	0.99

PPV – Positive predictive value; NPV – Negative predictive value; AUC – Area under the curve; RFs – Radiomics features

(AUC: 0.92 and 0.89 for the training and validation cohorts) than the logistic regression method (AUC: 0.72 and 0.71) for detecting patients who did not respond to nCRT.[25] In our study, in 8 (16%) patients, nonresponse or disease progression occurred after nCRT (AUC: 0.97).

In some studies in this field, reduction of tumor stage was reported. The main outcome measure of the study was the rate of pathologic good response, defined as the sum of tumor regression grade 3 and 4 according to Dworak's classification.[21]

In a more recent study of rectal cancer patients who had nCRT, by using the features of CT images, a model which is based on radiomics and clinical features was obtained that could predict different survival modalities were investigated. This prediction was based on two models of neoadjuvant rectal score of minimum absolute shrinkage and selection operator (LASSO) and survival models.[26] Other approaches have been proposed, including different segmentations in LARC, which showed a complete response of 26.8% with synthetic minority over-sampling technique.[23]

Today, the problems of radiomics analysis even with the same images and with different types of software are the huge number of different features and variables that is produced, since there are no standardized definitions of features with a verifiable number of references.[25,27] This study should be considered as a hypothesis-generating study. Since it has been proved that a physician can just notice about five variables while treating a patient, it is necessary to involve physicists and computer professionals in this field if clinical decision is desired to be made based on radiomics features.[28,29] The current study was conducted with a sample size of 50 patients, which is relatively small. More reliable data can be obtained by increasing the sample size, obviously.

Conclusions

The potential role of radiomics features of CT imaging has been highlighted in recent studies on rectal cancer. We have presented an approach combining pretreatment CT imaging radiomics features with clinical data to build a disturbed forest model, predicting pCR in a single center cohort of patients with LARC treated with nCRT, followed by surgical resection. We found that this combined model properly predicted pCR after nCRT in rectal cancer patients. Finally, the result of the current study could be helpful in treatment escalation in whom a complete response is expected by pretreatment RM features.

Authors' Contribution

Reza Paydar and Seyed Hosein Mousavie Anijdan: Idea development, wrote the main manuscript text, ML and Modeling. Daryoush. Moslemi, Hamid Fallah Taftiand Ali Akbar Moghadamnia: Data gathering and analysis. Reza Reiazi: Reviewing the manuscript and data curation. All authors reviewed the manuscript.

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Conflicts of interest

There are no conflicts of interest.

References

1. Xi Y, Xu P. Global colorectal cancer burden in 2020 and projections to 2040. Transl Oncol 2021;14:101174.
2. Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: Incidence, mortality, survival, and risk factors. Prz Gastroenterol 2019;14:89-103.
3. van Gijn W, Marijnen CA, Nagtegaal ID, Kranenbarg EM, Putter H, Wiggers T, *et al.* Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer: 12-

year follow-up of the multicentre, randomised controlled TME trial. Lancet Oncol 2011;12:575-82.
4. Heald RJ, Karanjia ND. Results of radical surgery for rectal cancer. World J Surg 1992;16:848-57.
5. Rafaelsen SR, Sørensen T, Jakobsen A, Bisgaard C, Lindebjerg J. Transrectal ultrasonography and magnetic resonance imaging in the staging of rectal cancer. Effect of experience. Scand J Gastroenterol 2008;43:440-6.
6. Kim NK, Kim MJ, Yun SH, Sohn SK, Min JS. Comparative study of transrectal ultrasonography, pelvic computerized tomography, and magnetic resonance imaging in preoperative staging of rectal cancer. Dis Colon Rectum 1999;42:770-5.
7. Garcia-Aguilar J, Pollack J, Lee SH, Hernandez de Anda E, Mellgren A, Wong WD, *et al.* Accuracy of endorectal ultrasonography in preoperative staging of rectal tumors. Dis Colon Rectum 2002;45:10-5.
8. MERCURY Study Group. Diagnostic accuracy of preoperative magnetic resonance imaging in predicting curative resection of rectal cancer: Prospective observational study. BMJ 2006;333:779.
9. Habr-Gama A, Perez RO, Wynn G, Marks J, Kessler H, Gama-Rodrigues J. Complete clinical response after neoadjuvant chemoradiation therapy for distal rectal cancer: Characterization of clinical and endoscopic findings for standardization. Dis Colon Rectum 2010;53:1692-8.
10. Smith FM, Chang KH, Sheahan K, Hyland J, O'Connell PR, Winter DC. The surgical significance of residual mucosal abnormalities in rectal cancer following neoadjuvant chemoradiotherapy. Br J Surg 2012;99:993-1001.
11. Guillem JG, Ruby JA, Leibold T, Akhurst TJ, Yeung HW, Gollub MJ, *et al.* Neither FDG-PET Nor CT can distinguish between a pathological complete response and an incomplete response after neoadjuvant chemoradiation in locally advanced rectal cancer: A prospective study. Ann Surg 2013;258:289-95.
12. Perez RO, Habr-Gama A, Gama-Rodrigues J, Proscurshim I, Julião GP, Lynn P, *et al.* Accuracy of positron emission tomography/computed tomography and clinical assessment in the detection of complete rectal tumor regression after neoadjuvant chemoradiation: Long-term results of a prospective trial (National Clinical Trial 00254683). Cancer 2012;118:3501-11.
13. Lambregts DM, Maas M, Bakers FC, Cappendijk VC, Lammering G, Beets GL, *et al.* Long-term follow-up features on rectal MRI during a wait-and-see approach after a clinical complete response in patients with rectal cancer treated with chemoradiotherapy. Dis Colon Rectum 2011;54:1521-8.
14. Perez RO, Habr-Gama A, Pereira GV, Lynn PB, Alves PA, Proscurshim I, *et al.* Role of biopsies in patients with residual rectal cancer following neoadjuvant chemoradiation after downsizing: Can they rule out persisting cancer? Colorectal Dis 2012;14:714-20.
15. Duldulao MP, Lee W, Streja L, Chu P, Li W, Chen Z, *et al.* Distribution of residual cancer cells in the bowel wall after neoadjuvant chemoradiation in patients with rectal cancer. Dis Colon Rectum 2013;56:142-9.
16. Filitto G, Coppola F, Curti N, Giampieri E, Dall'Olio D, Merlotti A, *et al.* Automated prediction of the response to neoadjuvant chemoradiotherapy in patients affected by rectal cancer. Cancers (Basel) 2022;14:2231.
17. Yi X, Walia E, Babyn P. Generative adversarial network in medical imaging: A review. Med Image Anal 2019;58:101552.
18. Shahzadi I, Zwanenburg A, Lattermann A, Linge A, Baldus C, Peeken JC, *et al.* Analysis of MRI and CT-based radiomics features for personalized treatment in locally advanced rectal cancer and external validation of published radiomics models. Sci Rep 2022;12:10192.
19. Ramireddy JK, Sathya A, Sasidharan BK. Can pretreatment MRI and planning CT radiomics improve prediction of complete pathological response in locally advanced rectal cancer following neoadjuvant treatment? J Gastrointest Cancer 2024;55;1199-211. [doi: 10.1007/s12029-024-01073-z].
20. Huang CM, Huang MY, Huang CW, Tsai HL, Su WC, Chang WC, *et al*. Machine learning for predicting pathological complete response in patients with locally advanced rectal cancer after neoadjuvant chemoradiotherapy. Scientific reports. 2020;10:12555.
21. Yi X, Pei Q, Zhang Y, Zhu H, Wang Z, Chen C, *et al.* MRI-based radiomics predicts tumor response to neoadjuvant chemoradiotherapy in locally advanced rectal cancer. Front Oncol 2019;9:552.
22. Wang J, Chen J, Zhou R, Gao Y, Li J. Machine learning-based multiparametric MRI radiomics for predicting poor responders after neoadjuvant chemoradiotherapy in rectal cancer patients. BMC Cancer 2022;22:420.
23. Kaval G, Dagoglu Kartal MG, Azamat S, Cingoz E, Ertas G, Karaman S, *et al.* Evaluating complete response prediction rates in locally advanced rectal cancer with different radiomics segmentation approaches. Pathol Oncol Res 2024;30:1611744. [doi: 10.3389/pore.2024.1611744].
24. Peng H, Long F, Ding C. Feature selection based on mutual information criteria of max-dependency, max-relevance, and min-redundancy. IEEE Trans Pattern Anal Mach Intell 2005;27:1226-38.
25. Zwanenburg A, Vallières M, Abdalah MA, Aerts HJ, Andrearczyk V, Apte A, *et al.* The image biomarker standardization initiative: Standardized quantitative radiomics for high-throughput image-based phenotyping. Radiology 2020;295:328-38.
26. Bibault JE, Giraud P, Housset M, Durdux C, Taieb J, Berger A, *et al.* Deep learning and radiomics predict complete response after neo-adjuvant chemoradiation for locally advanced rectal cancer. Sci Rep 2018;8:12611.
27. Anijdan SH, Reiazi R, Tafti HF, Moslemi D, Moghadamnia AA, Paydar R. Application of Radiomics in Radiotherapy: Challenges and Future Prospects. Caspian Journal of Pediatrics 2022;24:127-40.
28. Abernethy AP, Etheredge LM, Ganz PA, Wallace P, German RR, Neti C, *et al.* Rapid-learning system for cancer care. J Clin Oncol 2010;28:4268-74.
29. Obermeyer Z, Lee TH. Lost in thought – The limits of the human mind and the future of medicine. N Engl J Med 2017;377:1209-11.