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Enhanced MRI Radiomics Based Model for Predicting Recurrence or Metastasis of Nasopharyngeal Cancer (NC) Undergoing Concurrent Chemoradiotherapy: A Retrospective Study

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Abstract

Nasopharyngeal Carcinoma (NC) refers to the malignant tumor that occurs at the top and side walls of the nasopharyngeal cavity. The NC incidence rate always dominates the first among the malignant tumors of the ear, nose and throat, and mainly occurs in Asia. NC cases are mainly concentrated in southern provinces in China, with about 4 million existing NC. With the pollution of environment and pickled diet, and the increase of life pressure, the domestic NC incidence rate has reached 4.5-6.5/100000 and is increasing year by year. It was reported that the known main causes of NC include hereditary factor, genetic mutations, and EB virus infection, common clinical symptoms of NC include nasal congestion, bloody mucus, etc. About 90% of NC is highly sensitive to radiotherapy which is regard as the preferred treatment method; However, for NC with lower differentiation, larger volume, and recurrence after treatment, surgical resection and local protons and heavy ions therapy are also indispensable means. According to reports, the subtle heterogeneity and diversity exists in some NC, with about 80% of NC undergone radiotherapy and about 25% experienced recurrence and death within five years after radiotherapy in China. Therefore, screening the NC population with suspected recurrence after concurrent chemoradiotherapy may improve survival rates in current clinical decision-making.

Plain language summary

NC is one of the prevalent malignancies of the head and neck region with poor prognosis. The aim of this study is to establish a predictive model for assessing NC prognosis using clinical and MR radiomics data.

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NC, also known as nasopharyngeal carcinoma, is a type of cancer that develops in the upper and lateral regions of the nasopharyngeal cavity.[1-4] The NC incidence rate always dominates the first among the malignant tumors of the ear, nose and throat, and mainly occurs in Asia. NC cases are mainly concentrated in southern provinces in China, with about 4 million existing NC. With the pollution of environment and pickled diet, and the increase of life pressure, the domestic NC incidence rate has reached 4.5-6.5/100000 and is increasing year by year. It was reported that the known main causes of NC include hereditary factor, genetic mutations, and EB virus infection, frequent clinical signs of NC comprise stuffy nose, bloody nasal discharge, sore throat, etc. Approximately 90% of patients with NC exhibit remarkable responsiveness to radiation therapy which is regard as the preferred treatment method; However, for NC with lower differentiation, larger volume, and recurrence after treatment, surgical resection and local protons and heavy ions therapy are also indispensable means. According to reports, the subtle heterogeneity and diversity exists in some NC, with about 80% of NC undergone radiotherapy and

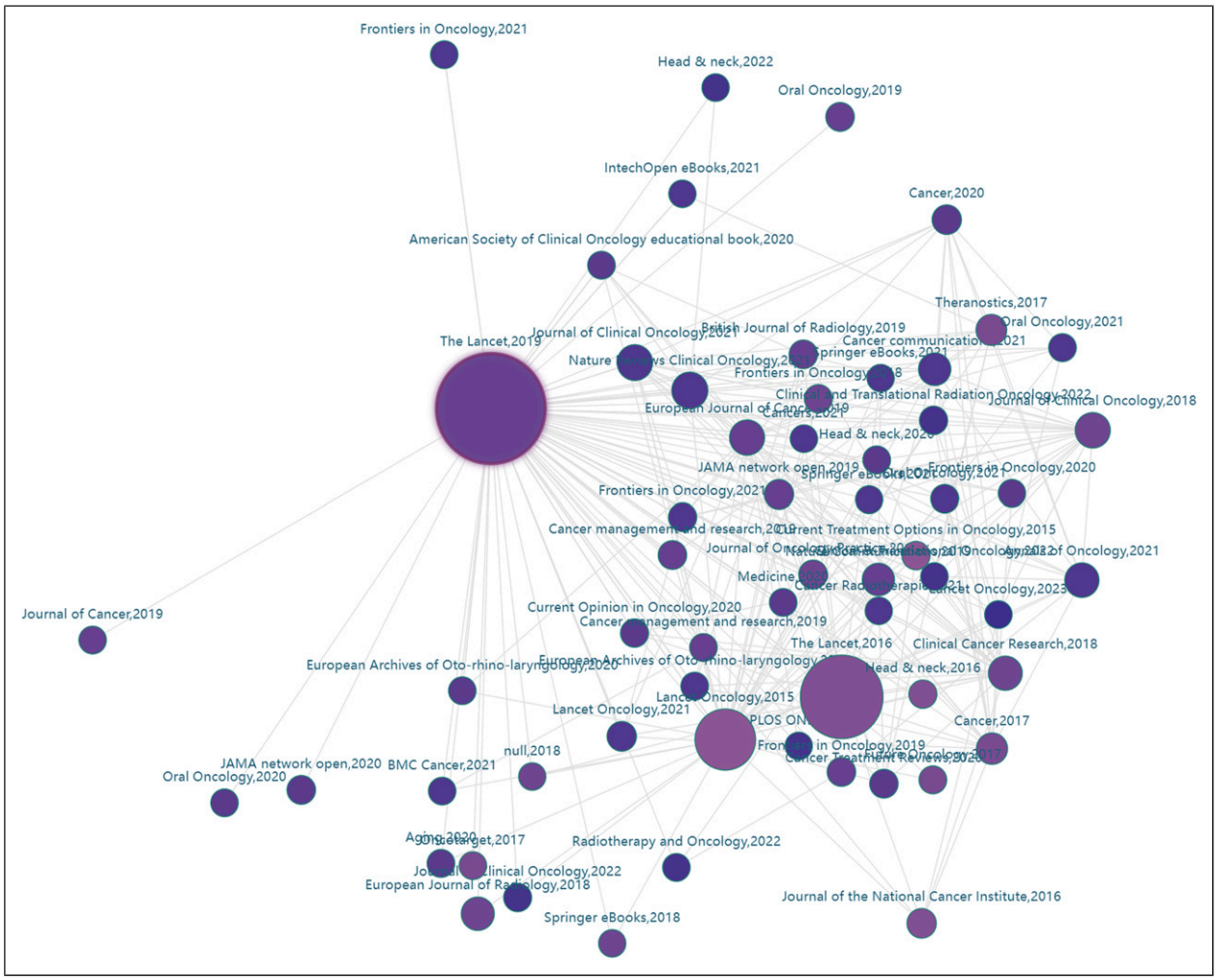

Figure 1. Our team searched 100 highly cited references on NC from 1994 to 2024. From the major content of the search, NC has always been a hot topic of research, but most of it focuses on the molecular mechanisms of tumor metastasis and subsequent treatment management of NC, while there is little research on multimodal radiomics for predicting the recurrence or metastasis of NC. The novelty of this paper is to build an efficient prediction model using the magnetic resonance imaging delta radiomics differences before and after chemoradiotherapy by incorporating clinicopathological data, which has rarely been extensively explored in prior research.

about 25% experienced recurrence and death within five years after radiotherapy in China. Therefore, screening the NC population with suspected recurrence after concurrent chemo-radiotherapy may improve survival rates in current clinical decision-making.[1-4] At present, AJCC guidelines recommend MR as the preferred screening method before NC surgery and after chemoradiotherapy. However, there may be minor defects or missed diagnosis in the interpretation of MR by human naked eyes, and it may also miss out on suspicious subtle signs of MR that cannot be distinguished by the eyes, such as slight thickening and uneven signal of nasopharyngeal soft tissue,etc. As a result, our team has introduced a relatively new method called Delta radiomics in predicting the recurrence or metastasis of NC, leading to a substantial enhancement in performance of the prediction model and NC poor prognosis screening through time-region-related radiomics texture difference analysis.[5-7] We have reviewed the previous references in PUBMED over past 30 years, there have been no topic reports on related research content. In this study, we divided 215 enrolled NC patients as a recurrence or metastasis group (n = 79) and a normal NC cases group (n = 136) via inclusion, exclusion criteria and 5-10 years follow-up, the clinical and enhanced MR data of the above NC cases were collected for retrospective study. And then all NCs were divided into training set and testing set by a time cutoff and 7/3 ratio. Then, three prediction models were established in the training set by incorporating NC clinicopathological data and Delta enhanced MR Radiomics scores. The combined model demonstrated superior predictive ability [AUC:0.880, 95% CI(.818-.927)] compared to both the clinical data model [AUC: 0.660, 95%CI(.579-.735);$P < .05$] and the radiomics model [AUC:0.842, 95%CI(.774-.896); $P = .08$]. The combined model had higher clinical net benefits was also confirmed by decision curve, and next, these same findings were confirmed in the validation set{combined model [AUC:0.848, 95%CI(.735-.926)] excelled over the clinical data model [AUC:0.702, 95% CI(.574-.811),$P = .02$] and radiomics model [AUC:0.786, 95% CI(.664-.878)],$P = .09$}. Finally, the combined nomogram constructed using the combined model also received better clinical use, providing reliable information support for NC clinical treatment decision making and improving NC survival rates (Figures 1-6 & Tables 1-3).[8-11]

This is a single-center, non-prospective and small-sample study, and the results may be subject to selection bias. More clinical and imaging quantitative data are required to additionally verify the model's efficacy. Furthermore, this paper did not include classification screening using multiple machine learning methods and semi-automatic lesion image delineation, which may also affect the study results.

In conclusion, the combined nomogram established derived from Delta MR radiomics shows significant clinical

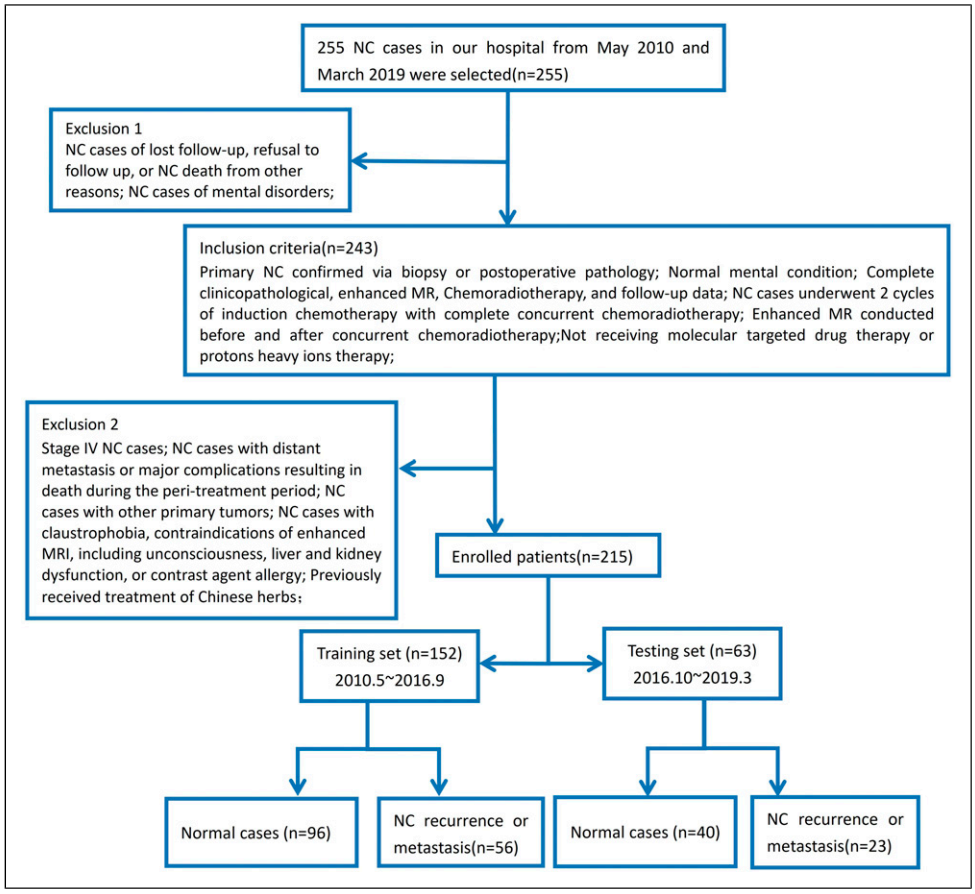

Figure 2. The simplified schematic diagram of NC cases enrollment and grouping in this study.

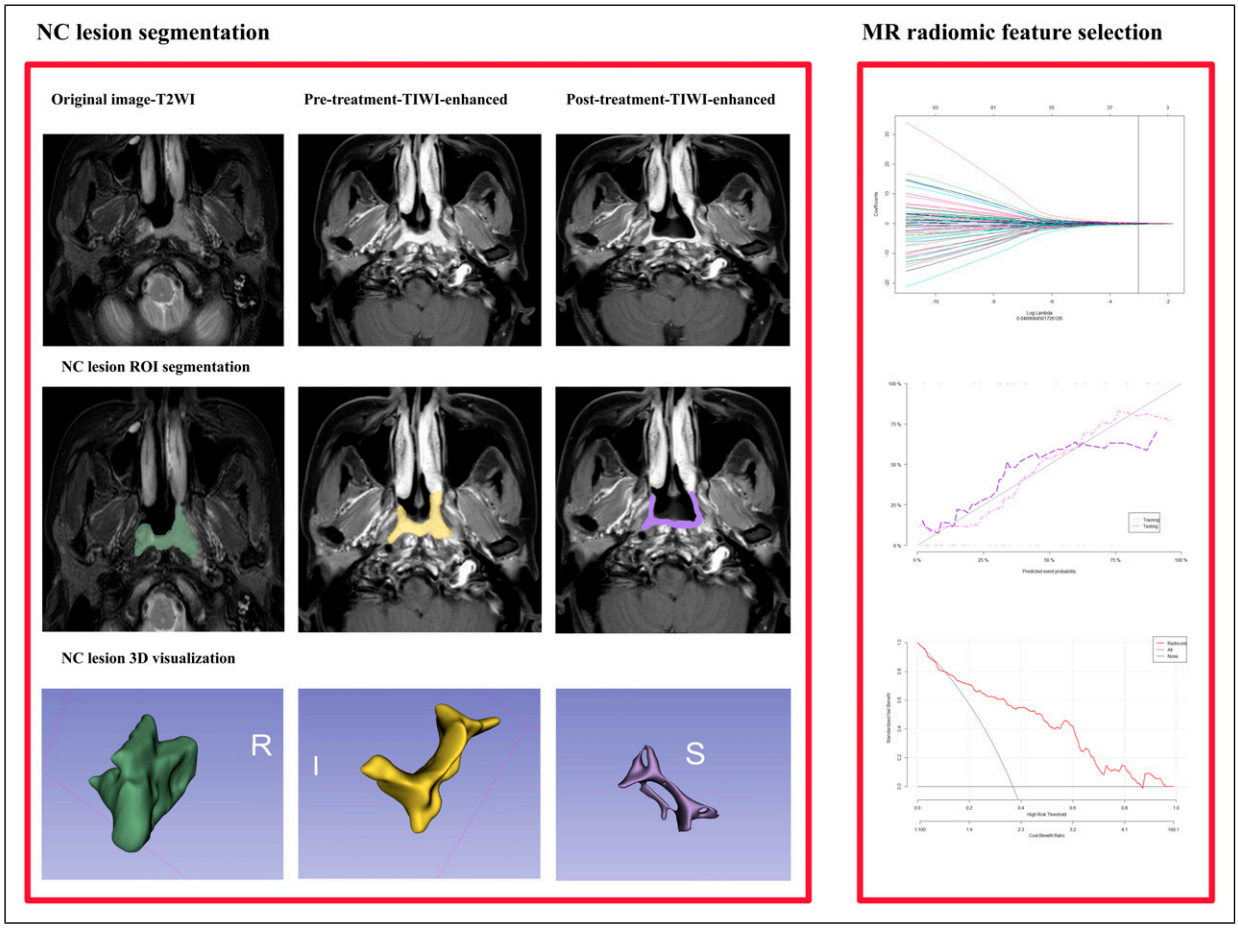

Figure 3. The flow-process diagram of delta enhanced MR radiomic analysis of NC lesion in this study. The depiction on the left illustrated the NC lesion's outline, the delineation of the volume of interest, and the three-dimensional reconstruction; the right figure represented the extraction of NC radiomic texture features and generation of radscore using the method of Least absolute shrinkage and selection operator (LASSO) with 10-fold cross-validation. Notes: Delta radiomic features = enhanced MRI radiomic feature value (after concurrent chemoradiotherapy - before concurrent chemoradiotherapy), and then generate delta radscore.

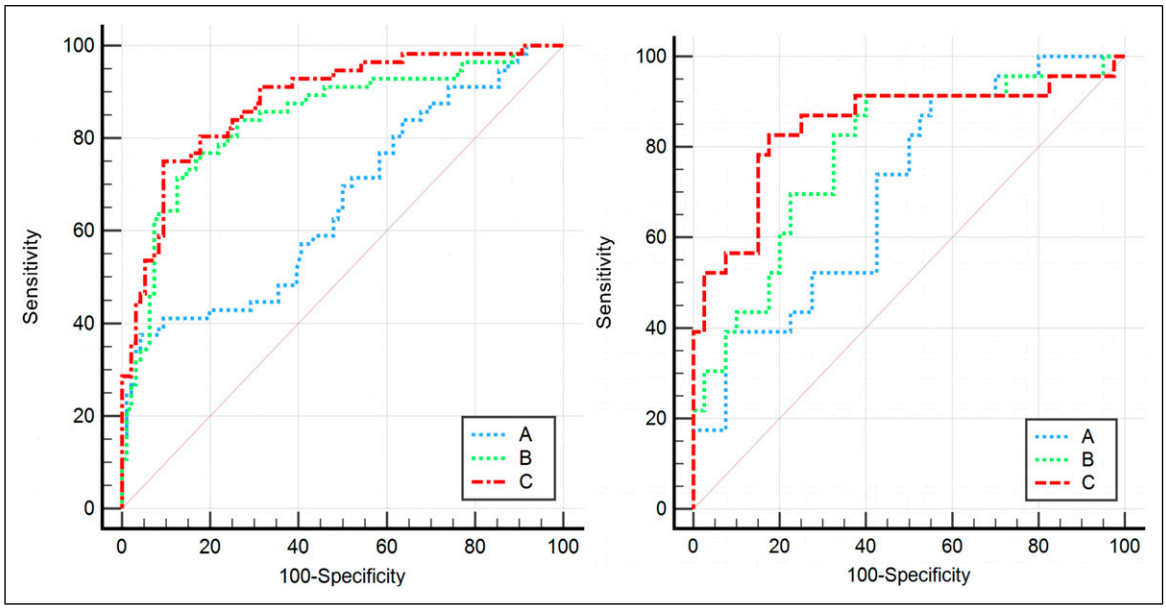

Figure 4. The Delong test curve confirmed that the combined model (C) outperformed both the clinical data model (A) and the radiomics model (B) in terms of predictive performance in both the training (left) and test sets (right). This suggests that integrating all available data sources can lead to more accurate predictions compared to using only clinical or radiomics data alone.

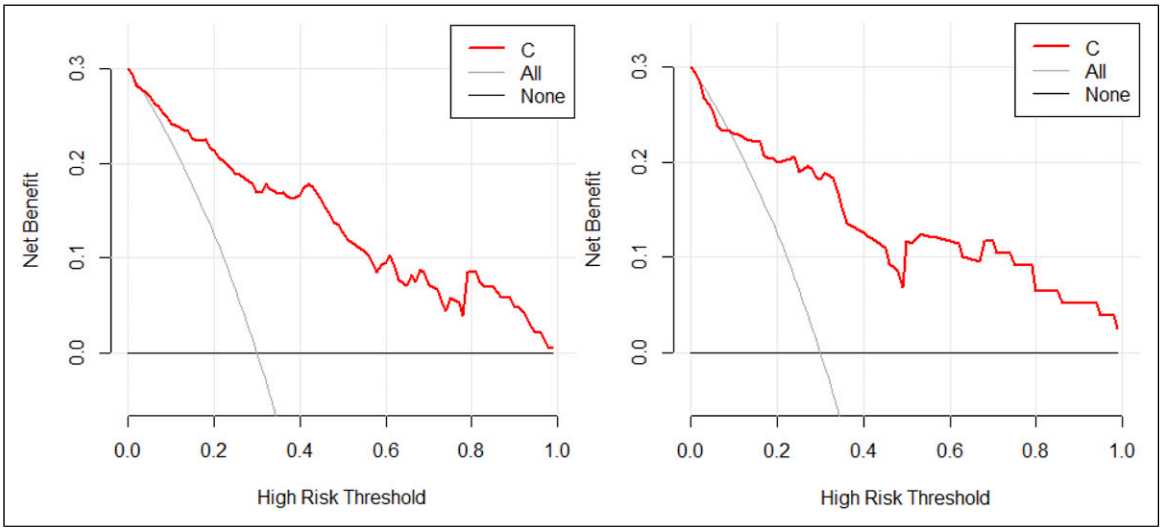

Figure 5. The decision curve confirmed that the combined model (C) demonstrated high predictive accuracy and clinical net benefit in both the training (on the left) and test sets (on the right).

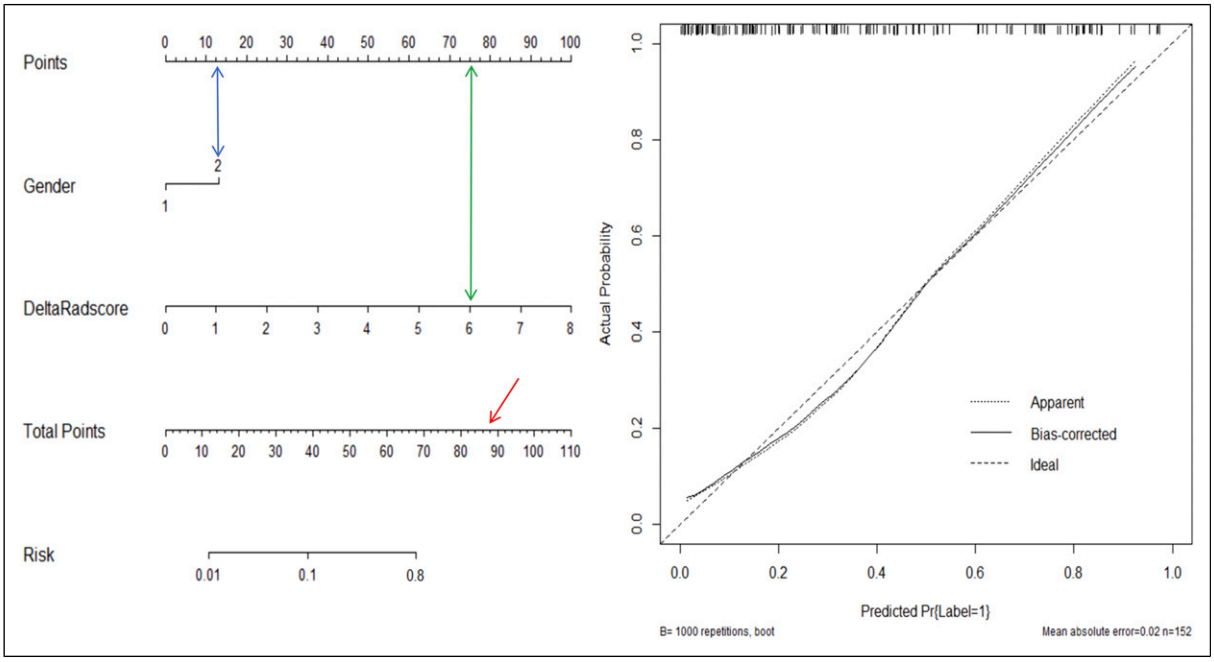

Figure 6. The novel nomogram developed using the screened independent risk factors received better clinical evaluation. We selected a case and scored it according to the nomogram, and compared it with the actual results, explaining the better use and value of the nomogram (Patient 52: Female (nomogram score 13,blue arrow), Delta-Radscore 6 (nomogram score 75,green arrow), a total of 88 nomogram score (red arrow). The nomogram indicates a 90% risk of recurrence, and the recurrence was confirmed by follow up) (left.nomogram, right. calibration curve).

Table 1. The Table Outcomes From Clinical Univariate and Multivariate Logistic Analysis Influencing the Recurrence or Metastasis of NC(Clinical Data Model), *$P < .05$.

Clinical Data Model	Univariate Analysis		Multivariate Analysis	
Factors	*P*	Hazard Ratio	*P*	Hazard Ratio
Age	.13	1.04 (.98-1.09)		
Gender	.03*	2.20 (1.09-4.41)	.03*	2.34 (1.10-4.96)
BMI	.87	1.01 (.93-1.09)		
Smoking history	.08	1.04 (.99-1.10)		
Alcohol use	.21	.97 (.93-1.02)		
Hypertension history	.85	1.01 (.96-1.05)		
Diabetes history	.45	1.02 (.96-1.09)		
Tumor volume	.66	.99 (.97-1.02)		
Peripheral lymph node metastasis	.71	.95 (.72-1.25)		
NC pathological differentiation	.03*	1.91 (1.09-3.37)		
Pathology type	.04*	1.77 (1.01-3.13)		
Clinical stage	.56	1.18 (.68-2.05)		
MR enhanced pattern	.03*	1.67 (1.04-2.70)		
NLR	.04*	1.06 (1.01-1.12)		
WBC	.51	.93 (.75-1.15)		
PLT	.33	1.01 (.99-1.02)		
PLR	.66	1.01 (.96-1.07)		

Table 2. The Table Outcomes From Radiomic Univariate and Multivariate Logistic Analysis Influencing the Recurrence or Metastasis of NC(Radiomics Model), *$P < .05$.

Radiomics Model	Univariate Analysis		Multivariate Analysis	
Factors	*P*	Hazard Ratio	*P*	Hazard Ratio
Delta radscore	<.05*	2.85 (1.99-4.06)	<.05*	2.85 (1.99-4.06)

Table 3. The Table Outcomes From Clinical-Radiomic Univariate and Multivariate Logistic Analysis Influencing the Recurrence or Metastasis of NC(Combined Model), *$P < .05$.

Combined Model	Univariate Analysis		Multivariate Analysis	
Factors	*P*	Hazard Ratio	*P*	Hazard Ratio
Gender	.03*	2.20 (1.09-4.41)	.01*	3.49 (1.33-9.21)
NLR	.04*	1.06 (1.01-1.12)		
Pathology type	.04*	1.77 (1.01-3.13)		
NC pathological differentiation	.03*	1.91 (1.09-3.37)		
MR enhanced pattern	.03*	1.67 (1.04-2.70)		
Delta radscore	<.05*	2.85 (1.99-4.06)	<.05*	3.19 (2.14-4.76)

utility in the prediction of NC recurrence and metastasis, and it is of significance for subsequent clinical decision-making changes and improving survival.

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Author Contributions

All authors conceived and drafted the manuscript, contributed to the literature review and are responsible for collecting and collating clinical data, revised the manuscript critically for important intellectual content. Dr An was responsible for the quality control of article statistics. Dr An, and Dr Ji approved the final version to be published and agreed to act as guarantors of the work. Dr Yu Shang, Junjie Liu, and Lina Song contributed equally to this work.

Declaration of Conflicting Interests

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Ethical Statement

Ethical Approval

This study ethics has been approved by the Human Ethics Committee of Xiangyang No.1 People's Hospital Ethics Committee (approval No.: XYYYE20230090). Our present medical research was conducted according to the principles expressed in the Declaration of Helsinki.

Consent to Participate

We also obtained, written consent from the patient's family.

Consent for Publication

Written informed consent was obtained from the individuals or patient's family.

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Data Availability Statement

All relevant data supporting the conclusions of this article are included within the article.

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