Pre-radiotherapy modified prognostic nutritional index predicts acute radiation enteritis in patients with cervical cancer undergoing radiotherapy: A retrospective study

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Abstract. Acute radiation enteritis (ARE) is a common complication of pelvic radiotherapy in patients with cervical cancer and may adversely affect treatment tolerance and nutritional status. The present retrospective study investigated whether the pre-radiotherapy modified prognostic nutritional index (mPNI), a cholesterol-modified nutritional and immune-related score, is associated with ARE in patients with cervical cancer receiving radiotherapy. A total of 92 patients with pathologically confirmed cervical cancer who completed radiotherapy at Fuyang People's Hospital Affiliated to Anhui Medical University (Fuyang, China) between January 2023 and December 2025 were included. ARE was graded according to the Radiation Therapy Oncology Group acute lower gastrointestinal toxicity criteria, with grade ≥1 ARE defined as the primary endpoint. Sensitivity analyses were conducted using grade ≥2 and grade ≥3 ARE as more clinically relevant endpoints. mPNI was calculated from pre-radiotherapy total cholesterol level, albumin level and total lymphocyte count. During radiotherapy, 67 patients developed grade ≥1 ARE. Pre-radiotherapy mPNI was higher in the ARE group than in the non-ARE group [median, 88.27 (interquartile range, 81.26-97.02) vs. 76.41 (interquartile range, 70.22-80.38); P<0.001]. In the clinically adjusted logistic regression model, a higher mPNI remained significantly associated with grade ≥1 ARE [odds ratio (OR), 1.163; 95% confidence interval (CI), 1.072-1.261; P<0.001]. Sensitivity analyses likewise demonstrated significant associations between mPNI and grade ≥2 ARE (OR, 1.069; 95% CI, 1.023-1.117; P=0.003) and grade ≥3 ARE (OR, 1.071; 95% CI, 1.013-1.133; P=0.016). Receiver operating characteristic curve analysis showed good discriminatory performance for grade ≥1 ARE, with an area under the curve of 0.835 (95% CI, 0.732-0.917), an optimal cut-off value of 80.406, a sensitivity of 79.1% and a specificity of 76.0%. These findings suggest that pre-radiotherapy mPNI may serve as a practical laboratory-based indicator for identifying patients with cervical cancer at increased risk of developing ARE during radiotherapy.

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Introduction

Cervical cancer is one of the most common gynaecological malignancies, with approximately 660,000 new cases and 350,000 deaths estimated worldwide in 2022 (1,2). Radiotherapy is a cornerstone of the multimodal management of cervical cancer and is widely used as postoperative adjuvant therapy for early-stage disease, definitive treatment for locally advanced disease and palliative treatment for selected patients with advanced disease (3,4). Although radiotherapy substantially improves local tumour control in cervical cancer, treatment-related toxicities remain a major clinical concern. Previous studies have reported that nearly 80% of patients with cervical cancer receiving pelvic radiotherapy develop early acute toxicities, whereas ~20% experience late toxicities (5,6).

Acute radiation enteritis (ARE) is one of the most common acute adverse events during pelvic radiotherapy (7,8). ARE not only impairs quality of life but may also lead to treatment interruption or dose reduction, thereby compromising tumour control (9,10). Therefore, reliable biomarkers or clinical indicators that enable early prediction of ARE risk in patients with cervical cancer undergoing radiotherapy are clinically needed, as they may facilitate proactive prevention and individualised intervention to reduce the incidence and severity of ARE.

Accumulating evidence suggests that systemic nutrition-immune indicators, such as the prognostic nutritional index (PNI) (11,12), may be useful for predicting radiotherapy-related toxicities (13,14). The recently proposed modified prognostic nutritional index (mPNI) (15,16), which incorporates serum cholesterol levels, may provide a more comprehensive laboratory-based profile of nutritional status, immune function and metabolic reserve than the conventional PNI. However, its predictive value for ARE during radiotherapy in patients with cervical cancer remains unclear. Accordingly, the present study aimed to investigate the association between pre-radiotherapy mPNI and the development of ARE in patients with cervical cancer, thereby providing preliminary

evidence for early identification and clinical intervention in high-risk populations.

Patients and methods

Patient selection. In the present retrospective study, 98 patients with cervical cancer who underwent radiotherapy at Fuyang People's Hospital (Fuyang, China) between 1 January, 2023, and 31 December, 2025, were initially screened. A total of 6 patients were excluded as they did not complete the prescribed course of radiotherapy. The final cohort comprised 92 female patients, with a median age of 59 years (range, 32-84 years). The requirement for informed consent was waived due to the retrospective nature of the study. This study was approved by the Ethics Committee of Fuyang People's Hospital (approval no. 2026-22).

Inclusion criteria. The inclusion criteria were as follows: i) Pathologically confirmed cervical cancer; ii) a diagnosis of International Federation of Gynecology and Obstetrics (FIGO) stage IB-IV disease (17), with planned definitive radiotherapy or postoperative adjuvant radiotherapy; and iii) a Karnofsky performance status (18) score of ≥70.

Exclusion criteria. The exclusion criteria were as follows: i) Incomplete clinical, laboratory or radiotherapy planning data; and ii) failure to complete the prescribed course of radiotherapy for any reason.

Computed tomography (CT) simulation. All patients were instructed to empty their bladder and bowel in the morning and to drink 800 ml water before simulation. CT simulation was performed after adequate bladder filling, indicated by a clear sensation of urinary urgency. The procedure was conducted by two experienced radiotherapists. Patients were placed in the supine position and underwent CT simulation using a large-bore CT simulator (Somatom go.Sim; Siemens AG). The scanning range extended from the superior border of the 11th thoracic vertebra to 5 cm below the ischial tuberosities, with a slice thickness of 3 mm.

All CT images were transferred to the Monaco treatment planning system (version 5.11; Elekta Instrument AB). Target volumes and organs at risk (OARs) were delineated according to the recommendations of the Radiation Therapy Oncology Group (RTOG) (19) and relevant dose constraints for OARs. Delineation was performed with reference to magnetic resonance imaging and contrast-enhanced CT findings, including the primary cervical lesion, local tumour extension and metastatic lymph nodes. Target delineation was performed by an attending radiation oncologist and jointly reviewed by a senior physician with the title of associate chief physician or above.

Target design and dosimetric requirements. The planning target volume (PTV) was defined as the clinical target volume with a 3-cm extension in the superior and inferior directions. Treatment plans were generated using the Monaco treatment planning system. A seven-field intensity-modulated radiotherapy (IMRT) plan was designed using 6-MV photon beams. At least 95% of the PTV was required to receive the prescribed dose, and dose hotspots outside the PTV were not allowed to exceed 110% of the prescription dose.

The OARs included the rectum, bladder, spinal cord, bilateral femoral heads, colon and small intestine. The bowel bag was defined as the intestinal region encompassing the entire small and large bowel, excluding the rectum and anus. Dose-volume histogram (DVH) (20) parameters were used to calculate the volumes of the bowel bag and rectum receiving doses of ≥40, ≥45 and ≥50 Gy, denoted as V40, V45 and V50, respectively. These DVH parameters were recorded as relative volumes (%).

Treatment delivery. All patients received external-beam radiotherapy with 6-MV X-rays. The total prescribed dose to the target volume was 45-54.4 Gy, delivered to 95% of the PTV in 25 fractions, once daily, at five fractions per week, with a fractional dose of 1.8-2.0 Gy. Positive metastatic lymph nodes could receive a simultaneous integrated boost of up to 59.94 Gy. For patients with para-aortic or common iliac lymph node metastases, extended-field irradiation was administered when clinically indicated. The use of concurrent chemotherapy was determined according to clinical stage, risk stratification and overall patient condition.

Assessment criteria for ARE. An ARE diagnosis was based on clinical manifestations, endoscopic findings and imaging features, after exclusion of infectious and other non-radiation-related intestinal disorders. ARE was graded according to the RTOG acute radiation morbidity scoring criteria (19).

ARE was evaluated according to the RTOG acute lower gastrointestinal toxicity criteria (19) as follows: Grade 0, no obvious intestinal symptoms; grade 1, mild changes in bowel habits, increased stool frequency or rectal discomfort without medication; grade 2, diarrhoea requiring medication, mucus discharge, or abdominal or rectal pain requiring analgesics; grade 3, severe diarrhoea requiring parenteral support, marked mucus or bloody discharge, or abdominal distension with radiographic evidence of bowel dilatation; grade 4, severe complications, such as obstruction, fistula, perforation, transfusion-requiring bleeding, or symptoms requiring decompression or diversion; and grade 5, death related to intestinal toxicity.

The primary endpoint was grade ≥1 acute lower gastrointestinal toxicity during radiotherapy. As grade 1 toxicity may be mild and of limited clinical significance, the distribution of RTOG grades was summarized. Sensitivity analyses using grade ≥2 and grade ≥3 endpoints were performed to evaluate more clinically meaningful toxicity.

Calculation of the mPNI. The mPNI was calculated using the following formula: mPNI=4.8 x total cholesterol (mmol/l)-1.5 x albumin (g/l)-7.7 x total lymphocyte count ($x10^9$/l) + 126 (21).

The directionality of this score differs from that of conventional PNI, which is usually calculated from serum albumin and lymphocyte count with positive coefficients. In the formula used in the present study, lower albumin and lower lymphocyte count increase mPNI, but higher cholesterol also increases mPNI. Therefore, a higher mPNI should be interpreted as a less favourable cholesterol-modified nutrition-immune-metabolic profile, rather than better nutritional status.

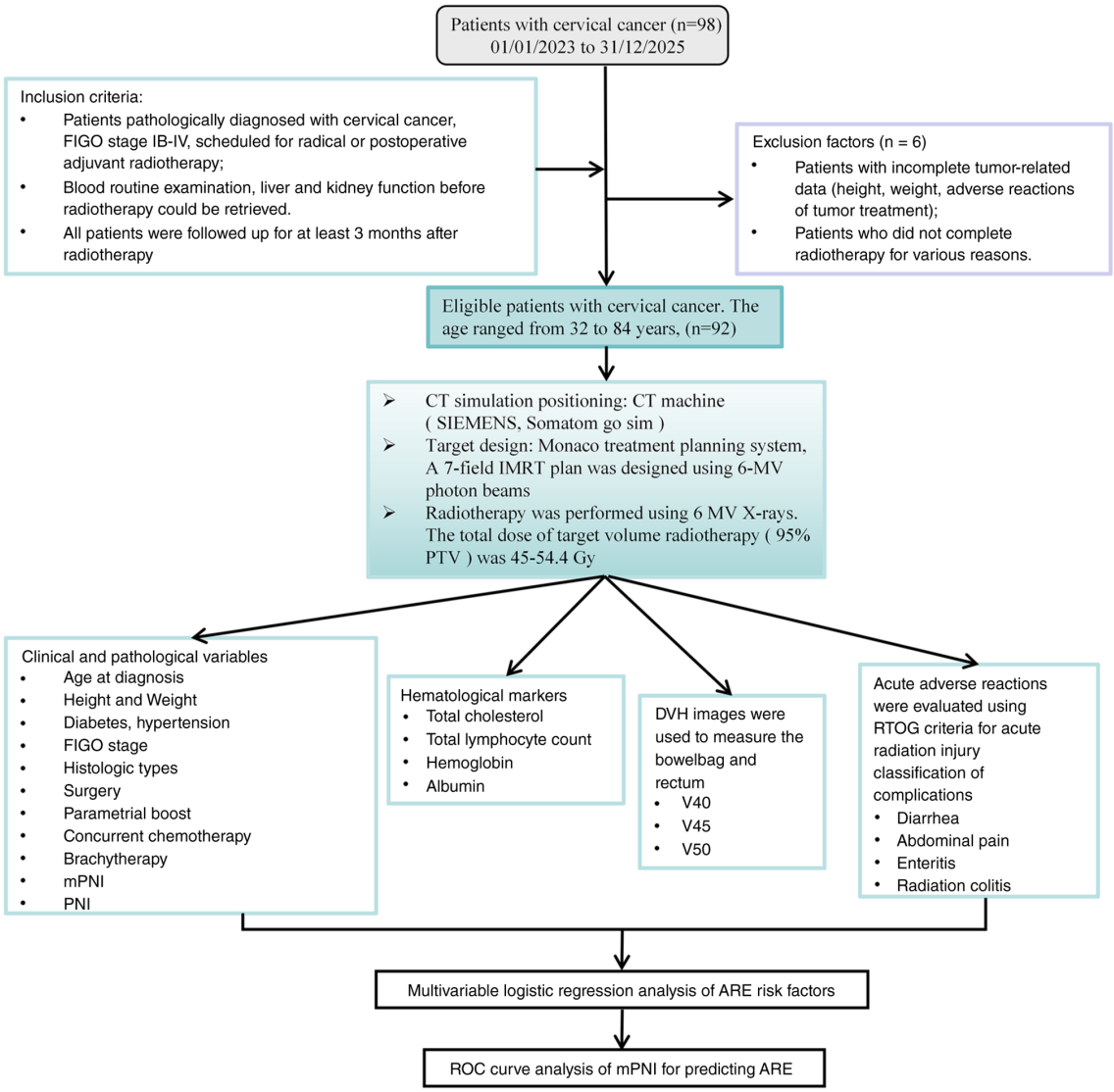

Figure 1. Patient selection and study design. FIGO, International Federation of Gynecology and Obstetrics; CT, computed tomography; IMRT, intensity-modulated radiotherapy; PTV, planning target volume; mPNI, modified prognostic nutritional index; DVH, dose-volume histogram; RTOG, Radiation Therapy Oncology Group; ROC, receiver operating characteristic; ARE, acute radiation enteritis; V40, relative volume (%) receiving at least 40 Gy.

Conventional PNI was calculated for comparison as albumin (g/l) + 5 x total lymphocyte count (x10^9/l).

Statistical analysis. All statistical analyses were performed using SPSS software (version 26.0; IBM, Corp.). Continuous variables were first assessed for normality. Normally distributed continuous variables are presented as the mean ± standard deviation, and comparisons between two groups were performed using the independent-samples t-test. Non-normally distributed continuous variables are expressed as the median (interquartile range) and were compared using the Mann-Whitney U test. Categorical variables are presented as the frequency (percentage), and between-group comparisons were performed using a χ^2 test or Fisher's exact test, as appropriate.

Multivariable logistic regression analysis was used to identify independent risk factors for ARE in patients with cervical cancer receiving radiotherapy. A limited multivariable model that included FIGO stage and mPNI was first constructed to reassess the original model. A clinically adjusted model was then established to account for clinically relevant confounding factors, including age, FIGO stage, surgery, concurrent chemotherapy, brachytherapy, prescription dose >50 Gy, boost treatment, bowel bag V40 (%) and rectum V40 (%). Due to the limited sample size and potential collinearity among DVH parameters, bowel bag V40 (%) and rectum V40 (%) were selected as representative dosimetric covariates. Sensitivity analyses were performed using grade ≥2 and grade ≥3 ARE as endpoints. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated.

Receiver operating characteristic (ROC) curve analysis was used to evaluate the discriminatory performance of mPNI and associated indicators. The optimal cut-off value was determined using the Youden index. Bootstrap resampling was used to estimate AUC stability and compare paired AUCs. Decision-curve analysis was performed to assess potential clinical usefulness. Two-sided $P<0.05$ was considered to indicate a statistically significant difference.

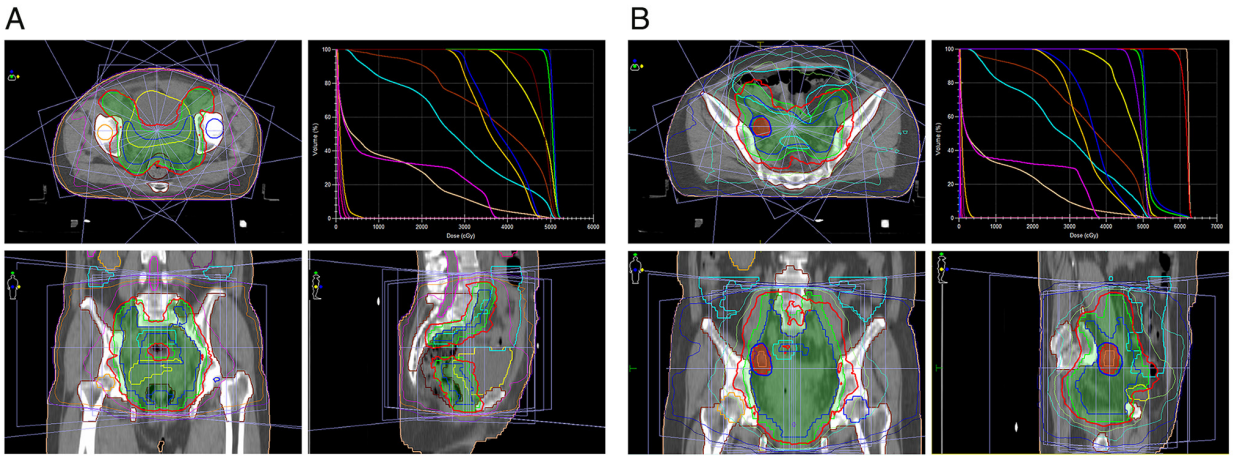

Figure 2. Representative external beam radiation therapy treatment plans in patients with and without ARE. (A) Representative dose distribution and DVH of a patient without ARE. (B) Representative dose distribution and DVH of a patient with ARE. ARE, acute radiation enteritis; DVH, dose-volume histogram.

Results

Incidence of ARE and baseline clinical characteristics of patients with cervical cancer during radiotherapy. Among the 92 eligible patients, 25 did not develop ARE and 67 developed grade ≥1 ARE, corresponding to an incidence rate of 72.8%. The RTOG grade distribution was as follows: grade 0, 25 patients (27.2%); grade 1, 21 patients (22.8%); grade 2, 28 patients (30.4%); grade 3, 18 patients (19.6%); and grade 4/5, 0 patients (0.0%) (Table SI). The patient selection process is shown in Fig. 1.

The FIGO stages ranged from I-IV, with 62 patients having stage I-II disease and 30 having stage III-IV disease. Stage I-II disease was present in 19 patients in the non-ARE group and 43 patients in the ARE group, whereas stage III-IV disease was present in 6 and 24 patients, respectively. This distribution was not statistically significant (Pearson χ^2=1.158; P=0.282). Hypertension and diabetes mellitus were present in 36 and 24 patients, respectively. In total, 63 patients underwent radical surgery for cervical cancer, 33 received brachytherapy after external-beam radiotherapy and 10 received boost treatment, with boost doses ranging from 50 to 59.94 Gy. Concurrent chemotherapy was administered to 55 patients. Before treatment, anaemia was observed in 62 patients. In total, 20 patients received >50 Gy, whereas 72 received ≤50 Gy (Table I).

Univariate analysis of factors associated with ARE during radiotherapy in patients with cervical cancer. The mean pre-radiotherapy mPNI was significantly higher in the ARE group than in the non-ARE group (89.72±11.14 vs. 76.45±8.59; t=-5.381; P<0.001). Conventional PNI was significantly lower in the ARE group than in the non-ARE group [43.60 (39.03-48.33) vs. 47.85 (45.05-51.30); Z=-2.83; P=0.005]. No significant differences were observed in age, BMI, hypertension, diabetes, FIGO stage, surgery, parametrial boost, concurrent chemotherapy, brachytherapy, prescription dose, anaemia or pathological type between the two groups (all P>0.05) Table I.

Association between dosimetric parameters and ARE occurrence. Comparison of radiotherapy dosimetric parameters showed no significant differences in bowel bag V40, V45 or V50, or in rectal V40, V45 or V50 between the ARE and non-ARE groups (P>0.05). These DVH parameters are expressed as relative volumes (%). These findings suggest that, in this cohort, the analysed bowel bag and rectal DVH parameters were not significantly associated with the occurrence of ARE during radiotherapy in patients with cervical cancer. Detailed results are presented in Table II.

Representative external-beam radiotherapy plans from the ARE and non-ARE groups are shown in Fig. 2. In both representative plans, adequate dose coverage of the PTV was achieved and the dose distribution to OARs, including the rectum, small intestine and bladder, met the clinical planning requirements.

Multivariable logistic regression analysis of risk factors for ARE. In the limited multivariable logistic model that included FIGO stage and pre-radiotherapy mPNI, pre-radiotherapy mPNI was significantly associated with grade ≥1 ARE [odds ratio (OR), 1.154; 95% confidence interval (CI), 1.075-1.239; P<0.001], whereas FIGO stage was not independently associated with ARE (OR, 1.477; 95% CI, 0.426-5.126; P=0.539). To address potential confounding by clinically relevant factors, a clinically adjusted model was constructed. Given the limited sample size and potential collinearity among DVH parameters, bowel bag V40 (%) and rectum V40 (%) were selected as representative dosimetric covariates in the clinically adjusted model. In this model, mPNI remained associated with grade ≥1 ARE (OR, 1.163; 95% CI, 1.072-1.261; P<0.001). The principal regression results are summarised in Table III, and the full clinically adjusted model is provided in Table SII.

Sensitivity analyses using more clinically meaningful endpoints showed that mPNI remained associated with grade ≥2 ARE (OR, 1.069; 95% CI, 1.023-1.117; P=0.003) and grade ≥3 ARE (OR, 1.071; 95% CI, 1.013-1.133; P=0.016) in models adjusted for age, FIGO stage, surgery, concurrent chemotherapy, brachytherapy, prescription dose >50 Gy and boost treatment. The grade ≥3 model should be interpreted as exploratory due to the limited number of severe events. Additional details are shown in Table SII.

Table I. Comparison of general data between the non-ARE (n=25) and ARE (n=67) groups.

Clinical features	Non-ARE group	ARE group	χ^2/t	P-value
Mean age ± SD, years	55.12±11.41	59.4±8.91	-1.89	0.062
Mean BMI ± SD, kg/m^2	24.10±3.69	23.87±3.0	0.31	0.761
Hypertension, n (%)				
No	13 (52.0)	43 (64.18)	1.13	0.287
Yes	12 (48.0)	24 (35.82)		
Diabetes, n (%)				
No	18 (72.0)	50 (74.63)	0.07	0.799
Yes	7 (28.0)	17 (25.37)		
FIGO stage, n (%)				
I-II	19 (76.0)	43 (64.18)	1.16	0.282
III-IV	6 (24.0)	24 (35.82)		
Surgery, n (%)				
No	5 (20.0)	24 (35.82)	2.11	0.146
Yes	20 (80.0)	43 (64.18)		
Parametrial boost, n (%)				
No	24 (96.0)	58 (86.57)	0.84	0.359
Yes	1 (4.0)	9 (13.43)		
Concurrent chemotherapy, n (%)				
No	14 (56.0)	23 (34.33)	3.56	0.059
Yes	11 (44.0)	44 (65.67)		
Brachytherapy, n (%)				
No	17 (68.0)	42 (62.69)	0.22	0.636
Yes	8 (32.0)	25 (37.31)		
Prescription dose, n (%)				
≤50 Gy	18 (72.0)	54 (80.60)		
>50 Gy	7 (28.0)	13 (19.40)	0.79	0.374
Anemia, n (%)				
HB <120 g/l	15 (60.0)	47 (70.15)	0.85	0.356
HB ≥120 g/l	10 (40.0)	20 (29.85)		
Pathological type (%)				
Squamous cell carcinoma	24 (96.0)	66 (98.51)	0.00	>0.999
Adenocarcinoma	1 (4.0)	1 (1.49)		
Mean mPNI ± SD	76.45±8.59	89.72±11.14	-5.38	<0.001
Conventional PNI[a]	47.85 (45.05-51.30)	43.60 (39.03-48.33)	-2.83	0.005

[a]Data are presented as median (interquartile range). ARE, acute radiation enteritis; HB, haemoglobin; SD, standard deviation; mPNI, modified prognostic nutritional index; BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics.

ROC curve analysis of mPNI for predicting ARE during radiotherapy in patients with cervical cancer. ROC curve analysis was performed to evaluate the predictive performance of pre-radiotherapy mPNI for ARE in patients with cervical cancer undergoing radiotherapy (22). ROC analysis showed that mPNI had an AUC of 0.835 (95% CI, 0.732-0.917) for grade ≥1 ARE. The optimal cut-off value was 80.406, with a sensitivity of 79.1% and a specificity of 76.0% (P<0.001). The bootstrap mean AUC was 0.835. ROC comparisons with albumin, lymphocyte count, total cholesterol and conventional PNI are shown in Fig. 3 and Table SIII, mPNI had the highest AUC, although its discriminatory performance was close to that of total cholesterol. Apparent calibration of the mPNI logistic model was acceptable in this dataset (Brier score, 0.139; Hosmer-Lemeshow χ^2 value, 3.004; P=0.934). Decision-curve analysis showed that the mPNI model provided a higher net benefit than the treat-all and treat-none strategies across most threshold probabilities from 0.25 to 0.80 (Fig. 4).

Compared with its individual components and conventional PNI, mPNI had the highest AUC, although its discrimination was close to that of total cholesterol. Paired bootstrap comparisons showed that the AUC of mPNI was higher than that of albumin (difference, 0.138; P=0.048), total lymphocyte count (difference, 0.226; P<0.001) and conventional PNI (difference,

Table II. DVH parameters between the non-ARE and ARE groups.

DVH (%)	Non-ARE group (n=25)	ARE group (n=67)	t/Z	P-value
Bowel bag V40	26.05±8.37	25.97±11.49	0.034	0.973
Bowel bag V45	19.62±7.74	17.95±8.66	1.087	0.28
Bowel bag V50	6.67 (1.56-11.56)	3.86 (0.00-18.44)	-1.516	0.124
Rectum V40	90.16±9.29	86.54±16.20	1.053	0.295
Rectum V45	73.33±19.75	67.72±22.22	1.108	0.271
Rectum V50	26.08 (7.94-40.27)	24.75 (0.00-39.89)	-0.485	0.643

Data are presented as mean ± standard deviation or median (interquartile range). Normally distributed variables were compared using the independent-samples t-test, whereas non-normally distributed variables were compared using the Mann-Whitney U test. V40, relative volume (%) receiving at least 40 Gy; DVH, dose-volume histogram; ARE, acute radiation enteritis.

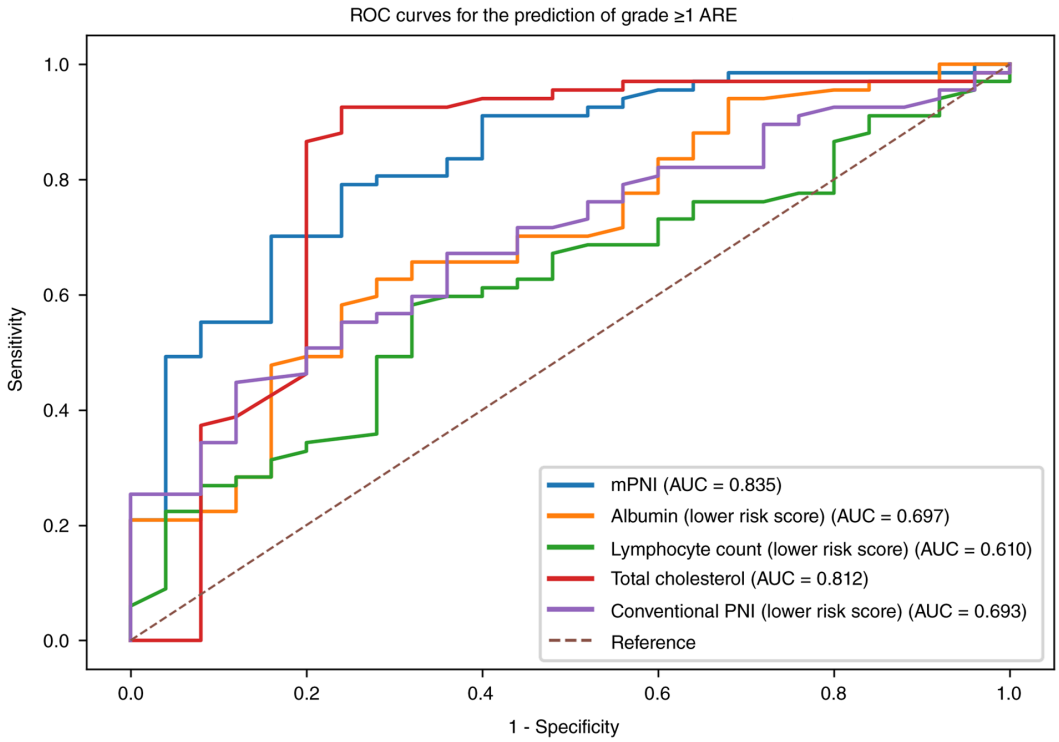

Figure 3. ROC curves for pre-radiotherapy mPNI, albumin, total lymphocyte count, total cholesterol and conventional PNI in predicting grade ≥1 ARE. mPNI, modified prognostic nutritional index; ARE, acute radiation enteritis; ROC, receiver operating characteristic; AUC, area under the curve.

0.143; P=0.022), but was not significantly higher than that of total cholesterol (difference, 0.023; P=0.644). These findings suggest that mPNI may provide additional discriminatory information beyond albumin, lymphocyte count and conventional PNI in this cohort; however, its advantage over total cholesterol alone was not statistically significant.

Discussion

Radiotherapy remains one of the primary effective treatment modalities for the comprehensive management of cervical cancer (23,24); however, its associated toxicities should not be overlooked. ARE is a common adverse reaction during pelvic radiotherapy (25); it typically appears in the second week after the initiation of radiotherapy and peaks at weeks 4-5. In severe cases, ARE may reduce the tolerance of a patient to radiotherapy and even lead to interruption or discontinuation of treatment, thereby adversely affecting tumour control and overall treatment efficacy (26). Previous studies have shown that the occurrence and progression of ARE are associated with radiotherapy technique, total dose, total irradiated volume, fractional dose, dose-volume ratio and the homogeneity of radiation dose distribution (3,5-7). In recent years, IMRT (27) has been used for radiotherapy in gynecological tumours. Although advances in IMRT have reduced the radiation exposure of OARs, ARE is difficult to avoid completely. Therefore, simple pretreatment indicators that can identify patients at increased risk of ARE may help guide individualised monitoring and early supportive intervention.

Table III. Multivariable logistic regression analysis of factors associated with acute radiation enteritis.

Model/variable	OR	95% CI	P-value
Limited model: FIGO III-IV vs. I-II	1.477	0.426-5.126	0.539
Limited model: mPNI	1.154	1.075-1.239	<0.001
Clinically adjusted model: mPNI	1.163	1.072-1.261	<0.001
Grade ≥2 sensitivity endpoint: mPNI	1.069	1.023-1.117	0.003
Grade ≥3 sensitivity endpoint: mPNI	1.071	1.013-1.133	0.016

Clinically adjusted model included age, FIGO stage, surgery, concurrent chemotherapy, brachytherapy, prescription dose >50 Gy, boost treatment, bowel bag V40 (%) and rectal V40 (%). Sensitivity models were adjusted for age, FIGO stage, surgery, concurrent chemotherapy, brachytherapy, prescription dose >50 Gy and boost treatment. CI, confidence interval; OR, odds ratio; FIGO, International Federation of Gynecology and Obstetrics; mPNI, modified prognostic nutritional index.

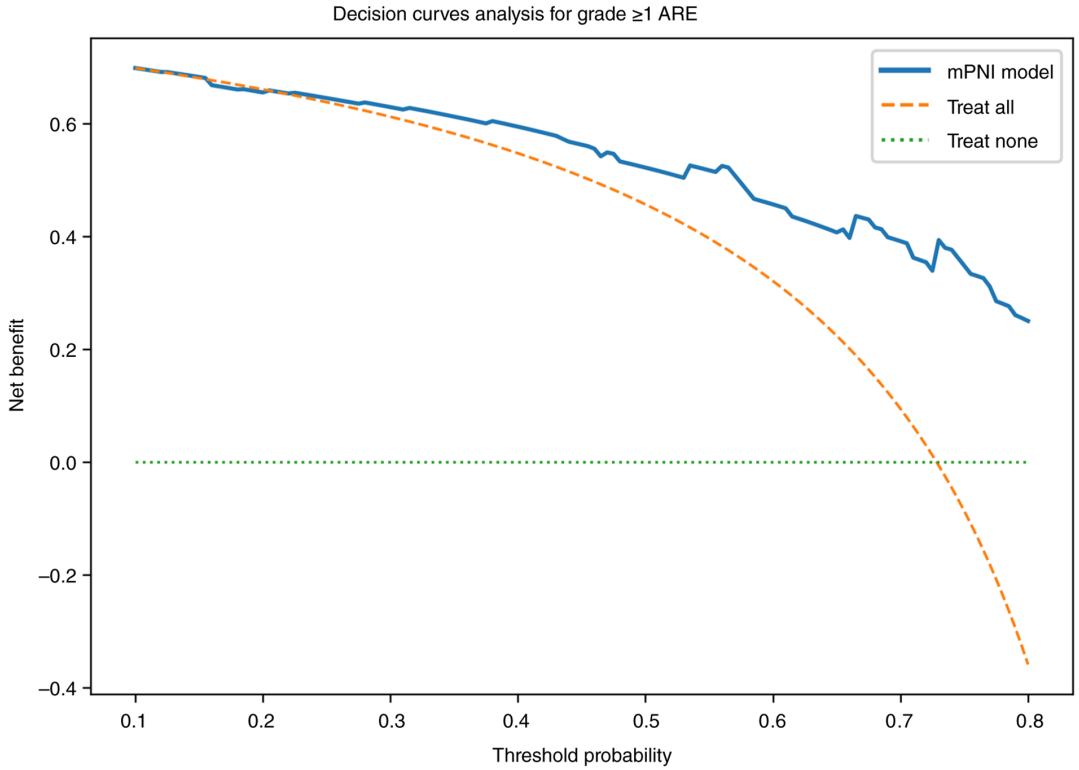

Figure 4. Decision-curve analysis of the mPNI model for predicting grade ≥1 ARE. mPNI, modified prognostic nutritional index; ARE, acute radiation enteritis.

Malnutrition is relatively common in patients with cervical cancer and has clinical significance (28). Impaired nutritional status may weaken immune function, reduce treatment tolerance and increase susceptibility to treatment-related adverse reactions. The PNI, calculated from serum albumin and peripheral blood lymphocyte count, reflects nutritional and immune status to some extent and has been investigated in perioperative and oncological settings, including retroperitoneal sarcoma, as well as in patients with nasopharyngeal and head and neck malignancies undergoing radiotherapy (11-14). The mPNI is an indicator that further incorporates serum cholesterol level based on the traditional PNI. Compared with conventional PNI, mPNI may more comprehensively reflect the nutritional status, immune function and metabolic reserve of patients. Previous studies have shown that mPNI has good predictive value for overall survival and recurrence-free survival in malignant tumours such as colorectal cancer, breast cancer and hepatocellular carcinoma (15,16,21), and that its predictive performance may be superior to that of the original PNI and some traditional nutritional assessment tools, such as the Global Leadership Initiative on Malnutrition criteria (29), the controlling nutritional status score (30) and the nutritional risk index (31). However, evidence regarding the value of mPNI in predicting radiotherapy-related adverse events, particularly ARE in cervical cancer, remains limited.

In the present study, higher pre-radiotherapy mPNI was associated with grade ≥1 ARE in patients with cervical cancer undergoing radiotherapy. As grade 1 toxicity reflects mild bowel habit changes, the use of grade ≥1 ARE as the primary endpoint may partly explain the relatively high incidence of

ARE in the present cohort. However, the association between mPNI and ARE persisted when grades ≥2 and ≥3 endpoints were used, suggesting that the finding was not solely driven by mild events. The grade ≥3 analysis should still be interpreted cautiously due to the limited number of severe events. ROC analysis also showed that pre-radiotherapy mPNI had good discriminatory performance for grade ≥1 ARE, with an AUC of 0.835, an optimal cut-off value of 80.406, a sensitivity of 79.1% and a specificity of 76.0%. The discriminatory performance of mPNI was close to that of total cholesterol, suggesting that cholesterol may have contributed substantially to the predictive signal in this cohort. Nevertheless, mPNI integrates metabolic, nutritional and immune-related information and remained associated with ARE after clinical adjustment. Therefore, it should be interpreted as a composite risk indicator rather than as evidence of superiority over all individual components.

The direction of the mPNI formula should be clearly distinguished from that of conventional PNI. In the formula used in the present study, albumin and lymphocyte count have negative coefficients; therefore, a higher mPNI may indicate a less favourable nutrition-immune-metabolic profile rather than better nutritional status. Patients with poorer nutritional and immune reserves before radiotherapy may have weaker intestinal mucosal repair capacity and may be more susceptible to radiation-induced intestinal injury, more severe symptoms and delayed recovery (32). Therefore, mPNI may serve as a simple laboratory-based indicator for preliminary ARE risk assessment before radiotherapy. For patients with elevated mPNI, closer symptom monitoring, early nutritional evaluation and supportive care may be considered during treatment.

Dosimetric variables are central determinants of intestinal toxicity. In the present study, bowel bag and rectal V40-V50 values were verified as relative volumes (%) and did not differ significantly between the ARE and non-ARE groups. This finding should not be interpreted as excluding the role of dosimetry in ARE. Rather, the available retrospective dosimetric dataset was limited to routinely extracted V40-V50 parameters. Lower-dose intestinal parameters, such as V15, V30 and V35, as well as mean and maximum dose, were not available. Future studies should incorporate more comprehensive DVH parameters and standardised bowel contouring to further clarify the interaction between nutritional status, metabolic indicators and radiation dose distribution.

The present study has several limitations. First, this was a single-centre retrospective study with a relatively limited sample size; therefore, selection bias may have been present, and the stability of the multivariable and predictive analyses requires further validation. Second, although mPNI is an easily obtainable laboratory-based indicator, it cannot replace a comprehensive nutritional assessment. Validated nutritional assessment tools were not used, and data on recent weight loss, dietary intake, nutritional support, prior malnutrition and body composition were unavailable. Third, only pre-radiotherapy mPNI was evaluated, and dynamic changes in nutritional, immune and inflammatory statuses during radiotherapy were not assessed. In addition, albumin and cholesterol levels may be influenced by non-nutritional factors, such as inflammation, infection, lipid-lowering therapy and metabolic disorders. Finally, external validation was not available. Despite these limitations, the present findings support the potential role of pre-radiotherapy mPNI as a practical screening indicator for ARE risk. Future prospective studies should determine whether mPNI-guided nutritional assessment and supportive care can reduce clinically meaningful gastrointestinal toxicity.

In conclusion, pre-radiotherapy mPNI was independently associated with ARE in patients with cervical cancer undergoing radiotherapy, and this association remained consistent when grades ≥2 and ≥3 toxicity endpoints were evaluated. Given that mPNI is derived from routinely available laboratory parameters, it may provide a practical, low-cost approach for pretreatment risk stratification. Incorporating mPNI into clinical assessment may help identify patients who could benefit from closer gastrointestinal toxicity monitoring, early nutritional evaluation and timely supportive intervention during radiotherapy. These findings should be interpreted as associative rather than causal and warrant validation in larger prospective multicentre studies.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WZ designed the study. YZ designed the study, interpreted the clinical data and wrote the manuscript. RH analyzed and interpreted data. WQ and CW conducted the literature search, interpreted data and revised the manuscript. WZ and YZ confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Fuyang People's Hospital (Fuyang, China; approval no. 2026-22). Due to the retrospective nature of the study, the requirement for informed consent was waived.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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