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Original Research

Developing a Pretreatment Risk Stratification Model: A Clinical Prediction Tool for Guiding Prognostic Grouping in Cervical Cancer Patients Undergoing Chemoradiotherapy

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Abstract

Background: Despite many reported pretreatment prognostic factors in cervical cancer patients, no integrated model has been established. This study aimed to evaluate the prognostic significance of established pretreatment factors in cervical cancer patients undergoing concurrent chemoradiotherapy (CCRT) and to develop a simple and practical model for pretreatment risk stratification. **Methods**: Fifty-one patients with cervical cancer treated with CCRT between September 2009 and July 2022 were retrospectively analyzed. The median follow-up period was 74.6 months, and the median patient age was 58 years. Clinicopathological and hematological factors, including age, body mass index (BMI), pathology, hemoglobin (Hgb), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), squamous cell carcinoma antigen (SCC-Ag), and International Federation of Gynecology and Obstetrics (FIGO) stage, were collected. Radiological and metabolic factors were assessed using magnetic resonance imaging (MRI), computed tomography (CT), and fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT), from which the primary tumor volume (pTV) and the maximum standardized uptake value (SUV_{max}) were measured. The prognostic significance of factors for progression-free survival (PFS) and overall survival (OS) was evaluated using the Cox proportional hazards models. **Results**: The 5-year OS and PFS rates were 75.5% and 72.6%, respectively. In univariate analyses, BMI ($p = 0.020$) and FIGO stage ($p < 0.001$) were associated with PFS, while age, pathology, Hgb, NLR, PLR, SCC-Ag, pTV, and SUV_{max} were not. Multivariate analysis identified FIGO stage as the only independent prognostic factor for PFS (hazard ratio [HR]: 4.385; 95% CI: 1.865–10.310; $p < 0.001$). For OS, Hgb ($p = 0.044$), BMI ($p = 0.024$, and FIGO stage ($p < 0.001$) were significant in univariate analyses, whereas BMI (HR: 3.207; 95% CI: 1.157–8.893; $p = 0.025$), and FIGO stage (HR: 3.604; 95% CI: 1.559–8.334; $p = 0.003$) remained significant in the multivariate analysis. The optimal BMI cut-off, determined by the receiver operating characteristic (ROC) analysis, was 21.2 kg/m^2. **Conclusions**: FIGO stage and BMI were the most influential pretreatment factors associated with survival in cervical cancer patients undergoing CCRT. These findings support a straightforward pretreatment risk-stratification approach based on readily obtainable information, intended to assist baseline risk communication rather than guide treatment decisions. External validation in larger, multicenter cohorts is needed to confirm its clinical reliability, but these findings suggest a practical approach to identifying patients with distinct prognostic risks before treatment.

Keywords: cervical cancer; chemoradiotherapy; prognostic factor

1. Introduction

Cervical cancer remains one of the most common malignancies in the world and is still associated with a high risk of death. According to data from the International Cancer Research Institute and the World Health Organization, 604,000 new cervical cancer cases were diagnosed in 2020, resulting in 342,000 deaths [1,2]. The cause of cervical cancer is strongly related to persistent human papillomavirus (HPV) infection, particularly HPV-16 and HPV-18, which together account for the most cases of invasive disease [3]. Early detection of cervical cancer commonly starts with Pap smear screening, followed by biopsy for confirmation and imaging studies for staging [4]. However, despite improvements in screening and HPV vaccination, many patients are still diagnosed at locally advanced stages, indicating that reliable pretreatment markers that can guide clinical decisions are still needed [5] and that cervical cancer remains a major cause of death. When surgery is not an option—often because the disease is too advanced or the patient is not a suitable surgical candidate—the main

treatment strategy shifts to concurrent chemoradiotherapy (CCRT). The definitive radiotherapy (RT) approach typically starts with external beam radiation therapy (EBRT) delivered to the pelvis and is then followed by intracavitary brachytherapy (ICR) to boost the dose directly to the tumor while minimizing exposure to the surrounding healthy tissues [6,7]. When assessing the prognosis of patients with cervical cancer treated with RT, several pretreatment factors are already known to be important. These can be grouped into a few broad categories that clinicians commonly evaluate before starting treatment. The clinicopathological factors included age, body mass index (BMI), clinical stage, and pathology. The hematological and radiological factors, including hemoglobin (Hgb), hematocrit (Hct), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), squamous cell carcinoma antigen (SCC-Ag), primary tumor volume (pTV) or size, are also routinely evaluated. In addition, metabolic factors, including the maximum standardized uptake value (SUV_{max}) in fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (F-18 FDG PET/CT) and, when available, metabolic tumor volume (MTV) and total lesion glycolysis (TLG), provide further insight into the overall disease burden [8–19]. Despite such well-known pretreatment clinicopathological, hematological, radiological, and metabolic factors, their relative prognostic value has not been systematically compared, and no simple model integrating these factors has been established. Therefore, this study aimed to evaluate the prognostic significance of major and readily obtainable pretreatment factors and to develop a practical, clinically applicable risk-prediction score for cervical cancer patients undergoing CCRT.

2. Materials and Methods

2.1 Patient Selection

A total of 51 patients with histologically verified uterine cervical cancer underwent RT at our institution between September 2009 and July 2022. The patients in this study were staged according to the 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system [20]. The study inclusion criteria were: (a) age $\geq$18 years, (b) pathologically confirmed SCC or adenocarcinoma (ADC), (c) FIGO stage IB-IVA without evidence of distant metastasis, (d) Eastern Cooperative Oncology Group performance status of 0–2, (e) receipt of EBRT with concurrent chemotherapy, followed by ICR. The study exclusion criteria were: (a) incomplete clinical records, (b) insufficient or missing pretreatment laboratory or imaging data, (c) incomplete RT, (d) received RT as palliative treatment, (e) prior surgical or therapeutic intervention before CCRT, (f) a previous malignancy in another organ, and (g) evidence of active infection or inflammatory disease (e.g., pneumonia or inflammatory joint disease), or hematologic disorders prior to CCRT.

Clinical factors collected included BMI, pathology, Hgb, NLR, PLR, SCC-Ag, and FIGO stage. Radiological and metabolic factors were evaluated using magnetic resonance imaging (MRI), CT, and PET/CT. The pTV was recorded as the radiological factor, and the SUV_{max} of the primary lesion was used as the metabolic factor.

The BMI and pTV were calculated using the following formulas:

$$\text{BMI} = \text{weight (kg)}/[\,\text{height (m)}]^2$$

$$\text{pTV} = \text{L} \times \text{W} \times \text{H} \times (\pi/6)$$

where L, W, and H represent the maximal tumor length, width, and height, respectively.

2.2 Treatment

All patients first underwent pelvic EBRT delivered with 10- or 15-megavoltage (MV) photon beams using a four-field box technique. Total EBRT doses ranged from 50.4 to 84.9 Gy (median, 59.4 Gy), administered in daily fractions of 1.8–2 Gy, five days per week. Concurrent chemotherapy was given during EBRT for all patients; one patient received weekly carboplatin (290 mg/m^2), whereas the remaining 50 patients received weekly cisplatin (40–60 mg/m^2). In accordance with international guidelines [21,22], cisplatin-based CCRT was used as the standard definitive treatment for all patients with FIGO stages IB2–IVA. Since no patient underwent primary surgery, stage-based variations in surgical management did not apply to this cohort.

After completing a median EBRT dose of 45 Gy, high-dose-rate (HDR) ICR was initiated using a Microselectron HDR system (Ir-192 source; Nucletron, Veenendaal, The Netherlands). Before each ICR session, an MRI or CT was performed to evaluate the most recent tumor response. If marked tumor reduction was observed or if the cumulative EBRT dose indicated that organ at risk (OAR) limits for the rectum, bladder, or bowel could be reached, the ICR fraction dose was adjusted accordingly to remain within safe tolerance levels. These dose modifications were made on an individual basis as part of routine clinical practice. A total HDR-ICR dose of 20–32 Gy (median, 24 Gy) was delivered twice weekly in fractions of 3–5 Gy. No patient received consolidation chemotherapy after completion of CCRT. The primary endpoint included both treatment response and treatment failure, which were assessed by gynecological examination, Pap smear test, cross-sectional imaging (CT or MRI from chest to pelvis), and PET/CT when available.

2.3 Statistical Analysis

All statistical analyses were conducted using R software (version 4.2.1; R Foundation for Statistical Computing, Vienna, Austria). Categorical variables were reported as counts and percentages. For continuous variables, we checked normality with the Shapiro-Wilk test and presented them as median and interquartile range. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan–Meier method, with group comparisons performed via the log-rank test. Continuous variables, including BMI, Hgb, NLR, PLR, SCC-Ag, pTV, and SUV_{max}, were dichotomized according to optimal cut-off values identified through receiver operating characteristic (ROC) curve analysis. The ROC procedure identified thresholds that maximized sensitivity and specificity, and these cut-off points were subsequently applied for classification in the survival analyses. For the PFS analysis, disease recurrence—either locoregional or distant—was defined as the endpoint, whereas death was considered the endpoint for the OS analysis. In this study, univariate analyses were performed using the log-rank test. For the multivariate analysis, prognostic variables were evaluated using Cox proportional hazards regression. Variables with $p < 0.10$ in the univariate analysis were initially considered, and the final multivariable model was selected using a stepwise procedure based on the Akaike Information Criterion (AIC), which identified the model with the best balance between goodness of fit and parsimony. Hazard ratios (HR) and 95% CI were reported, and statistical significance was defined as $p < 0.05$. A risk-based classification model was generated based on β-coefficients from the multivariate analysis. β-coefficients were obtained directly from the multivariable Cox proportional hazards model, which estimates the log-hazard for each prognostic factor. HRs were derived as the exponential transformation of these coefficients [HR = exp(β)]. The β-coefficients from the final multivariable model were used as the basis for assigning points in the risk-score calculation. Model calibration and discriminatory performance were internally validated through bootstrap resampling with 400 replicates (B = 400), which generated bias-corrected estimates for assessing model stability. This approach allowed evaluation of potential overfitting by comparing apparent and bias-adjusted calibration curves. The bootstrap procedure further ensured robustness by repeatedly re-estimating the prognostic model across resampled datasets.

3. Results

The baseline characteristics of the 51 patients are presented in Table 1. The Shapiro–Wilk test results for all continuous variables are provided in **Supplementary Table 1**. The median age was 58 years (range, 37–81 years), and 84.3% of patients were younger than 75 years. Most patients (72.5%) had FIGO stage III or IV disease, and all underwent CCRT.

Table 1. Baseline patient's characteristics.

Characteristics	Number (%)
Pathology	
SCC	48 (94.1)
ADC	3 (5.9)
FIGO stage	
I	3 (5.9)
II	11 (21.6)
III	31 (60.8)
IV	6 (11.7)
Age (years)* median [IQR]	58.0 [51.2–69.5]
<75	43 (84.3)
≥75	8 (15.7)
BMI (kg/m^2)* median [IQR]	22.8 [20.9–25.0]
<21.2	17 (33.3)
≥21.2	34 (66.7)
Hb (g/dL)* median [IQR]	11.7 [9.7–12.8]
<10.2	17 (33.3)
≥10.2	34 (66.7)
NLR* median [IQR]	2.6 [2.0–3.8]
<2.2	33 (64.7)
≥2.2	18 (35.3)
PLR* median [IQR]	161.3 [111.1–212.8]
<170.0	27 (52.9)
≥170.0	24 (47.1)
SCC-Ag* median [IQR]	9.7 [2.3–34.5]
<27.5	34 (66.7)
≥27.5	17 (33.3)
pTV (cm^3)* median [IQR]	74.2 [37.9–121.6]
<35.3	10 (19.6)
≥35.3	41 (80.4)
SUV_{max}* median [IQR]	10.6 [8.2–14.6]
<10.1	23 (45.1)
≥10.1	28 (54.9)

IQR, interquartile range; BMI, body mass index; SCC, squamous cell carcinoma; ADC, adenocarcinoma; FIGO, International Federation of Gynecology and Obstetrics; Hgb, hemoglobin; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; SCC-Ag, squamous cell carcinoma antigen; pTV, primary tumor volume; SUV_{max}, maximum standardized uptake value; *The optimal cut-off for continuous variables was determined using receiver operating characteristic (ROC) curve analysis.

The median follow-up duration was 74.6 months (range, 9.9–156.4 months). The median age of the cohort was 58 years (range: 37–81 years). The 5-year OS and PFS outcomes were 75.5% and 72.6%, respectively (Fig. 1).

3.1 PFS Analysis

In the univariate analysis, age ($p = 0.202$), pathology ($p = 0.843$), Hgb ($p = 0.166$), NLR ($p = 0.210$), PLR ($p = 0.552$), SCC-Ag ($p = 0.444$), pTV ($p = 0.435$), and SUV_{max} ($p = 0.342$) were not associated with PFS. In contrast, BMI

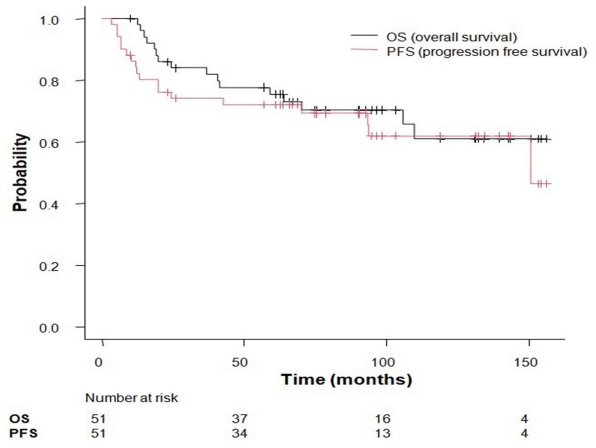

Fig. 1. Kaplan–Meier plots of progression-free survival (PFS) and overall survival (OS).

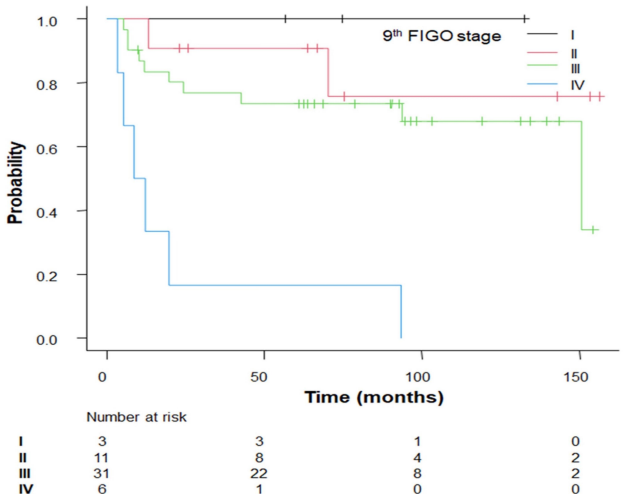

Fig. 2. Kaplan–Meier survival curves for progression-free survival stratified by factor (FIGO stage), demonstrating statistically significant differences.

(p = 0.020) and FIGO stage ($p < 0.001$) were associated with PFS (Table 2). According to the multivariate analysis, FIGO stage (HR: 4.385; 95% CI: 1.865–10.310; $p < 0.001$) was a significant prognostic factor for PFS (Fig. 2) (Table 3).

3.2 OS Analysis

Age (p = 0.284), pathology (p = 0.689), NLR (p = 0.399), PLR (p = 0.470), SCC-Ag (p = 0.231), pTV (p = 0.188), and SUV_{max} (p = 0.269) were not correlated, while Hgb (p = 0.044), BMI (p = 0.024), and FIGO stage ($p < 0.001$) were correlated (Table 2). In the multivariate analysis, BMI (HR: 3.207; 95% CI: 1.157–8.893 p = 0.025), and FIGO stage (HR: 3.604; 95% CI: 1.559–8.334; p = 0.003) showed prognostic significance for OS (Fig. 3) (Table 3). As BMI was the only continuous variable significantly associated with OS, we performed an ROC analysis to determine its optimal cut-off value. The ROC curve for BMI is presented in **Supplementary Fig. 1**.

The results of the univariate analyses for PFS and OS of all factors are summarized in Table 2. A summary of significant and non-significant prognostic factors for both PFS and OS is provided in **Supplementary Table 2**.

3.3 Risk Stratification Model Based on Prognostic Scoring

A prognostic risk score for PFS was developed based on the β-coefficients of the risk factors. In this scoring model applied for PFS, FIGO stage (I, II, III, or IV) was incorporated as a prognostic variable, with points assigned based on stage. FIGO stages I–III were allocated a point of 0, whereas FIGO stage IV was allocated a point of 14. Risk stratification for PFS was categorized as follows: low-risk group (point = 0; n = 45, 88.2%), high-risk group (point = 14; n = 6, 11.8%). The two groups showed a significant difference in 5-year PFS (79.5% [95% CI: 64.20%–88.80%] vs. 16.7% [95% CI: 0.77%–51.70%], $p < 0.001$) (Fig. 4). The prognostic risk score for OS was constructed using the following prognostic factors, with weights assigned accordingly: BMI <21.2 kg/m^2 (assigned a point of 11), and FIGO stage I, II, III, or IV (assigned a point of 0 for stage I–III and 12 for stage IV).

OS risk stratification resulted in three groups: low-risk group (point = 0, n = 31, 60.8%), intermediate-risk group (point = 11, n = 17, 33.3%), and high-risk group (point = 23, n = 3, 5.9%). A statistically significant differences in the 5-year OS rates was found across the three groups: 93.2% [95% CI: 75.7% to 98.3%] for low-risk group, 57.8% [95% CI: 31.1% to 77.3%] for intermediate-risk group, and 0% [95% CI: NA] for high-risk group $p < 0.001$) (Fig. 4).

Table 3 summarizes the multivariate analysis results for all factors related to PFS and OS, along with the resulting risk stratification scoring model.

4. Discussion

In our study, BMI and FIGO stage were significant factors for survival outcomes among patients receiving CCRT for cervical cancer. In our study, the prognostic impact of FIGO stage and BMI was clearly demonstrated by the observed survival differences. Patients with stage I–III had a 5-year PFS of 79.5% and a 5-year OS of 93.2%, whereas those with stage IV showed markedly poorer outcomes, with both 5-year PFS and OS at 16.7%. BMI also showed a significant association with OS, with patients in the higher BMI group achieving a 5-year OS of 87.7% compared with 51.3% in the lower BMI group. Regarding radiotherapy, there was a wide EBRT dose range; however, the higher doses of 84.9 Gy and 70.4 Gy were given only to two patients with bulky pelvic nodal disease, for whom escalation was clinically appropriate while respecting OAR constraints. All other patients received EBRT within the standard range of 50.4–66.6 Gy, and no toxicities were

Table 2. Univariate Log-Rank analysis of progression-free and OS in cervical cancer patients treated with chemoradiotherapy.

Variable	Univariate analysis			
	PFS		OS	
	5-year PFS (95% CI)	*p*-value*	5-year OS (95% CI)	*p*-value*
Age (years)				
<75	69.0% (52.6%–80.7%)	0.202	73.2% (56.8%–84.2%)	0.284
≥75	87.5% (38.7%–98.1%)		87.5% (38.7%–98.1%)	
Pathology				
SCC	72.4% (57.2%–83.0%)	0.843	76.8% (62.0%–86.4%)	0.689
ADC	66.6% (54.1%–94.5%)		66.7% (54.1%–94.5%)	
FIGO stage				
I	100%	<0.001	100%	<0.001
II	90.9% (50.8%–98.7%)		90.9% (53.9%–98.8%)	
III	73.6% (54.0%–85.8%)		80.0% (60.8%–90.5%)	
IV	16.7% (7.7%–51.7%)		16.7% (7.7%–51.7%)	
BMI (kg/m^2)				
<21.2	64.7% (37.7%–82.3%)	0.020	51.3% (25.7%–72.1%)	0.024
≥21.2	85.0% (67.6%–93.5%)		87.7% (70.4%–95.2%)	
NLR				
<2.2	83.0% (55.9%–94.2%)	0.210	83.0% (55.9%–94.2%)	0.399
≥2.2	66.0% (47.0%–79.5%)		71.5% (52.3%–84.0%)	
PLR				
<170.0	73.9% (52.9%–86.6%)	0.552	73.6% (52.4%–86.4%)	0.470
≥170.0	69.8% (46.9%–84.3%)		78.0% (55.0%–90.2%)	
Hgb (g/dL)				
<10.2	58.8% (32.5%–77.8%)	0.166	58.8% (32.5%–77.8%)	0.044
≥10.2	78.8% (60.6%–89.3%)		84.5% (66.6%–93.2%)	
SUV_{max}				
<10.1	72.8% (49.0%–86.8%)	0.342	76.6% (52.5%–89.5%)	0.269
≥10.1	71.2% (50.6%–84.5%)		74.7% (54.1%–87.1%)	
SCC-Ag				
<27.5	79.2% (61.2%–89.5%)	0.444	81.8% (63.9%–91.4%)	0.231
≥27.5	57.0% (30.3%–76.8%)		62.5% (34.9%–81.1%)	
pTV (cm^3)				
<35.3	80.0% (40.9%–94.6%)	0.435	90.0% (47.3%–98.5%)	0.188
≥35.3	70.1% (53.3%–81.8%)		72.0% (55.2%–83.4%)	

* Log-rank test.

observed in those treated with higher doses. Because all patients subsequently underwent HDR brachytherapy, the overall biological dose to the cervix remained relatively consistent, making it unlikely that these dose variations influenced the results of the study.

Previous study has investigated the relationship between BMI and survival outcomes in gynecological cancers. While obesity has traditionally been considered a negative prognostic factor, recent systematic reviews and meta-analyses have shown that a high BMI does not necessarily confer a survival benefit, and in some cases may even be associated with worse overall survival [14]. Additionally, a recent study have also shown favorable outcomes in higher BMI groups; for example, overweight patients demonstrated significantly better survival than both underweight and obese patients [23]. Furthermore, a qualitative study found that some overweight patients reported better tolerance to therapy, especially RT [24]. In another study, cachexia risk stratification using BMI showed shorter survival (median 4.83 months) in the low BMI groups [25]. Consistent with the studies mentioned above, in our study, BMI was significant for PFS and also for OS. The reasons why BMI might be linked to survival prognosis could be explained as follows: nutritional reserves could buffer against treatment-related cachexia [26], altered pharmacokinetics can lead to improved drug tolerance [27,28], earlier detection due to more frequent screening could be performed in some regions [29], hormonal milieu possibly affects tumor growth dynamics differently [30], and sarcopenia, rather than BMI alone, serves as a more decisive prognostic factor for OS. Patients with higher BMI and preserved muscle mass tend to exhibit more favorable clinical outcomes [28,31].

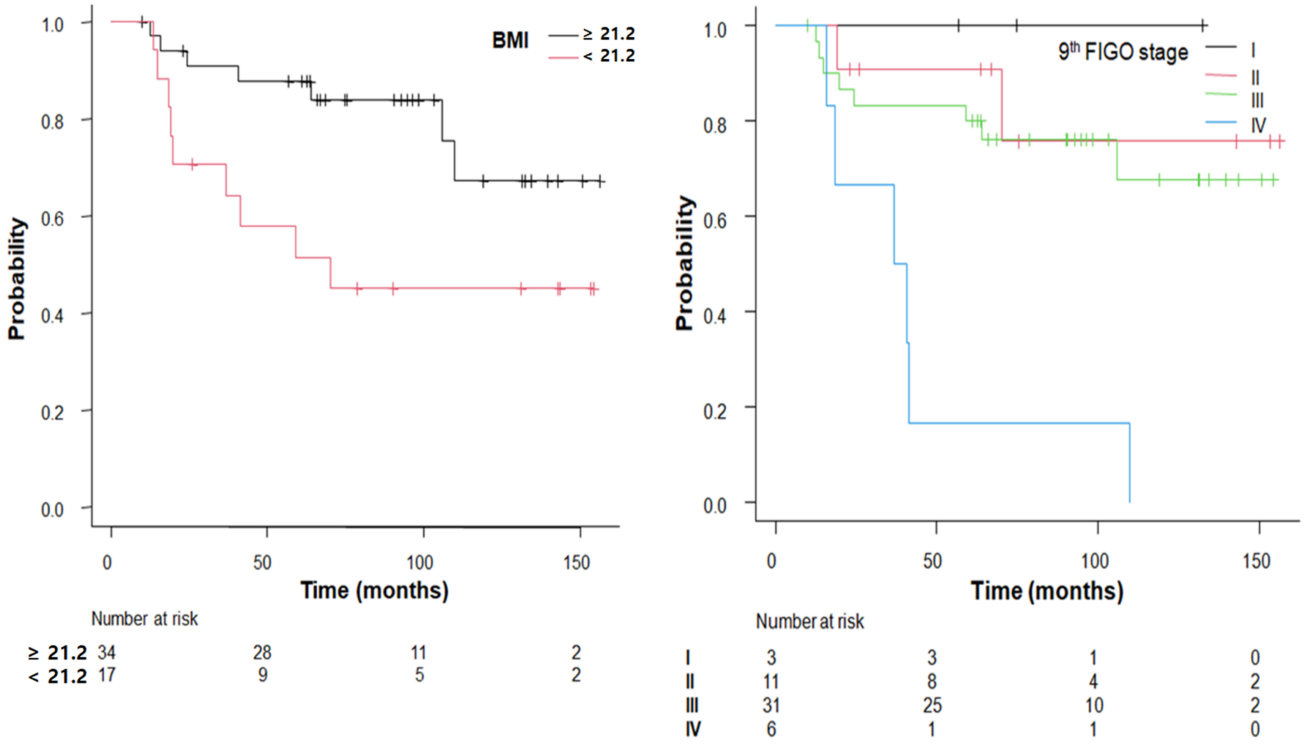

Fig. 3. Kaplan–Meier survival curves for OS stratified by factors (BMI and FIGO stage) demonstrating statistically significant differences.

Table 3. Summary of prognostic factors identified by multivariate Cox proportional hazards regression for PFS and OS, including the β-coefficient and risk scoring algorithm.

Variables	Risk factors	HR (95% CI)	β-coefficient	Risk score	p^*
		PFS			
FIGO stage	I, II, III vs. IV (ref = I, II, III)	4.385 (1.865–10.310)	1.478	14	<0.001
BMI (kg/m^2)	≥21.2 vs. <21.2 (ref = ≥21.2)	2.575 (0.9745–6.805)	0.946	0	0.056
		OS			
BMI (kg/m^2)	≥21.2 vs. <21.2 (ref = ≥21.2)	3.207 (1.157–8.893)	1.165	11	0.025
FIGO stage	I, II, III vs. IV (ref = I, II, III)	3.604 (1.559–8.334)	1.282	12	0.003
Hgb (g/dL)	≥10.2 vs. <10.2 (ref = ≥10.2)	2.366 (0.858–6.526)	0.861	0	0.096

HR, hazard ratio; *Cox proportional hazards regression.

In this study, prognostic factor analysis was performed on patients classified according to the 2018 FIGO staging system. Due to the limited number of patients, the FIGO stages were divided into four groups (I, II, III, and IV) for analytical purposes. When FIGO stage was dichotomized (I–III vs. IV), the prognostic significance remained unchanged, further supporting the robustness of our findings. The results confirmed that the FIGO stage was a statistically significant prognostic factor for both OS and PFS. The 2018 revision of the FIGO staging system, which incorporates imaging and nodal status, is widely recognized as a major advance in predicting cancer outcomes [20,32]. Studies have demonstrated that these changes allow for earlier intervention, more accurate risk stratification, and tailored treatment, all of which improve outcomes [33–35]. Overall, these results highlight the complementary value of BMI and FIGO stage as pretreatment prognostic markers. Because our study period included years before the introduction of the 2018 FIGO system, earlier cases were reclassified according to the updated criteria to maintain consistent staging. Since no patient underwent surgery, and the change in staging did not influence the CCRT approach, this reclassification is unlikely to have affected clinical management or the validity of the prognostic analyses. FIGO stage remained the most influential factor, reflecting the overall extent of disease. BMI provided additional insight into treatment tolerance and general health, with lower BMI linked to poorer survival. Because both measures are simple to obtain and represent different aspects of the patient's status, they offer practical utility in estimating prognosis

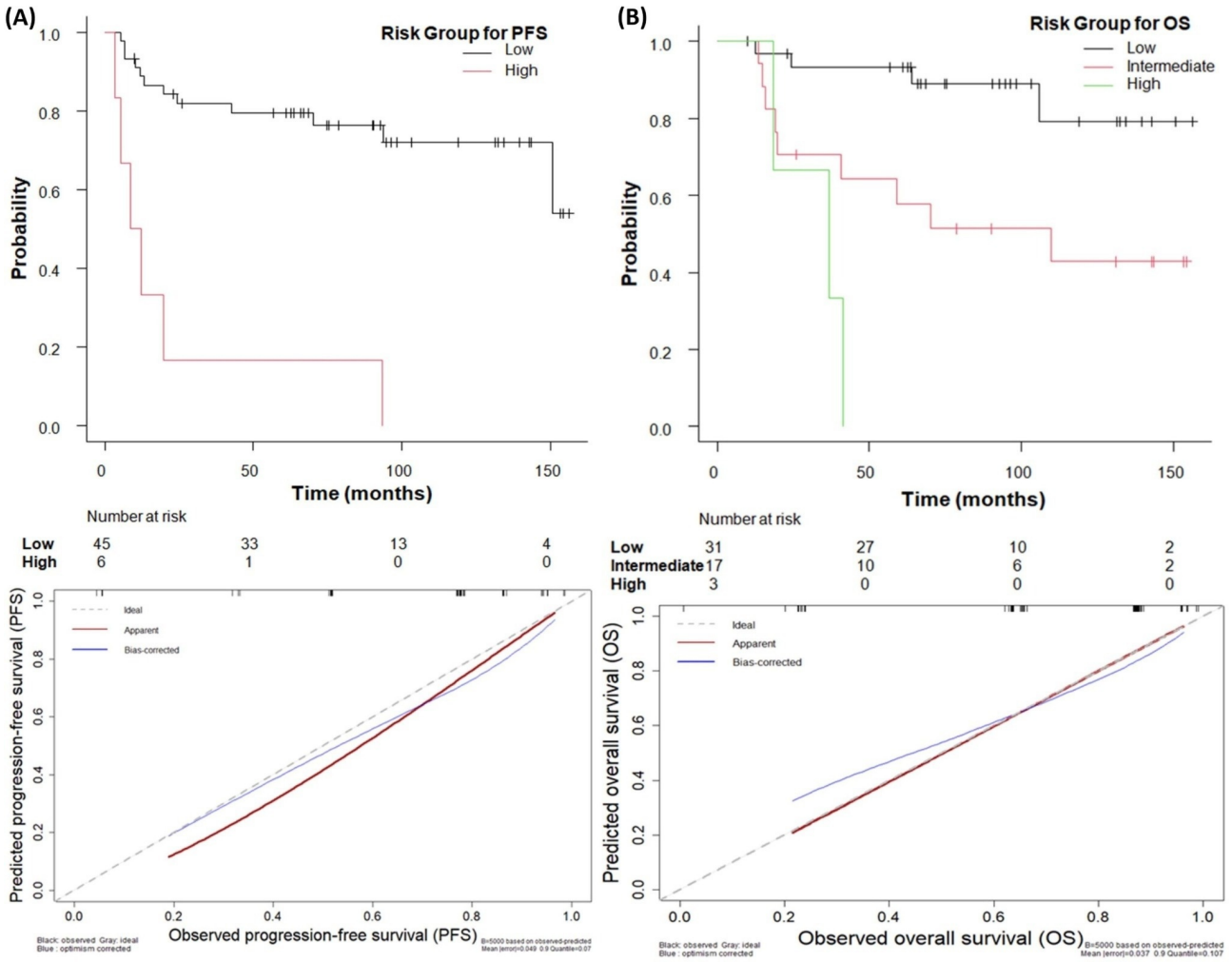

Fig. 4. Kaplan–Meier plots and calibration curves of (A) PFS and (B) OS according to risk stratification. (A) Kaplan–Meier plot and calibration curve for PFS. (B) Kaplan–Meier plot and calibration curve for OS. The *p*-values of the Kaplan–Meier survival curves for PFS and OS for risk stratification were $p < 0.001$ and $p < 0.001$, respectively. The prognostic performance of the models was evaluated by comparing predicted probabilities with observed outcomes using calibration plots. The left panel illustrates calibration for PFS, while the right panel shows OS. In both plots, the dashed gray diagonal line represents perfect calibration, where predicted probabilities align perfectly with observed outcomes. The brown curves represent the apparent calibration, which shows how the model performed on its training data. The bias-corrected calibration (shown in blue) was performed using bootstrap resampling (B = 400) to account for potential overfitting. Black ticks at the top of each plot denote the distribution of predicted survival probabilities. The calibration curves for both the PFS and OS models demonstrated good agreement between the predicted and observed probabilities, closely tracking the ideal diagonal line (especially for OS). Deviations in the lower probability range were noted for PFS, possibly due to sparse data in that region. The proximity of the bias-corrected curves to the apparent calibration lines suggested minimal overfitting and good internal validity of the models. Because the number of patients in the high-risk group was small (n = 6 for PFS; n = 3 for OS), both the PFS and OS estimates are associated with wide confidence intervals and should be interpreted with caution as imprecise estimates driven by sparse data.

and can support a straightforward, clinically useful risk-stratification model.

In the present study, hematological factors were not identified as a significant prognostic factor for survival. The prognosis of cervical cancer is significantly affected by anemia, which is commonly indicated by low Hgb and Hct levels. Numerous studies have confirmed that pretreatment anemia correlates with poor tumor oxygenation, leading to reduced radiotherapy efficacy, increased tumor hypoxia, and shorter overall and disease-free survival [11,12,36]. These results underscore the clinical importance of monitoring and managing anemia both prior to and during treatment to optimize patient outcomes. In the present study, Hgb demonstrated a significant association with OS in the

univariate analysis. In the multivariate analysis, it showed a marginally significant association (HR: 2.366; 95% CI: 0.8578–6.5260; $p = 0.096$). The multivariate Cox analysis yielded a hazard ratio of 2.366, indicating more than a twofold increased risk of mortality associated with this factor. With a larger cohort, the confidence interval would be expected to narrow, and the observed trend might reach conventional levels of statistical significance. Furthermore, although NLR, PLR, and SCC-Ag have been previously reported as significant prognostic indicators for survival, they were not identified as independent prognostic factors in the multivariate analysis of the present study. Consistent with the findings of the present study, in some studies, NLR, PLR, and SCC-Ag have shown statistical significance in the univariate analyses; however, they were not identified as independent prognostic factors for survival in multivariate analyses [37,38]. These findings were consistent with the results of the present study and suggested that the interactions among multiple variables should be considered in prognostic evaluations.

While the literature on cervical cancer and age as a prognostic factor is mixed, a study has suggested that advanced age may be an independent negative prognostic factor for mortality [15], whereas others have indicated no significant age-related differences in survival outcomes [8,39]. Some studies have suggested that younger women may have a higher risk of local recurrence; however, unlike older women, they do not experience worsening outcomes due to recurrence [40,41]. In our study, age did not have a significant effect on the survival outcomes.

In the present study, prognostic analyses were conducted using pTV as the radiological factor and SUV_{max} as the metabolic factor. Both factors lacked statistical significance in predicting survival outcomes. Consistent with our findings, other studies consistently reported that pTV was not a statistically significant predictor of survival [13,16]. While previous studies have demonstrated that the tumor volume reduction rate (TVRR) during treatment is a significant prognostic factor for survival, calculating TVRR requires imaging obtained during radiotherapy, such as CT or MRI [13,16]. Because the present study aimed to evaluate only pretreatment prognostic factors, TVRR was not included in our analysis. For the same reason, MTV, which also requires post-baseline imaging data, was not incorporated into this study. Yoo *et al*. [42] reported that SUV_{max} and average SUV were not independent prognostic indicators for survival. Although a correlation was observed between tumor size and SUV_{max}, multivariate analysis revealed no direct association with survival. Similarly, several other studies have demonstrated that SUV_{max} is not significantly associated with survival in multivariate systems and shows only a borderline relationship with OS, indicating that it is not an independent prognostic factor [10,43]. Although metabolic prognostic indicators, such as MTV and TLG, which reflect the total metabolic burden, have been reported to demonstrate greater prognostic value than SUV_{max} [44,45], they are more complex and difficult to measure in routine clinical practice. Therefore, this study included only the SUV_{max}, which is widely measured and used in most hospitals. In our analysis, radiological and metabolic factors such as pTV and SUV_{max} were evaluated, but did not show independent prognostic value. This suggests that patient-related systemic factors may exert a greater influence on outcomes than tumor-based measurements. The limited independent significance of pTV and SUV_{max} appears to reflect their strong correlation with FIGO stage, which already incorporates major elements of tumor burden and nodal involvement. When analyzed with the FIGO stage, much of their prognostic contribution was absorbed by the stage variable. Although SUV_{max} is less informative than volumetric PET factors such as MTV or TLG, these measures could not be assessed because the required imaging data were unavailable. Nevertheless, SUV_{max} is widely reported and routinely used in clinical practice, making its inclusion as a pretreatment metabolic factor reasonable in settings where volumetric PET metrics are not accessible. The results of our multivariate analysis using all these factors confirmed that BMI and the FIGO stage were significantly associated with survival. Based on these results, we developed a risk-score stratification model. Although FIGO staging requires assessment through imaging studies, other factors, such as BMI, can be readily obtained in clinical settings, suggesting that this classification model is easily feasible and can be applied to guide treatment decisions. One of the strengths of this study is that it identifies pretreatment prognostic factors that are clinically relevant in routine practice. Building on these findings, we developed a risk-score classification model intended to aid clinicians in planning treatment. To the best of our knowledge, no previous study has integrated multiple established pretreatment prognostic factors into a single predictive model for cervical cancer. By consolidating these factors into a unified framework, this study provides a structured approach that may support more consistent and informed patient assessment before therapy.

Limitations

This study has several limitations. The number of patients who met the eligibility criteria was modest, which limits the strength of the conclusions. Even so, the cohort was sufficient for the scope of the analysis because only a small number of variables were included in the multivariable Cox proportional hazards model, the events-per-variable ratio remained acceptable, and all patients were treated with a consistent CCRT protocol. However, the single-institution nature of the study suggests that the results should be interpreted with some caution. Accordingly, the prognostic tool derived from this study is intended solely to facilitate baseline risk communication and should not be used to inform or direct treatment decisions. Overall,

the findings are best viewed as exploratory and will need to be confirmed in larger studies involving multiple centers.

5. Conclusions

In this study, FIGO stage and BMI were the most influential pretreatment factors for survival in patients receiving CCRT for cervical cancer. Their independent prognostic value offers a practical basis for a straightforward risk-stratification approach that may help clinicians recognize higher-risk patients and make more informed treatment decisions. Because both factors are routinely assessed before therapy, they provide a useful means of estimating prognosis at the time of diagnosis. This tool is intended solely to assist with baseline risk communication, not to guide treatment decisions. Although the model shows promise, its clinical reliability will need to be confirmed through external validation in multicenter studies and in larger patient cohorts. These findings provide a sound basis for future work to develop dependable pretreatment prognostic tools.

Availability of Data and Materials

The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

SL and BO were responsible for the conceptualization and design of the study and performed the statistical analysis. Data collection was carried out by SL and HL. The interpretation of the results was contributed by HL, KL, and YK. All authors contributed to critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This Institutional Review Board of Gachon University Gil Medical Center (IRB approval number: GBIRB2025-302) approved this study, which was conducted in compliance with the Declaration of Helsinki. Because this retrospective study used only de-identified clinical data that had already been collected as part of routine care prior to the initiation of the study, no additional patient contact was required; therefore, the requirement for informed consent was waived.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG47038.

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