

Impact of Pretreatment Blood Parameters on Survival Outcomes in Patients with Locally Advanced Cervical Cancer Treated with Concurrent Chemoradiotherapy: A Retrospective Cohort Study

Pornnapas Chaowanasai, Worrawan Sirichai, Piyawan Pariyawateekul, Walanya Aonrawattanasrikul, Konkarn Bhamarapratana, Komsun Suwannarurk

Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Royal Thai Air Force, Bangkok, 10220, Thailand.

Abstract

Objectives: To evaluate the association between systemic inflammatory markers and the albumin–globulin ratio (AGR) with prognostic outcomes in patients with locally advanced cervical cancer (LACC) treated with concurrent chemoradiation therapy (CCRT). **Materials and Methods:** A retrospective cohort study was conducted at the Gynecologic Oncology Unit, Bhumibol Adulyadej Hospital, Royal Thai Air Force, Thailand. Medical records of patients with LACC treated between 2015 and 2019 were reviewed. Patients who completed definitive CCRT were included. Demographic characteristics, histopathological findings, FIGO stage, and pretreatment hematologic parameters were collected. Associations between inflammatory markers and survival outcomes were analyzed. **Results:** A total of 110 patients were included, with a mean age of 49.8 years. Squamous cell carcinoma was the predominant histological subtype, accounting for 80.9% (89/110) of cases. The 5-year overall survival (OS) and progression-free survival (PFS) rates were 61.8% and 57.8%, respectively. Patients with a neutrophil-to-lymphocyte ratio (NLR) <2.33 had significantly better PFS, while those with an NLR <3.2 demonstrated significantly better OS than patients with higher NLR values. A platelet-to-lymphocyte ratio (PLR) <154 and an AGR >1.2 were also significantly associated with improved survival outcomes. Specifically, a higher AGR was associated with better PFS. **Conclusion:** Pretreatment systemic inflammatory markers may provide useful prognostic information in patients with LACC undergoing definitive CCRT. Lower NLR and PLR values, together with a higher AGR, were associated with more favorable survival outcomes, supporting their potential role as inexpensive and readily available prognostic biomarkers.

Keywords: locally advanced cervical cancer, concurrent chemoradiation therapy, neutrophil-to-lymphocyte ratio

Rep Radiother Oncol, 12 (1), 35-42

Submission Date: 05/19/2026 Acceptance Date: 07/03/2026

Introduction

Cervical cancer (CC) is the fourth most commonly diagnosed cancer and the fourth leading cause of cancer-related death among women worldwide, with persistent infection by high-risk human papillomavirus (HPV) recognized as its principal etiologic factor [1]. In Thailand, cervical cancer remains a major public health concern and is the second most common malignancy among women after breast cancer, accounting for approximately 13.8% of newly diagnosed female cancers in 2021 [2].

Management of cervical cancer depends primarily on disease stage according to the International Federation of Gynecology and Obstetrics (FIGO) classification. Early-stage disease (FIGO IA–IB2 and IIA1) is generally treated with radical surgery, while radiotherapy is reserved for patients who are not suitable surgical candidates. For FIGO stages IB3 and IIA2, concurrent chemoradiotherapy (CCRT) is the standard treatment. Patients with locally advanced cervical cancer (LACC; FIGO IIB–IVA) are routinely treated with platinum-based CCRT, whereas

Corresponding Author:

Dr. Worrawan Sirichai

Department of Obstetrics and Gynecology, Bhumibol Adulyadej Hospital, Royal Thai Air Force, Bangkok, 10220, Thailand.

Email: pornnapaschaowanasai@gmail.com

systemic therapy is recommended for metastatic disease (FIGO IVB) [3].

Despite advances in radiotherapy techniques and concurrent chemotherapy, survival outcomes for patients with LACC remain unsatisfactory because of persistent, recurrent, or metastatic disease following definitive treatment [4]. Established prognostic factors associated with poorer progression-free survival (PFS) and overall survival (OS) include advanced FIGO stage, large tumor size, lymph node metastasis, and non-squamous histology [5–8]. However, these clinicopathological characteristics alone do not fully explain the considerable heterogeneity in treatment response and long-term outcomes among patients with LACC.

Increasing evidence suggests that systemic inflammation plays a critical role in tumor progression, immune evasion, angiogenesis, and resistance to therapy. Consequently, several inflammation-based hematologic biomarkers derived from routine complete blood counts have been investigated as potential prognostic indicators in cervical cancer. These include the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), and aggregate index of systemic inflammation (AISI). Although numerous studies have demonstrated associations between these biomarkers and survival outcomes, their prognostic value remains inconsistent across different patient populations and treatment settings [9–15].

Serum albumin and globulin are additional biomarkers that reflect both nutritional status and systemic inflammatory activity. Hypoalbuminemia is commonly associated with malnutrition, chronic inflammation, and poor clinical outcomes in patients with cancer, whereas elevated globulin levels reflect activation of inflammatory pathways mediated by cytokines, growth factors, and angiogenic factors that contribute to tumor progression and metastasis [16, 17]. Accordingly, the albumin-to-globulin ratio (AGR) has emerged as a promising prognostic biomarker in several malignancies, including lung, colorectal, prostate, renal, and bladder cancers, with lower AGR values consistently associated with poorer survival outcomes [18–22]. However, evidence regarding the prognostic significance of AGR in patients with LACC treated with definitive CCRT remains limited.

Therefore, the present study aimed to evaluate the prognostic value of pretreatment systemic inflammatory markers and the albumin-to-globulin ratio in patients with locally advanced cervical cancer undergoing definitive concurrent chemoradiotherapy, with particular emphasis on their associations with progression-free and overall survival.

Materials and Methods

Study Design and Setting

This retrospective cohort study was conducted at the Gynecologic Oncology Unit of Bhumibol Adulyadej Hospital (BAH), Royal Thai Air Force (RTAF), Bangkok,

Thailand. The study protocol was approved by the Institutional Review Board of Bhumibol Adulyadej Hospital (IRB No. 98/67).

Study Population

Patients diagnosed with locally advanced cervical cancer (LACC; FIGO stage IIB or higher) who underwent definitive concurrent chemoradiotherapy (CCRT) at BAH between January 2015 and December 2019 were eligible for inclusion.

The inclusion criteria were: (1) histopathologically confirmed cervical cancer; (2) age between 18 and 75 years; (3) no previous cancer treatment; (4) completion of the planned course of definitive CCRT; and (5) an Eastern Cooperative Oncology Group (ECOG) performance status of ≤ 2 . Patients were excluded if they had incomplete clinical records, multiple primary malignancies, hematologic disorders, autoimmune diseases, chronic liver or kidney disease, or missing laboratory data required for analysis.

All patients were staged according to the 2018 International Federation of Gynecology and Obstetrics (FIGO) staging system.

Treatment Protocol

At our institution, all patients with LACC received definitive platinum-based CCRT. External beam radiotherapy (EBRT) was delivered to the pelvis using a linear accelerator (Varian Inc., CA, USA) at a total dose of 45–50 Gy in 2 Gy daily fractions over approximately five weeks. This was followed by high-dose-rate intracavitary brachytherapy using Cobalt-60, delivering 6.5 Gy per fraction for 4–5 fractions over approximately one month.

Concurrent chemotherapy consisted of weekly intravenous cisplatin (40 mg/m²) administered throughout the course of external beam radiotherapy.

Data Collection

Clinical and demographic data were retrieved from the hospital's electronic medical records. The collected variables included age, body mass index (BMI), ECOG performance status, HIV status, histopathological subtype, FIGO stage, primary tumor size, treatment details, recurrence or progression status, survival status, and follow-up duration.

Pretreatment laboratory parameters were obtained from blood samples collected within one month before initiation of CCRT. Hematologic variables included hemoglobin (Hb), white blood cell (WBC) count, absolute neutrophil count, absolute lymphocyte count, platelet count, serum albumin, and serum globulin levels.

Inflammatory biomarkers, including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), systemic inflammation response index (SIRI), aggregate index of systemic inflammation (AISI), and the albumin-to-globulin ratio (AGR), were calculated using standard published formulas.

Sample Size Calculation

The minimum sample size was estimated based on the comparison of two survival curves with unequal group sizes using the method described by Koulis et al. [9]. Assuming a two-sided significance level (α) of 0.05, a statistical power of 80% ($\beta = 0.20$), and an allocation ratio of 3:1 between comparison groups, the expected 5-year overall survival rates were 34% for the high-risk group and 60% for the low-risk group. These assumptions yielded a required sample size of 84 patients (21 in the high-risk group and 63 in the low-risk group). The final study cohort consisted of 110 eligible patients, exceeding the minimum sample size required for adequate statistical power.

Statistical Analysis

Statistical analyses were performed using R software (version 3.2.3; R Foundation for Statistical Computing, Vienna, Austria). Baseline characteristics were summarized as mean $\pm$ standard deviation (SD) for continuous variables and frequency (percentage) for categorical variables. Between-group comparisons were performed using the Mann–Whitney U test for continuous variables and the Chi-square test or Fisher's exact test, as appropriate, for categorical variables.

Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan–Meier method, and survival curves were compared using the log-rank test. Receiver operating characteristic (ROC) curve analysis was performed to determine the optimal cutoff values for the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and albumin-to-globulin ratio (AGR). Optimal thresholds were selected using the Youden index, corresponding to the maximum combined sensitivity and specificity for predicting PFS and OS.

Variables demonstrating statistical significance in univariable analyses or considered clinically relevant were entered into multivariable Cox proportional hazards regression models to identify independent prognostic factors. Results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs). A two-sided p value <0.05 was considered statistically significant throughout the study.

Results

During the study period from 2015 to 2019, a total of 346 patients were diagnosed with locally advanced cervical cancer (LACC). After applying the eligibility criteria, 110 patients were included in the final analysis, as shown in Figure 1.

The mean age of the study population was 49.8 years. Most patients had a normal body mass index (BMI), with a median BMI of 23.8 kg/m², and the majority had good functional status (ECOG performance status 0: 98.2%). More than half of the patients (54/110, 49.1%) were diagnosed with FIGO stage IIB disease, and 89 patients (80.9%) had squamous cell carcinoma histology. Additional demographic, clinical, and laboratory characteristics are presented in Table 1. The estimated

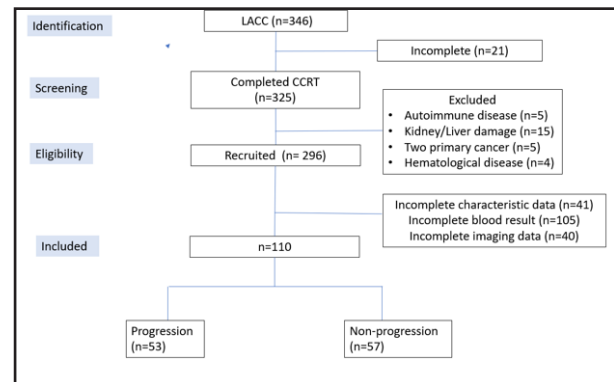


Figure 1. Flow Diagram of the Study Population. LACC: locally advanced cervical cancer; CCRT: concurrent chemoradiotherapy.

5-year overall survival (OS) and progression-free survival (PFS) rates were 61.8% and 57.8%, respectively.

When comparing patients with disease progression (P group) and those without progression (NP group), patients in the NP group were more likely to have earlier locally advanced disease (FIGO stage IIB) compared with the progression group (57.9% vs. 39.6%, $p = 0.04$). Among the evaluated inflammatory and nutritional biomarkers, only the neutrophil-to-lymphocyte ratio (NLR) and albumin-to-globulin ratio (AGR) demonstrated significant associations with progression outcomes.

Similarly, comparison between surviving patients (alive group) and deceased patients (death group) showed that FIGO stage IIB was more common among survivors (56.9%) compared with patients who died (40.4%, $p = 0.04$). Among the evaluated biomarkers, only NLR was significantly associated with overall survival ($p = 0.04$). Other demographic and clinical characteristics were

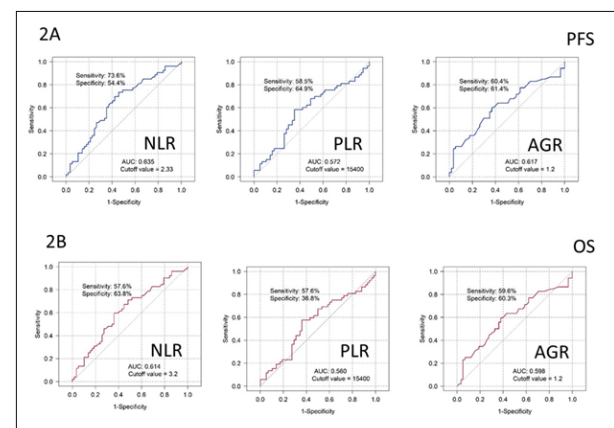


Figure 2. Receiver Operating Characteristic (ROC) Curves of Inflammatory Biomarkers for Predicting Progression-free Survival and Overall Survival in Patients with Locally Advanced Cervical Cancer. Panel A. ROC curves of NLR, PLR, and AGR for prediction of progression-free survival (PFS). Panel B. ROC curves of NLR, PLR, and AGR for prediction of overall survival (OS). Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; AGR, albumin-to-globulin ratio; PFS, progression-free survival; OS, overall survival.

Table 1. Baseline Characteristics of Patients with Locally Advanced Cervical Cancer and Association of Clinical Variables with Progression-free Survival and Overall Survival (n=110).

Characteristic	Total (n=110)	Progression (n=53)	Non-progression (n=57)	p-value	Death (n=52)	Alive (n=58)	p-value
Age (years)	49.8 ± 12.7	50.1 ± 12.7	49.6 ± 12.9	0.83	50.6 ± 12.8	49.1 ± 12.7	0.54
BMI (kg/m ²)	23.8 ± 4.4	23.8 ± 4.3	23.8 ± 4.6	0.99	23.6 ± 4.5	24.1 ± 4.4	0.58
FIGO stage				0.04			0.03
IIB	54 (49.1)	21 (39.6)	33 (57.9)		21 (40.4)	33 (56.9)	
IIIA	4 (3.6)	4 (7.5)	0 (0)		4 (7.7)	0 (0)	
IIIB	31 (28.2)	20 (37.7)	11 (19.3)		20 (38.5)	11 (19.0)	
IIIC1	11 (10.0)	4 (7.5)	7 (12.3)		4 (7.7)	7 (12.1)	
IIIC2	8 (7.3)	3 (5.7)	5 (8.8)		3 (5.8)	5 (8.6)	
IVA	2 (1.8)	1 (1.9)	1 (1.8)		0 (0)	2 (3.4)	
Histology				0.24			0.23
Squamous cell carcinoma	89 (80.9)	42 (79.2)	47 (82.5)		41 (78.8)	48 (82.8)	
Adenocarcinoma	14 (12.7)	5 (9.4)	9 (15.8)		5 (9.6)	9 (15.5)	
Adenosquamous carcinoma	3 (2.7)	2 (3.8)	1 (1.8)		2 (3.8)	1 (1.7)	
Others	4 (3.6)	4 (7.6)	0 (0)		4 (7.6)	0 (0)	
Tumor size >4 cm	67 (60.9)	37 (69.8)	30 (52.6)	0.10	36 (69.2)	31 (53.4)	0.13
ECOG performance status 0	108 (98.2)	52 (98.1)	56 (98.2)	1.00	51 (98.1)	57 (98.3)	1.00
HIV negative	106 (96.4)	50 (94.3)	56 (98.2)	0.35	49 (94.2)	57 (98.3)	0.34
Hemoglobin (g/dL)	11.4 (10.3–12.4)	11.3 (10.3–11.8)	11.6 (10.5–12.7)	0.10	11.4 (10.3–12.0)	11.6 (10.4–12.6)	0.32
Neutrophil-to-lymphocyte ratio (NLR)	3.0 (2.0–4.9)	3.6 (2.3–5.3)	2.3 (1.8–4.0)	0.02	3.5 (2.1–5.5)	2.3 (1.9–4.4)	0.04
Platelet-to-lymphocyte ratio (PLR)	NR	16.3 (9.8–23.1)	11.7 (8.7–23.6)	0.19	16.3 (9.6–22.8)	12.0 (8.7–24.0)	0.28
Albumin (g/dL)	4.4 (4.1–4.9)	4.3 (4.0–4.9)	4.4 (4.2–4.9)	0.15	4.3 (4.0–4.9)	4.4 (4.1–4.9)	0.29
Globulin (g/dL)	3.7 ± 0.6	3.8 ± 0.7	3.6 ± 0.5	0.09	3.7 ± 0.7	3.6 ± 0.6	0.21
Albumin-to-globulin ratio (AGR)	1.3 ± 0.2	1.1 (1.0–1.4)	1.3 (1.1–1.5)	0.03	1.1 (1.0–1.4)	1.3 (1.1–1.5)	0.08

Values are presented as mean ± standard deviation (SD), median (interquartile range [IQR]), or n (%), as appropriate. Abbreviations: BMI, body mass index; FIGO, International Federation of Gynecology and Obstetrics; ECOG, Eastern Cooperative Oncology Group; HIV, human immunodeficiency virus; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; AGR, albumin-to-globulin ratio; NR, not reported/needs verification.

comparable between the progression/non-progression groups and the alive/death groups (Table 1).

Receiver operating characteristic (ROC) curve analyses were performed to determine optimal cutoff values for NLR, PLR, and AGR in predicting PFS and OS (Figure 2). Patients with an NLR <2.33 had significantly better PFS, while those with an NLR <3.20 demonstrated significantly improved OS compared with patients with higher NLR values ($p = 0.002$ and $p = 0.009$, respectively).

Patients with a PLR <15.4 had significantly better PFS and OS than those with higher PLR values (both $p = 0.016$). Furthermore, patients with an AGR >1.2 showed significantly improved PFS and OS compared with those with lower AGR values ($p = 0.023$ and $p = 0.048$, respectively). The survival analyses based on these cutoff values are presented in Figure 3.

Discussion

During the study period, 110 patients with locally advanced cervical cancer (LACC) were included in the final analysis, as shown in Figure 1. Approximately half of the patients had early-stage LACC. The estimated 5-year overall survival (OS) and progression-free survival

(PFS) rates were 61.8% and 57.8%, respectively. Previous studies have reported 5-year OS and PFS rates ranging from 55% to 86.7% and 49.1% to 94%, respectively [9, 10, 23–26]. Studies reporting comparable survival outcomes generally included patients with similar clinicopathological characteristics to those in the present cohort (Table 2) [9–12, 23–29].

In the current study, only the neutrophil-to-lymphocyte ratio (NLR) and albumin-to-globulin ratio (AGR) were significantly associated with PFS. Previous studies by Elmali, Yu, Chen, and Fullerton similarly identified NLR as an independent prognostic factor [11, 12, 27, 28]. In contrast, Kumar et al. reported that only the platelet-to-lymphocyte ratio (PLR) was associated with PFS in patients with cervical cancer [24]. Other studies by Yu and Fullerton demonstrated that both NLR and PLR were significant predictors of survival outcomes [27, 28]. These findings support the concept that inflammation-related biomarkers, particularly ratios reflecting the balance between immune suppression and systemic inflammation, may provide valuable prognostic information in patients with LACC.

Lymphocytes play an essential role in antitumor immunity, whereas neutrophils and platelets contribute

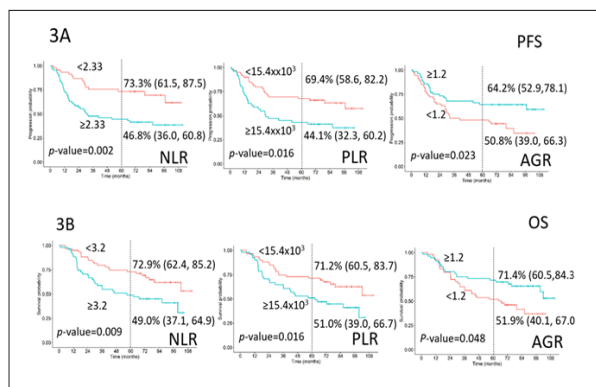


Figure 3. Kaplan-Meier Survival Curves for Progression-free Survival and Overall Survival According to Inflammatory Biomarkers in Patients with Locally Advanced Cervical Cancer. Kaplan-Meier curves demonstrate the association of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and albumin-to-globulin ratio (AGR) with progression-free survival (PFS) and overall survival (OS). Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; AGR, albumin-to-globulin ratio; PFS, progression-free survival; OS, overall survival.

to tumor progression through inflammatory activation, angiogenesis, and immune modulation. Therefore, elevated neutrophil or platelet levels relative to lymphocyte counts may reflect an unfavorable tumor microenvironment and impaired host immune response. The association between NLR and PLR with survival outcomes observed in previous studies and the present study suggests their potential utility as accessible prognostic biomarkers in cervical cancer management [11, 12, 24, 27, 28].

Previous studies have also reported hemoglobin (Hb) as a prognostic factor for PFS. Koulis et al. and Elmali et al. identified pretreatment anemia as associated with poorer outcomes; however, approximately one-third of patients in those studies had FIGO stage III or more advanced disease [9, 12]. In patients with LACC, particularly those with advanced-stage disease, definitive treatment commonly involves intensive CCRT, including pelvic and para-aortic

irradiation when indicated. Radiation exposure to the pelvic bones and spinal marrow may transiently suppress hematopoiesis, resulting in reductions in red blood cell, white blood cell, and platelet production.

Hemoglobin levels may influence radiotherapy response because adequate tissue oxygenation is required for the generation of radiation-induced reactive oxygen species, which contribute to tumor cell killing. Previous studies have suggested that correction of anemia may improve local tumor control by enhancing oxygen delivery during radiotherapy; however, large prospective trials confirming the clinical benefit of increasing tumor oxygenation remain limited [30]. In the present study, Hb was not significantly associated with either PFS or OS, possibly reflecting differences in disease stage distribution, treatment intensity, and baseline patient characteristics compared with previous reports.

The present study demonstrated that AGR was a significant prognostic factor for PFS, consistent with findings reported by Yoshino et al., who found that lower AGR was associated with poorer survival outcomes [29]. Albumin is synthesized by hepatocytes, and its production may be suppressed by systemic inflammation mediated by cytokines such as interleukin-6 (IL-6), which are frequently elevated in cancer patients. Therefore, reduced albumin levels may reflect both poor nutritional status and an active inflammatory state [31].

Globulin consists of various serum proteins produced by the liver and immune cells, including B lymphocytes and plasma cells. It contains several inflammatory components, such as C-reactive protein-related proteins, complement factors, and immunoglobulins. Elevated globulin levels may therefore indicate persistent systemic inflammation. Consequently, a reduced AGR may represent a combination of malnutrition, chronic inflammation, and tumor-related immune activation, explaining its association with poorer outcomes [31, 32].

Although hemoglobin levels may reflect oxygen-carrying capacity during radiotherapy, the present study found no significant association between Hb or platelet count and OS. In contrast, Koulis et al.

Table 2. Comparison of Clinical Characteristics and Prognostic Significance of Blood Parameters between the Present Study and Previous Studies in Patients with Locally Advanced Cervical Cancer.

Author	Year	Country	Sample size	Stage	Age (years)	SCC (%)	OS (%)	PFS (%)
Koulis	2017	Canada	257	IB–IVA	50	86.4	60	52
Cho	2017	India	105	IIB	NR	94.3	86.7	81.8
Gennigens	2020	Belgium	103	NR	50	88.3	81.4	76.8
Elmali	2024	Turkey	261	NR	57	100	NR	69.6
Yu	2024	China	180	IB2–IIB	52.7	NR	NR	NR
Chen	2024	Taiwan	138	NR	60.1	78.3	NR	NR
Fullerton	2024	Canada	196	IB1–IVB	51	50	NR	NR
Kumar	2022	India	1051	NR	50	94.7	69	65
Garg	2024	India	123	NR	61	76.4	66.8	64
Oymak	2023	Turkey	139	NR	61	Most cases	55	49.1
Yoshino	2019	Japan	128	NR	65	89	NR	NR
Present study	2024	Thailand	110	IIB–IVA	49.8	80.9	61.8	57.8

Table 2 continued. Prognostic Significance of Blood Parameters Reported in Previous Studies and the Present Study.

Biomarker	PFS association reported	OS association reported
Hemoglobin (Hb)	Koulis (S), Elmali (S), Oymak (NS), Present (NS)	Koulis (S), Gennigens (NS), Garg (S), Present (NS)
Neutrophil-to-lymphocyte ratio (NLR)	Elmali (S), Yu (S), Chen (S), Fullerton (S), Present (S)	Chen (S), Garg (S), Present (S)
Platelet-to-lymphocyte ratio (PLR)	Elmali (S), Yu (S), Fullerton (S), Kumar (S), Present (NS)	Fullerton (S), Kumar (S), Present (NS)
Albumin-to-globulin ratio (AGR)	Present (S)	Yoshino (S), Present (NS)
Platelet count (Plt)	Koulis (NS), Present (NS)	Koulis (S), Present (NS)

NR: not reported; SCC: squamous cell carcinoma; OS: overall survival; PFS: progression-free survival; Hb: hemoglobin; NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; AGR: albumin-to-globulin ratio; Plt: platelet; S: statistically significant association; NS: no statistically significant association.

reported Hb and PLR as significant prognostic factors for OS [9]. In their study, patients had a higher mean Hb level (12.8 g/dL) and a 5-year OS rate of approximately 60%. Similarly, Gennigens et al. reported no significant association between Hb and OS in a cohort with relatively favorable outcomes (3-year OS: 81.4%) and a higher mean Hb level (13.1 g/dL) [10]. In studies by Garg, Kumar, and the present study, the 5-year OS rates were 66.8%, 69%, and 57.8%, respectively, with corresponding mean Hb levels of approximately 11.5, 11.5, and 11.4 g/dL [24, 25]. The lower Hb levels observed in the latter cohorts may partly explain differences in survival outcomes and highlight the importance of considering baseline hematologic status when interpreting prognostic biomarkers.

NLR in the current study was a significant prognostic factor for 5-year OS. This finding was consistent with the results reported by Chen and Garg [11, 25]. However, Cho, Gennigens, Yu, Fullerton, and Kumar found no significant association between NLR and OS [9–10, 23–24, 27–28]. The proportion of stage IV cervical cancer cases in the present study and in the studies by Chen and Garg ranged from 1.8% to 13.4%, whereas the corresponding proportion in the studies by Koulis, Gennigens, Fullerton, and Kumar ranged from 0.8% to 5.1% [9–11, 23–25, 27–28]. Similarly, the proportion of squamous cell carcinoma (SCC) histology in the present study and the studies by Chen and Garg ranged from 76.4% to 80.9%, compared with higher proportions (84.0%–94.7%) reported in the studies by Koulis, Gennigens, Fullerton, and Kumar [9–11, 23–25, 27, 28]. These differences in disease characteristics may partly explain the variation in survival outcomes among studies. Patients included in the studies by Gennigens, Fullerton, and Kumar appeared to have more favorable prognostic profiles than those in the present study and the studies by Chen and Garg [9–11, 23–25, 27–28]. Although OS represents an important long-term outcome in cervical cancer survivors, pretreatment inflammatory markers may have limited predictive value for long-term survival due to the influence of multiple clinical and treatment-related factors.

PLR was not identified as a prognostic factor in the studies by Gennigens, Yu, Chen, Garg, or the present study. In contrast, Fullerton and Kumar reported PLR as

a significant prognostic factor, although the underlying reasons for these inconsistent findings remain unclear [10, 11] [24, 25] [27, 28]. Overall, previous studies have demonstrated heterogeneous results regarding the prognostic value of NLR and PLR for OS. Nevertheless, lymphocyte-related parameters appear to play an important role in reflecting the host inflammatory and immune responses associated with cancer progression.

In conclusion, NLR values below 2.33 and 3.2 were associated with improved PFS and OS, respectively. AGR was also significantly associated with PFS.

Strengths

This study represents one of the early investigations exploring the prognostic impact of AGR on PFS and OS in patients with cervical cancer.

Limitations

This study had several limitations. First, its retrospective design and incomplete clinical data may have affected the accuracy and reliability of the findings. Second, as this study was conducted at a single institution, the generalizability of the results to other populations and clinical settings may be limited. Future multicenter studies with larger sample sizes are warranted to validate these findings and improve external validity.

Applicability

These findings may provide a basis for future studies investigating whether optimization of nutritional status and maintenance of normal albumin levels could improve clinical outcomes in patients with cervical cancer.

Acknowledgements

The authors are grateful to the gynecologic oncology team of Bhumibol Adulyadej Hospital, Bangkok, Thailand, and the Bhumibol Adulyadej Research Fund.

Conflict of interest

The authors declare that there is no conflict of interest.

Funding

This study was supported by the hospital research center with a grant of 8,000 baht.

Contributions of authors

Conception and design: Pornnapas Chaowanasai, Administrative support: Piyawan Pariyawateekul, Collection and assembly of data: Pornnapas Chaowanasai, Data analysis and interpretation: Pornnapas Chaowanasai, Wanlaya Aonrawattanasrikul, Manuscript writing: Pornnapas Chaowanasai and Worrawan Sirichai.

Ethics declaration

Ethics approval and consent to participate: As this study was retrospective and all patient identities were anonymized, individual informed consent was not required. The authors declare that no financial support was received from any organization for the submitted work.

Competing interests

The authors declare no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: a cancer journal for clinicians*. 2021 05;71(3):209-249. <https://doi.org/10.3322/caac.21660>
2. National Cancer Institute. Hospital-based cancer registry 2021 [Internet]. Bangkok (TH): National Cancer Institute; c2022 [cited 2023 Jun 1]. Available from: https://www.nci.go.th/e-book/hosbased_2564/index.html...
3. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R. Cancer of the cervix uteri: 2021 update. *International Journal of Gynecology & Obstetrics*. 2021 Oct;155(S1):28-44. <https://doi.org/10.1002/ijgo.13865>
4. Reducing Uncertainties About the Effects of Chemoradiotherapy for Cervical Cancer: A Systematic Review and Meta-Analysis of Individual Patient Data From 18 Randomized Trials. *Journal of Clinical Oncology*. 2008 Dec 10;26(35):5802-5812. <https://doi.org/10.1200/JCO.2008.16.4368>
5. Koh W, Abu-Rustum NR, Bean S, Bradley K, Campos SM, Cho KR, Chon HS, et al. Cervical Cancer, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. *Journal of the National Comprehensive Cancer Network*. 2019 01;17(1):64-84. <https://doi.org/10.6004/jnccn.2019.0001>
6. Kong T, Ryu H, Kim SC, Enomoto T, Li J, Kim KH, Shim S, et al. Asian Society of Gynecologic Oncology International Workshop 2018. *Journal of Gynecologic Oncology*. 2019;30(2):e39. <https://doi.org/10.3802/jgo.2019.30.e39>
7. Bae HS, Kim Y, Lim MC, Seo S, Park S, Kang S, Kim SH, Kim J. Predictors of Radiation Field Failure After Definitive Chemoradiation in Patients With Locally Advanced Cervical Cancer. *International Journal of Gynecological Cancer*. 2016 05;26(4):737-742. <https://doi.org/10.1097/IGC.0000000000000662>
8. Joo J, Shin H, Park B, Park S, Yoo C, Yoon K, Kong S, Kim Y, Kim SS, Kim J. Integration Pattern of Human Papillomavirus Is a Strong Prognostic Factor for Disease-Free Survival After Radiation Therapy in Cervical Cancer Patients. *International Journal of Radiation Oncology*Biophysics*. 2017 07;98(3):654-661. <https://doi.org/10.1016/j.ijrobp.2017.02.226>
9. Koulis TA, Kornaga EN, Banerjee R, Phan T, Ghatage P, Magliocco AM, Lees-Miller SP, Doll CM. Anemia, leukocytosis and thrombocytosis as prognostic factors in patients with cervical cancer treated with radical chemoradiotherapy: A retrospective cohort study. *Clinical and Translational Radiation Oncology*. 2017 06;4:51-56. <https://doi.org/10.1016/j.ctro.2017.05.001>
10. Gennigens C, De Cuyper M, Seidel L, Hermesse J, Barbeaux A, Forget F, Albert A, Jerusalem G, Kridelka F. Correlation between hematological parameters and outcome in patients with locally advanced cervical cancer treated by concomitant chemoradiotherapy. *Cancer Medicine*. 2020 Nov;9(22):8432-8443. <https://doi.org/10.1002/cam4.3465>
11. Chen JL, Huang C, Shih I, Liou Y, Tai Y, Chiang Y, Kuo C. Prognostic nutritional index and neutrophil-lymphocyte ratio predict toxicities and prognosis in patients with cervical cancer treated with curative radiochemotherapy. *Journal of the Formosan Medical Association*. 2024 06;123(6):671-678. <https://doi.org/10.1016/j.jfma.2023.10.022>
12. Elmali A, Guler OC, Demirhan B, Yavuz M, Onal C. Long-term analysis of hematological parameters as predictors of recurrence patterns and treatment outcomes in cervical cancer patients undergoing definitive chemoradiotherapy. *Strahlentherapie und Onkologie*. 2024 Nov;200(11):949-957. <https://doi.org/10.1007/s00066-024-02278-8>
13. Guo J, Lv W, Wang Z, Shang Y, Yang F, Zhang X, Xiao K, et al. Prognostic Value of Inflammatory and Nutritional Markers for Patients With Early-Stage Poorly-to Moderately-Differentiated Cervical Squamous Cell Carcinoma. *Cancer Control: Journal of the Moffitt Cancer Center*. 2023;30:10732748221148913. <https://doi.org/10.1177/10732748221148913>
14. Ayhan S, Akar S, Kar İ, Turan AT, Türkmen O, Kiliç F, et al. Prognostic value of systemic inflammatory response markers in cervical cancer. *J Obstet Gynaecol*. 2022;42(6):2411-9. <https://doi.org/10.1080/01443615.2022.2069482>
15. Li Y, Chang J, He M, Wang H, Luo D, Li F, Li J, Ran L. Neutrophil-to-Lymphocyte Ratio (NLR) and Monocyte-to-Lymphocyte Ratio (MLR) Predict Clinical Outcome in Patients with Stage IIB Cervical Cancer. *Journal of Oncology*. 2021 09 08;2021:1-14. <https://doi.org/10.1155/2021/2939162>
16. McMillan DC, Watson WS, O'Gorman P, Preston T, Scott HR, McArdle CS. Albumin Concentrations Are Primarily Determined by the Body Cell Mass and the Systemic Inflammatory Response in Cancer Patients With Weight Loss. *Nutrition and Cancer*. 2001 03;39(2):210-213. https://doi.org/10.1207/S15327914nc392_8
17. Gupta D, Lis CG. Pretreatment serum albumin as a predictor of cancer survival: A systematic review of the epidemiological literature. *Nutrition Journal*. 2010 Dec;9(1):69. <https://doi.org/10.1186/1475-2891-9-69>
18. Lu P, Ma Y, Wei S, Liang X. A Low Albumin-to-Globulin Ratio Predicts a Poor Prognosis in Patients With Metastatic Non-small-cell Lung Cancer. *Frontiers in Medicine*. 2021 03 01;8:621592. <https://doi.org/10.3389/fmed.2021.621592>
19. Li J, Zhu N, Wang C, You L, Guo W, Yuan Z, Qi S, et al. Preoperative albumin-to-globulin ratio and prognostic nutritional index predict the prognosis of colorectal cancer: a retrospective study. *Scientific Reports*. 2023 Oct 12;13(1):17272. <https://doi.org/10.1038/s41598-023-43391-5>
20. Wang X, Yang G, Chai Y, Li Z, Che X, Wang Y, Yang L, Zhou Z. Decreased Preoperative Serum AGR as a Diagnostic Marker of Poor Prognosis after Radical Surgery of Upper Urinary Tract and Bladder Cancers from a Pooled Analysis

- of 9,002 Patients. *Disease Markers*. 2022;2022:6575605. <https://doi.org/10.1155/2022/6575605>
21. Saliccia S, Frisenda M, Bevilacqua G, Viscuso P, Casale P, De Berardinis E, Di Pierro GB, et al. Prognostic Value of Albumin to Globulin Ratio in Non-Metastatic and Metastatic Prostate Cancer Patients: A Meta-Analysis and Systematic Review. *International Journal of Molecular Sciences*. 2022 09 29;23(19):11501. <https://doi.org/10.3390/ijms231911501>
 22. Chen J, Xie C, Yang Y, Yang S, Huang J, Ye F, Lin Z, et al. Association between albumin-to-globulin ratio and the risk of overall survival in advanced non-small cell lung cancer patients with anlotinib treatment: a retrospective cohort study. *BMC pulmonary medicine*. 2023 07 25;23(1):275. <https://doi.org/10.1186/s12890-023-02574-6>
 23. Cho O, Noh OK, Oh Y, Chang S, Ryu H, Lee EJ, Chun M. Hematological parameters during concurrent chemoradiotherapy as potential prognosticators in patients with stage IIB cervical cancer. *Tumour Biology: The Journal of the International Society for Oncodevelopmental Biology and Medicine*. 2017 02;39(2):1010428317694306. <https://doi.org/10.1177/1010428317694306>
 24. Kumar A, Gurram L, Naga Ch P, Nayak P, Mulye G, Chopra S, Engineer R, et al. Correlation of Hematological Parameters With Clinical Outcomes in Cervical Cancer Patients Treated With Radical Radio(chemo)therapy: A Retrospective Study. *International Journal of Radiation Oncology, Biology, Physics*. 2024 01 01;118(1):182-191. <https://doi.org/10.1016/j.ijrobp.2023.07.022>
 25. Garg M, Bhati P, Balaji G, Sasidharan A, Kalavagunta S, Vs S, Dutta D. Hematological Parameters at Baseline: A Novel Prognostic Factor for Cervical Cancer Patients Undergoing Concurrent Chemoradiotherapy in South India. *Cureus*. 2024 09;16(9):e69461. <https://doi.org/10.7759/cureus.69461>
 26. Oymak E, Guler OC, Onal C. Prognostic significance of albumin and globulin levels in cervical cancer patients treated with chemoradiotherapy. *International Journal of Gynecological Cancer*. 2023 01;33(1):19-25. <https://doi.org/10.1136/ijgc-2022-003768>
 27. Yu J, Huang L, Dong T, Cao L. Prediction of outcomes after chemoradiotherapy for cervical cancer by neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio. *Journal of Obstetrics and Gynaecology*. 2024 Dec 31;44(1):2361858. <https://doi.org/10.1080/01443615.2024.2361858>
 28. Fullerton R, Martell K, Khanolkar R, Phan T, Banerjee R, Meyer T, Traptow L, et al. Impact of immune, inflammatory and nutritional indices on outcome in patients with locally advanced cervical cancer treated with definitive (chemo)radiotherapy. *Gynecologic Oncology*. 2024 Nov;190:291-297. <https://doi.org/10.1016/j.ygyno.2024.09.005>
 29. Yoshino Y, Taguchi A, Shimizuguchi T, Nakajima Y, Takao M, Kashiyaama T, Furusawa A, Kino N, Yasugi T. A low albumin to globulin ratio with a high serum globulin level is a prognostic marker for poor survival in cervical cancer patients treated with radiation based therapy. *International Journal of Gynecological Cancer*. 2019 01;29(1):17-22. <https://doi.org/10.1136/ijgc-2018-000025>
 30. Berek JS, Hacker NF. Radiation therapy. Berek and Hacker's. In: *Gynecologic Oncology* 7th ed.: Wolters Kluwer, Philadelphia; 2021; p232-287...
 31. Myron Johnson A, Merlini G, Sheldon J, Ichihara K. Clinical indications for plasma protein assays: transthyretin (prealbumin) in inflammation and malnutrition: International Federation of Clinical Chemistry and Laboratory Medicine (IFCC): IFCC Scientific Division Committee on Plasma Proteins (C-PP). *Clinical Chemical Laboratory Medicine*. 2007 01 01;45(3). <https://doi.org/10.1515/CCLM.2007.051>
 32. Ballou M. Mechanisms of action of intravenous immune serum globulin in autoimmune and inflammatory diseases. *Journal of Allergy and Clinical Immunology*. 1997 08;100(2):151-157. [https://doi.org/10.1016/S0091-6749\(97\)70217-3](https://doi.org/10.1016/S0091-6749(97)70217-3)



This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International License.