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Correlation Of Haemoglobin, Leukocytes, Platelet And Neutrophil-Lymphocyte Ratio To Radiotherapy Response In Stage IIB-IIIB Cervical Cancer Patients

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ABSTRACT

Background: Cervical cancer is a common gynaecological cancer, with high prevalence especially in advanced stages. Radiotherapy is one of the main therapies, but the response to radiotherapy is influenced by several factors. Some studies suggest that haemoglobin, leucocyte, platelet, and neutrophil lymphocyte ratio (NLR) levels may play a role as prognostic indicators in the effectiveness of radiotherapy in cervical cancer. This study aims to analyse the relationship of haemoglobin, leucocyte, platelet and NLR levels to radiotherapy response in stage IIB-IIIB cervical cancer patients.

Methods: Analytical observational study with a retrospective cohort approach involving 50 stage IIB-IIIB cervical cancer patients undergoing radiation therapy. Blood profile measurements and radiotherapy response were taken from medical records before and during radiotherapy. Statistical analysis was performed using Chi-square test and logistic regression to determine the relationship between haematological parameters and radiotherapy response.

Results: The Friedman test showed a significant decrease in leukocyte levels during radiotherapy (X^2=81.54; p<0.001) and platelet levels (X^2=61.50; p<0.001), with a downward trend beginning after the 10th radiation session. However, there were no significant differences between hematological parameters (hemoglobin, leukocytes, platelets, and NLR) and treatment response groups (p>0.05). Log-rank analysis of progression-free survival (PFS) indicated that only leukocyte levels had a significant association. Preradiation leukocyte counts ≥8.85 were associated with a higher risk of disease progression (HR=2.96; 95% CI = 1.26–6.94; p=0.013).

Conclusion: Leukocytes serve as a prognostic factor in determining progressive response.

Keywords: *cervical cancer, hemoglobin, neutrophil-to-lymphocyte ratio (NLR), platelet, radiotherapy, response evaluation criteria in solid tumor (RECIST), white blood cells*

1. INTRODUCTION

Cervical cancer is the most common gynecological malignancy worldwide and ranks 14th among all cancers and 4th among women.[1] In 2018, approximately 570,000 women were diagnosed globally, with around 311,000 deaths. The American Cancer Society (2022) estimated that in the United States, there would be 14,100 new invasive cervical cancer cases and approximately 4,280 related deaths in 2022.[2] In Indonesia, cervical cancer ranks second among the top ten most common cancers, with an incidence rate of 12.7% based on anatomical pathology data from 2010. The Indonesian Ministry of Health (2017) estimated 90 to 100 new cases per 100,000 population annually, translating to roughly 40,000 new cases each year.[3] The primary cause of cervical cancer is persistent infection with Human Papilloma Virus (HPV), particularly types 16 and 18, which are responsible for about 70% of global cervical cancer cases.[4]

Disease severity in cervical cancer, as in other cancers, is categorized by clinical stage, with more advanced stages indicating worse clinical outcomes.[1,5] Common treatment approaches include surgery (hysterectomy), radiotherapy, chemotherapy, or a combination of these modalities.[6] Increasing emphasis has been placed on identifying predictive markers for poor prognosis. Several studies have indicated that inflammatory responses within the tumor microenvironment play a role in cancer progression. Cytokine production by leukocytes, often triggered by HPV infection, has been shown to affect disease development. HPV can downregulate interferon expression and upregulate IL-10 and TGF-β1, creating an immunosuppressive local environment that contributes to tumor immune evasion.[7,8]

Inflammatory markers such as the neutrophil-to-lymphocyte ratio (NLR) have gained attention as simple, cost-effective prognostic tools. Elevated NLR levels have been associated with poorer survival outcomes in various solid tumors, including cervical cancer. Higher NLR is correlated with larger tumor size, advanced clinical stage, and lymph node metastasis—

factors strongly associated with worse prognosis and reduced long-term survival.[9–12] These findings suggest that patients with aggressive tumor characteristics could benefit from NLR evaluation to support clinical decision-making.[13]

Other hematologic parameters, such as hemoglobin concentration, platelet count, and coagulation status, also serve as potential prognostic indicators. Anemia has been associated with poor local disease control and lower survival rates in cervical cancer patients. A study comparing patients with hemoglobin levels below and above 12 g/dL found that those with lower hemoglobin had more advanced disease, worse tumor differentiation, a higher incidence of lymph node metastasis, and a significantly lower five-year survival rate.[14] Given that hematopoiesis is highly sensitive to radiation, routine blood tests are commonly performed during radiotherapy to identify patients at risk of cytopenia. In some institutions, weekly blood monitoring is standard practice.[12] This study aims to assess the association between hemoglobin, leukocyte count, platelet levels, and NLR with radiotherapy response among patients with stage IIB–IIIB cervical cancer in Makassar.

2. MATERIAL AND METHODS

This study was approved by the Ethics Committee of Biomedical Research on Human Subjects, Faculty of Medicine, Hasanuddin University, Makassar. The research was conducted over the period from July 1st 2023 to October 20th 2024.

Study subjects

This analytical observational study used a retrospective cohort approach based on medical record data of cervical cancer patients at stage IIB–IIIB who underwent radiotherapy at Dr. Wahidin Sudirohusodo General Hospital (RSUP Dr Wahidin Sudirohusodo) and the Teaching Hospital of Hasanuddin University (RSP Universitas Hasanuddin).

Sample size

The sampling in this study was conducted using total sampling. The sample size was calculated using OpenEpi version 3 software, with a confidence interval of 95%, power of 80%, and a sample ratio of 1:1 between the two groups. Based on the difference in means and standard deviations between the two groups (Group 1: 374.7 ± 118.2 and Group 2: 290.4 ± 73.2), a required sample size of 44 subjects was obtained (22 per group). To anticipate potential data loss or dropouts, 10% of the total sample (approximately 6 subjects) was added, resulting in a minimum required sample size of 50 subjects.

Inclusion and exclusion criteria

The inclusion criteria in this study were as follows: patients diagnosed with cervical cancer based on biopsy results, patients in stage IIB–IIIB, patients who agreed to undergo radiotherapy, and patients who had complete laboratory tests including hemoglobin, platelet count, leukocyte count, neutrophil, and lymphocyte levels. Meanwhile, the exclusion criteria included pregnant women, patients with comorbidities or other malignancies such as HIV infection, autoimmune diseases, or systemic infections, patients who did not complete the radiotherapy cycle, and those without radiological examinations before and/or after radiotherapy.

Assesment

Data collection was conducted after obtaining approval from the Ethics Committee of the Faculty of Medicine, Hasanuddin University, and permission from the directors of Dr. Wahidin Sudirohusodo General Hospital and the Teaching Hospital of Hasanuddin University. The researcher collected data from medical records of patients diagnosed with stage IIB–IIIB cervical cancer who underwent radiotherapy only at the two hospitals, within the period from October 1st, 2022, to September 30th 2024. The medical records had to include complete information such as name, age, education, occupation, parity, marital status, menopausal status, nutritional status histopathology, tumor extent, cancer stage, blood transfusion, duration of treatment, radiotherapy response, and survival status, laboratory blood tests, and radiological examinations before and after radiotherapy. The treatment response in this study was categorized according to Response Evaluation Criteria in Solid Tumors (RECIST) criteria ver 1.1. into four groups: complete response (CR), partial response (PR), stable disease (SD), and progressive disease (PD). This standardized method was used to objectively assess changes in tumor size and to categorize the therapeutic outcomes. Subjects who did not meet the inclusion and exclusion criteria were excluded from the study. The necessary data were recorded and subsequently analyzed using the IBM Statistical Package for Social Sciences (SPSS) ver 24.

Statistical analysis

Descriptive statistics were first used to summarize patient characteristics, including age, education, occupation, parity, marital status, menopausal status, nutritional status histopathology, tumor extent, cancer stage, blood transfusion, duration of treatment, radiotherapy response, and survival status. Bivariate analysis was then performed to assess the relationship between clinical variables (hemoglobin, leukocytes, and NLR) and radiotherapy response. Wilcoxon and Friedman test was used to evaluate changes in hematologic parameters throughout the radiotherapy sessions. One-Way ANOVA and Kruskal-Wallis tests were used to compare hematological parameters among the different treatment response groups. Survival analysis was performed. Overall survival (OS) and progression-free survival (PFS) were assessed to evaluate patient outcomes across different treatment response groups. The log-rank test was used to compare survival distributions between

different treatment response groups. A significance level of 0.05 was used for all statistical tests.

3. RESULT

A total of 50 cervical cancer patients were included in this study. Medical records from were reviewed at RSUP Dr. Wahidin Sudirohusodo and RSP Universitas Hasanuddin. Out of 168 patients who underwent only radiation therapy, 65 met the stage criteria (I, IIA, IIIC, IVB), but 26 did not complete 35 cycles of radiation and 27 lacked pre- and post-radiation imaging. Therefore, 50 patients with stage IIB–IIIB who completed radiotherapy and had complete radiological data were selected. The study was conducted from November 2023 to October 2024 (Figure 1).

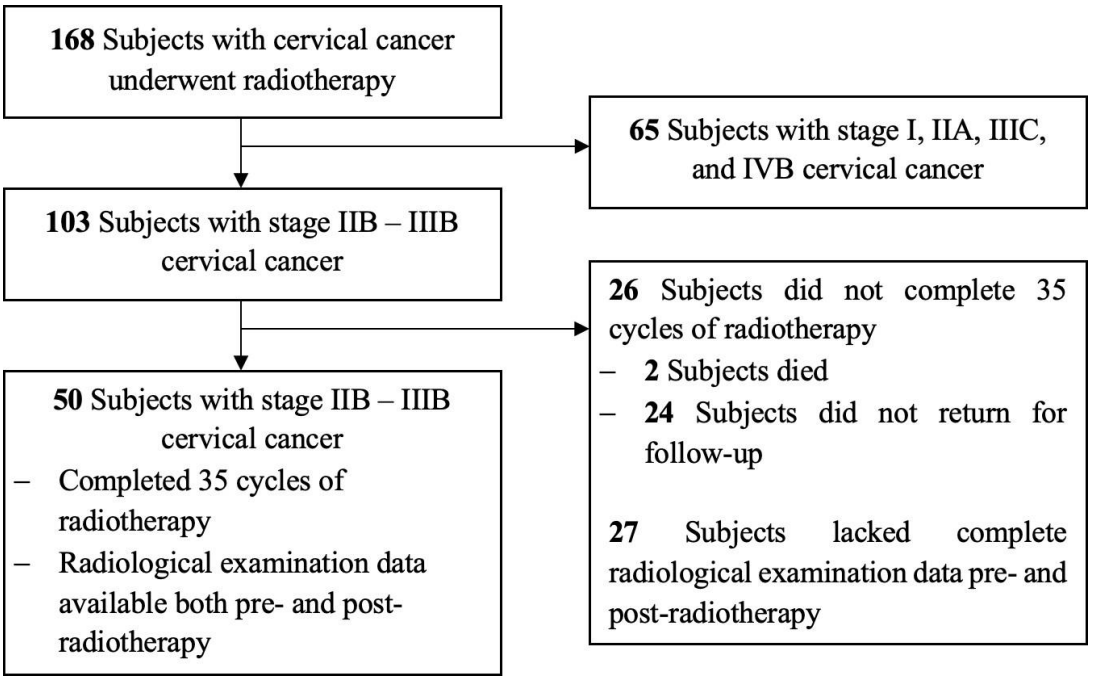

Figure 1. Subject Recruitment Flow

Table 1. Subjects Characteristics

Variable	Category	N	%
Age	≥49 years	23	54
	<49 years	27	46
Education	Elementary school	4	8
	Junior high school	5	10
	Senior high school	29	58
	University	12	24
Occupation	Employed	13	26
	Unemployed	37	74
Marital status	<2 times married	47	94
	≥2 times married	3	6
Parity	Nullipara	1	2
	Primipara	2	4
	Multipara	47	94

Menopause	Yes	20	40
	No	30	60
Nutritional status	Underweight	5	10
	Normal	18	36
	Overweight	11	22
	Obesity I	14	28
	Obesity II	2	4
Histopathology	Squamous Cell Carcinoma (SCC)	40	80
	Adenosquamous	2	4
	Adenocarcinoma	8	16
Tumor size	≤4 cm	9	18
	>4 cm	41	82
Lymph node spread	Present	18	36
	Absent	32	64
Lymphovascular space invasion	Negative	48	90
	Positive	2	4
Stage	IIB	40	80
	IIIA	3	6
	IIIB	7	14
Blood transfusion	Yes	26	52
	No	24	48
Duration of treatment	<68 days	25	50
	≥68 days	25	50
Radiotherapy response	Complete	4	8
	Partial	9	18
	Stable	12	24
	Progressive	25	50
Final status	Survived	46	92
	Deceased	4	8

The study population was predominantly composed of ≥49 years old patients with a relatively low level of formal employment. Most participants had been married once and had given birth more than once. The majority had not yet entered menopause perioed and presented with varied nutritional statuses, although overweight and obesity were common. Histopathological examination revealed that squamous cell carcinoma was the most frequent type. Most tumors were relatively large, with a notable proportion showing lymph node involvement, while lymphovascular space invasion was rare. The majority of cases were diagnosed at an advanced stage. Blood transfusions were frequently administered. In terms of therapeutic response, progressive disease was the most frequent outcome, and complete responses were uncommon. Despite this, the survival rate among participants was high.

Table 2. Changes in Laboratory Parameters during Radiotherapy

Parameter		Mean	SD	Median	p-value[a]	X^2	p-value[b]
Hemoglobin (g/dL)						5.65	0.581
	Preradiation	11.04	1.50	10.60			
	After 5th radiation	10.71	1.55	10.45	0.050		
	After 10th radiation	10.50	1.82	10.60	0.184		
	After 15th radiation	10.78	1.41	10.75	0.683		
	After 20th radiation	10.86	1.20	10.95	0.663		
	After 25th radiation	10.81	1.30	10.95	0.886		
	After 30th radiation	10.75	1.34	10.80	0.479		
	After 35th radiation	10.71	1.31	11.15	0.853		
Leukocyte ($x10^3/\mu L$)						81.54	<0.001*
	Preradiation	9.21	4.09	8.85			
	After 5th radiation	8.26	4.06	7.07	0.003*		
	After 10th radiation	6.77	3.97	5.80	<0.001*		
	After 15th radiation	6.39	2.76	5.88	0.413		
	After 20th radiation	6.04	2.30	5.61	0.212		
	After 25th radiation	5.82	2.05	5.25	0.465		
	After 30th radiation	5.83	2.59	5.29	0.604		
	After 35th radiation	6.51	3.25	5.73	0.086		
Platelet ($x10^3/\mu L$)						61.50	<0.001*
	Preradiation	337.52	95.60	333.00			
	After 5th radiation	327.02	95.19	334.00	0.367		
	After 10th radiation	273.52	85.12	252.00	<0.001*		
	After 15th radiation	265.62	69.51	255.50	0.299		
	After 20th radiation	267.16	65.62	266.50	0.581		
	After 25th radiation	269.70	63.54	265.50	0.713		
	After 30th radiation	264.98	63.36	270.50	0.472		
	After 35th radiation	278.16	82.23	283.00	0.142		
NLR						104.81	<0.001*
	Preradiation	4.04	3.19	2.78			
	After 5th radiation	5.65	3.89	4.82	0.002*		
	After 10th radiation	7.12	5.15	5.90	<0.001*		
	After 15th radiation	8.84	6.33	7.07	0.003*		
	After 20th radiation	9.64	7.86	7.28	0.233		

	After 25th radiation	9.45	7.64	7.32	0.540		
	After 30th radiation	7.93	6.80	5.58	0.039*		
	After 35th radiation	7.31	9.00	4.74	0.222		

[a] Wilcoxon test; [b] Friedmann test; * significant at 0.05 level

The mean hemoglobin level decreased slightly from 11.04 mg/dL before therapy to 10.71 mg/dL after the 35th session, but this change was not statistically significant (Friedman test $X^2 = 5.65$, $p = 0.581$). In contrast, leukocyte levels showed a significant decrease primarily after the 5th and 10th radiation sessions, dropping from 9.21×10^3 to 8.26×10^3 and further to 6.77×10^3, indicating an early and acute hematologic response to radiation. Platelet levels remained relatively stable after the 5th session but experienced a more marked decline only after the 10th session, from 327.02×10^3 to 273.52×10^3. The NLR values showed a noticeable increase throughout the course of radiation therapy, peaking at session 20 before gradually declining in later sessions. Although the overall change was statistically significant ($X^2 = 104.81$, $p < 0.001$), only the increases after sessions 5, 10, 15, and 30 were statistically significant in post-hoc analysis (Table 2 & Figure 2).

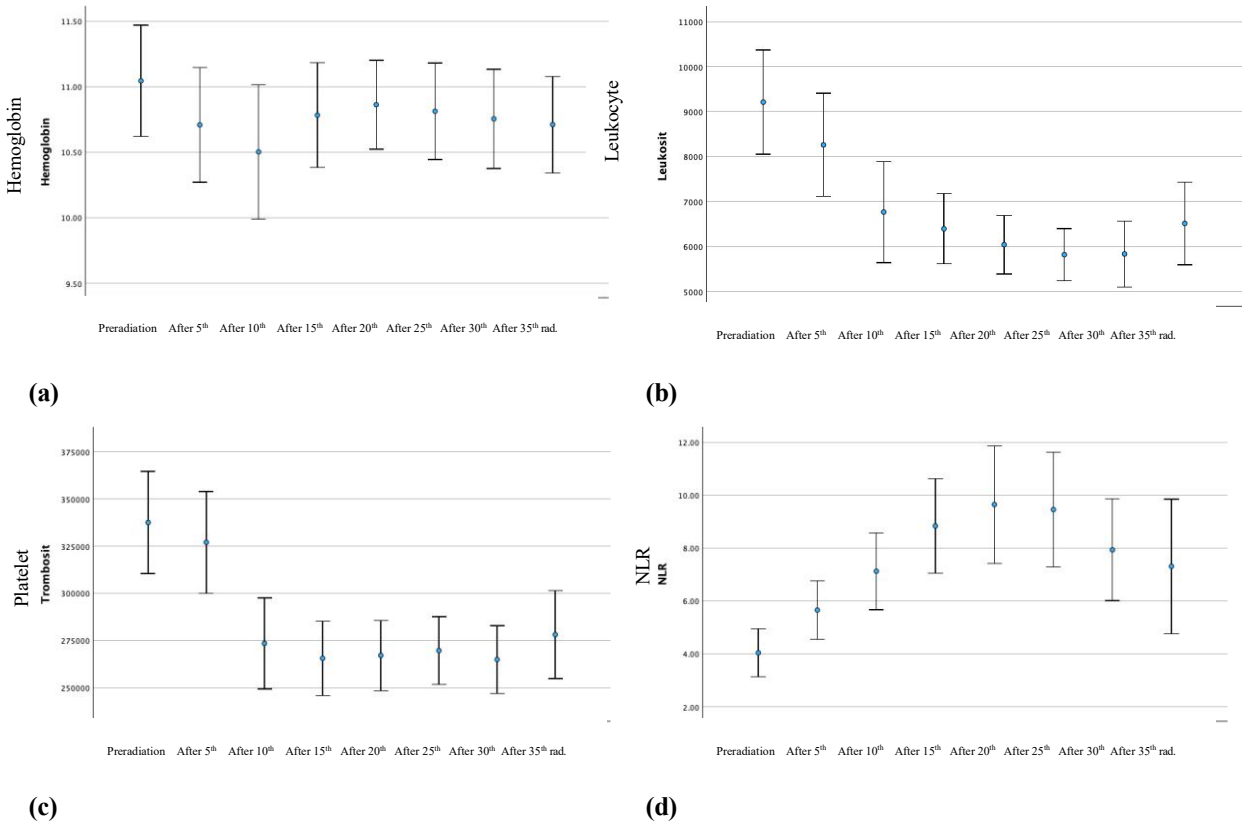

Figure 2. Error Bar of Changes in a) Hemoglobin, b) Leukocytes, c) Platelets, and d) Neutrophil-to-Lymphocyte Ratio

Hemoglobin levels remained relatively constant across all response groups, with no statistically significant differences observed at any measurement point ($p>0.05$). Leukocyte counts exhibited a general decline up to the 30th radiation session, followed by a slight increase at session 35, yet these changes were not statistically significant between the different response groups ($p>0.05$). Similarly, platelet levels showed a declining trend after the initiation of radiotherapy, but no significant intergroup differences were detected ($p>0.05$). NLR values increased after the fifth radiation, particularly in patients with stable or progressive disease. However, statistical analysis revealed no significant differences between response groups at most time points ($p>0.05$), except after the 15th session where a significant difference was noted ($p=0.046$) (Table 3).

Table 3. Difference in Hematological Parameter based on Radiotherapy Response

Parameter		Radiotherapy Response				p-value
		Complete	Partial	Stable	Progressive	
Hemoglobin (g/dL)[a]						
	Preradiation	10.60 ± 1.78	11.19 ± 1.91	11.07 ± 0.87	11.05 ± 1.62	0.937
	After 5th rad.	10.73 ± 1.35	11.52 ± 1.54	10.24 ± 1.14	10.64 ± 1.71	0.310
	After 10th rad.	10.30 ± 1.98	10.83 ± 1.49	10.25 ± 1.60	10.54 ± 2.06	0.905
	After 15th rad.	11.18 ± 1.21	11.11 ± 1.48	10.64 ± 1.24	10.67 ± 1.54	0.793
	After 20th rad.	11.03 ± 0.56	11.08 ± 1.13	10.75 ± 1.52	10.81 ± 1.17	0.921
	After 25th rad.	11.00 ± 0.69	10.94 ± 1.20	10.73 ± 1.40	10.78 ± 1.41	0.971
	After 30th rad.	11.05 ± 0.66	10.62 ± 1.34	10.78 ± 1.53	10.74 ± 1.38	0.964
	After 35th rad.	10.38 ± 0.76	10.52 ± 1.14	10.82 ± 1.45	10.78 ± 1.40	0.902
Leukocyte (x10^3/ µL)[b]						
	Preradiation	9.58 (3.34)	7.30 (3.66)	6.75 (3.41)	9.76 (4.72)	0.084
	After 5th rad.	7.45 (5.37)	6.80 (4.28)	6.16 (1.74)	7.61 (5.44)	0.718
	After 10th rad.	5.55 (0.95)	5.48 (1.99)	5.92 (5.62)	6.48 (3.85)	0.504
	After 15th rad.	5.30 (0.97)	5.70 (2.44)	5.75 (2.93)	6.12 (4.09)	0.362
	After 20th rad.	5.26 (0.57)	5.30 (2.93)	5.85 (5.03)	5.70 (2.60)	0.785
	After 25th rad.	5.38 (1.04)	4.39 (1.37)	6.20 (4.80)	5.29 (2.81)	0.297
	After 30th rad.	5.11 (1.03)	5.00 (1.74)	5.42 (2.58)	5.40 (2.31)	0.439
	After 35th rad.	6.57 (6.07)	6.26 (5.46)	4.83 (1.55)	6.00 (3.12)	0.466
Plaetelet (x10^3/ µL)[a]						
	Preradiation	324.0 ± 45.8	344.1 ± 135.7	321.1 ± 103.9	345.2 ± 84.1	0.894
	After 5th rad.	269.8 ± 36.7	307.8 ± 75.5	324.0 ± 117.1	344.6 ± 95.6	0.455
	After 10th rad.	24.,5 ± 5.6	227.7 ± 43.0	295.3 ± 132.7	284.0 ± 69.5	0.243
	After 15th rad.	230.3 ± 29.2	247.7 ± 83.4	283.1 ± 82.4	269.4 ± 61.9	0.494
	After 20th rad.	229.8 ± 37.6	270.8 ± 61.4	263.7 ± 76.6	273.5 ± 66.2	0.673
	After 25th rad.	256.0 ± 50.6	269.9 ± 80.9	252.5 ± 75.0	280.1 ± 53.6	0.643
	After 30th rad.	255.5 ± 25.7	257.6 ± 85.1	257.6 ± 73.6	272.7 ± 55.6	0.869
	After 35th rad.	257.0 ± 36.9	301.3 ± 145.5	237.9 ± 57.8	292.5 ± 61.4	0.204
NLR[b]						
	Preradiation	1.86 (1.24)	2.95 (3.55)	3.35 (3.99)	2.71 (4.82)	0.264
	After 5th rad.	5.94 (12.91)	5.20 (3.60)	5.05 (4.70)	4.46 (5.16)	0.916
	After 10th rad.	3.10 (2.19)	6.03 (2.29)	6.29 (3.05)	5.72 (7.74)	0.088
	After 15th rad.	3.96 (2.03)	6.92 (3.37)	6.94 (6.57)	8.07 (9.51)	0.046*

	After 20th rad.	4.98 (2.46)	7.30 (3.98)	7.69 (10.20)	7.99 (7.29)	0.082
	After 25th rad.	7.36 (4.94)	6.17 (3.89)	8.61 (6.71)	7.54 (7.52)	0.764
	After 30th rad.	3.99 (4.77)	4.68 (6.22)	6.59 (3.01)	6.56 (6.91)	0.471
	After 35th rad.	5.41 (12.88)	6.47 (20.70)	4.92 (4.93)	4.44 (4.11)	0.569

[a] mean ± standard deviation & tested using the One-Way ANOVA test; [b] median (interquartile range) & tested using the Kruskal-Wallis test; * significant at 0.05 level

Based on the log-rank test results for overall survival (OS), no statistically significant differences were found for any of the parameters analyzed. In contrast, the log-rank test for progression-free survival (PFS) revealed several parameters with statistically significant results, including lymph node spread (p<0.001), blood transfusion (p=0.002), leukocyte count (p=0.007), and age (p=0.032) (Table 4).

Based on the analysis of factors affecting OS, no statistically significant associations were found for any of the parameters tested. In contrast, the analysis of PFS revealed several variables with significant associations. Age ≥47.5 years showed a protective effect on PFS (HR 0.43; p=0.044). Additionally, the presence of lymph node spread (HR 3.93; p=0.001), blood transfusion (HR 3.75; p=0.005), and leukocyte levels ≥8.85 (HR 2.96; p=0.013) significantly increased the risk of disease progression. Other variables such as histopathology, tumor size, stage, duration of therapy, hemoglobin, platelet count, and NLR did not show a significant influence on PFS (p>0.05) (Table 5).

Table 4. Log-Rank Test of the Association Between Factors and OS and PFS

Parameter	**Log Rank**	
	OS	**PFS**
Age	0.284	0.032*
Histopathology	0.699	0.462
Tumor size	0.277	0.122
Lymph node spread	0.069	<0.001*
Lymphovascular invasion	0.671	0.461
Stage	0.825	0.102
Blood transfusion	0.313	0.002*
Duration of treatment	0.451	0.654
Hemoglobin	0.928	0.702
Leukocyte	0.183	0.007*
Platelet	0.996	0.800
NLR	0.996	0.618

* Significant at 0.05 level

4. DISCUSSION

Subject Characteristics

This study involved 50 patients with stage IIB–IIIB cervical cancer undergoing radiotherapy. Most patients were over 49 years old and had high school or college education, factors linked to early detection and diagnosis of cervical cancer.[15,16] The majority were employed and multiparous, contributing to increased risk due to hormonal changes and cervical trauma.[17,18] Squamous cell carcinoma was the most common histopathological type (78%), with 78% of patients at stage IIB and 60% premenopausal, consistent with previous studies [19,20]. Obesity was prevalent, and most tumors were >4 cm with 64% showing lymph node spread, indicating advanced disease.[21–23] Blood transfusions were required in 52% of cases to maintain hemoglobin levels during therapy.[24]

The response to radiotherapy in cervical cancer patients was evaluated using RECIST version 1.1, which assesses changes

in tumor size through imaging techniques such as MRI or CT scan. Target lesions are limited to a maximum of five in total and two per organ, selected based on size and measurability, with measurements taken as the longest diameter or short axis for lymph nodes. Non-target lesions are assessed qualitatively as CR, Non-CR/Non-PD, or PD, Evaluations are typically done using consistent imaging methods. Although this method provides standardized evaluation, it may have limitations in distinguishing necrotic tissue from residual active tumor, especially in gradually regressing cervical cancer.[25] Only 8% showed a complete response, while 50% experienced disease progression, contrasting with higher complete response rates reported in studies involving chemoradiotherapy.[22] Despite this, 92% of patients survived High progression rate may come from the use of radiotherapy alone, whereas current guidelines by ESMO and NCCN recommend combined chemoradiation and/or surgery for locally advanced cases.[26] Previous meta-analyses confirm that chemoradiation and/or surgery significantly improves complete response, regional control, and overall survival, despite increased acute toxicity risks.[27]

Table 5. Hazard Ratio Analysis of OS and PFS of Various Factors

Parameter		**OS**		**PFS**	
		HR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**
Age	<47.5 (Ref.)	0.31 (0.03 – 3.00)	0.311	0.43 (0.19 – 0.98)	0.044*
	≥47.5				
Histopathology	SCC (Ref.)	1.56 (0.16 – 15.04)	0.701	0.65 (0.19 – 2.17)	0.481
	Non-SCC				
Tumor size	≤4 cm (Ref.)	30.40 (0.00 – 68…)	0.505	2.27 (0.75 – 6.88)	0.148
	>4 cm				
Lymph node spread	Absent (Ref.)	6.43 (0.65 – 63.21)	0.111	3.93 (1.69 – 9.16)	0.001*
	Present				
Lymphovascular invasion	Negative (Ref.)	0.05 (0.00 – 994…)	0.779	0.05 (0.00 – 13…)	0.633
	Positve				
Stage	IIB (Ref.)	1.29 (0.13 – 124…)	0.826	1.96 (0.84 – 4.61)	0.121
	IIIA-IIIB				
Blood transfusion	No (Ref.)	3.06 (0.31 – 29.87)	0.337	3.75 (1.49 – 9.44)	0.005*
	Yes				
Duration of treatment	<68 days (Ref.)	2.34 (0.24 – 22.78)	0.464	1.19 (0.54 – 2.62)	0.667
	≥68 days				
Hemoglobin	<10.6 (Ref.)	0.91 (0.13 – 6.49)	0.928	0.86 (0.39 – 1.89)	0.713
	≥10.6				
Leukocyte	<8.85 (Ref.)	4.18 (0.43 – 40.78)	0.219	2.96 (1.26 – 6.94)	0.013*
	≥8.85				
Platelet	<333.0 (Ref.)	0.99 (0.14 – 7.07)	0.996	1.11 (0.50 – 2.46)	0.807
	≥333.0				
NLR	<2.78 (Ref.)	1.01 (0.14 – 7.13)	0.996	1.22 (0.55 – 2.70)	0.630
	≥2.78				

* Significant at 0.05 level

Analysis of Changes in Hematological Parameters

The mean hemoglobin level before radiotherapy was 11.04 ± 1.50 mg/dL, which decreased to 10.71 ± 1.55 mg/dL after the fifth radiation session. Although statistically insignificant (p=0,050), this result indicating an early hematological impact of radiotherapy.[28] This decline is attributed to radiation-induced cytotoxic effects on bone marrow and increased red blood cell destruction from oxidative stress.[29,30] Radiation, particularly in the pelvic area, impairs hematopoietic progenitor cells, leading to decreased erythropoiesis and persistent anemia.[31] Although hemoglobin levels remained below pre-radiation levels during therapy, they stabilized after the first cycle, consistent with findings that showed no significant change in hemoglobin across radiation cycles.[32] Blood transfusions, commonly administered after the first cycle to prevent anemia-related complications, played a role in maintaining hemoglobin stability.[33–36] The effectiveness of transfusions in maintaining stable hemoglobin was also supported by Mitsuhashi et al., who observed no significant changes in levels up to four weeks post-therapy.[37] Additionally, radiotherapy impairs hematopoietic stem cell function and bone marrow homeostasis, contributing to prolonged hematological changes.[38]

This study revealed a statistically significant decline in leukocyte counts after the 5th and 10th radiotherapy sessions, with mean levels dropping from 9.21 $\times 10^3/\mu L$ pre-radiation to 8.26 $\times 10^3/\mu L$ post-5th session (p=0.003) and further to 6.77 $\times 10^3/\mu L$ post-10th session (p<0.001), indicating an early impact of radiation on leukopenia.[39,40] These findings align with previous studies reporting acute leukopenia in cervical cancer patients during the early phase of treatment, influenced by factors such as radiation dose and baseline leukocyte levels.[41,42] Radiation damages hematopoietic cells in the bone marrow, where lymphocytes, the most radiosensitive white cells, may decline by up to 65% after a single low-dose exposure.[43] Granulocytes like neutrophils also decrease, with delayed recovery post-treatment, and neutrophil counts may drop by 11.2%, persisting even three months after therapy.[44] Moreover, radiation reduces monocyte viability by up to 30%, contributing to overall leukopenia.[45] These leukocyte reductions during early radiotherapy are attributed to high radiation exposure to active bone marrow, delayed cellular recovery, and the high radiosensitivity of white blood cells.[44]

This study observed a significant decline in platelet count after the 10th radiotherapy session, with mean levels decreasing from 327.02 $\times 10^3/\mu L$ post-5th session to 273.52 $\times 10^3/\mu L$ (p<0.001), indicating a cumulative radiation effect on thrombocyte production or destruction. Although platelet levels remained lower than baseline following this drop, no further statistically significant changes were observed in later sessions, suggesting that the most notable hematologic impact occurs during the early-mid phase of therapy. Radiation inhibits platelet production by suppressing bone marrow activity and damaging megakaryocytes through oxidative stress-induced DNA damage and apoptosis via mitochondrial and p53 pathways.[46,47] Moreover, radiation may reduce thrombopoietin levels, further impairing platelet production. Despite their relative radioresistance, megakaryocytes begin to show dysfunction as cumulative radiation doses increase, particularly beyond 50 Gy.[45,48] While early doses (e.g., after 5 sessions) may be insufficient to cause significant thrombocytopenia, the data suggest that reaching a certain threshold (around the 10th session) begins to impact bone marrow hematopoiesis.[45] Thus, careful monitoring of cumulative dose and its distribution across active bone marrow regions is essential to prevent hematologic complications such as thrombocytopenia.[49,50]

The neutrophil-to-lymphocyte ratio (NLR) showed a significant increase during the early to mid-phase of radiotherapy, rising from a mean of 4.04 pre-radiation to 5.65 after the 5th session (p=0.002) and peaking at 8.84 after the 15th session (p=0.003), reflecting an inflammatory response and lymphocyte depletion due to radiation exposure. Although NLR values remained elevated at the 20th and 25th sessions, changes were not statistically significant, with a decline beginning at the 30th session (p=0.039). Overall, changes in NLR throughout therapy were statistically significant (p<0.001). Radiotherapy induces damage to hematopoietic cells in the bone marrow, particularly affecting lymphocytes more than neutrophils due to their higher radiosensitivity, leading to early lymphocyte decline and increased NLR. As treatment progresses, neutrophil levels begin to decline as well, slowing the NLR rise and contributing to its eventual plateau and decrease.[45,51]

Hematological Factors on OS and PFS

Low hemoglobin levels prior to therapy are often associated with poor prognosis in cervical carcinoma due to tumor hypoxia, which reduces radiotherapy effectiveness by inducing pro-angiogenic factors like HIF-1α, leading to therapy resistance.[52,53] Adequate hemoglobin is crucial for optimal radiotherapy response as oxygenation enhances cancer cell sensitivity to radiation by facilitating DNA damage, whereas hypoxia impairs treatment outcomes.[54] However, in this study, hemoglobin levels (≥10.6 g/dL) were not significantly associated with OS or PFS, as indicated by hazard ratios of 0.91 and 0.86 (p=0.928 and p=0.713), consistent with Gennigens et al. (2020).[32] Several studies suggest that low hemoglobin levels do not always significantly impact tumor hypoxia or treatment response, as reoxygenation during therapy and partial effectiveness of anemia correction with EPO or transfusions may mitigate these effects.[55] Additionally, factors such as uniform patient distribution, uncontrolled confounders like transfusion therapy and nutritional status, as well as comorbidities and individual variations in treatment response may influence outcomes, warranting further research with better-controlled variables.[51,56]

Leukocyte count is often used as a marker of systemic inflammation and has been associated with poor prognosis in cervical cancer patients, with elevated levels linked to increased inflammatory response, metastasis, and aggressive disease

progression.[57,58] In this study, leukocyte levels ≥8.85 x10³ were significantly associated with worse progression-free survival (PFS), with a hazard ratio of 2.96 (95% CI: 1.26–6.94; p = 0.013), indicating leukocytosis as a negative predictor possibly due to enhanced tumor aggressiveness and therapy resistance.[32,59,60] However, some studies found no significant association, potentially due to sample size limitations, differences in measurement methods, or patient characteristics such as age, cancer stage, and therapeutic response.[61,62]

Platelets play a critical role in cancer progression by promoting tumor proliferation, angiogenesis, and metastasis, with several studies linking elevated pre-treatment platelet counts to poorer prognosis in cervical cancer patients undergoing radiotherapy.[63,64] However, this study found no significant association between platelet count and either OS or PFS (p=0.996 for OS and p=0.807 for PFS), indicating that higher platelet levels (≥333,000/µL) were not independent predictors of outcomes. These findings align with other research showing that platelet count is not always a reliable prognostic marker, potentially due to variability in cutoff values, patient heterogeneity, limited sample size, and confounding factors like coagulation markers and systemic inflammatory indices.[65,66]

The neutrophil-to-lymphocyte ratio (NLR) is recognized as an inflammatory biomarker reflecting systemic immune response to malignancy, with elevated pre-treatment NLR associated with poor prognosis in cervical cancer patients undergoing radiotherapy.[66] Pathophysiologically, a high NLR indicates neutrophil predominance promoting a tumor-supportive microenvironment through proinflammatory cytokines, while reduced lymphocyte counts reflect weakened antitumor immunity.[67] However, in this study, NLR showed no significant association with OS or PFS, as evidenced by high p-values (p=0.996 for OS and p=0.630 for PFS). Although previous studies have supported NLR's prognostic value, others found no statistical significance, possibly due to small sample sizes or high clinical heterogeneity affecting analytical power [68]. Additionally, variations in NLR cut-off values and multivariate analysis approaches may obscure its independent predictive value.[66]

Other Factors on OS and PFS

This study identified lymph node spread (HR: 3.93; p=0.001), blood transfusion (HR: 3.75; p=0.005), and age ≥47.5 years (HR: 0.43; p=0.044) as significant factors affecting progression-free survival (PFS), with older age associated with a lower risk of progression. Bogani et al. (2017) also found lymph node spread to be significantly associated with reduced PFS (HR: 2.4; 95% CI: 1.00–6.06; p=0.05), but blood transfusion did not show a statistically significant effect (HR: 2.71; 95% CI: 0.91–8.03; p=0.07).[69]

This study has limitations, including its retrospective design, which may introduce selection and information bias. The relatively small sample size and single-center setting also limit the generalizability of the findings. Additionally, potential confounding variables such as nutritional status, comorbidities, and concurrent treatments were not fully controlled. Despite these limitations, the findings highlight leukocyte count as a potential prognostic factor for progression-free survival in patients with stage IIB–IIIB cervical cancer undergoing radiotherapy. These results suggest the need for larger, prospective, and multicenter studies to validate the prognostic value of hematological markers and to explore their integration into clinical decision-making, possibly in combination with inflammatory indices and imaging parameters.

5. CONCLUSION

Based on this study, among the four hematological parameters analyzed—hemoglobin, leukocyte, platelet, and neutrophil-to-lymphocyte ratio (NLR)—only leukocyte count showed a significant association with radiotherapy response in patients with stage IIB–IIIB cervical cancer. This highlights the potential of leukocyte levels as a hematological indicator for evaluating treatment effectiveness in this patient group.

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Author's Contributions

Nugraha Utama Pelupessy, Nur Rakhmah, and Andi Alfian Zainuddin have been involved in drafting the manuscript. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare no conflict of interest.

Consent for Publication

There is consent for the publication of this paper.

REFERENCES

[1] Bejar FG, Oaknin A, Williamson C, Mayadev J, Peters PN, Secord AA, et al. Novel therapies in gynecologic cancer. American Society of Clinical Oncology Educational Book. 2022;(42):483–99.

[2] The American Cancer Society. Key Statistics Cervical Cancer. Atlanta: The American Cancer Society; 2022.

[3] Kementerian Kesehatan Republik Indonesia. Pedoman Nasional Pelayanan Kedokteran Kanker Serviks. Jakarta: Kementerian Kesehatan Republik Indonesia; 2017.

[4] Bai Y. Molecular Genetic Pathology Of Solid Tumors: Henry's Clinical Diagnosis and Management by Laboratory Methods. Elsevier; 2022.

[5] Bermúdez-Guzmán L. Pan-cancer analysis of non-oncogene addiction to DNA repair. Sci Rep. 2021;11(1):23264.

[6] The American Cancer Society. Treating Cervical Cancer. Atlanta: The American Cancer Society; 2021.

[7] Carrero YN, Callejas DE, Mosquera JA. In situ immunopathological events in human cervical intraepithelial neoplasia and cervical cancer: Review. Transl Oncol. 2021;14(5):101058.

[8] Choi N, Kim JH, Chie EK, Gim J, Kang HC. A meta-analysis of the impact of neutrophil-to-lymphocyte ratio on treatment outcomes after radiotherapy for solid tumors. Medicine. 2019;98(18):e15369.

[9] Kim HS, Yoon G, Ryu JY, Cho YJ, Choi JJ, Lee YY, et al. Sphingosine kinase 1 is a reliable prognostic factor and a novel therapeutic target for uterine cervical cancer. Oncotarget. 2015;6(29):26746–56.

[10] Rojas-Puentes L, Cardona AF, Carranza H, Vargas C, Jaramillo LF, Zea D, et al. Epithelial–mesenchymal transition, proliferation, and angiogenesis in locally advanced cervical cancer treated with chemoradiotherapy. Cancer Med. 2016;5(8):1989–99.

[11] Xie XZ, Song K, Cui B, Jiang J, Zhang YZ, Wang B, et al. Clinical and pathological factors related to the prognosis of chinese patients with stage Ib to IIb cervical cancer. Asian Pacific Journal of Cancer Prevention. 2012;13(11):5505–10.

[12] Yang Y, Song K ling, Chang H, Chen L. Decreased expression of microRNA-126 is associated with poor prognosis in patients with cervical cancer. Diagn Pathol. 2014;9(1):220.

[13] Wu J, Chen M, Liang C, Su W. Prognostic value of the pretreatment neutrophil-to-lymphocyte ratio in cervical cancer: a meta-analysis and systematic review. Oncotarget. 2017;8(8):13400–12.

[14] Li B, Shou Y, Zhu H. Predictive value of hemoglobin, platelets, and D-dimer for the survival of patients with stage IA1 to IIA2 cervical cancer: a retrospective study. Journal of International Medical Research. 2021;49(12).

[15] Allahqoli L, Dehdari T, Rahmani A, Fallahi A, Gharacheh M, Hajinasab N, et al. Delayed cervical cancer diagnosis: a systematic review. Eur Rev Med Pharmacol Sci. 2022;26(22):8467–80.

[16] Abu SH, Woldehanna BT, Nida ET, Tilahun AW, Gebremariam MY, Sisay MM. The role of health education on cervical cancer screening uptake at selected health centers in Addis Ababa. PLoS One. 2020;15(10):e0239580.

[17] Isabirye A. Individual and intimate-partner factors associated with cervical cancer screening in Central Uganda. PLoS One. 2022;17(9):e0274602.

[18] Tekalegn Y, Sahiledengle B, Woldeyohannes D, Atlaw D, Degno S, Desta F, et al. High parity is associated with increased risk of cervical cancer: Systematic review and meta-analysis of case-control studies. Women's health. 2022;18:1.

[19] Wang M, Huang K, Wong MCS, Huang J, Jin Y, Zheng ZJ. Global cervical cancer incidence by histological subtype and implications for screening methods. J Epidemiol Glob Health. 2024;14(1):94–101.

[20] Ojha N, Jha M, Shrestha E, Dangal G. Late stage cervical cancer among confirmed cervical cancer cases in a tertiary care centre: A descriptive cross-sectional study. JNMA J Nepal Med Assoc. 2021;59(239):630–4.

[21] Urbute A, Frederiksen K, Thomsen LT, Kesmodel US, Kjaer SK. Overweight and obesity as risk factors for cervical cancer and detection of precancers among screened women: A nationwide, population-based cohort study. Gynecol Oncol. 2024;181:20–7.

[22] Liang C, Wang W, Yang G, Xu Z, Li J, Wu K, et al. Utility of interim apparent diffusion coefficient value in predicting treatment response among patients with locally advanced cervical cancer treated with radiotherapy. Clin Transl Radiat Oncol. 2024;48:100827.

[23] Olthof EP, van der Aa MA, Adam JA, Stalpers LJA, Wenzel HHB, van der Velden J, et al. The role of lymph nodes in cervical cancer: incidence and identification of lymph node metastases—a literature review. Int J Clin

Oncol. 2021;26(9):1600–10.

[24] Zayed S, Nguyen TK, Lin C, Boldt G, Beriwal S, Creutzberg CL, et al. Red blood cell transfusion practices for patients with cervical cancer undergoing radiotherapy. JAMA Netw Open. 2021;4(4):e213531.

[25] Ruchalski K, Anaokar JM, Benz MR, Dewan R, Douek ML, Goldin JG. A call for objectivity: Radiologists' proposed wishlist for response evaluation in solid tumors (RECIST 1.1). Cancer Imaging. 2024;24(1):154.

[26] Marth C, Landoni F, Mahner S, McCormack M, Gonzalez-Martin A, Colombo N. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2017;28:iv72–83.

[27] Datta NR, Stutz E, Liu M, Rogers S, Klingbiel D, Siebenhüner A, et al. Concurrent chemoradiotherapy vs . radiotherapy alone in locally advanced cervix cancer: A systematic review and meta-analysis. Gynecol Oncol. 2017;145(2):374–85.

[28] Berta DM, Teketelew BB, Chane E, Bayleyegn B, Tamir M, Cherie N, et al. Hematological changes in women with cervical cancer before and after cancer treatment: Retrospective cohort study. Sci Rep. 2024;14(1):27630.

[29] Jameus A, Kennedy AE, Thome C. Hematological changes following low dose radiation therapy and comparison to current standard of care cancer treatments. Dose Response. 2021;19(4):15593258211056196.

[30] Corbeau A, Kuipers SC, de Boer SM, Horeweg N, Hoogeman MS, Godart J, et al. Correlations between bone marrow radiation dose and hematologic toxicity in locally advanced cervical cancer patients receiving chemoradiation with cisplatin: a systematic review. Radiotherapy and Oncology. 2021;164:128–37.

[31] Vitzthum LK, Heide ES, Park H, Williamson CW, Sheridan P, Huynh-Le MP, et al. Comparison of hematologic toxicity and bone marrow compensatory response in head and neck vs. cervical cancer patients undergoing chemoradiotherapy. Front Oncol. 2020;10.

[32] Gennigens C, DeCuypere M, Seidel L, Hermesse J, Barbeaux A, Forget F, et al. Correlation between hematological parameters and outcome in patients with locally advanced cervical cancer treated by concomitant chemoradiotherapy. Cancer Med. 2020;9(22):8432–43.

[33] Duskin-Bitan H, Leibner A, Amitai O, Diker-Cohen T, Hirsch D, Benbassat C, et al. Bone-marrow suppression in elderly patients following empiric radioiodine therapy: Real-life data. Thyroid. 2019;29(5):683–91.

[34] Huang J, Gu F, Ji T, Zhao J, Li G. Pelvic bone marrow sparing intensity modulated radiotherapy reduces the incidence of the hematologic toxicity of patients with cervical cancer receiving concurrent chemoradiotherapy: a single-center prospective randomized controlled trial. Radiation Oncology. 2020;15(1):180.

[35] Shimura K, Mabuchi S, Komura N, Yokoi E, Kozasa K, Sasano T, et al. Prognostic significance of bone marrow FDG uptake in patients with gynecological cancer. Sci Rep. 2021;11(1):2257.

[36] Ran Q, Guo C, Sun C, Liu Q, He H, Zhao W, et al. Loss of FGFR3 accelerates bone marrow suppression-induced hematopoietic stem and progenitor cell expansion by activating FGFR1-ELK1-Cyclin D1 signaling. Transplant Cell Ther. 2021;27(1):45.e1-45.e10.

[37] Mitsuhashi N, Ikeda H, Nemoto Y, Kuronuma M, Kamiga M, Hiroshima Y. Hemostatic effect of palliative radiation therapy in preventing blood transfusions from bleeding occurring within advanced gastric cancer. Palliat Med Rep. 2021;2(1):355–64.

[38] Rafieemehr H, Maleki Behzad M, Azandeh S, Farshchi N, Ghasemi Dehcheshmeh M, Saki N. Chemo/radiotherapy-induced bone marrow niche alterations. Cancer Invest. 2020;1–15.

[39] Jia W, Li X, Zhang T, Wang C, Zhen M. Efficiently normalizing leukopoiesis by gadofullerene nanoparticles to ameliorate radiation-triggered myelosuppression. J Mater Chem B. 2023;11(31):7401–9.

[40] Sun S, Chen Z, Li P, Wu J, Zhu B, Zhang X, et al. Clinical study of acute toxicity of pelvic bone marrow-sparing intensity-modulated radiotherapy for cervical cancer. Ginekol Pol. 2023;94(2):101–6.

[41] Trindade AJ, Thaniyavarn T, Townsend K, Klasek R, Tsveybel KP, Kennedy JC, et al. Alemtuzumab as a therapy for chronic lung allograft dysfunction in lung transplant recipients with short telomeres. Front Immunol. 2020;11.

[42] Ye X, Zhou J, Guo S, Lou P, Ma R, Guo J. The undervalued acute leukopenia induced by radiotherapy in cervical cancer. Curr Radiopharm. 2023;16(1):50–6.

[43] Wild AT, Herman JM, Dholakia AS, Moningi S, Lu Y, Rosati LM, et al. Lymphocyte-sparing effect of stereotactic body radiation therapy in patients with unresectable pancreatic cancer. International Journal of Radiation Oncology Physics. 2016;94(3):571–9.

[44] Miszczyk M, Majewski W. Hematologic toxicity of conformal radiotherapy and intensity modulated radiotherapy in prostate and bladder cancer patients. Asian Pac J Cancer Prev. 2018;19(10):2803–6.

[45] Swanson GP, Hammonds K, Jhavar S. Reference results for blood parameter changes and recovery after pelvic radiation without chemotherapy. Hematol Rep. 2022;14(2):155–64.

[46] Tang S, Li L, Yuan S. Effects of radiotherapy and chemotherapy on platelet in patients with lung cancer. Frontiers in Bioscience-Landmark. 2023;28(11).

[47] Zheng Z, Su J, Bao X, Wang H, Bian C, Zhao Q, et al. Mechanisms and applications of radiation-induced oxidative stress in regulating cancer immunotherapy. Front Immunol. 2023;14.

[48] DiCarlo AL, Poncz M, Cassatt DR, Shah JR, Czarniecki CW, Maidment BW. Medical countermeasures for platelet regeneration after radiation exposure. Report of a workshop and guided discussion sponsored by the National Institute of Allergy and Infectious Diseases, Bethesda, MD, March 22–23, 2010. Radiat Res. 2011;176(1):e0001-15.

[49] Fan X, Krzyzanski W, Wong RSM, Liu D, Yan X. Novel combination of erythropoietin and romiplostim to treat chemotherapy-induced anemia and thrombocytopenia via pharmacodynamic interaction on hematopoietic stem and progenitor cells. ACS Pharmacol Transl Sci. 2023;6(12):1884–97.

[50] Yi W, Kim BH, Kim M, Ryang SR, Jang MH, Kim JM, et al. Short-term bone marrow suppression in differentiated thyroid cancer patients after radioactive iodine treatment. Endocr J. 2020;67(12):1193–8.

[51] Muhammed AABM, Thakur N, Patel S. Prognostic significance of neutrophil lymphocyte ratio in patients of carcinoma cervix treated with radiotherapy. Oncology Journal of India. 2020;4(3):92.

[52] Kunos CA, Fabian D, Fredericks T, Baldwin L, Dietrich C, Miller RW, et al. Hemoglobin level associates with survival in women from Appalachian Kentucky with uterine cervix cancer. Front Oncol. 2023;13.

[53] Jeong MH, Kim H, Kim TH, Kim MH, Kim BJ, Ryu SY. Prognostic significance of pretreatment lymphocyte percentage and age at diagnosis in patients with locally advanced cervical cancer treated with definite radiotherapy. Obstet Gynecol Sci. 2019;62(1):35.

[54] Chen HH, Meng WY, Li RZ, Wang QY, Wang YW, Pan HD, et al. Potential prognostic factors in progression-free survival for patients with cervical cancer. BMC Cancer. 2021;21(1):531.

[55] Welsh L, Panek R, Riddell A, Wong K, Leach MO, Tavassoli M, et al. Blood transfusion during radical chemo-radiotherapy does not reduce tumour hypoxia in squamous cell cancer of the head and neck. Br J Cancer. 2017;116(1):28–35.

[56] Fachini AMD, Zuliani AC, Sarian LO, Teixeira JC, Esteves SCB, da Costa Machado H, et al. Long-term outcomes of concomitant cisplatin plus radiotherapy versus radiotherapy alone in patients with stage IIIB squamous cervical cancer: A randomized controlled trial. Gynecol Oncol. 2021;160(2):379–83.

[57] 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 (Lahore). 2022;42(6):2411–9.

[58] Chao B, Ju X, Zhang L, Xu X, Zhao Y. A novel prognostic marker Systemic Inflammation Response Index (SIRI) for operable cervical cancer Patients. Front Oncol. 2020;10.

[59] Wisdom AJ, Hong CS, Lin AJ, Xiang Y, Cooper DE, Zhang J, et al. Neutrophils promote tumor resistance to radiation therapy. Proc Natl Acad Sci U S A. 2019;116(37):18584–9.

[60] Yildirim BA, Guler OC, Kose F, Onal C. The prognostic value of haematologic parameter changes during treatment in cervical cancer patients treated with definitive chemoradiotherapy. J Obstet Gynaecol (Lahore). 2019;39(5):695–701.

[61] Maulard A, Chargari C, Faron M, Alwohaibi A, Leary A, Pautier P, et al. A new score based on biomarker values to predict the prognosis of locally advanced cervical cancer. Gynecol Oncol. 2020;159(2):534–8.

[62] Ferioli M, Benini A, Malizia C, Forlani L, Medici F, Laghi V, et al. Classical prognostic factors predict prognosis better than inflammatory indices in locally advanced cervical cancer: Results of a comprehensive observational study including tumor-, patient-, and treatment-related data (ESTHER Study). J Pers Med. 2023;13(8):1229.

[63] Cao W, Yao X, Cen D, Zhi Y, Zhu N, Xu L. Prognostic role of pretreatment thrombocytosis on survival in patients with cervical cancer: a systematic review and meta-analysis. World J Surg Oncol. 2019;17(1):132.

[64] Li N, Zhang Y, Qu W, Zhang C, Ding Z, Wang L, et al. Analysis of systemic inflammatory and coagulation biomarkers in advanced cervical cancer: Prognostic and predictive significance. Int J Biol Markers. 2023;38(2):133–8.

[65] Ergen S, Barlas C, Dagdelen M, Can G, Sahinler I. The prognostic role of the pretreatment peripheral neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in patients with cervical cancer. Ann Med Res. 2021;28(4):778.

[66] Xu R, Lu H, Guo Q, Qian J, Fan Q, Zhao P, et al. The prognostic value of peripheral inflammatory cell ratios in patients with cervical cancer after radiotherapy. 2021.

[67] Han X, Liu S, Yang G, Hosseinifard H, Imani S, Yang L, et al. Prognostic value of systemic hemato-immunological indices in uterine cervical cancer: A systemic review, meta-analysis, and meta-regression of observational studies. Gynecol Oncol. 2021;160(1):351–60.

[68] Punjabi A, Barrett E, Cheng A, Mulla A, Walls G, Johnston D, et al. Neutrophil–lymphocyte ratio and absolute lymphocyte count as prognostic markers in patients treated with curative-intent radiotherapy for non-small cell lung cancer. Clin Oncol. 2021;33(8):e331–8.

[69] Bogani G, Ditto A, Martinelli F, Signorelli M, Chiappa V, Lopez C, et al. Impact of blood transfusions on survival of locally advanced cervical cancer patients undergoing neoadjuvant chemotherapy Plus Radical Surgery. International Journal of Gynecological Cancer. 2017;27(3):514–22.