
Radiotherapy-induced changes in electrolyte levels and hematological parameters among endometrial cancer patients

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ABSTRACT

Background and Objective: Endometrial cancer, originating in the uterus's inner epithelial lining, is treated with radiotherapy, including external beam radiotherapy and brachytherapy. However, radiotherapy may disrupt electrolyte balance and affect blood components. This study aimed to evaluate the effect of radiation on hematological and electrolyte parameters in patients with endometrial cancer.

Methods: The study was conducted at the Awat Center, Erbil, Iraq, between December 25, 2024, and February 22, 2025, involving 25 patients. Blood samples were collected before, during, and after therapy, and parameter analyses were performed. The Elekta Infinity machine was used for curative treatment, including Volumetric Modulated Arc Therapy (VMAT). The local Ethics Committee approved the study and protocol.

Results: Radiotherapy significantly reduced white blood cell counts (WBC) from $6.94 \pm 2.59 \times 10^9/L$ before treatment to $4.70 \pm 1.45 \times 10^9/L$ during treatment ($p < 0.001$), with partial recovery post-treatment ($5.18 \pm 1.84 \times 10^9/L$, $p = 0.001$). Platelet counts also declined from $234.84 \pm 63.34 \times 10^3/\mu L$ to $199.08 \pm 47.69 \times 10^3/\mu L$ after radiotherapy ($p = 0.008$). Hemoglobin, red blood cells, and most electrolytes (sodium, potassium, chloride, magnesium, phosphate) showed no significant variation. However, serum calcium levels declined modestly but significantly after radiotherapy (from 9.69 ± 0.54 to 9.36 ± 0.58 mg/dL, $p = 0.034$).

Conclusion: Adjuvant VMAT radiotherapy in endometrial cancer patients induces significant hematological suppression, particularly of WBCs and platelets, while maintaining stable electrolyte levels. These findings highlight the hematologic sensitivity of pelvic radiotherapy and the importance of regular monitoring to reduce cytopenic risks.

Keywords: Adjuvant, Electrolytes, Hemoglobin, Blood platelets, Radiotherapy (intensity-modulated), Hematocrit

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INTRODUCTION

Endometrial cancer (EC) originates from the epithelial lining of the uterus and is characterized by increasing global incidence and mortality rates. EC comprises multiple histological subtypes and distinct molecular classifications. The disease exists in two main categories: Type I, which develops from unopposed estrogen exposure and includes low-grade tumors with favorable outcomes, and Type II, which lacks estrogen involvement and contains high-grade tumors with poor clinical results. The majority of Type I EC consists of grade I and grade II endometrioid adenocarcinomas, but Type II includes grade III endometrioid adenocarcinomas together with serous, clear cell, undifferentiated carcinomas, and carcinosarcomas. The International Agency for Research on Cancer reported 417,336 new endometrial cancer cases worldwide in 2020, placing it as the sixth most prevalent cancer among women. The disease most commonly affects women between the ages of 65 and 75. Incidence and survival outcomes are notably influenced by racial, socioeconomic, and geographic factors. While approximately 67% of cases are diagnosed at an early stage, with a five-year overall survival (OS) rate of 81%, the prognosis for advanced stages is significantly worse, with five-year OS rates of 17% for stage IVA and 15% for stage IVB (1-4).

Radiation therapy functions as a common cancer treatment that employs high-energy rays to eliminate cancer cells and reduce tumor size. It can be delivered through two primary methods: External Beam Radiotherapy (EBRT) and Internal Radiotherapy (Brachytherapy). EBRT involves delivering radiation from a machine outside the body, aiming high-energy photons at the tumor, while brachytherapy involves placing a small radiation source inside the body near or within the

cancerous area. EBRT employs advanced techniques such as 3D Conformal Radiation Therapy (3DCRT), which uses 3D imaging to shape the radiation beam around the tumor but delivers a uniform dose across the beam; Intensity-Modulated Radiation Therapy (IMRT), which enhances precision by adjusting beam intensity to minimize exposure to healthy tissues; and Volumetric Modulated Arc Therapy (VMAT), which uses 360-degree gantry rotation and variable dose rates for superior dose conformity and efficiency. Radiotherapy works by utilizing ionizing radiation, which produces electrically charged particles that deposit energy in tissues, causing damage to the cell nucleus and ultimately killing cancer cells to halt their division and growth. The success of radiotherapy depends on delivering sufficient radiation to the tumor, as insufficient doses can leave tumor cells behind, potentially causing resistant cells to form. Advances in radiotherapy focus on optimizing dose delivery to the target, minimizing exposure to organs at risk (OARs), and increasing the therapeutic index. Among these methods, EBRT is the most common technique in clinical settings, requiring extensive planning and often involving super-voltage machines to target tumors precisely and effectively (5-15); locally, single-institution experience in Erbil with combined chemoradiotherapy approaches for pelvic malignancies has similarly underscored the importance of systematic response and toxicity monitoring across treatment phases (16).

Radiotherapy, while effective in treating cancer, can disrupt the delicate balance of electrolytes in the body. Especially, curative radiotherapy can potentially lead to electrolyte imbalances. Curative radiotherapy, aimed at eradicating the cancer, often involves higher doses of radiation over a longer period, increasing the risk of electrolyte disturbances (17).

Radiotherapy, particularly in curative settings, can negatively impact blood cell production. Radiation exposure to areas with dense bone marrow tissue, like the pelvis or spine, leads to decreased hematopoietic activity, which causes anemia, leukopenia, and thrombocytopenia (18, 19), a pattern also documented locally among radiation-exposed personnel in Erbil, where prolonged exposure was associated with measurable changes in red and white blood cell counts and platelet numbers (20). The extent of these effects depends on the radiation dose and treatment site, as well as individual patient characteristics. Given these potential hematological and biochemical disturbances, this study aimed to evaluate the changes in electrolyte levels and hematological parameters in endometrial cancer patients receiving adjuvant pelvic radiotherapy using VMAT.

METHODS

Study Design and Ethical Approval

This prospective study was conducted at the Awat Radiation Oncology Center, a facility specializing in advanced radiation therapies, in Erbil, Iraq, between December 25, 2024, and February 22, 2025 (Hawler Medical University–College of Medicine Ethics Committee, document code 45, dated 22-9-2024). The local Ethics Committee approved the research protocol.

Patient Selection and Enrollment

Twenty-five individuals with endometrial cancer were enrolled. Convenience sampling was used to choose participants, who had to meet certain requirements, including being between the ages of 40 and 70, having a confirmed histological diagnosis of endometrial cancer, and giving written consent.

Blood Sample Collection

Before, during, and after therapy, each patient had five milliliters of blood drawn by trained nurses

(A = before radiotherapy; B = mid-treatment, after fraction 13; C = after completion of radiotherapy).

Hematological Analysis

White blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), hematocrit (Hct), and platelets (PLT) were measured using the Swelab Alfa Plus analyzer after 2 mL of blood was placed in EDTA tubes for hematological analysis.

Electrolyte Analysis

After centrifuging the remaining 3 mL, the serum was used for electrolyte analysis. The Jokoh EX-DS analyzer was used to test the levels of sodium, potassium, and chloride, while the Roche Integra 400 Plus analyzer was used to detect the levels of magnesium, calcium, and phosphate.

Radiotherapy Protocol

Using the Elekta Infinity machine, radiotherapy techniques included Volumetric Modulated Arc Therapy for curative treatments, with a total dose of 4,500 centi-gray (cGy) administered over 25 fractions.

Statistical Analysis

Statistical analysis was performed using the Shapiro-Wilk test to assess data normality. Based on the distribution, the paired-samples t-test was applied for normally distributed variables, while the Wilcoxon signed-rank test was used for non-normally distributed data. A p-value <0.05 was considered statistically significant. Analysis was performed using SPSS software, version 29.

RESULTS

The analysis focused on evaluating changes in hematological and biochemical parameters among patients with endometrial cancer who underwent adjuvant VMAT radiotherapy. Data were collected at three timepoints — before treatment, during radiotherapy, and after treatment — to assess the

extent and pattern of radiotherapy-induced alterations in blood components and serum electrolyte levels, (Table 1).

All 25 patients received curative treatment using VMAT, with all cases female and treated with an adjuvant prescription. Each patient received a total

radiation dose of 4500 cGy, delivered in 25 fractions of 180 cGy per session, with no variation in technique, dose, or fractionation across the group. Regarding geographic distribution, 60% of patients were from Hawler, 32% from Duhok, and 8% from Mosul, (Table 2).

Table 1. Descriptive statistics summary for qualitative data

Variable	Category	Frequency	%
Type of treatment	Curative	25	100.0
Gender	Female	25	100.0
Address	Hawler	15	60.0
	Duhok	8	32.0
	Mosul	2	8.0
Technique/Modality	VMAT	25	100.0
Rx type	Adjuvant	25	100.0
Rx dose (cGy)	4500	25	100.0
Fractional dose (cGy)	180	25	100.0
No. of fractions	25	25	100.0

Table 2. Descriptive statistics (mean±SD) for quantitative data

Variable	Mean	SD
Age (years)	59.16	12.99
A_Ca ²⁺ (mg/dL)	9.69	0.54
A_Mg ²⁺ (mg/dL)	1.91	0.24
A_PO ₄ ³⁻ (mg/dL)	3.21	0.65
A_Na ⁺ (mmol/L)	135.25	2.44
A_K ⁺ (mmol/L)	5.03	0.77
A_Cl ⁻ (mmol/L)	108.98	2.72
A_WBC (×10 ⁹ /L)	6.94	2.59
A_RBC (×10 ¹² /L)	4.08	0.81
A_HGB (g/dL)	12.06	1.25
A_HCT (%)	34.89	3.31

Variable	Mean	SD
A_PLT ($\times 10^3/\mu\text{L}$)	234.84	63.34
B_Ca ²⁺ (mg/dL)	9.46	0.74
B_Mg ²⁺ (mg/dL)	2.05	0.46
B_PO ₄ ³⁻ (mg/dL)	3.31	0.59
B_Na ⁺ (mmol/L)	135.42	2.45
B_K ⁺ (mmol/L)	5.11	1.18
B_Cl ⁻ (mmol/L)	108.34	2.52
B_WBC ($\times 10^9/\text{L}$)	4.70	1.45
B_RBC ($\times 10^{12}/\text{L}$)	4.00	0.76
B_HGB (g/dL)	12.39	1.53
B_HCT (%)	36.37	3.87
B_PLT ($\times 10^3/\mu\text{L}$)	198.16	55.63
C_Ca ²⁺ (mg/dL)	9.36	0.58
C_Mg ²⁺ (mg/dL)	1.97	0.25
C_PO ₄ ³⁻ (mg/dL)	3.30	0.47
C_Na ⁺ (mmol/L)	135.59	2.67
C_K ⁺ (mmol/L)	5.23	1.03
C_Cl ⁻ (mmol/L)	108.98	2.85
C_WBC ($\times 10^9/\text{L}$)	5.18	1.84
C_RBC ($\times 10^{12}/\text{L}$)	3.97	0.71
C_HGB (g/dL)	11.97	2.08
C_HCT (%)	35.00	5.08
C_PLT ($\times 10^3/\mu\text{L}$)	199.08	47.69

A = before radiotherapy, B = mid-treatment (after fraction 13), C = after completion of radiotherapy.

The patients had a mean age of 59.16 years (SD=12.99). Across the three time points (A, B, C), various hematological and biochemical parameters were measured. Serum calcium (Ca^{2+}) levels were relatively stable, with means of 9.69, 9.46, and 9.36 mg/dL, respectively. Magnesium, phosphate, sodium, potassium, and chloride levels showed minimal fluctuation, maintaining near-normal ranges across all stages, (Figure 1).

White blood cell (WBC) counts decreased from a mean of $6.94 \times 10^9/\text{L}$ at baseline (A) to 4.70 at point

B and slightly increased to 5.18 at point C. Red blood cell (RBC) counts and hemoglobin (HGB) values remained relatively stable, with mild variation across the stages. Hematocrit (HCT%) showed a slight increase from 34.89% at A to 36.37% at B before decreasing to 35.00% at C. Platelet (PLT) counts showed a notable decline from $234.84 \times 10^3/\mu\text{L}$ at baseline to around 198–199 at later points, suggesting a treatment-related hematologic effect, (Figure 2).

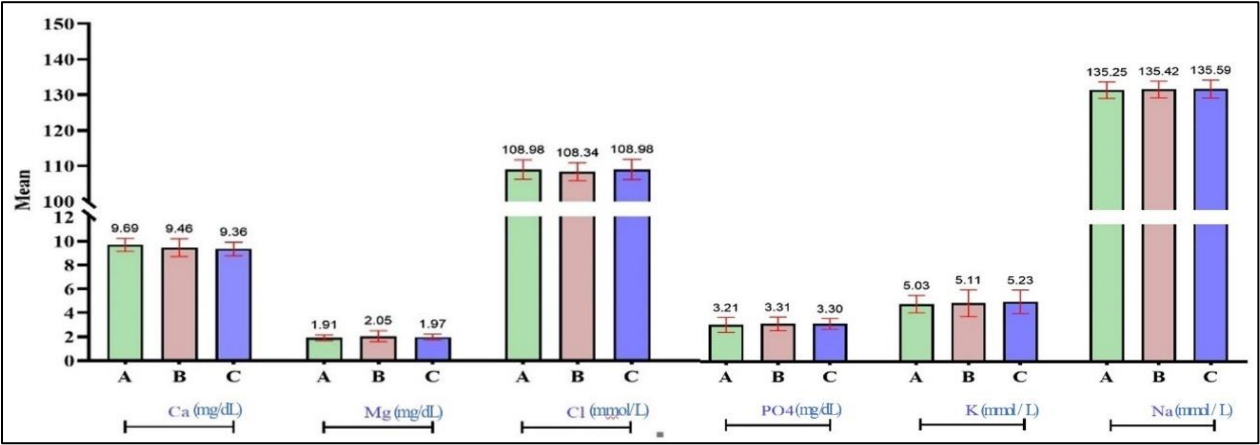


Figure 1. Mean serum electrolyte levels [Na^+ , K^+ , Cl^- (mmol/L); Ca^{2+} , Mg^{2+} , PO_4^{3-} (mg/dL)] across radiotherapy stages

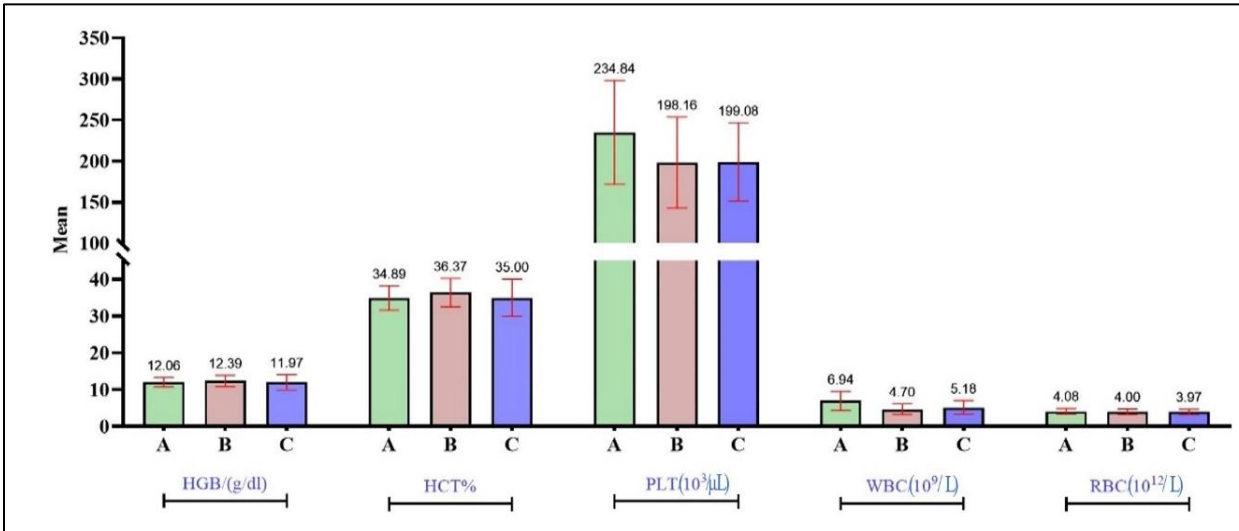


Figure 2. Mean hematological parameters [WBC ($\times 10^9/\text{L}$), RBC ($\times 10^{12}/\text{L}$), HGB (g/dL), HCT (%), PLT ($\times 10^3/\mu\text{L}$)] across radiotherapy stages

Figures 1 and 2 present the mean values of hematological parameters and serum electrolytes; both visually support the statistical findings, showing noticeable declines in WBC and platelet counts during treatment, along with stable electrolyte levels. Overall, the data indicate modest biochemical and hematological changes over time, potentially related to treatment effects.

The Shapiro-Wilk test of normality was used to assess the distribution of biochemical and hematological parameters across the three time points. At time point A, all variables were normally distributed except RBC ($p=0.007$), which showed a significant deviation from normality; Ca^{2+} , Mg^{2+} , PO_4^{3-} , Na^+ , K^+ , Cl^- , WBC, HGB, HCT, and PLT all had p -values >0.05 , supporting the use of parametric tests at baseline. At time points B and C, more variables deviated from normality: at B, Mg^{2+} ($p=0.032$), K^+ ($p=0.001$), and WBC ($p=0.006$) were non-normal; by C, Ca^{2+} ($p=0.021$), PO_4^{3-} ($p=0.031$), K^+ ($p=0.001$), and HCT ($p=0.022$) were also non-normal, potentially requiring non-parametric

tests for these variables in further analyses, (Table 3 A & B).

Between time points A and B, significant differences were observed in WBC ($p < 0.001$), HCT ($p=0.042$), and PLT ($p=0.006$), indicating notable hematological alterations likely influenced by treatment. Other parameters — Ca^{2+} , Mg^{2+} , Na^+ , K^+ , Cl^- , RBC, HGB, and PO_4^{3-} — showed no statistically significant changes between these timepoints. Comparisons between A and C confirmed continued significant changes in WBC ($p=0.001$) and PLT ($p=0.008$), suggesting a persistent hematologic response; Ca^{2+} also showed a statistically significant decrease from A to C ($p=0.034$), while all other parameters remained non-significant. The B vs. C comparison revealed only one significant result: WBC again showed a significant increase ($p=0.011$), emphasizing its sensitivity to treatment effects. The majority of other parameters across all comparisons remained statistically non-significant, indicating general biochemical stability despite some hematologic fluctuations over time.

Table 3 A. Comparison of electrolyte parameters across treatment pairs

Parameter	Pair	A/B/C Mean $\pm$ SD	Test value	p
Ca^{2+}	A vs B	9.686 $\pm$ 0.544 / 9.461 $\pm$ 0.737	1.316	0.201†
Mg^{2+}	A vs B	1.910 $\pm$ 0.239 / 2.052 $\pm$ 0.460	-1.765	0.078‡
PO_4^{3-}	A vs B	3.209 $\pm$ 0.647 / 3.307 $\pm$ 0.592	-0.733	0.470†
Na^+	A vs B	135.248 $\pm$ 2.445 / 135.420 $\pm$ 2.451	-0.316	0.755†
K^+	A vs B	5.028 $\pm$ 0.771 / 5.107 $\pm$ 1.176	-0.122	0.903‡
Cl^-	A vs B	108.980 $\pm$ 2.724 / 108.336 $\pm$ 2.516	1.196	0.243†
Ca^{2+}	A vs C	9.686 $\pm$ 0.544 / 9.364 $\pm$ 0.577	-2.114	0.034‡
Mg^{2+}	A vs C	1.910 $\pm$ 0.239 / 1.974 $\pm$ 0.254	-1.554	0.133†
PO_4^{3-}	A vs C	3.209 $\pm$ 0.647 / 3.295 $\pm$ 0.465	-0.646	0.524†
Na^+	A vs C	135.248 $\pm$ 2.445 / 135.588 $\pm$ 2.669	-0.551	0.587†

Parameter	Pair	A/B/C Mean±SD	Test value	p
K ⁺	A vs C	5.028±0.771 / 5.232±1.033	-1.036	0.300‡
Cl ⁻	A vs C	108.980±2.724 / 108.984±2.850	-0.006	0.995†
Ca ²⁺	B vs C	9.461±0.737 / 9.364±0.577	-0.325	0.745‡
Mg ²⁺	B vs C	2.052±0.460 / 1.974±0.254	-0.373	0.709‡
PO ₄ ³⁻	B vs C	3.307±0.592 / 3.295±0.465	0.120	0.906†
Na ⁺	B vs C	135.420±2.451 / 135.588±2.669	-0.346	0.732†
K ⁺	B vs C	5.107±1.176 / 5.232±1.033	-1.185	0.236‡
Cl ⁻	B vs C	108.336±2.516 / 108.984±2.850	-1.398	0.175†

Table 3 B. Comparison of hematological parameters across treatment pairs

Parameter	Pair	A/B/C Mean±SD	Test value	p
WBC	A vs B	6.938±2.587 / 4.696±1.449	-3.829	<0.001‡
RBC	A vs B	4.076±0.805 / 3.997±0.758	-1.332	0.183‡
HGB	A vs B	12.060±1.251 / 12.387±1.534	-1.088	0.287†
HCT	A vs B	34.888±3.311 / 36.368±3.874	-2.150	0.042†
PLT	A vs B	234.840±63.339 / 198.160±55.634	2.992	0.006†
WBC	A vs C	6.938±2.587 / 5.180±1.844	3.890	0.001†
RBC	A vs C	4.076±0.805 / 3.968±0.710	-0.886	0.376‡
HGB	A vs C	12.060±1.251 / 11.968±2.079	0.288	0.776†
HCT	A vs C	34.888±3.311 / 34.996±5.084	-0.171	0.864‡
PLT	A vs C	234.840±63.339 / 199.080±47.690	2.889	0.008†
WBC	B vs C	4.696±1.449 / 5.180±1.844	-2.543	0.011‡
RBC	B vs C	3.997±0.758 / 3.968±0.710	0.263	0.795†
HGB	B vs C	12.387±1.534 / 11.968±2.079	1.303	0.205†
HCT	B vs C	36.368±3.874 / 34.996±5.084	-1.380	0.168‡
PLT	B vs C	198.160±55.634 / 199.080±47.690	-0.079	0.937†

† = paired-samples t-test (parametric); ‡ = Wilcoxon signed-rank test (non-parametric).

DISCUSSION

This prospective study investigated the impact of adjuvant volumetric modulated arc therapy (VMAT) on electrolyte and hematological parameters in 25 endometrial cancer patients across three treatment phases: pre-radiotherapy, mid-treatment, and post-radiotherapy. The results indicate that radiotherapy induced statistically significant reductions in white blood cell (WBC) and platelet (PLT) counts, with relatively stable levels of red blood cells (RBC), hemoglobin (HGB), and most serum electrolytes.

The observed decrease in WBCs (from $6.94 \pm 2.59 \times 10^9/\text{L}$ pre-treatment to $4.70 \pm 1.45 \times 10^9/\text{L}$ mid-treatment, $p < 0.001$) aligns with previous reports highlighting the myelosuppressive effects of pelvic irradiation due to bone marrow exposure, even with advanced techniques like VMAT (21). Similarly, the reduction in PLT counts (from 234.84 ± 63.34 to 199.08 ± 47.69 , $p = 0.008$) reflects platelet sensitivity to radiation, which may predispose patients to thrombocytopenia in prolonged or high-dose regimens (22). However, hemoglobin and RBC levels showed no statistically significant changes, suggesting that VMAT may spare erythropoietic function to some extent due to its improved dose conformality and reduced exposure of active marrow (23, 24).

In terms of biochemical parameters, most electrolyte levels — including sodium, potassium, magnesium, chloride, and phosphate — remained within normal range and showed no significant variation across treatment phases. This suggests that systemic electrolyte disturbances are uncommon in VMAT-treated pelvic radiotherapy for endometrial cancer, consistent with reports indicating lower systemic toxicity profiles for modern techniques (26, 27). Nonetheless, calcium levels declined modestly but significantly from 9.69 ± 0.54 mg/dL to 9.36 ± 0.58 mg/dL post-

treatment ($p = 0.034$), possibly reflecting subclinical effects of radiation on bone metabolism or renal handling, as hypothesized in prior studies (25). The lack of a major electrolyte imbalance may also relate to patient selection, limited treatment volume, and effective hydration during radiotherapy. This finding aligns with conclusions from studies that hematological suppression is a reliable marker of acute radiation effects, while electrolyte shifts are less consistent and often influenced by comorbid conditions or concurrent medications (26, 27).

Taken together, these findings support that adjuvant VMAT in early-stage endometrial cancer is associated with transient yet statistically significant hematological suppression, especially of WBCs and platelets, without causing overt biochemical disturbances. The preserved erythropoietic and electrolyte balance suggests that VMAT offers a favorable toxicity profile, which is essential for long-term survivorship, particularly in early-stage and low-intermediate-risk patients who constitute the majority of cases (24).

CONCLUSION

The present study demonstrates that adjuvant VMAT radiotherapy in endometrial cancer patients results in significant reductions in white blood cell and platelet counts during and after treatment, while maintaining stable levels of serum electrolytes and red blood cell indices. These results underscore the hematologic sensitivity of pelvic bone marrow to radiation exposure but also highlight the safety and tolerability of VMAT in preserving biochemical homeostasis. Regular hematological monitoring during treatment is recommended to detect and manage cytopenias. Further studies with larger cohorts are warranted to validate these findings and explore their correlation with clinical outcomes.

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COMPETING INTEREST

The authors declare that they have no competing interests.

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