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Research Article

Pretreatment Platelet Indices and Red Cell Distribution Width as a Predictor of Endometrial Carcinoma Among Patients with Abnormal Uterine Bleeding

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Abstract

Introduction: Endometrial carcinoma is the sixth most common cancer for females in the world and the seventh most common gynecological cancer in developing countries. The values of platelet indices (MPV, PDW) and red cell distribution width (RDW) are associated with different stages of endometrial and cervical carcinoma. Thus, this study aimed to determine the relation of MPV, PDW, and RDW with endometrial carcinoma. Methods: This cross-sectional study was conducted in the Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh from July 2022 to July 2023. This study included 61 women with histopathologically confirmed endometrial carcinoma (FIGO stage I to IV) as cases and 122 women with histopathologically confirmed benign endometrial disease as the control group. Result: This study found that the case group had a higher mean age (55.62 years vs. 43.75 years). Blood parameter findings showed higher mean MPV (10.46 vs. 9.96) and RDW (46.64 vs. 43.05) in cases. PDW mean was lower in cases (11.33 vs. 14.39). MPV correlated positively with the FIGO stage and histological type, while PDW had a negative correlation. ROC analysis of MPV yielded an AUC of 0.645, with a cut-off of 10.50 showing sensitivity 58%, specificity 72%, and accuracy 57%. ROC analysis of PDW yielded an AUC of 0.789, with a cut-off of 13.50 showing sensitivity 44%, specificity 97%, and accuracy 61%. Multivariant regression revealed MPV to be the strongest factor of endometrial carcinoma (OR-6.20, p=0.039). Conclusion: This study showed that the mean platelet volume (MPV) and red cell distribution width (RDW) are potential markers for detecting endometrial carcinoma.

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Keywords

Platelet Indices, Red Cell Distribution Width (RDW), Endometrial Carcinoma, Uterine Bleeding

1. Introduction

Endometrial carcinoma is the sixth most common cancer for females in the world and the seventh most common gynecological cancer in developing countries. [1, 2] The strongest known risk factor for endometrial cancer is unopposed estrogen exposure which includes obesity, sedentary working, and hormone replacement therapy. [3] Early accurate diagnosis is important because patients with endometrial carcinoma have a favorable prognosis if diagnosed early. [4] Because of the high disease death rate and increasing number of new diagnoses, endometrial cancer has a substantial impact on women's health. Most endometrial malignancies are carcinomas, while sarcomas account for the remaining proportion. Endometrial carcinomas can be classified into histological subtypes including endometrioid, serous, and clear cell carcinomas. Histological subtyping is currently routinely used to guide prognosis and treatment decisions [5]. Cancer is widely accepted as both a cause and result of chronic inflammation. [6-8] Platelets are important for both blood coagulation and tumor angiogenesis. They contain both pro and anti-angiogenetic molecules and are sequestered in intracellular granules. Thus, platelets play an important role in tumor angiogenesis. Secreted angiogenic molecules from platelets increase their secretion by autocrine pathways. [9-12]

Platelets play roles in tumor growth and invasion with some other molecules such as cytokines, growth factors, and local mediators. [13] PDW represented the changes in morphological shape and reactivity of platelets. An increased PDW always indicates a change in platelet activity by some factors. [14] MPV was the marker indicating platelet activity and its increase in value mostly was associated with evaluated inflammatory process and malignancy. Platelets with larger MPV are supposed to carry more mediators, thus to some extent contributing to cancer development and progress. [15] MPV can be regarded as an easy predictive factor in judging the severity of disease and selecting further options before endometrial biopsy and pathology result in higher-risk patients. [16] Red cell distribution width (RDW) is a routinely examined parameter in complete blood count (CBC), which is a quantitative measure of the variation of circulating red blood cell size and is routinely assessed in the differential diagnosis of anemia [17-19]. RDW reflects chronic inflammation, and increased levels of circulatory cytokines, such as IL-6, TNF-alfa, and hepcidin [20, 21]. RDW has also been reported as an inflammatory marker in patients with inflammatory conditions. [19] There are no specific tumor markers for endometrial carcinoma till now. For early detection and monitoring of high-risk patients, it is necessary to find some markers.

Therefore, this study was done to find out the relation of platelet indices (MPV, PDW) and red cell distribution width (RDW) with endometrial carcinoma among patients with abnormal uterine bleeding (intermenstrual bleeding, menorrhagia, and postmenopausal bleeding).

2. Methodology & Materials

This was a cross-sectional study conducted in the Department of Gynecological Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh during the period from July 2022 to July 2023. In our study, we took 61 women with histopathologically confirmed endometrial carcinoma (FIGO stage I to IV) as cases and 122 women with histopathologically confirmed benign endometrial disease as the control group. So, a total of 183 patients were included in this study.

These are the following criteria to be eligible for enrollment as our study participants: a) Patients aged more than 18 years; b) Patients with abnormal uterine bleeding during admission; c) Patients with histopathologically confirmed endometrial cancer; d) Patients with International Federation of Gynecology and Obstetrics (FIGO) stage I-IV disease; e) Patients with histopathologically confirmed benign endometrial disease; f) Patients who were willing to participate were included in the study And a) Patients with other primary cancer with or without metastasis; b) Patients with history of using recombinant granulocyte colony stimulating factor or taking corticosteroids; c) Patients with prior radiotherapy and/or chemotherapy; d) Patients with known hematological disease & inflammatory disease; e) Patients with local or systemic infection; f) Patients with any history of acute illness (e.g., Uncontrolled DM, renal or pancreatic diseases, ischemic heart disease, asthma, COPD etc.) were excluded from our study.

Data collection: After obtaining verbal consent from the patients following the introduction and informing the study's purpose and objectives, data was collected through face-to-face interviews ensuring privacy and confidentiality using the questionnaire. All other required data was collected from history sheets, investigation papers, per-operative findings, and follow-up records. After that, all data was compiled, modified, and finalized. All data were recorded systematically in the preformed data collection form.

Statistical Analysis: Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. The differences between groups were analyzed with an independent t-test, Pearson's chi-square (X^2) test, Fisher's exact test, etc. ROC curves were compared to test the statistical significance of the difference between areas. The area under the curve (AUCs) was measured using the MedCalc statistical Software, revealing the sensitivity and specificity of a single or combined diagnosis. A p-value <0.05 was considered as significant. Statistical analysis was performed using SPSS 22 (Statistical Package for Social Sciences) for Windows version 10. Ethical approval was taken from the ethical review committee of Bangabandhu Sheikh Mujib Medical University.

3. Results

Table 1. *Distribution of the participants according to sociodemographic characteristics (n=183).*

Variables	Cases (61)	Control (122)	P value
Age			
24-43	7 (11.5%)	59 (48.4%)	
44-63	40 (65.6%)	63 (51.6%)	[b]0.001[s]
≥64	15 (23%)	0	
Mean±SD	55.62±10.24	43.75±6.63	[c]0.001[s]
Mean±SD	47.70±9.76		
Median (min-max)	46 (24-72)		
Educational Qualification			
Illiterate	13 (21.3%)	4 (3.3%)	
Primary pass	19 (31.1%)	21 (17.2%)	[b]0.001[s]
Secondary pass	10 (16.4%)	38 (31.1%)	
Higher Secondary	18 (29.5%)	45 (36.9%)	
Graduate	1 (1.6%)	14 (11.5%)	
Marital status			
Married	40 (26.1%)	113 (73.9%)	[a]0.001[s]
Widow/widower	21 (70%)	9 (30%)	
Associated disease			
HTN	30 (93.8%)	2 (6.2%)	
DM	31 (88.6%)	4 (11.4%)	[b]0.001[s]
No comorbidity	0	116 (100%)	
BMI kg/m^2			
Normal (18.5-24.9)	1 (1.6%)	105 (86.1%)	
Overweight (25-29.9)	23 (37.7%)	12 (9.8%)	[b]0.001[s]
Obesity (>30)	37 (60.7%)	38 (4.1%)	

a= chi square test, b= Fisher's Exact test, c= independent t-test, s= significant

Table 1 shows that age between 44-63 years was more prevalent in both groups (65.6% vs 51.6%) but the mean distribution showed that patients in the case group (55.62±10.24) had higher mean age than the control group (43.75±6.63). In the case group, the highest prevalence of education was up to the primary level where whereas the control group was more educated than them (31.1% 36.9%). An important finding is that co-morbidity was highly prevalent (both DM and HTN; 88.6% and 93.8%) in the cases group than the control group. The majority of the control group was free of comorbidities. While studying the BMI of the patients, it was observed that obesity was most prevalent among the case group (60.7%) even overweight was prevalent too (37.7%) whereas most of the participants of the control group had normal BMI.

Table 2. *Distribution of the participants according to reproductive history.*

Variables	Cases (61)	Control (122)	P value
Menstrual history			
Menorrhagia	3 (3.1%)	94 (96.9%)	
Menorrhagia+ dysmenorrhea	0	14 (100%)	[b]0.001[s]
Intermenstrual bleeding	12 (85.7%)	2 (14.3%)	
Post-menopausal bleeding	30 (100%)	0	
Menorrhagia+ Intermenstrual bleeding	16 (57.1%)	12 (42.9%)	

Variables	Cases (61)	Control (122)	P value
Parity			
Nullipara	6 (9.8%)	19 (15.6%)	[b]0.001[s]
Para (1-2)	22 (36.1%)	14 (11.5%)	
Miltipara	33 (54.1%)	89 (73%)	
Contraceptive use			
OCP	27 (27.8%)	70 (72.2%)	
OCP+IUCD	0	1 (100%)	
OCP+Implanon	0	4 (100%)	
IUCD	0	1 (100%)	[b]0.001[s]
Implanon	0	15 (100%)	
Tubal ligation	2 (15.3%)	11 (84.61%)	
Nothing	27 (51.9%)	25 (48.70%)	
History of HRT			
Yes	2 (100%)	0	
No	0	0	

a= chi square test, b= Fisher's Exact test, c= independent t-test, s= significant

Table 2 shows that patients with a high count of intermenstrual bleeding, postmenopausal bleeding, and menorrhagia + intermenstrual bleeding were in the case group (3.1%, 85.7%, 100%, 57.1%). This distribution was also significant ($p<0.001$). Multiparous patients were mostly affected by endometrial carcinoma (54.1%, $p<0.001$).

Table 3. *Distribution of the participants according to malignancy history.*

Variables	Cases (61)	Control (122)	P value
Family member suffering from endometrial cancer			
Yes	4 (100%)	0	[a]0.004[s]
No	57 (31.8%)	122 (68.2%)	
Duration of symptoms (months)			
mean±SD	6.31±2.16	23.25±8.02	[c]0.001[s]
mean±SD	17.61±10.41		
Median (min-max)	18 (2-48)		

a= chi square test, c= independent t-test, s= significant

Table 3 shows that 4 patients in the case group had a family history of endometrial carcinoma but most of the participants in the control group (68.2%) had no such family history. The mean duration of symptoms was 6.31±2.16 months in the case group and 23.25±8.02 months in the control group.

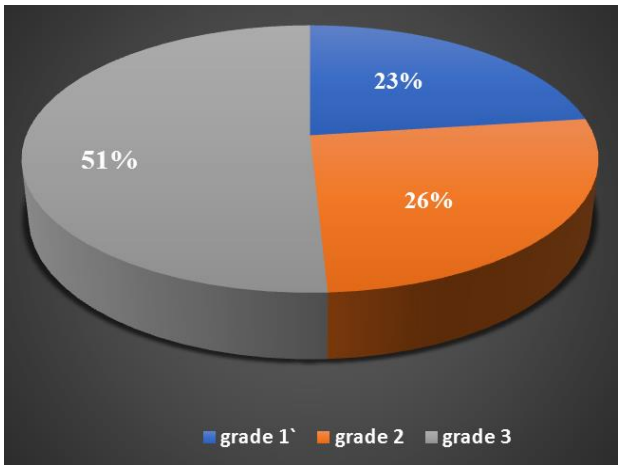

Figure 1. *Distribution of the participants according to histological grade.*

The pie chart shows the percentages of different grades of endometrial cancer in the participants. Here about 51% of patients presented with grade 3 lesions, 26 % of patients presented with grade 2 lesions, and 23% of patients presented with grade 1 lesions at the time of diagnosis.

Table 4. *Distribution of the participants according to MPV, PDW, and RDW.*

Variables	Cases (61)	Control (122)	P value
MPV			
Mean±SD	10.46±1.26	9.96±1.25	[c]0.012[s]
Mean±SD	10.16±1.27		
Median (min-max)	10 (5-16)		
PDW			
Mean±SD	11.33±1.78	14.39±4.62	[c]0.001[s]
Mean±SD	13.37±4.16		
Median (min-max)	12 (2-53)		
RDW			
Mean±SD	46.64±6.18	43.05±7.03	[c]0.001[s]
Mean±SD	44.26±6.95		
Median (min-max)	44 (2-62)		

Data presented as n (%), mean±SD, median (min-max), a= chi-square test, c= independent sample t-test, s= significant

Table 4 shows that in MPV, RDW, and PDW, there are statistically significant differences between cases (endometrial cancer) and controls. The p-values for these variables are less than the conventional significance level of 0.05, indicating that the differences are unlikely to have occurred by chance.

Table 5. *Correlation of the MPV, PDW, and RDW with clinicopathological characteristics.*

Variables	MPV Correlation coefficient	P value
FIGO stage	0.334	[d]0.009[s]
Histological grade	0.166	[d]0.204[ns]
PDW		
Age	-0.357	[d]0.001[s]
FIGO stage	-0.202	[d]0.122[ns]
Histological grade	-0.284	[d]0.028[s]
RDW		
FIGO stage	0.031	[d]0.815[ns]

d= Spearman's correlation, s=significant, ns=not significant

Table 5 shows that MPV has a positive correlation with the FIGO stage and histological grade, indicating that as the FIGO stage increases, MPV tends to increase. PDW has a strong negative correlation with age, FIGO staging, and histological grade indicating as histological grade and FIGO grade increases, PDW tends to decrease significantly. RDW has no significant but positive correlation with the FIGO stage.

Table 6. *Logistic regression of FIGO staging of cases group.*

Variables	Univariate regression (OR)	P value	Multivariate logistic regression (OR)	P value
PDW	1.68 (1.37-2.07)	[e]0.001[s]		
MPV	4.27 (1.72-10.58)	[e]0.002[s]	6.20 (1.09-35.1)	[f]0.039[s]
Histological grade	1.0	[e]0.001[s]		
Age	1.5 (1.15-2.08)	[e]0.004[s]		

e= univariate logistic regression, f= multivariate logistic regression, s= statistically significant

Table 6 shows that logistic regression (binary regression among the case group and multinomial regression among FIGO stages of endometrial carcinoma) revealed MPV, PDW, histological type, and age were strong influencers of endometrial carcinoma. However, through multivariant analysis, only MPV came through as the strongest influencer of endometrial carcinoma (OR- 6.20, p=0.039).

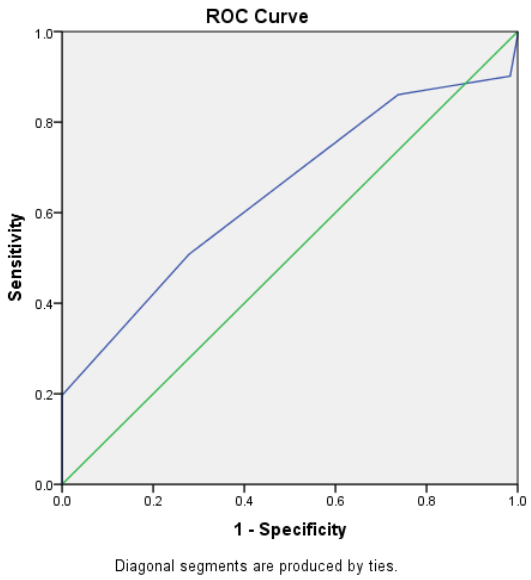

Figure 2. *ROC for MPV.*

ROC analysis of MPV to predict endometrial carcinoma found an AUC value of 0.645 (95% CI 0.565-0.724) which was statistically significant (P <0.0.001).

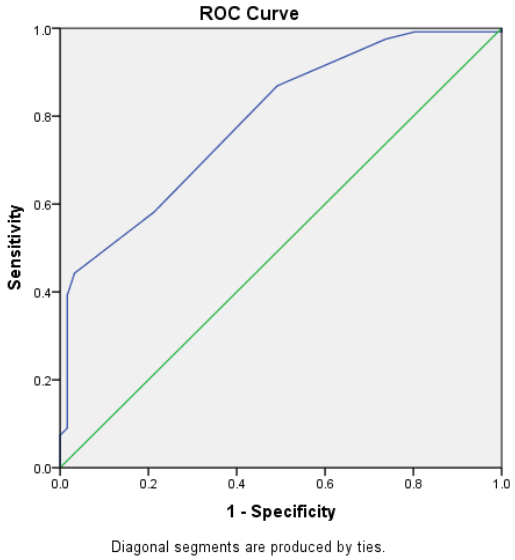

Figure 3. *ROC for PDW.*

ROC analysis of PDW to predict endometrial carcinoma found an AUC value of 0.789 (95% CI 0.722-0.856) which was statistically significant (P <0.0.001).

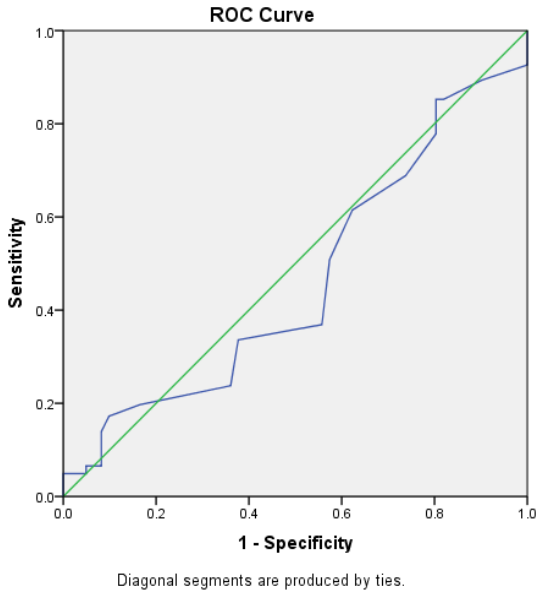

Figure 4. *ROC for RDW.*

ROC analysis of RDW to predict endometrial carcinoma found an AUC value of 0.463 (95% CI 0.374-0.552) which was statistically nonsignificant (P =0.414).

Table 7. *Determination of cut-off value with Youden index.*

	Cutoff value	Sensitivity	Specificity	PPV	NPV	Accuracy	Youden index (j=sen+spe-1)
MPV	10.50	0.580	0.721	0.42	0.78	0.57	0.230
PDW	13.50	0.443	0.967	0.46	0.96	0.61	0.410
RDW	49.50	0.172	0.902	0.389	0.725	0.233	0.074

Table 7 shows that a cut-off value of MPV of 10.50 showed the highest Youden index (0.230) with a sensitivity of 58%, specificity of 72%, PPV of 42 %, NPV of 78%, and accuracy of 57%. A cut-off value of PDW of 13.50 showed the highest Youden index (0.410) with a sensitivity of 44%, specificity of 97%, PPV of 46%, NPV of 96%, and accuracy of 61%. A cut-off value of RDW of 49.50 showed the highest Youden index (0.074) with a sensitivity of 17%, specificity of 90%, PPV of 39%, NPV of 73%, and accuracy of 23%.

4. Discussion

The age distribution of participants in our study revealed a significant difference between the case and control groups. The majority of participants in both groups were aged between 44 and 63 years (65.6% in the case group vs. 51.6% in the control group). However, the mean age of the case group (55.62 ± 10.24) was notably higher than that of the control group (43.75 ± 6.63). Similar findings of increased age among cancer patients were reported by Yayla Abide et al. (2018). [22]

Our study also highlighted a high prevalence of co-morbidities such as diabetes mellitus (DM) and hypertension (HTN) in the case group, with rates of 88.6% and 93.8%, respectively, compared to the control group, where most participants were disease-free. This aligns with the findings of Yayla Abide et al. (2018), who also noted a significant association between DM, HTN, and endometrial carcinoma. [22] Song et al. (2019) further confirmed that these conditions were most prevalent among patients with malignant cases. [23]

While studying the BMI of our patients, it was observed that obesity was most prevalent among the case group (60.7%) even overweight was prevalent too (37.7%) whereas most of the participants in the control group had normal BMI (86.1%). While Oge et al., (2013) found no significant association of endometrial cancer with BMI. [24]

Multiparous patients were mostly affected by endometrial carcinoma (54.1%, p<0.001) in our study and Yayla Abide et al., (2018) also supported our findings as they have observed the same findings that higher parity showed a highly significant association with endometrial cancer. [22] Our study also observed that IUCD use has a significant association (66.7%, p<0.001) with endometrial carcinoma (66.7%, p<0.001). Gao et al., (2020) found use of HRT and OCP was related to endometrial and cervical carcinoma. [25]

When evaluating hematological parameters, our study found that the mean platelet volume (MPV) was significantly higher in the case group (10.46 ± 1.26) compared to the control group (9.96 ± 1.25). Similarly, the red cell distribution width (RDW) mean was also elevated in cases (46.64 ± 6.18 vs. 43.05 ± 7.03, p < 0.001). However, the platelet distribution width (PDW) mean was significantly lower in the case group (11.33 ± 1.78) than in the controls (14.39 ± 4.62). While Song et al. (2019) reported contrasting findings regarding PDW, our results were supported by studies from Kurtoglu et al. (2015), Oge et al. (2013), and Yayla Abide et al. (2018), who noted higher MPV levels in cancer patients. [22, 24, 26] Zhang et al. (2020) and Kemal et al. (2015) also observed elevated RDW levels in endometrial cancer cases, further supporting our findings. [14, 27] Karateke A (2015) et al found the highest MPV (p<0.001), and PDW (p=0.002) were in the endometrial cancer group, and the lowest levels were in the control group. [28]

This study showed that MPV had positive correlations with the FIGO stage and histological grade, indicating that as the FIGO stage increases, MPV tends to increase. PDW had a strong negative correlation with age, FIGO staging, and histological grade indicating as histological grade and FIGO grade increase, PDW tends to decrease significantly. RDW has a non-significant but positive correlation with the FIGO stage. Shen et al, (2017) found a significant correlation between FIGO staging with MPV. [29] Chen et al., (2020) also found a positive correlation of the FIGO stage with increasing MPV and RDW. [30]

Logistic regression analysis in our study identified MPV, PDW, histological type, and age as significant predictors of endometrial carcinoma. Among these, multivariate analysis revealed MPV as the strongest independent predictor (OR = 6.20, p = 0.039). This is consistent with findings by Petric et al. (2023), who reported age as a significant predictor (OR = 1.02, p < 0.05), and Ji et al. (2013), who highlighted histological type as a key influencer (OR = 3.13, p < 0.05). [31, 32]

Our study also assessed the predictive power of hematological parameters through ROC analysis. MPV showed an AUC of 0.645 (95% CI: 0.565–0.724; p < 0.001), comparable to Yayla Abide et al. (2018), who reported an AUC of 0.587. [22] PDW demonstrated a statistically significant AUC of 0.789 (95% CI: 0.722–0.856; p < 0.001), whereas RDW had a nonsignificant AUC of 0.463 (95% CI: 0.374–0.552; p = 0.414).

5. Limitations of the Study

Our study was a single-center study. We took a small sample size due to our short study period. After evaluating those patients, we did not follow up with them for the long term and did not know other possible interference that may happen in the long term with these patients.

6. Conclusion and Recommendations

In our study, we found that mean platelet volume (MPV) and red cell distribution width (RDW) were higher in the case group, while platelet distribution width (PDW) was lower. MPV showed positive correlations with the FIGO stage and histological grade, indicating that more advanced stages of the disease are associated with higher MPV. On the other hand, PDW had a strong negative correlation with age, FIGO staging, and histological grade, suggesting that higher grades and stages were linked to lower PDW. ROC analysis indicated that MPV and PDW could be potential predictors of endometrial carcinoma, with varying sensitivities, specificities, and accuracy rates at different cut-off values.

So further study with a prospective and longitudinal study design including a larger sample size needs to be done to validate the findings of our study.

Abbreviations

BSMMU	Bangabandhu Sheikh Mujib Medical University

Ethical Approval

This study was approved by the ethical review committee.

Funding

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Conflicts of Interest

The authors declare no conflicts of interest.

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