Association of Preoperative HbA1c and Perioperative Glucose Fluctuation With Coagulation Status and Bleeding Outcomes in Diabetic Women Undergoing Cesarean Section: A Retrospective Cohort Study

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AIM: To investigate the associations between preoperative glycated hemoglobin (HbA1c) levels and a three-point perioperative glucose coefficient of variation (CV) with perioperative coagulation status and bleeding outcomes in diabetic women undergoing cesarean section.
METHODS: This single-center retrospective cohort study included 150 diabetic women who underwent cesarean section at our institution between October 2022 and December 2025. Preoperative HbA1c was used as an indicator of chronic glycemic control. A three-point perioperative glucose CV, derived from the preoperative glucose value, the highest intraoperative glucose value, and the highest postoperative glucose value, was used as an exploratory marker of short-term perioperative glucose fluctuation. The primary outcome was postpartum hemorrhage (PPH), defined as estimated blood loss (EBL) $\geq$1000 mL. Secondary outcomes included EBL, escalation of hemostatic interventions, transfusion, and perioperative coagulation parameters, including fibrinogen, platelet count, prothrombin time, international normalized ratio, activated partial thromboplastin time, and D-dimer levels.
RESULTS: Among the 150 women, 112 had HbA1c $<$7.0% and 38 had HbA1c $\geq$7.0%. Compared with the good glycemic control group, the poor glycemic control group exhibited higher intraoperative and postoperative glucose levels, lower postoperative hemoglobin, platelet count, and fibrinogen levels, and higher international normalized ratio and D-dimer levels. The poor glycemic control group also had higher incidences of perioperative hyperglycemia, PPH, hemostatic escalation, and transfusion. EBL was significantly higher in the poor-control group [630.00 (512.25, 1336.25) mL vs. 492.00 (375.75, 597.50) mL], and the incidence of PPH was also increased (39.47% vs. 3.57%). Univariable logistic regression analysis showed that HbA1c was associated with increased odds of PPH (odds ratio (OR) 4.68, 95% confidence interval (CI) 2.58–8.48), while three-point glucose CV was similarly associated with increased PPH risk (OR 1.19, 95% CI 1.08–1.30). After adjustment for age and body mass index, standardized HbA1c and standardized three-point glucose CV remained associated with PPH (OR 6.86, 95% CI 3.10–15.15; and OR 3.07, 95% CI 1.66–5.67, respectively). Exploratory discrimination analysis demonstrated that the combined model achieved a higher area under the curve than HbA1c alone (0.963 vs. 0.900).
CONCLUSIONS: Elevated preoperative HbA1c levels and greater perioperative three-point glucose fluctuation were associated with impaired coagulation profiles and an increased risk of perioperative bleeding in diabetic women undergoing cesarean section. Given that the glucose fluctuation metric was derived from only three perioperative measurements and the number of PPH events was relatively limited, these findings should be considered exploratory rather than definitive evidence of a validated clinical prediction model.

Keywords: cesarean section; postpartum hemorrhage; gestational diabetes; glycated hemoglobin; blood glucose

Introduction

With the increasing prevalence of obesity, advanced maternal age, and type 2 diabetes mellitus, the incidence of gestational diabetes mellitus (GDM) and pregestational diabetes has risen substantially, affecting approximately 14% of pregnancies worldwide [1]. During early pregnancy and the perinatal period, diabetic women experience increased metabolic demand and systemic inflammatory activation. Impaired glycemic control is associated with multiple adverse maternal and fetal outcomes, including preeclampsia, preterm delivery, and perioperative complications [2,3].

Among these complications, postpartum hemorrhage (PPH) remains one of the most severe and continues to be a leading cause of maternal morbidity and mortality worldwide [4,5]. Although pregnancy is physiologically characterized by a hypercoagulable state, this hemostatic balance may rapidly deteriorate during major obstetric bleeding, with progressive consumption of coagulation factors and activation of fibrinolysis as hemorrhage advances [6]. Among perioperative hemostatic markers, fibrinogen has received considerable attention as a clinically relevant indicator for evaluating the severity of obstetric bleeding [7], while changes in platelet count, prothrombin time

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(PT), activated partial thromboplastin time (APTT), and D-dimer levels may provide additional information regarding coagulation impairment during clinical deterioration [8,9]. Accordingly, perioperative coagulation assessment remains clinically relevant for the early recognition and management of obstetric hemorrhage [10].

Beyond mean glucose exposure, short-term glucose fluctuation has increasingly been recognized as a marker of metabolic instability. Unlike glycated hemoglobin (HbA1c), which reflects long-term glycemic exposure, glucose fluctuation may be more sensitive to acute physiological stress and may capture pathophysiological information not fully reflected by average glucose levels alone [11,12]. A previous perioperative study has shown that marked blood glucose fluctuations are associated with increased risks of infection, organ dysfunction, and mortality [13]. However, whether these findings apply to diabetic women undergoing cesarean section remains unclear, and the clinical relevance of perioperative glucose fluctuation in this population has not been fully elucidated. Continuous glucose monitoring is considered the gold standard for evaluating glycemic variability. However, its routine use in perioperative obstetric care is limited by cost, accessibility, and increased clinical workload. Therefore, in the present study, we adopted a pragmatic approach by calculating a three-point perioperative glucose coefficient of variation (CV) using preoperative glucose, peak intraoperative glucose, and peak postoperative glucose values. This parameter was intended as an exploratory surrogate marker of short-term perioperative glucose fluctuation rather than a validated measure of glycemic variability.

Most previous studies involving diabetic pregnancy have focused primarily on overall adverse maternal and neonatal outcomes, with relatively few specifically evaluating women undergoing cesarean section. Moreover, evidence remains limited regarding whether preoperative HbA1c and perioperative glucose fluctuation are jointly associated with coagulation status and bleeding outcomes in this population. Therefore, we conducted this retrospective cohort study to investigate associations among preoperative HbA1c, perioperative glucose fluctuation, perioperative coagulation parameters, and bleeding outcomes in diabetic women undergoing cesarean section.

Methods

Research Design and Study Population

This single-center, retrospective cohort study enrolled consecutively diabetic women who underwent cesarean delivery at Wenzhou People's Hospital between October 2022 and December 2025. Study subjects were identified from the hospital electronic medical record system, laboratory information system, anesthesia record system, and blood transfusion/blood utilization database. The inclusion criteria were as follows: (1) a confirmed diagnosis of gestational diabetes mellitus (GDM) or pre-existing diabetes mellitus; (2) delivery by cesarean section at Wenzhou People's Hospital; and (3) availability of complete preoperative HbA1c, perioperative blood glucose monitoring records, perioperative coagulation indicators, and bleeding outcome data. The exclusion criteria were as follows: (1) missing key exposure or outcome variables; (2) known congenital or acquired coagulation disorder; (3) long-term use of anticoagulant or antiplatelet medications; and (4) medical records containing substantial logical inconsistencies that could not be verified. Ultimately, 150 patients were included in the final analysis.

According to preoperative HbA1c levels, patients were categorized into a good glycemic control group (HbA1c $<$7.0%) and a poor glycemic control group (HbA1c $\geq$7.0%), comprising 112 and 38 patients, respectively. The study protocol was approved by the Ethics Committee of Wenzhou People's Hospital (approval number: KY-202603-014), and all procedures were conducted following the principles of the Declaration of Helsinki.

Data Collection and Variable Definitions

This study was based on de-identified clinical data generated during routine medical care and did not involve additional interventions. Demographic and clinical variables collected included age, body mass index (BMI), gestational age at delivery, parity, history of previous cesarean section, emergency cesarean section, preeclampsia, high-risk placental factors, and anesthesia methods. Laboratory parameters included preoperative and postoperative hemoglobin (Hb), platelet count (Plt), prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (APTT), fibrinogen concentration and D-dimer level.

Preoperative laboratory values were defined as the most recent measurements obtained before surgery. Intraoperative glucose was defined as the highest glucose value recorded during surgery, while postoperative glucose was defined as the highest glucose value recorded during routine postoperative monitoring. Postoperative coagulation parameters were obtained on the morning of postoperative day 1 (approximately 20–28 hours after surgery), corresponding to the first routine morning blood collection according to our institutional clinical protocol. Delta variables (preoperative minus postoperative values) were calculated to reflect perioperative changes in laboratory parameters.

Two glycemia-related exposure variables were prespecified. First, preoperative HbA1c was used as an indicator of chronic glycemic status and analyzed both as a continuous variable and according to the clinically relevant threshold of 7.0%. Second, a three-point perioperative glucose coefficient of variation (three-point glucose CV) was calculated using three routinely available glucose values: the preoperative glucose value, the highest intraoperative glucose value, and the highest postoperative glucose value, according to the formula: standard deviation / mean $\times$ 100%.

This metric reflects glucose fluctuations across only these three perioperative time points and was therefore used as an exploratory surrogate marker of short-term glycemic fluctuation rather than as a standardized measure of glycemic variability [14].

Definition of Outcome

The primary outcome was postpartum hemorrhage (PPH), defined as estimated blood loss (EBL) ≥1000 mL during the perioperative period, extending from skin incision to 24 hours after surgery.

Secondary outcomes included: (1) continuous EBL, defined as the total estimated blood loss (mL) from skin incision to 24 hours after surgery; (2) hemostatic escalation, defined as any additional pharmacological or mechanical intervention beyond routine oxytocin administration, including but not limited to supplementary uterotonic agents, intrauterine tamponade, compression sutures, or interventional procedures, as determined by clinical judgment and documented in the medical records; (3) transfusion or blood product utilization, defined as perioperative administration of any blood component (e.g., red blood cells, plasma, or coagulation factor preparations) according to clinical indications; and (4) perioperative coagulation changes, including alterations in fibrinogen concentration, platelet count, prothrombin time (PT), activated partial thromboplastin time (APTT), international normalized ratio (INR), and D-dimer level.

Statistical Analysis

All statistical analyses were performed using R software (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria). Continuous variables were assessed for normality using the Shapiro-Wilk test. Normally distributed variables are presented as mean ± standard deviation and were compared using the independent-samples *t*-test. Non-normally distributed variables are presented as median (interquartile range [IQR]) and were compared using the Mann-Whitney *U* test. Categorical variables are presented as frequency (percentage) and were compared using the chi-square test or Fisher's exact test, as appropriate.

To further characterize the combined distribution of chronic glycemic status and short-term perioperative glucose fluctuations, four combined exposure groups were constructed based on HbA1c level and three-point glucose CV. Spearman correlation analysis was performed to evaluate the associations of HbA1c and three-point glucose CV with perioperative coagulation changes and EBL. Delta variables were calculated as preoperative minus postoperative values; therefore, negative values indicated postoperative increases.

Using PPH as the binary outcome variable, logistic regression analysis was conducted to evaluate the associations of HbA1c and three-point glucose CV with PPH risk. Univariable logistic regression models and a mutually adjusted model incorporating both glycemic indicators were initially fitted. Variables included in multivariable analyses were selected based on clinical relevance and univariable associations with PPH. HbA1c and three-point glucose CV were standardized to Z-scores (mean = 0, SD = 1) to facilitate comparison of effect sizes. Three multivariable logistic regression models were constructed. Model 1 (crude model) included both glycemic indicators without adjustment. Model 2 (primary model) additionally adjusted for age and body mass index (BMI). Model 3 (exploratory model) further adjusted for parity, previous cesarean section, emergency cesarean section, preeclampsia, high-risk placental factors, gestational age, and preoperative hemoglobin, platelet count, APTT, fibrinogen, and D-dimer levels. Given the limited number of PPH events (n = 19), Model 2 was prespecified as the primary analytical model with limited covariate adjustment to reduce the risk of model overfitting. Model 3 was considered an exploratory analysis, and its findings were interpreted cautiously due to the increased likelihood of overfitting and wider confidence intervals.

Variance inflation factors (VIF) were calculated to assess multicollinearity among covariates. VIF values were used for diagnostic evaluation rather than as criteria for variable exclusion. Variables with VIF <5 were considered to demonstrate acceptable collinearity.

Receiver operating characteristic (ROC) curve analysis, restricted cubic spline (RCS) analysis, and subgroup analyses were performed as secondary exploratory analyses to describe potential patterns in the data rather than to establish validated prediction models. These analyses should be interpreted cautiously, given the limited sample size and the number of events. Areas under the curve (AUCs) were compared using the DeLong test.

In subgroup analyses, the association between HbA1c and PPH was stratified by the median glucose CV. Due to the sparse outcome events in the low-glucose CV subgroup, effect estimates within this subgroup were unstable. Accordingly, these stratified analyses are presented as supportive exploratory findings only. All statistical tests were two-sided, and p-values < 0.05 were considered statistically significant.

Results

Baseline Characteristics

A total of 150 diabetic women undergoing cesarean section were included in this study, comprising 112 patients in the good glycemic control group and 38 patients in the poor glycemic control group. No statistically significant differences were observed between the two groups in age, BMI, gestational age at delivery, preoperative Hb, preoperative Plt count, parity, history of previous cesarean section, emergency cesarean section, preeclampsia, or high-risk placental factors. No statistically significant differences were observed between the two groups in age, BMI, gestational age

Table 1. Baseline characteristics of patients stratified by glycemic control status.

Variables	Total (n = 150)	Good glycemic control (n = 112)	Poor glycemic control (n = 38)	Statistic	*p*-value
Age (years), mean ± SD	31.56 ± 5.05	31.51 ± 5.38	31.71 ± 3.95	$t = -0.21$	0.832
BMI (kg/m^2), mean ± SD	29.18 ± 4.72	28.72 ± 4.30	30.57 ± 5.62	$t = -1.86$	0.069
Gestational age (weeks), mean ± SD	37.86 ± 1.16	37.81 ± 1.23	38.02 ± 0.96	$t = -0.95$	0.342
Preoperative Hb (g/L), mean ± SD	120.59 ± 10.26	120.43 ± 10.22	121.08 ± 10.50	$t = -0.34$	0.737
Preoperative Plt ($\times 10^9$/L), mean ± SD	211.34 ± 47.41	213.42 ± 46.94	205.21 ± 48.90	$t = 0.92$	0.358
Preoperative HbA1c (%), median (Q_1, Q_3)	5.82 (5.42, 7.04)	5.58 (5.32, 5.92)	7.78 (7.56, 8.50)	$Z = -9.19$	<0.001
Preoperative glucose (mmol/L), median (Q_1, Q_3)	6.10 (5.30, 7.18)	5.90 (5.07, 6.53)	7.65 (6.17, 8.10)	$Z = -5.68$	<0.001
Preoperative PT (s), median (Q_1, Q_3)	8.88 (8.34, 9.21)	8.93 (8.36, 9.25)	8.45 (8.21, 9.04)	$Z = -2.57$	0.010
Preoperative INR, median (Q_1, Q_3)	0.89 (0.85, 0.93)	0.90 (0.86, 0.93)	0.84 (0.83, 0.92)	$Z = -3.43$	<0.001
Preoperative APTT (s), median (Q_1, Q_3)	28.76 (26.50, 32.08)	29.80 (26.37, 32.24)	27.61 (26.50, 29.47)	$Z = -1.67$	0.095
Preoperative fibrinogen (g/L), median (Q_1, Q_3)	4.47 (3.95, 5.01)	4.70 (4.11, 5.21)	3.96 (3.81, 4.40)	$Z = -4.72$	<0.001
Preoperative D-dimer (mg/L), median (Q_1, Q_3)	1.69 (1.02, 2.33)	1.71 (1.05, 2.37)	1.55 (0.74, 2.12)	$Z = -0.96$	0.337
Parity, median (Q_1, Q_3)	1.00 (0.00, 1.00)	1.00 (0.00, 1.00)	1.00 (0.00, 1.00)	$Z = -0.04$	0.972
Diabetes type, n (%)				$\chi^2 = 72.18$	<0.001
GDM	100 (66.67)	96 (85.71)	4 (10.53)		
Pre-existing DM	50 (33.33)	16 (14.29)	34 (89.47)		
Previous C-section, n (%)				$\chi^2 = 1.31$	0.253
No	95 (63.33)	68 (60.71)	27 (71.05)		
Yes	55 (36.67)	44 (39.29)	11 (28.95)		
Emergency C-section, n (%)				$\chi^2 = 2.80$	0.094
No	102 (68.00)	72 (64.29)	30 (78.95)		
Yes	48 (32.00)	40 (35.71)	8 (21.05)		
Preeclampsia, n (%)				$\chi^2 = 0.01$	0.909
No	133 (88.67)	100 (89.29)	33 (86.84)		
Yes	17 (11.33)	12 (10.71)	5 (13.16)		
High-risk placental factors, n (%)				$\chi^2 = 1.98$	0.159
No	141 (94.00)	103 (91.96)	38 (100.00)		
Yes	9 (6.00)	9 (8.04)	0 (0.00)		

Abbreviations: BMI, body mass index; Hb, hemoglobin; Plt, platelet count; PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time; GDM, gestational diabetes mellitus; DM, diabetes mellitus; Q_1, first quartile; Q_3, third quartile; HbA1c, glycated hemoglobin.

at delivery, preoperative Hb, preoperative Plt count, preoperative APTT, parity, history of previous cesarean section, emergency cesarean section, preeclampsia, or high-risk placental factors. The mean ages in the good-control and poor-control groups were 31.51 ± 5.38 years and 31.71 ± 3.95 years, respectively ($p = 0.832$). Mean BMI values were 28.72 ± 4.30 kg/m^2 and 30.57 ± 5.62 kg/m^2, respectively ($p = 0.069$), while gestational ages were 37.81 ± 1.23 weeks and 38.02 ± 0.96 weeks, respectively ($p = 0.342$). Preoperative Hb levels were 120.43 ± 10.22 g/L and 121.08 ± 10.50 g/L ($p = 0.737$), and preoperative Plt counts were 213.42 ± 46.94 × 10^9/L and 205.21 ± 48.90 ×10^9/L ($p = 0.358$), respectively.

Consistent with the grouping criteria, HbA1c (%) and preoperative blood glucose levels (mmol/L) were significantly higher in the poor-control group than in the good-control group. Median HbA1c increased from 5.58% in the good-control group to 7.78% in the poor-control group ($p < 0.001$), while the median preoperative blood glucose increased from 5.90 mmol/L to 7.65 mmol/L ($p < 0.001$). Among the preoperative coagulation indices, significant between-group differences were observed in PT, INR, and fibrinogen levels. Notably, preoperative fibrinogen concentration was significantly lower in the poor-control group than in the good-control group [3.96 (3.81, 4.40) g/L vs. 4.70 (4.11, 5.21) g/L, $p < 0.001$]. In addition, the distribution of diabetes types differed significantly between the two groups. The poor-control group consisted predominantly of women with pre-existing diabetes, while the good-control group was mainly composed of women with GDM ($p < 0.001$) (Table 1).

Perioperative Outcomes and Coagulation Function

Intraoperative and postoperative glucose levels were significantly higher in the poor-control group than in the good-control group. The median intraoperative glucose level was 8.20 mmol/L in the poor-control group compared with 6.90 mmol/L in the good-control group ($p < 0.001$). Similarly, the median postoperative glucose level was 9.40 mmol/L in the poor-control group and 6.90 mmol/L in the good-control

Table 2. Perioperative outcomes and coagulation profiles according to glycemic control status.

Variables	Total (n = 150)	Good glycemic control (n = 112)	Poor glycemic control (n = 38)	Statistic	*p*-value
Postoperative Hb (g/L), mean ± SD	105.27 ± 16.40	108.36 ± 12.71	96.16 ± 22.02	$t = 3.24$	0.002
Postoperative Plt ($\times 10^9$/L), mean ± SD	193.89 ± 54.25	206.77 ± 49.76	155.95 ± 49.42	$t = 5.45$	<0.001
Intraoperative glucose (mmol/L), median (Q_1, Q_3)	7.35 (6.23, 8.20)	6.90 (6.10, 7.93)	8.20 (7.15, 9.17)	$Z = -4.53$	<0.001
Postoperative glucose (mmol/L), median (Q_1, Q_3)	7.15 (6.20, 8.50)	6.90 (5.88, 7.90)	9.40 (7.55, 10.30)	$Z = -5.84$	<0.001
Glucose CV (%), median (Q_1, Q_3)	13.58 (8.76, 16.69)	13.42 (8.51, 17.17)	13.67 (9.58, 15.51)	$Z = -0.30$	0.766
Postoperative PT (seconds), median (Q_1, Q_3)	8.99 (8.58, 9.30)	8.99 (8.51, 9.28)	9.00 (8.80, 9.44)	$Z = -1.86$	0.063
Postoperative INR, median (Q_1, Q_3)	0.91 (0.87, 0.96)	0.90 (0.86, 0.94)	0.97 (0.94, 1.01)	$Z = -5.32$	<0.001
Postoperative APTT (s), median (Q_1, Q_3)	30.38 (27.16, 32.32)	29.93 (26.93, 32.40)	30.48 (29.34, 32.30)	$Z = -1.90$	0.058
Postoperative fibrinogen (g/L), median (Q_1, Q_3)	4.33 (3.55, 5.03)	4.63 (3.90, 5.21)	3.37 (1.91, 4.10)	$Z = -5.66$	<0.001
Postoperative D-dimer (mg/L), median (Q_1, Q_3)	2.23 (1.50, 2.88)	2.13 (1.19, 2.80)	2.62 (1.76, 3.17)	$Z = -3.37$	<0.001
Estimated blood loss (mL), median (Q_1, Q_3)	523.50 (397.00, 663.75)	492.00 (375.75, 597.50)	630.00 (512.25, 1336.25)	$Z = -4.14$	<0.001
Anesthesia type, n (%)				$\chi^2 = 2.21$	0.137
General anesthesia	16 (10.67)	9 (8.04)	7 (18.42)		
Neuraxial anesthesia	134 (89.33)	103 (91.96)	31 (81.58)		
Perioperative hyperglycemia, n (%)				$\chi^2 = 47.40$	<0.001
No	125 (83.33)	107 (95.54)	18 (47.37)		
Yes	25 (16.67)	5 (4.46)	20 (52.63)		
PPH, n (%)				$\chi^2 = 29.89$	<0.001
No	131 (87.33)	108 (96.43)	23 (60.53)		
Yes	19 (12.67)	4 (3.57)	15 (39.47)		
Hemostatic escalation, n (%)				$\chi^2 = 12.55$	<0.001
No	88 (58.67)	75 (66.96)	13 (34.21)		
Yes	62 (41.33)	37 (33.04)	25 (65.79)		
Any transfusion, n (%)				$\chi^2 = 15.37$	<0.001
No	134 (89.33)	107 (95.54)	27 (71.05)		
Yes	16 (10.67)	5 (4.46)	11 (28.95)		

Abbreviations: CV, coefficient of variation; PPH, postpartum hemorrhage.

group ($p < 0.001$). However, no statistically significant difference in the median three-point glucose CV was observed between the two groups (13.67% vs. 13.42%, $p = 0.766$).

In terms of perioperative hematologic and coagulation outcomes, postoperative Hb levels were significantly lower in the poor-control group than in the good-control group (96.16 ± 22.02 vs. 108.36 ± 12.71, $p = 0.002$). Postoperative platelet counts were likewise lower in the poor-control group (155.95 ± 49.42 vs. 206.77 ± 49.76, $p < 0.001$). In contrast, postoperative INR and D-dimer levels were higher in the poor-control group, whereas postoperative fibrinogen levels were lower. PT and APTT showed a similar unfavorable trend in the poor-control group. However, the between-group differences reached only borderline statistical significance.

Bleeding-related outcomes also differed significantly between the two groups. Median EBL was higher in the poor-control group than in the good-control group [630.00 (512.25, 1336.25) mL vs. 492.00 (375.75, 597.50) mL, $p < 0.001$]. Furthermore, the incidence of PPH was markedly greater in the poor-control group (39.47% vs. 3.57%, $p < 0.001$). The poor-control group also demonstrated higher proportions of hemostatic escalation, transfusion, and perioperative hyperglycemia events (all $p < 0.001$) (Table 2).

Correlation Analysis

Spearman correlation analysis demonstrated that both HbA1c and three-point glucose CV were positively correlated with EBL. HbA1c was positively correlated with delta platelet count and delta fibrinogen, and negatively correlated with delta PT, delta INR, delta APTT, and delta D-dimer. Because delta values were calculated as preoperative minus postoperative measurements, positive delta values indicate postoperative decreases, whereas negative delta values indicate postoperative increases or prolongation. Therefore, the positive correlations of HbA1c with delta platelet count and delta fibrinogen suggest greater postoperative decreases in platelet count and fibrinogen, while the negative correlations with delta PT, delta INR, delta APTT, and delta D-dimer suggest greater postoperative increases or prolongation in these parameters. Three-point glucose CV was positively correlated with EBL and negatively correlated with delta D-dimer, while its associations with other coagulation-related delta variables were

weak and inconsistent in direction. Changes in PT, INR, and APTT showed moderate correlations in the same direction (Fig. 1).

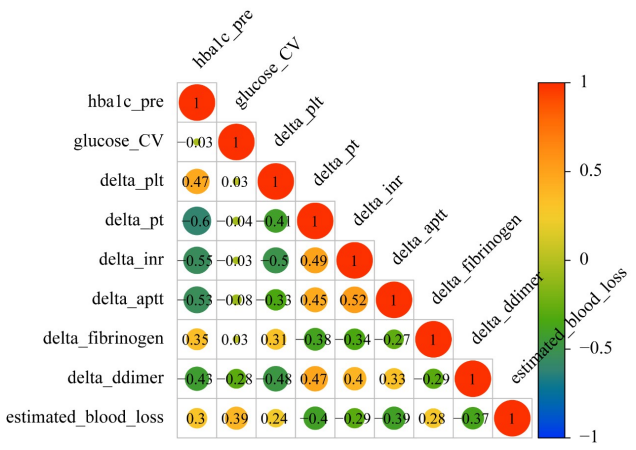

Fig. 1. Spearman correlation heatmap illustrating the relationships among preoperative glycated hemoglobin (HbA1c), three-point perioperative glucose coefficient of variation (CV), perioperative changes in coagulation parameters (delta values), and estimated blood loss (EBL) in 150 diabetic women undergoing cesarean section. Delta values were calculated as preoperative minus postoperative measurements; therefore, positive delta values indicate postoperative decreases, whereas negative delta values indicate postoperative increases or prolongation.

Combined Analysis of HbA1c and Glucose CV

After stratification into four groups based on HbA1c level and glucose CV, bleeding outcomes demonstrated significant differences across the combined metabolic categories. The median EBL values in the low HbA1c + low CV group, low HbA1c + high CV group, and high HbA1c + low CV group were 439.00, 537.00, and 525.00 mL, respectively, while the median EBL in the high HbA1c + high CV group increased markedly to 1226.00 mL ($p < 0.001$). Similarly, the distribution of hemostatic escalation interventions differed significantly among the four groups ($p = 0.005$).

PPH and blood transfusion events showed a similar trend, with higher incidences in the high HbA1c + high CV group. The incidence of PPH was highest in the high HbA1c + high CV group, while no PPH events were observed in the low HbA1c + low CV group. Given the relatively small and uneven subgroup sample sizes (range: n = 19–56), this four-group analysis should be regarded as descriptive supportive evidence rather than as a basis for definitive clinical inference (Table 3).

Associations of HbA1c and Glucose CV With PPH

Univariable and mutually adjusted logistic regression analyses demonstrated that both HbA1c and glucose CV were associated with PPH risk. In univariable analysis, each 1% increase in HbA1c was associated with higher odds of PPH (odds ratio (OR) 4.68, 95% confidence interval (CI) 2.58–8.48, $p < 0.001$). Similarly, each 1% increase in glucose CV was associated with increased odds of PPH (OR 1.19, 95% CI 1.08–1.30, $p < 0.001$). When both variables were simultaneously included in the same regression model, these associations remained statistically significant (Table 4).

In exploratory receiver operating characteristic (ROC) analysis, the area under the curve (AUC) was 0.900 for HbA1c alone, 0.772 for glucose CV alone, and 0.963 for the combined model. The combined model demonstrated significantly greater discriminative performance than HbA1c alone ($Z = -2.628$, $p = 0.009$). However, because this study was not designed as a formal prediction model development and validation study, these ROC findings should be interpreted as exploratory discrimination analyses rather than as evidence supporting an established clinical prediction tool (Fig. 2).

Parsimonious Multivariable Analysis

In the crude regression model, both standardized HbA1c and standardized glucose CV were significantly associated with PPH. After adjustment for age and BMI, both variables remained independently associated with the outcome. Given the limited number of PPH events, this parsimoniously adjusted model was designated as the primary multivariable analysis.

A more extensively adjusted model (Model 3) was also explored. However, its effect estimates were accompanied by substantially wider confidence intervals (e.g., standardized

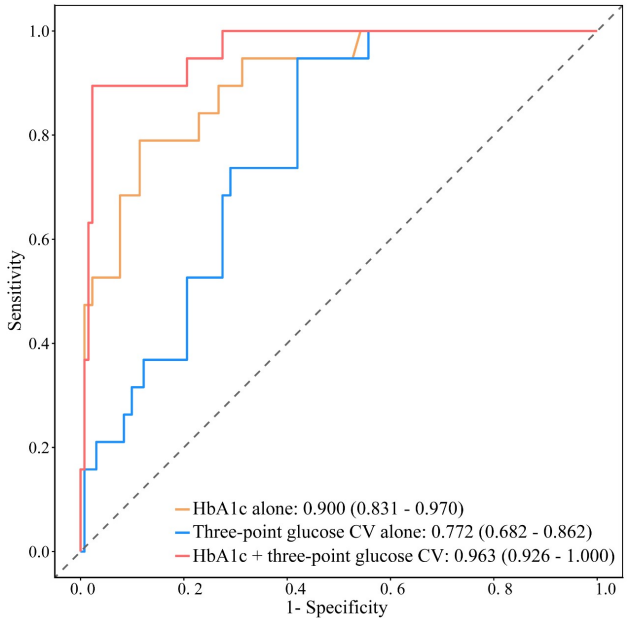

Fig. 2. Receiver operating characteristic (ROC) curves for the prediction of postpartum hemorrhage.

Table 3. Bleeding outcomes according to combined HbA1c and three-point glucose CV.

Variables	Total (n = 150)	Low HbA1c + Low CV (n = 56)	High HbA1c + Low CV (n = 19)	Low HbA1c + High CV (n = 56)	High HbA1c + High CV (n = 19)	Statistic	*p*-value
Estimated blood loss, median (Q_1, Q_3)	523.50 (397.00, 663.75)	439.00 (368.00, 549.25)	525.00 (440.50, 639.00)	537.00 (415.00, 674.00)	1226.00 (628.00, 1373.00)	H = 32.66	<0.001
Postpartum hemorrhage, n (%)						-	<0.001
No	131 (87.33)	56 (100.00)	16 (84.21)	52 (92.86)	7 (36.84)		
Yes	19 (12.67)	0 (0.00)	3 (15.79)	4 (7.14)	12 (63.16)		
Hemostatic escalation, n (%)						χ^2 = 12.99	0.005
No	88 (58.67)	39 (69.64)	7 (36.84)	36 (64.29)	6 (31.58)		
Yes	62 (41.33)	17 (30.36)	12 (63.16)	20 (35.71)	13 (68.42)		
Any transfusion, n (%)						-	<0.001
No	134 (89.33)	54 (96.43)	16 (84.21)	53 (94.64)	11 (57.89)		
Yes	16 (10.67)	2 (3.57)	3 (15.79)	3 (5.36)	8 (42.11)		
Among transfused patients (n = 16)							
Red blood cell units, median (Q_1, Q_3)	1.50 (1.00, 2.00)	2.00 (2.00, 2.00)	1.00 (1.00, 1.50)	4.00 (2.50, 4.00)	1.00 (1.00, 2.00)		
Fresh frozen plasma units, median (Q_1, Q_3)	1.00 (0.00, 3.00)	0.00 (0.00, 0.00)	3.00 (1.50, 3.00)	0.00 (0.00, 0.00)	3.00 (1.50, 3.00)		
Cryoprecipitate units, median (Q_1, Q_3)	2.00 (0.00, 6.00)	0.00 (0.00, 0.00)	4.00 (2.00, 4.00)	0.00 (0.00, 0.00)	8.00 (3.00, 12.00)		
Fibrinogen concentrate, median (Q_1, Q_3)	0.95 (0.00 2.20)	0.00 (0.00, 0.00)	2.20 (1.10, 2.20)	0.00 (0.00, 0.00)	2.20 (1.42, 2.30)		

Statistical tests: H, Kruskal–Wallis test; χ^2, chi-square test; -, Fisher's exact test.

Given the relatively small and uneven subgroup sizes (range: n = 19–56), this four-group analysis should be interpreted as descriptive and supportive rather than confirmatory.

Table 4. Univariate and bivariate logistic regression analyses for postpartum hemorrhage.

Variables	HbA1c alone		Three-point glucose CV alone		HbA1c + three-point glucose CV	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Preoperative HbA1c	4.68 (2.58–8.48)	<0.001			9.17 (3.54–23.78)	<0.001
Three-point glucose CV			1.19 (1.08–1.30)	<0.001	1.40 (1.18–1.67)	<0.001

Abbreviations: OR, odds ratio; CI, confidence interval.

Table 5. Parsimonious and exploratory multivariable logistic regression models for postpartum hemorrhage using standardized predictors.

Variables	Model 1		Model 2		Model 3	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Standardized preoperative HbA1c	5.51 (2.86–10.62)	<0.001	6.86 (3.10–15.15)	<0.001	13.19 (3.10–56.05)	<0.001
Standardized glucose CV	2.69 (1.57–4.58)	<0.001	3.07 (1.66–5.67)	<0.001	3.68 (1.23–10.96)	0.019

Model definitions:

• Model 1: Crude model.

• Model 2: Primary parsimonious model adjusted for age and body mass index.

• Model 3: Exploratory fully adjusted model additionally adjusted for parity, prior cesarean section, emergency cesarean section, preeclampsia, high-risk placenta, gestational age, preoperative hemoglobin, platelet count, activated partial thromboplastin time, fibrinogen, and D-dimer.

HbA1c OR 13.19, 95% CI 3.10–56.05), indicating greater statistical uncertainty. Accordingly, these findings were interpreted cautiously and were not considered the primary inferential findings of the study (Table 5).

Multicollinearity diagnostics showed that all variance inflation factors (VIF) values were below the prespecified threshold of 5. In the primary parsimonious model, VIF values ranged from 1.02 to 1.06, and in the exploratory fully adjusted model, VIF values ranged from 1.07 to 1.72, indicating acceptable collinearity among the included variables.

Restricted Cubic Spline (RCS) Analysis

In the exploratory RCS analysis, with log-transformed EBL as the dependent variable, the overall association for HbA1c was statistically significant (overall $p < 0.001$), and the nonlinearity test was also significant ($p = 0.011$). For glucose CV, the overall association was significant ($p = 0.001$), while the nonlinearity test was not significant ($p = 0.972$). Given the exploratory nature of the analysis, these findings are presented primarily as descriptive information regarding potential exposure-response patterns rather than as evidence of definitive threshold effects (Fig. 3).

Sensitivity Analysis

In exploratory subgroup analyses stratified according to the median glucose CV, the association between HbA1c and PPH remained evident within the high-glucose CV subgroup (OR 4.59, 95% CI 2.39–8.81). In contrast, effect estimation within the low-glucose CV subgroup was unstable because of sparse outcome events (only three PPH cases). Therefore, these subgroup findings should be interpreted cautiously and considered only as supportive exploratory findings (Table 6).

Discussion

This study demonstrated that poor preoperative glycemic control was associated with a more unfavorable perioperative bleeding phenotype in diabetic women undergoing cesarean section. Compared with patients with good glycemic control, those with poor glycemic control exhibited lower postoperative Hb and platelet levels, higher INR and D-dimer levels, and lower fibrinogen levels. Additionally, estimated blood loss, PPH, hemostatic escalation interventions, and blood transfusion-related outcomes were more frequently observed in the poor-control group. Further analysis suggested that both HbA1c and glucose CV were statistically associated with PPH, and that the combined model demonstrated superior discriminative performance compared with the HbA1c-only model. Based on these observational findings, we propose that long-term glycemic status and perioperative glucose fluctuation may be associated with perioperative coagulation status and bleeding-related outcomes in diabetic women undergoing cesarean section. However, causal relationships cannot be established from this retrospective analysis.

First, the association between HbA1c and bleeding-related outcomes may reflect the relationship between long-term metabolic status and overall perioperative physiological vulnerability. In the management of diabetic pregnancy, a single static biomarker may not sufficiently characterize the complex metabolic state throughout gestation. Perioperative and perinatal management, therefore, requires integration of more dynamic glycemic information [15]. A review by Szmuilowicz *et al.* [16] emphasized the significance of capturing dynamic blood glucose patterns and short-term glycemic fluctuations during pregnancy to reduce maternal and fetal malformations. Therefore, reliance on HbA1c

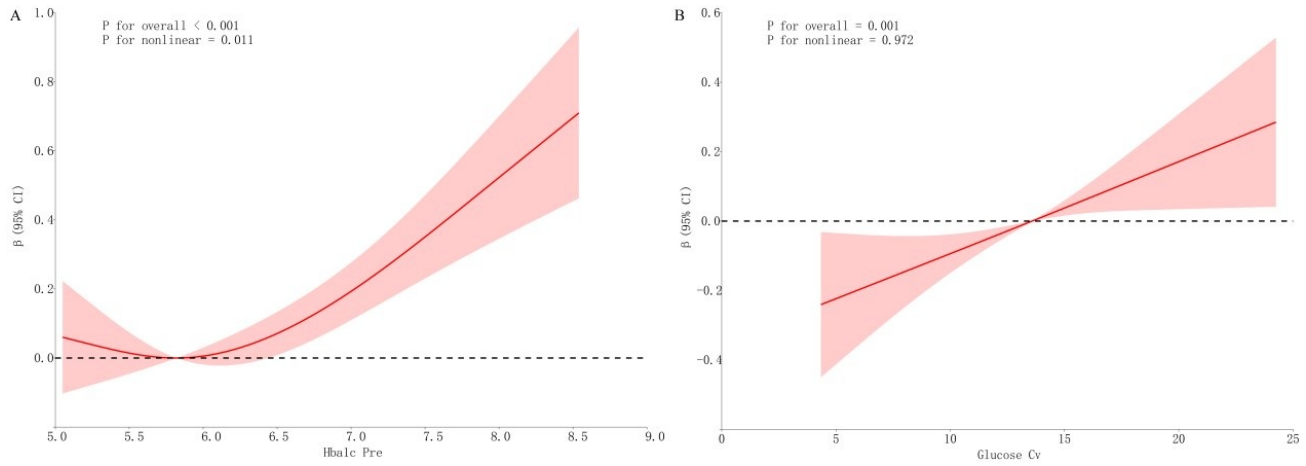

Fig. 3. Restricted cubic spline (RCS) analysis of the relationships between glycemic parameters and estimated blood loss. (A) Preoperative HbA1c and (B) three-point glucose CV. Four knots were placed at the 5th, 35th, 65th, and 95th percentiles of each exposure variable. Linear regression models were fitted using log-transformed EBL as the dependent variable to improve distributional normality. Solid lines represent the predicted log(EBL), and shaded regions indicate 95% confidence intervals. Nonlinearity *p*-values were calculated by testing the null hypothesis that all spline-transformed terms, excluding the linear term, were jointly equal to zero.

Table 6. Subgroup analysis of the association between HbA1c and postpartum hemorrhage stratified by median glucose CV.

Variables	n (%)	OR (95% CI)	*p*-value	*p* for interaction
All patients	150 (100.00)	4.68 (2.58–8.48)	<0.001	
Median glucose CV				0.024
Low CV	75 (50.00)	Not reliably estimated	0.997	
High CV	75 (50.00)	4.59 (2.39– 8.81)	<0.001	

Abbreviations: Inf, infinity.

Patients were stratified into low- and high-CV groups based on the median glucose CV (13.6%). Odds ratios for HbA1c (per 1% increase) were estimated using logistic regression within each subgroup. In the low-CV subgroup, the OR could not be reliably estimated due to sparse events (only three postpartum hemorrhage cases).

alone may not fully reflect the perioperative metabolic burden. In the present study, higher HbA1c levels were associated with increased risk of PPH and greater EBL, as well as lower postoperative fibrinogen and platelet levels. These findings are consistent with the hypothesis that poor long-term glycemic control may coexist with a less favorable perioperative hemostatic profile. Previous research has also suggested that diabetic pregnancy may be accompanied by abnormalities in hemostatic and fibrinolytic pathways [17], although the current data cannot determine whether these alterations represent causal mechanisms or epiphenomena associated with greater disease severity.

Secondly, perioperative glucose fluctuation, as reflected by glucose CV, also provided independent information in the present study. Unlike HbA1c, glucose CV describes the degree of short-term perioperative glucose dispersion and may therefore more closely reflect acute physiological stress and metabolic instability. Previous research has suggested a stable association between blood glucose fluctuations and vascular dysfunction, and this association does not appear to depend solely on mean blood glucose levels [18]. Furthermore, the relationship between continuous glucose-related indicators and adverse pregnancy outcomes has become clearer, and accumulating evidence supports the view that dynamic glycemic indicators may complement the limitations of conventional static indicators [19].

In this study, glucose CV was calculated from only three perioperative glucose measurements and should therefore be regarded as an exploratory surrogate marker rather than a validated measure of glycemic variability [14]. Notably, although the median CV did not differ significantly between the two groups, glucose CV remained significantly associated with PPH in the regression model, and the AUC of the combined model improved modestly. These findings suggest that glucose CV captures aspects of immediate perioperative metabolic instability beyond those reflected by HbA1c alone. However, given that this metric was derived from limited perioperative time points, this interpretation remains speculative and requires further validation in studies incorporating continuous glucose monitoring.

Thirdly, the direction of coagulation-related changes observed in this study demonstrated good clinical consistency. In the poor-control group, postoperative fibrinogen levels were lower, while D-dimer and INR levels were higher,

and platelet counts were lower. In contrast, changes in PT and APTT were relatively modest. This pattern is broadly consistent with recent observations in postpartum hemorrhage research, indicating that fibrinogen and fibrinolysis-related indicators may be more sensitive markers of perioperative bleeding severity than traditional coagulation time parameters [6]. Regarding fibrinogen, previous evidence has reported associations between lower fibrinogen levels and severe PPH phenotypes [7], although this should not be interpreted to mean that fibrinogen is the sole or primary driver of bleeding severity in all cases. Moreover, accurate quantification of blood loss remains challenging in clinical practice and may influence the assessment of coagulation impairment [20]. Therefore, the more pronounced alterations in fibrinogen, platelet count, and D-dimer observed in this study suggest that perioperative coagulation assessment in diabetic women undergoing cesarean section may benefit from increased attention to these relatively sensitive indicators, particularly in the setting of high bleeding load, while recognizing that such abnormalities may represent both contributors to and consequences of hemorrhage.

From a potential physiological perspective, long-term hyperglycemia and perioperative blood glucose fluctuation may be associated with vascular dysfunction and altered platelet phenotype. A previous study has demonstrated links between blood glucose fluctuation and vascular dysfunction [18], while platelets in diabetic patients are more likely to exhibit a hyperreactive phenotype. Additionally, platelet-related parameters have been reported to correlate with glycemic control status [21], suggesting that platelet dysfunction may contribute to the relationship between abnormal glucose metabolism and perioperative hemostatic abnormalities. In this study, HbA1c and glucose CV were correlated with changes in platelet count and several coagulation-related indices, further supporting this potential clinical correlation. However, given the observational design of this study, these findings should be regarded as hypothesis-generating rather than as evidence of direct causality.

The four-group combined exposure analysis further enhanced the clinical interpretability of the findings. Compared with stratification based on HbA1c or glucose CV alone, the combined exposure phenotype more closely reflects perioperative risk patterns encountered in clinical practice. The results showed that the high-HbA1c/high-CV group exhibited the most unfavorable outcomes in EBL, PPH, hemostatic escalation interventions, and blood transfusion requirements, consistent with the hypothesis that patients with both poor chronic glycemic control and marked perioperative glucose fluctuation may present a more adverse bleeding phenotype when long-term metabolic control is poor and perioperative blood glucose fluctuations are large. Different glycemic profile patterns are often associated with varying distributions of adverse pregnancy outcomes [19,22]. From a clinical perspective, risk stratification based solely on a single preoperative glycemic control index may be insufficient. Simultaneous consideration of long-term glycemic control and perioperative glucose fluctuations may better reflect actual perioperative risk-stratification requirements.

Regarding the ROC findings, while the combined model showed a higher AUC than HbA1c alone (0.963 vs. 0.900), this improvement should be interpreted as "information gain" rather than evidence of a validated clinical prediction tool. Recent studies have emphasized that neither machine-learning models nor conventional statistical models should be translated into clinical decision-making without rigorous external validation [23,24]. Therefore, the ROC findings in the present study should be regarded as exploratory discrimination analyses only. Furthermore, RCS analysis suggested a non-linear relationship between HbA1c and log(EBL), while the relationship between glucose CV and log(EBL) appeared approximately linear. These findings indicate that the correlation between the two glycemic indicators and the bleeding phenotype may differ mechanistically. As an indicator of medium- and long-term glycemic exposure, HbA1c may reflect a progressively unfavorable metabolic background at higher levels. In contrast, glucose CV, as a short-term fluctuation index, may exhibit a more continuous association with perioperative bleeding-related changes. Therefore, the present findings support the interpretation of HbA1c and glucose CV as complementary rather than interchangeable glycemic indicators.

In terms of clinical significance, the findings of this study support the concept of perioperative risk identification. In recent years, studies on cesarean section and PPH have increasingly focused on blood-loss assessment, blood transfusion support, cell recovery, and optimization of hemostatic strategies [20,25]. A study suggests that earlier identification of bleeding tendency and optimization of perioperative preparation may be clinically valuable in high-risk cesarean deliveries [10]. In this study, HbA1c and glucose CV may provide additional information for bleeding risk stratification in diabetic women undergoing cesarean section. Patients with higher HbA1c levels or greater perioperative blood glucose fluctuations may warrant closer perioperative coagulation monitoring and more comprehensive bleeding preparedness. However, these implications currently remain at the level of risk awareness and stratification and should not be directly extrapolated into specific intervention strategies without prospective validation studies.

Several important limitations should be considered when interpreting the present findings. First, as a single-center retrospective study, the results are inherently susceptible to selection bias and residual confounding. Unmeasured differences in disease severity, perioperative management, or clinical decision-making between the good-control and poor-control groups may have partially contributed to the observed associations. Second, and most importantly with respect to statistical robustness, the number of PPH events

was limited (n = 19). This restricted the potential to simultaneously adjust for multiple covariates without increasing the risk of model overfitting, resulting in relatively wide 95% confidence intervals in the fully adjusted model (e.g., standardized HbA1c OR 13.19, 95% CI 3.10–56.05), and precluded stable estimation of stratum-specific effects in the low-CV subgroup, in which only 3 PPH events occurred. Consequently, the multivariable and subgroup analyses should be interpreted primarily as exploratory hypothesis- generating rather than as evidence of definitive causal inference or validated risk-stratification models. Third, although the three-point glucose CV was pragmatically derived from routinely available perioperative glucose measurements, it was calculated from only three discrete time points, including intraoperative and postoperative peak values, and therefore cannot comprehensively characterize true glycemic variability as assessed by continuous glucose monitoring. Accordingly, its validity as a surrogate marker for short-term glucose fluctuation remains to be established.

Fourth, postoperative coagulation parameters were obtained at a single time point approximately 20–28 hours after surgery, which may not fully capture the dynamic progression of perioperative coagulation disturbances during the immediate perioperative period. Additionally, estimated blood loss was based on routine clinical assessment methods that are subject to inter-observer variability, potentially affecting the precision of outcome ascertainment. Future studies should include multicenter prospective cohorts with greater event numbers to validate these associations with adequate statistical power. Additionally, incorporating continuous glucose monitoring systems would help determine whether glycemic variability metrics derived from dense longitudinal glucose data demonstrate consistent or stronger associations with coagulation abnormalities and bleeding-related outcomes. Only after prospective replication and external validation should the exploratory findings regarding the combined effects of HbA1c and perioperative glucose fluctuation be considered for integration into clinical perioperative risk-assessment strategies.

Conclusions

This study suggests that preoperative HbA1c and perioperative glucose CV are associated with perioperative coagulation dysfunction and bleeding-related outcomes in diabetic women undergoing cesarean section. The coexistence of elevated HbA1c and higher glucose CV was associated with the most unfavorable bleeding phenotype, suggesting that a combined assessment of chronic glycemic status and short-term perioperative glucose fluctuations may provide complementary information for perioperative risk assessment. However, given the single-center retrospective design and the limited number of PPH events, these findings should be regarded as exploratory and require validation in larger prospective studies.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

YHZ designed and performed the research study. LXC analyzed the data. YHZ drafted the article. Both authors have been involved in revising the manuscript critically for important intellectual content. Both authors gave final approval of the version to be published. Both authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Wenzhou People's Hospital (approval number: KY-202603-014), and all procedures followed the principles of the Declaration of Helsinki. Because this was a retrospective study based on de-identified clinical data generated during routine medical care and involved no additional interventions, the requirement for informed consent was waived by the Ethics Committee of Wenzhou People's Hospital.

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Conflict of Interest

The authors declare no conflict of interest.

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