Predictive Value of Intraoperative Glucose Variability for Chronic Postsurgical Pain After Arthroscopic Rotator Cuff Repair: A Retrospective Cohort Study

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AIM: To investigate the predictive value of intraoperative glucose variability (GV) for chronic postsurgical pain (CPSP) in patients undergoing arthroscopic rotator cuff repair (ARCR).

METHODS: A retrospective study was conducted on 211 ARCR patients admitted to Tongxiang First People's Hospital from January 2021 to December 2024. Patients were divided into CPSP group (n = 35) and non-CPSP group (n = 176). Influencing factors were analyzed with univariate and binary logistic regression. The predictive value of these factors for CPSP in ARCR patients was evaluated with receiver operating characteristic (ROC) curve analysis. Shoulder joint indicators of patients with different levels of intraoperative GV were compared before and after treatment. GV was expressed as the ratio of the standard deviation to the mean value of intraoperative blood glucose.

RESULTS: There were no statistically significant differences ($p > 0.05$) in age, sex, body mass index (BMI), surgery time, intraoperative blood loss, length of hospital stay, tear location, tear area, glycated hemoglobin (HbA1c), fasting blood glucose and full-thickness tear between the groups. However, there were statistically significant differences ($p < 0.05$) in the number of torn tendons, shoulder acromioplasty, coefficient of variance (CV), largest amplitude of glycemic excursions (LAGE), and preoperative pain. Binary logistic regression analysis revealed that the number of torn tendons, LAGE, and CV were influencing factors for CPSP in ARCR patients ($p < 0.05$). The area under the ROC curve for CV was 0.864, standard error 0.027 (95% CI: 0.812–0.916, $p < 0.001$), with a Youden index of 0.62, sensitivity of 91.43%, and specificity of 70.45%. Post-treatment Constant–Murley Score (CMS) and American Shoulder and Elbow Surgeons Score (ASES) scores were significantly better in patients with CV $\leq$0.18 compared to CV >0.18 ($p < 0.001$).

CONCLUSIONS: Intraoperative GV has predictive value for CPSP in ARCR patients.

Keywords: glucose variability; arthroscopic rotator cuff repair; chronic pain

Introduction

Shoulder pain has become a significant health issue affecting quality of life, ranking third among musculoskeletal pain sites and representing a major cause of musculoskeletal disability. In the United States, approximately 4.5 million patients seek medical care annually for shoulder pain [1]. Rotator cuff injuries, a primary cause of shoulder pain for most patients, increase in incidence with age [2]. In the treatment of rotator cuff injuries, arthroscopic rotator cuff repair (ARCR) has become the gold standard due to advantages such as minimal incision, reduced muscle damage, and significant improvement in shoulder joint function [3]. However, despite advancements in surgical techniques, postoperative pain management following shoulder arthroscopy remains challenging.

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The pathogenesis of chronic pain after ARCR is complex. Surgical trauma triggers a local inflammatory response, releasing inflammatory mediators to stimulate nerve endings; it may also cause nerve damage, leading to neuropathic pain, while postoperative scar adhesions and limited joint movement can further contribute to persistent pain [4]. Moderate to severe pain is common after surgery, and chronic pain lasting more than three months, referred to as chronic postsurgical pain (CPSP), significantly impairs patients' well-being [5]. CPSP not only hinders recovery but also increases economic burden, healthcare resource utilization, and negatively affects quality of life.

Historically, opioid drugs have played a crucial role in postoperative pain management in orthopedic surgery and have been considered the gold standard for ensuring adequate pain control [6]. However, opioids are associated with adverse effects such as nausea, vomiting, constipation, and, at high doses, serious complications including respiratory depression and hypoxemia. Moreover, opioid dependence is a major concern in CPSP management, underscoring the importance of identifying high-risk patients and planning personalized postoperative pain strategies. Current research on pain following ARCR has predominantly focused on risk

factors like age, sex, and type of surgery [7], with limited study on identifying patients predisposed to CPSP. Additionally, although shoulder repair surgery effectively alleviates shoulder pain and restores function, many patients often experience varying degrees of prolonged postoperative pain, which adversely impacts sleep and overall quality of life. Therefore, improving perioperative pain conditions and enhancing postoperative outcomes remain a pressing clinical challenge for shoulder surgeons.

Blood glucose is a key metabolic substrate, and its stability is crucial for maintaining normal organ function. During the physiological state of surgery, the patient's body is in a state of stress and the endocrine system undergoes significant changes, resulting in fluctuations in blood glucose levels [8]. Intraoperative glucose variability (GV) refers to the fluctuations in blood glucose levels during surgery, reflecting variability over time rather than a single glucose measurement. GV has been used as a risk predictor of cardiovascular disease [9,10], but its application in CPSP has not been established. Hence, this study aims to explore the predictive value of intraoperative GV for CPSP in ARCR, providing new insights for optimizing perioperative pain management strategies.

Methods

Research Objects

Sample size calculation was performed using the formula $N = Z_{\alpha/2}{}^2\pi(1-\pi)/\delta^2$. Based on previous literature on the occurrence of chronic pain following ARCR [4], where π was taken as 13.74%, with a significance level of $\alpha = 0.05$ and an allowable error of $\delta = 0.06$, the calculated sample size was at least 127. Considering the possibility of invalid samples, the sample size was expanded by 20% to a minimum of 153. For this retrospective study, a total of 240 ARCR patients admitted to Tongxiang First People's Hospital from January 2021 to December 2024 were initially screened. After applying inclusion and exclusion criteria, 211 patients were included in the study. Patients were categorized into the CPSP group (n = 35) and the non-CPSP group (n = 176) based on the presence of CPSP, defined as post-ARCR pain (numerical rating scale score $\geq$4) persisting for more than three months [5]. Follow-up in this study was based on monthly visits by patients returning to the hospital. The inclusion criteria were as follows: (1) patients meeting the clinical diagnostic criteria for rotator cuff tear and undergoing ARCR in Tongxiang First People's Hospital; (2) age $\geq$18 years; (3) ARCR performed by the same group of surgeons; (4) patients undergoing their first rotator cuff repair surgery. The exclusion criteria were as follows: (1) patients with malignant tumors or other conditions causing persistent pain; (2) patients with mental disorders or communication barriers; (3) patients experiencing pain outside the surgical site; (4) patients with concurrent diabetes. The flowchart of patients recruitment and selection is shown in Fig. 1.

This study was conducted is in accordance with the Declaration of Helsinki. Approval was obtained from the Medical Ethics Committee of Tongxiang First People's Hospital (2025-014-01). The requirement for informed consent was waived due to the use of anonymized patient data.

Data Collection Methods

General Data Collection

Patient general information was collected using the electronic medical records system, including age, sex, body mass index (BMI), surgery time, intraoperative blood loss, length of hospital stay, number of torn tendons, tear location, tear area, full-thickness tear, acromioplasty, preoperative pain (based on numerical rating scale (NRS), with an NRS score $\geq$4), and other relevant data.

Blood Glucose Monitoring Indicators

The following blood glucose monitoring indicators were recorded: mean blood glucose (MBG), standard deviation of blood glucose (SDBG), glucose variability (GV) represented by the coefficient of variance (CV) of intraoperative blood glucose levels [11], and the largest amplitude of glycemic excursions (LAGE). Blood glucose was monitored using point-of-care testing (POCT) within the hospital, recorded every 30 minutes from the beginning of surgery. Calculation methods were as follows: MBG, average blood glucose level during surgery; SDBG, standard deviation of blood glucose during surgery; CV, ratio of the standard deviation to the mean blood glucose level during surgery (SDBG/MBG); and LAGE, difference between the highest and lowest blood glucose levels during surgery.

Functional Outcomes

Preoperative (one day before surgery) and postoperative (one month after surgery) functional outcomes were assessed using the Constant–Murley Score (CMS) [12] and the American Shoulder and Elbow Surgeons Score (ASES) [13].

Postoperative Blood Glucose Management

Patients' blood glucose levels were closely monitored. If hyperglycemia persisted, oral antidiabetic drugs or insulin were administered as appropriate. When glucocorticoids or other drugs that increase blood glucose were used during the operation, the frequency of monitoring was increased, and the intensity of treatment was adjusted promptly. Patients were encouraged to engage in moderate early exercise to promote glucose metabolism. Medical staff provided education on blood glucose management to patients and their families to enhance awareness, cooperation, and adherence, thereby supporting postoperative blood glucose stability, wound healing, and physical recovery.

Statistical Analysis

The collected data were analyzed using SPSS 27.0 (International Business Machines Corporation, Armonk, NY,

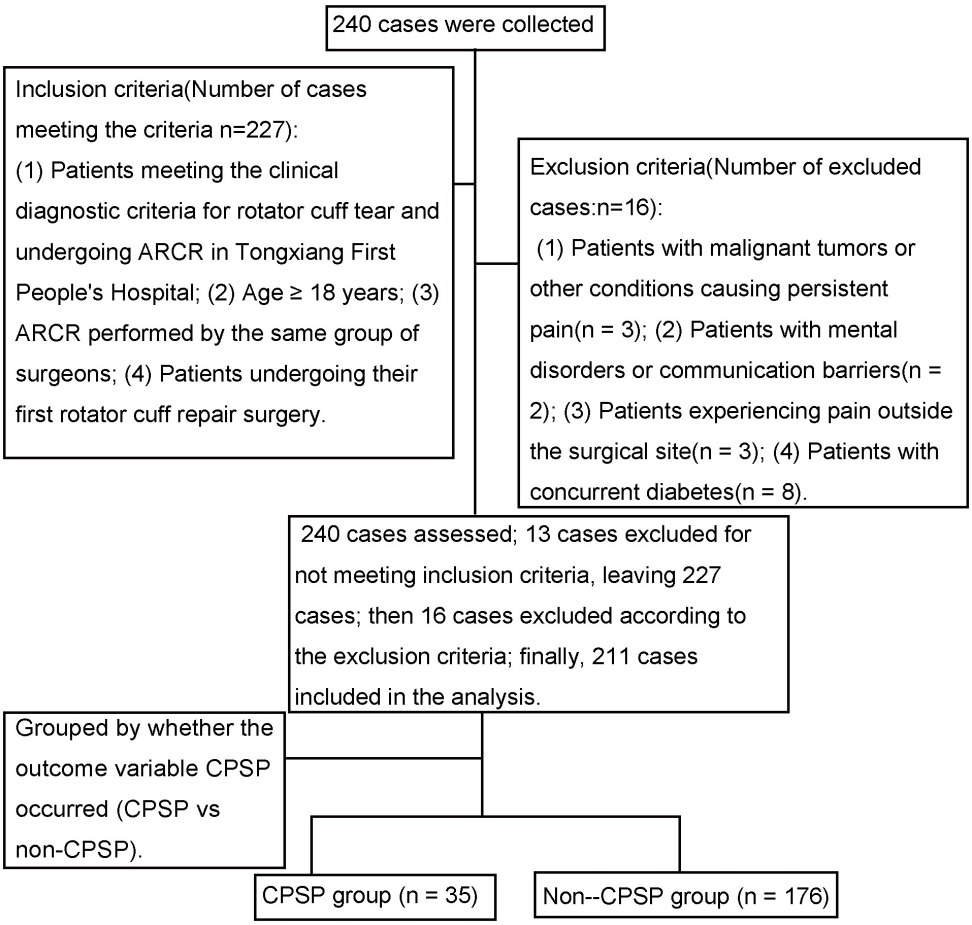

Fig. 1. Flowchart of participant recruitment in this study. ARCR, arthroscopic rotator cuff repair; CPSP, chronic postsurgical pain.

USA). The Shapiro-Wilk test was employed for normality testing. For normally distributed continuous data, results are presented as $\bar{X} \pm S$. Comparisons were made using independent samples *t*-tests. For data that did not follow a normal distribution, results were presented as the median and interquartile range (IQR) denoted as median quartiles 2 (MQ2) (Q1, Q3), and analyzed using the Mann-Whitney U test. Categorical data was presented as frequencies or rates, and comparisons were conducted using the χ^2 test or Fisher's exact test. Factors were analyzed with univariate and binary logistic regression analysis. The predictive value of factors for CPSP in ARCR patients was evaluated using receiver operating characteristic (ROC) curves. A significance level of $p < 0.05$ was considered statistically significant.

Results

Univariate Analysis of Influencing Factors

Comparisons of patient age, sex, BMI, surgery time, intraoperative blood loss, length of hospital stay, tear location, tear area, glycated hemoglobin (HbA1c), fasting blood glucose, full-thickness tear showed no statistically significant differences ($p > 0.05$). In contrast, comparisons of the number of torn tendons, acromioplasty, CV, LAGE, and preoperative pain showed statistically significant differences ($p < 0.05$), as shown in Table 1.

Binary Logistic Regression Analysis of Influencing Factors

Using significant factors identified in the univariate analysis as independent variables, a binary logistic regression analysis was conducted with CPSP as the dependent variable (CPSP = 1, non-CPSP = 0). The collinearity diagnosis indicates that there was no meaningful multicollinearity (tolerance: 0.940–0.992, VIF: 1.008–1.064). The results of the binary logistic regression analysis indicated that the number of torn tendons, LAGE, and CV are influencing factors for CPSP in ARCR patients ($p < 0.05$) (Tables 2,3).

ROC Curve Analysis of Predictive Value of Indicators

The ROC analysis showed that the area under the curve (AUC) for predicting the number of torn tendons was 0.598 with a standard error of 0.054 (95% CI: 0.491–0.705, $p = 0.068$). The Youden index was 0.20, with a sensitivity

Table 1. Univariate analysis of influencing factors.

Indicator		CPSP group (n = 35)	Non-CPSP group (n = 176)	$Z/t/\chi^2$ value	p value
Age (years)		59.54 ± 8.45	58.99 ± 8.13	0.363	0.717
Sex	Male	18	80	0.121	0.728
	Female	17	86		
BMI (kg/m^2)		21.64 ± 2.84	21.94 ± 2.63	0.608	0.544
Surgery time (min)		190.54 ± 20.54	186.54 ± 18.54	1.145	0.254
Intraoperative blood loss (mL)		245.54 ± 34.54	239.87 ± 31.95	0.946	0.345
Length of hospital stay (days)		7.24 ± 1.34	7.11 ± 1.16	0.590	0.556
Number of torn tendons		1 (1, 2)	1 (1, 1)	–2.317	0.021
Tear location	Supraspinatus	24	119	0.151	0.985
	Infraspinatus	2	8		
	Subscapular	2	10		
	Multiplesites	7	39		
Tear area (cm^2)	<1	6	20	3.334	0.189
	1–<3	21	132		
	≥3	8	24		
Full-thickness tear	No	28	135	0.180	0.671
	Yes	7	41		
Acromioplasty	Yes	29	165	4.676	0.031
	No	6	11		
CV		0.21 ± 0.02	0.16 ± 0.03	–10.642	<0.001
LAGE (mmol/L)		3.19 ± 0.75	2.10 ± 0.72	–7.856	<0.001
Preoperative pain	Yes	13	31	6.746	0.009
	No	22	145		
HbA1c (%)		5.55 ± 0.70	5.45 ± 0.81	0.681	0.496
Fasting glucose (mmol/L)		5.46 ± 0.55	5.51 ± 0.61	0.450	0.653

Note: BMI, body mass index; CPSP, chronic postsurgical pain; HbA1c, glycated hemoglobin; CV, coefficient of variance; LAGE, largest amplitude of glycemic excursions. Intraoperative blood glucose variability is represented by CV and LAGE.

Table 2. Variable assignment.

Influencing factors	Assignment
Torn tendons	Original value
Acromioplasty	Yes = 0, No = 1
LAGE	Original value
CV	Original value
Preoperative pain	No = 0, Yes = 1

of 45.71% and a specificity of 73.86%. For the prediction of LAGE, the AUC was 0.833 with a standard error of 0.035 (95% CI: 0.765–0.900, $p < 0.001$). The Youden index was 0.49, with a sensitivity of 97.14% and a specificity of 51.14%. For CV, the AUC was 0.864 with a standard error of 0.027 (95% CI: 0.812–0.916, $p < 0.001$). The Youden index was 0.62, with a sensitivity of 91.43% and a specificity of 70.45%. The predictive value of CV was the highest among the three variables (i.e., highest AUC and Youden index), as shown in Table 4 and Fig. 2.

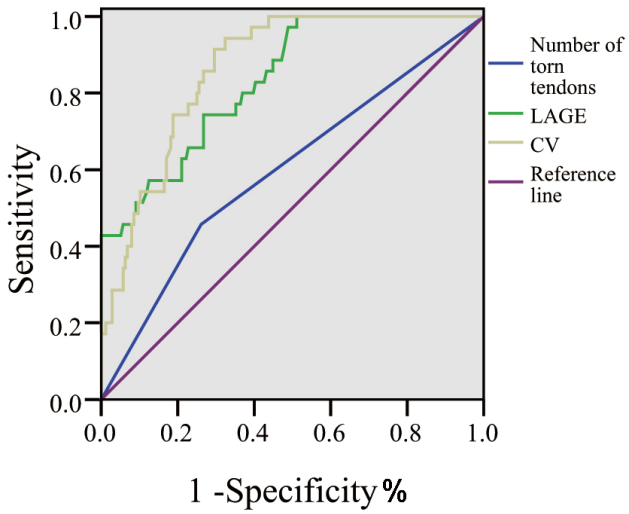

Fig. 2. ROC curve. ROC, receiver operating characteristic; CV, coefficient of variance; LAGE, largest amplitude of glycemic excursions.

Comparison of Shoulder Joint Indices Before and After Treatment in Patients With Different CV Values

Patients in the CV ≤0.18 group showed better post-treatment CMS and ASES scores compared with the CV >0.18 group, with a statistically significant difference ($p < 0.001$), as shown in Table 5.

Discussion

In the univariate analysis, this study showed significant differences in factors such as the number of torn tendons, acromioplasty, CV, LAGE, and preoperative pain between

Table 3. Binary logistic regression analysis of influencing factors.

Factor	β	Standard error	Wald	p value	Exp(β)	95% CI		Collinearity analysis	
						Lower limit	Upper limit	Tolerance	VIF
Torn tendon count	1.574	0.627	6.305	0.012	4.825	1.412	16.481	0.992	1.008
Acromioplasty	1.149	0.942	1.489	0.222	3.155	0.498	19.978	0.992	1.008
LAGE	2.129	0.462	21.211	<0.001	8.410	3.398	20.816	0.940	1.064
CV	0.626	0.137	20.825	<0.001	1.871	1.429	2.448	0.946	1.057
Preoperative pain	0.944	0.668	1.993	0.158	2.569	0.693	9.520	0.983	1.018

VIF, variance inflation factor.

Table 4. ROC analysis results.

Indicator	AUC	Standard error	95% CI	Youden	Sensitivity	Specificity	p value	Cut-off value
Torn tendon count	0.598	0.054	0.491~0.705	0.20	45.71	73.86	0.068	-
LAGE	0.833	0.035	0.765~0.900	0.49	97.14	51.14	<0.001	2.02
CV	0.864	0.027	0.812~0.916	0.62	91.43	70.45	<0.001	0.18

ROC, receiver operating characteristic; AUC, area under the curve. -, there is no best cut-off value for classification indicators.

Table 5. Comparison of shoulder joint indices before and after treatment in patients with different CV values.

Indicator		CV ≤0.18 group (n = 135)	CV >0.18 group (n = 76)	t/χ^2 value	p value
CMS (points)	Before treatment	54.64 ± 8.54	56.46 ± 7.66	1.541	0.125
	After treatment	83.54 ± 9.54	78.65 ± 9.45	3.586	<0.001
ASES (points)	Before treatment	32.98 ± 2.64	33.23 ± 2.94	0.659	0.511
	After treatment	63.54 ± 4.64	60.21 ± 4.54	5.043	<0.001

CMS, Constant–Murley Score; ASES, American Shoulder and Elbow Surgeons Score.

the CPSP and non-CPSP groups. Further binary logistic regression analysis clarified that the number of torn tendons, LAGE, and CV are important risk factors for CPSP occurrence in ARCR patients ($p < 0.05$). These results suggest that in the ARCR surgical process, in addition to traditional surgical factors such as the number of torn tendons, intraoperative glycemic variability should not be overlooked, as it may play a crucial role in the occurrence and development of CPSP [9].

From a mechanistic perspective, although the specific mechanisms through which CV influences the occurrence of CPSP after ARCR are not fully elucidated, existing research provides some potential clues. Study by Giri A *et al.* [14] has shown that diabetes is a risk factor for rotator cuff disease, supporting the rationale of this study. Glucose serves as the primary energy source for numerous cells, including the brain, which is highly sensitive to serum glucose levels. The brain consumes about 50% of the body's glucose and relies on it as a major energy source that is difficult to substitute with other forms of energy [15]. Within the brain, glucose-sensing neurons regulate glucose metabolism and homeostasis [16]. High intraoperative glycemic variability indicates significant fluctuations in blood glucose levels, which may have adverse effects on the nervous system [17]. Severe fluctuations in intraoperative blood glucose levels, particularly episodes of severe hypoglycemia, can reduce adenosine triphosphate (ATP) levels in neuronal cells. ATP is the direct energy source for cells, and its depletion can lead to neuronal depolarization, affecting normal neuronal function. This may activate nociceptive receptors, rendering patients more sensitive to pain stimuli and thereby increasing the risk of CPSP [18].

High intraoperative blood glucose levels should also not be overlooked. Hyperglycemia can trigger oxidative stress reactions, generating large amounts of free radicals that damage neurons, disrupt neural signal transmission, impair nervous system function, and lead to cognitive and sensory abnormalities, potentially including abnormal pain perception, thereby promoting the occurrence of CPSP [19,20]. Moreover, high blood glucose levels are not only a consequence of perioperative inflammation but also a contributing factor. Research by Choi H *et al.* [21] suggests that CV is an important mechanism in the development of postoperative delirium (POD). Neuroinflammation can be induced by systemic inflammation, and the close interplay between systemic inflammation, blood glucose homeostasis, and oxidative stress may be influenced by significant intraoperative glycemic variability, impairing neural function and promoting POD after ARCR surgery. This mechanistic analysis aligns closely with the findings of this study.

In this study, the predictive value of CV for CPSP in ARCR patients was evaluated with ROC curves. The results indicated that the AUC for the CV prediction model was 0.864, with a standard error of 0.027 (95% CI: 0.812–0.916, $p < 0.001$). The Youden index was 0.62, with a sensitivity of 91.43% and specificity of 70.45%. These findings suggest

that CV has acceptable predictive accuracy for CPSP after ARCR, effectively distinguishing high-risk patients likely to develop CPSP. Furthermore, we compared shoulder joint indices before and after treatment in patients with different CV values. Patients in the CV $\leq$0.18 group showed better post-treatment CMS and ASES scores compared to those in the CV $>$0.18 group. This further supports the association between intraoperative glycemic variability and postoperative shoulder joint functional recovery and pain relief. The results also suggest that pre-existing chronic pain or neuropathy may increase the risk of postoperative GV and CPSP. Chronic pain sensitizes the nervous system, and neuropathy impairs sensory conduction, both of which may change the body's response to surgical stress and thereby increase disease risk.

This study holds significant clinical implications. Currently, the prediction of CPSP after ARCR mainly relies on traditional risk factors such as age, sex, and surgical type, but the predictive power of these factors is limited. For the first time, this study incorporates intraoperative glycemic variability into the predictive index system for CPSP after ARCR, providing clinicians with a more accurate prediction method. By identifying high-risk patients for developing CPSP before surgery, clinicians can tailor personalized perioperative pain management strategies, such as enhancing blood glucose monitoring and regulation or optimizing pain management protocols, to reduce the incidence of CPSP, improve postoperative recovery, and enhance patients' quality of life. Moreover, these findings provide both a theoretical basis and a clinical reference for further research into the relationship between intraoperative glycemic variability and postoperative pain, thereby contributing to the advances in this field.

However, this study also has certain limitations. The single-center recruitment and use of the same surgical team limit sample representativeness, risking selection and information bias. Excluding diabetic patients restricts clinical applicability, as many patients have this condition. Monthly follow-ups for only three months may miss long-term pain trends and late-onset CPSP. This study does not stratify pain phenotypes, which may mask differences between pain mechanisms. Monitoring blood glucose every 30 minutes may underestimate its variability. Additionally, it overlooks psychological factors like anxiety and depression, which are important predictors of CPSP. This study's single-center retrospective design increases the risk of selection and information bias. Subsequently, data should be collected from multiple centers to capture more key indicators, such as baseline psychology. The short follow-up period means that long-term outcomes and complications were not fully observed; longer follow-up is needed for comprehensive evaluation. Moreover, the CV dichotomy at 0.18 is data-driven, which introduces optimism bias since no cut-off value was pre-specified. In addition, univariate screening did not adjust for multiple comparisons, affecting the reliability of results. Pairwise comparisons of ROC AUCs did not use the DeLong test. Other limitations include reliance on a single surgeon group, lack of diabetes stratification, short follow-up time, and unverified pain phenotypes. The study also lacked prospective intervention data and therefore could not explore the impact of intraoperative GV reduction measures on CPSP incidence. Future research should aim to expand the sample size and conduct prospective studies to validate the reliability and stability of the findings. Additionally, exploration of the specific molecular mechanisms through which intraoperative glycemic variability influences CPSP after ARCR is needed to provide theoretical support for the development of targeted intervention strategies.

Conclusions

In summary, CV is of great value in predicting CPSP in patients undergoing ARCR. Further improvements are needed to enhance the accuracy of CPSP prediction and to provide patients with more scientific perioperative management and postoperative recovery guidance.

Availability of Data and Materials

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

Author Contributions

XZ designed the research study and performed the research. LX analyzed the data. XZ wrote the manuscript. 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

This study is in accordance with the Declaration of Helsinki. The study was approved by the Medical Ethics Committee of Tongxiang First People's Hospital (2025-014-01). The requirement for informed consent was waived due to the use of anonymized patient data.

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Conflict of Interest

The authors declare no conflict of interest.

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