Postoperative Glycemic Variability in Diabetic Orthopedic Patients: Association with DVT/Myocardial Infarction and Interactive Risk with HbA1c

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Abstract: This study explored the association of postoperative glycemic variability with 30-day deep vein thrombosis (DVT) and myocardial infarction (MI) in diabetic orthopedic patients, and its interaction with glycated hemoglobin (HbA1c). A retrospective analysis of 826 diabetic patients undergoing elective major orthopedic surgeries (total hip arthroplasty [THA], total knee arthroplasty [TKA], spinal fusion) (2019–2024) was conducted. Glycemic variability indices included mean amplitude of glycemic excursions (MAGE), blood glucose standard deviation (SD), and maximum glycemic fluctuation (Max-G). Multivariate logistic regression and interaction analyses were performed. Results showed 109 (13.2%) DVT cases and 38 (4.6%) MI cases. After adjusting for confounders, each 1 mmol/L increase in MAGE was associated with 2.13-fold higher DVT risk (OR=2.13, 95% CI: 1.68–2.70, P<0.001) and 2.57-fold higher MI risk (OR=2.57, 95% CI: 1.81–3.65, P<0.001). Significant interaction between glycemic variability and HbA1c was observed (Pinteraction<0.05): in patients with HbA1c>9%, DVT (OR=3.02) and MI (OR=3.61) risks were higher than in those with HbA1c<7% (DVT: OR=1.58; MI: OR=1.87). Sensitivity analysis confirmed robustness. Conclusion: Postoperative glycemic variability (especially MAGE) is an independent risk factor for DVT/MI in diabetic orthopedic patients, with significant interaction with HbA1c. Strengthening glycemic variability management is crucial.

***Keywords*:** diabetes mellitus, orthopedic surgery, glycemic variability, deep vein thrombosis, myocardial infarction, glycated hemoglobin

1. Introduction

With population aging and rising diabetes prevalence, diabetic patients account for 20%–30% of major orthopedic surgery (THA, TKA) populations [1]. Postoperative DVT and MI are life-threatening: DVT may progress to pulmonary embolism, and MI causes early postoperative death, prolonging hospital stays and increasing 1-year mortality by 3–5 times in diabetics [2–3]. Identifying their risk factors is clinically critical.

Glycemic control is core to perioperative management. Previous studies focused on long-term indices (e.g., HbA1c>8% linked to infection [4]), but growing evidence shows glycemic variability (short-term glucose fluctuations) is a stronger cardiovascular risk indicator—even with normal fasting glucose/HbA1c, fluctuations damage vascular endothelium via oxidative stress and inflammation [5–6]. A cohort study found each 1 mmol/L MAGE increase raised cardiovascular event risk by 1.8-fold [7], but it did not target orthopedic patients or analyze DVT/MI interactions.

Orthopedic surgery (trauma, bleeding, immobilization) exacerbates glycemic variability—postoperative 72-hour MAGE is 1.5–2.0 times preoperative levels [8]. Whether short-term variability and long-term HbA1c have a "synergistic hazard" effect (poor HbA1c increasing variability sensitivity) remains unclear. This study analyzed 826 diabetic orthopedic patients to explore variability-DVT/MI associations and variability-HbA1c interactions, providing evidence for glycemic management.

2. Materials and methods

2.1 Study Subjects

Diabetic patients undergoing elective THA (CPT: 27130, 27132), TKA (CPT: 27447, 27449), or spinal fusion (CPT: 22612, 22630, 22633) (2019–2024) were included if they: (1) met China Guidelines for the Prevention and Treatment of Type 2 Diabetes Mellitus (2023 Edition), diabetes duration ≥6 months; (2) were aged ≥18 years; (3) had ≥6 blood glucose monitors (every 4–6 hours, fasting/postprandial) within 72 hours postoperatively; (4) had complete data. Exclusions: preoperative DVT/MI (1 month), coagulation disorders, non-discontinuable anticoagulants, malignant tumors (survival <1 year), severe liver/kidney dysfunction, death/loss to follow-up (24 hours postoperatively), or acute stress. Final sample: 826

patients.

2.2 Data Collection

Baseline data: Age, gender, BMI, diabetes type/duration, preoperative HbA1c (3 months), comorbidities (hypertension, coronary heart disease, CKD), preoperative medications.

Surgery-related data: Surgery type, duration (skin incision to suture), intraoperative blood loss, anesthesia, postoperative anticoagulants (LMWH, fondaparinux).

Glycemic variability indices [9–10]: MAGE (average peak-trough differences >1 SD from daily mean), SD (dispersion of glucose values), Max-G (highest–lowest glucose within 72 hours).

Outcomes: 30-day DVT (diagnosed via Doppler/CTA [11]) and MI (per Fourth Universal Definition of Myocardial Infarction (2018) [12]).

2.3 Statistical Methods

SPSS 26.0 was used. Normally distributed data: mean ± SD (x±s), t-test; non-normal data: median (IQR) [M (Q1, Q3)], Mann-Whitney U test; count data: n (%), χ^2/Fisher's test.

Multivariate logistic regression analyzed variability-DVT/MI associations (three models):

Model 1: Unadjusted;

Model 2: Adjusted for age, gender, BMI;

Model 3: Further adjusted for diabetes duration, HbA1c, hypertension, coronary heart disease, surgery type, duration, blood loss, anticoagulants.

Interaction terms (e.g., MAGE×HbA1c) were added to Model 3. Patients were stratified by HbA1c (<7%, 7%–9%, >9%) for trend analysis. Sensitivity analyses: (1) exclude 24-hour postoperative glucose; (2) adjust for postoperative infection (temperature >38.5℃, WBC >10×10^9/L). $P<0.05$ was significant.

3. Results

3.1 Baseline data and complication occurrence

A total of 826 diabetic patients undergoing elective major orthopedic surgeries (total hip arthroplasty [THA], total knee arthroplasty [TKA], spinal fusion) were included in this study, with a follow-up of 30 days postoperatively to record the occurrence of deep vein thrombosis (DVT) and myocardial infarction (MI). To clarify the distribution of baseline characteristics in the total population and differences between patients with and without complications, the following sections present the overall baseline data and inter-group comparisons.

3.1.1 Overall baseline characteristics of the total population

In the total cohort, the mean age was (65.8±8.7) years, with 432 males (52.3%) and 394 females (47.7%), showing a slight male predominance. The mean body mass index (BMI) was (26.3±3.5) kg/m², which was in the overweight range (BMI 24~28 kg/m²) according to the Chinese adult BMI classification standard. Regarding diabetes-related indicators: 798 patients (96.6%) had type 2 diabetes, and only 28 patients (3.4%) had type 1 diabetes, consistent with the high prevalence of type 2 diabetes in the elderly population; the mean duration of diabetes was (8.2±4.5) years, indicating a long-term disease course in most patients; the preoperative glycated hemoglobin (HbA1c) level was (7.8±1.6)%, with 289 patients (35.0%) having HbA1c<7% (good long-term glycemic control), 392 patients (47.5%) having HbA1c 7%~9% (moderate control), and 145 patients (17.5%) having HbA1c>9% (poor control), suggesting that nearly one-fifth of patients had inadequate long-term glycemic management before surgery.

For comorbidities: 459 patients (55.6%) had hypertension, 194 patients (23.5%) had coronary heart disease, and 124 patients (15.0%) had chronic kidney disease, reflecting a high incidence of cardiovascular and renal comorbidities in this population—consistent with the common comorbidity profile of elderly diabetic patients.

In terms of surgical indicators: the distribution of surgery types was balanced, including 296 cases of THA (35.8%), 348 cases of TKA (42.1%), and 182 cases of spinal fusion (22.0%); the mean surgical duration was (135.6±38.2) minutes, and the mean intraoperative blood loss was (328.5±146.7) ml, which are within the normal range for major orthopedic surgeries; 783 patients (94.8%) received postoperative anticoagulation (low-molecular-weight heparin or fondaparinux), in line with the clinical guideline recommendations for venous thromboembolism prevention in major orthopedic surgeries

Postoperatively, 109 patients (13.2%) developed DVT within 30 days: 38 cases (12.8%) in THA patients, 47 cases (13.5%) in TKA patients, and 24 cases (13.2%)—showing no significant difference in DVT incidence among different surgery types ($\chi^2=0.189$, $P=0.910$). A total of 38 patients (4.6%) developed MI: 12 cases (4.1%) in THA patients, 17 cases

(4.9%) in TKA patients, and 9 cases (4.9%) in spinal fusion patients—also with no significant difference in MI incidence across surgery types (χ^2=0.356, P=0.837).

3.1.2 Comparison of baseline characteristics between patients with and without complications

The DVT group had older age (68.9±9.1 vs. 65.2±8.5 years, P=0.001), higher BMI (27.5±3.8 vs. 26.1±3.4 kg/m², P=0.001), longer diabetes duration (9.5±4.8 vs. 8.0±4.4 years, P=0.002), higher HbA1c (8.9±1.8 vs. 7.6±1.5%, P<0.001), more coronary heart disease (33.0% vs. 22.0%, P=0.009), longer surgery duration (148.5±39.6 vs. 133.2±37.5 minutes, P=0.001), and more blood loss (365.8±152.9 vs. 322.3±144.1 ml, P=0.003) than the non-DVT group.

The MI group showed similar trends: older age (70.3±9.5 vs. 65.6±8.6 years, P=0.002), higher BMI (27.8±4.0 vs. 26.2±3.5 kg/m², P=0.030), longer diabetes duration (9.8±5.1 vs. 8.1±4.5 years, P=0.041), higher HbA1c (9.2±1.9 vs. 7.7±1.6%, P<0.001), and longer surgery duration (149.8±41.2 vs. 135.1±38.0 minutes, P=0.026). No significant differences in gender, diabetes type, hypertension, CKD, surgery type, or anticoagulation rate were observed (all P>0.05; Table 1).

Table 1. Comparison of baseline characteristics between patients with and without complications

Characteristic	Total population (n=826)	Non-DVT group (n=717)	DVT group (n=109)	Statistic (t/χ^2)	P-value	Non-MI group (n=788)	MI group (n=38)	Statistic (t/χ^2)	P-value
Demographic features									
Age (years)	65.8±8.7	65.2±8.5	68.9±9.1	3.872	0.001	65.6±8.6	70.3±9.5	3.215	0.002
Gender, male [n(%)]	432 (52.3)	368 (51.3)	64 (58.7)	2.351	0.125	410 (52.0)	22 (57.9)	0.689	0.406
BMI (kg/m²)	26.3±3.5	26.1±3.4	27.5±3.8	3.426	0.001	26.2±3.5	27.8±4.0	2.198	0.030
Diabetes-related indicators									
Diabetes type [n(%)]				0.892	0.345			0.517	0.473
- Type 1	28 (3.4)	24 (3.3)	4 (3.7)			27 (3.4)	1 (2.6)		
- Type 2	798 (96.6)	693 (96.7)	105 (96.3)			761 (96.6)	37 (97.4)		
Diabetes duration (years)	8.2±4.5	8.0±4.4	9.5±4.8	3.154	0.002	8.1±4.5	9.8±5.1	2.073	0.041
Preoperative HbA1c (%)	7.8±1.6	7.6±1.5	8.9±1.8	6.783	<0.001	7.7±1.6	9.2±1.9	4.528	<0.001
HbA1c stratification [n(%)]				18.256	<0.001			12.367	<0.001
- <7%	289 (35.0)	265 (36.9)	24 (22.0)			281 (35.7)	8 (21.1)		
- 7%~9%	392 (47.5)	338 (47.1)	54 (49.5)			376 (47.7)	16 (42.1)		
- >9%	145 (17.5)	114 (15.9)	31 (28.4)			131 (16.6)	14 (36.8)		
Comorbidities [n(%)]									
- Hypertension	459 (55.6)	392 (54.7)	67 (61.5)	2.103	0.147	435 (55.2)	24 (63.2)	0.985	0.325
- Coronary heart disease	194 (23.5)	158 (22.0)	36 (33.0)	6.842	0.009	181 (23.0)	13 (34.2)	2.874	0.090
- Chronic kidney disease	124 (15.0)	103 (14.4)	21 (19.3)	2.457	0.117	118 (15.0)	6 (15.8)	0.042	0.837
Surgery-related indicators									
Surgery type [n(%)]				0.189	0.910			0.356	0.837
- THA	296 (35.8)	255 (35.6)	41 (37.6)			284 (36.0)	12 (31.6)		
- TKA	348 (42.1)	299 (41.7)	49 (45.0)			331 (42.0)	17 (44.7)		
- Spinal fusion	182 (22.0)	163 (22.7)	19 (17.4)			173 (21.9)	9 (23.7)		
Surgical duration (min)	135.6±38.2	133.2±37.5	148.5±39.6	3.689	0.001	135.1±38.0	149.8±41.2	2.257	0.026
Intraoperative blood loss (ml)	328.5±146.7	322.3±144.1	365.8±152.9	2.947	0.003	327.1±146.2	372.6±158.4	1.892	0.062
Postoperative anticoagulation	783 (94.8)	676 (94.3)	107 (98.2)	3.201	0.074	749 (95.1)	34 (89.5)	1.753	0.186

3.2 Comparison of glycemic variability indices between groups with and without complications

Patients were divided into DVT group (109 cases) vs. non-DVT group (717 cases), and MI group (38 cases) vs. non-MI group (788 cases). Glycemic variability indices were compared between the groups (Table 1). Results showed that MAGE, blood glucose SD, and Max-G in the DVT group were significantly higher than those in the non-DVT group (all P<0.001)—MAGE was (5.2±1.4) mmol/L in the DVT group and (3.1±1.1) mmol/L in the non-DVT group; MAGE, blood glucose SD, and Max-G in the MI group were also significantly higher than those in the non-MI group (all P<0.001)—MAGE reached (5.8±1.6) mmol/L in the MI group and (3.2±1.2) mmol/L in the non-MI group. In addition, HbA1c levels in the DVT group

and MI group were significantly higher than those in the non-complication groups (all P<0.05), suggesting that poor long-term glycemic control and short-term glycemic variability may jointly affect the risk of complications.

Table 2. Comparison of glycemic variability indices between groups with and without complications ($\bar{x}\pm s$, mmol/L)

Indicator	Non-DVT group (n=717)	DVT group (n=109)	t-value/ U-value	P-value	Non-MI group (n=788)	MI group (n=38)	t-value/ U-value	P-value
Mean amplitude of glycemic excursions (MAGE)	3.1±1.1	5.2±1.4	15.623	<0.001	3.2±1.2	5.8±1.6	12.345	<0.001
Blood glucose standard deviation (SD)	1.8±0.6	3.2±0.8	18.751	<0.001	1.9±0.7	3.5±0.9	10.892	<0.001
Maximum glycemic fluctuation (Max-G)	4.5±1.3	7.8±1.7	17.236	<0.001	4.7±1.4	8.5±1.9	11.567	<0.001

3.3 Multivariate logistic regression analysis of glycemic variability with DVT and MI

DVT and MI were used as dependent variables, and MAGE, blood glucose SD, and Max-G were included as independent variables for multivariate logistic regression analysis (Table 2, Table 3). Results showed that after adjusting for age, gender, BMI, diabetes duration, HbA1c, comorbidities, surgical factors, and anticoagulant use (Model 3):

Association with DVT: Each 1 mmol/L increase in MAGE was associated with a 2.13-fold higher DVT risk (OR=2.13, 95% CI: 1.68~2.70, P<0.001); each 1 mmol/L increase in blood glucose SD was associated with a 1.89-fold higher DVT risk (OR=1.89, 95% CI: 1.52~2.35, P<0.001); each 1 mmol/L increase in Max-G was associated with a 1.67-fold higher DVT risk (OR=1.67, 95% CI: 1.35~2.07, P<0.001).

Association with MI: Each 1 mmol/L increase in MAGE was associated with a 2.57-fold higher MI risk (OR=2.57, 95% CI: 1.81~3.65, P<0.001); each 1 mmol/L increase in blood glucose SD was associated with a 2.24-fold higher MI risk (OR=2.24, 95% CI: 1.60~3.13, P<0.001); each 1 mmol/L increase in Max-G was associated with a 1.92-fold higher MI risk (OR=1.92, 95% CI: 1.50~2.46, P<0.001).

The above results indicate that postoperative glycemic variability (especially MAGE) is an independent risk factor for DVT and MI, and the risk effect remains significant after adjusting for multiple factors.

Table 3. Multivariate logistic regression analysis of glycemic variability with DVT (OR, 95% CI)

Independent variable	Model 1 (crude)	Model 2 (adjusted for demographic factors)	Model 3 (fully adjusted)	P-value
MAGE (per 1 mmol/L increase)	2.87 (2.31~3.58)	2.56 (2.03~3.23)	2.13 (1.68~2.70)	<0.001
Blood glucose SD (per 1 mmol/ L increase)	2.53 (2.05~3.13)	2.28 (1.84~2.82)	1.89 (1.52~2.35)	<0.001
Max-G (per 1 mmol/L increase)	2.21 (1.80~2.72)	2.05 (1.66~2.53)	1.67 (1.35~2.07)	<0.001

Table 4. Multivariate logistic regression analysis of glycemic variability with MI (OR, 95% CI)

Independent variable	Model 1 (crude)	Model 2 (adjusted for demographic factors)	Model 3 (fully adjusted)	P-value
MAGE (per 1 mmol/L increase)	3.25 (2.41~4.38)	3.01 (2.20~4.12)	2.57 (1.81~3.65)	<0.001
Blood glucose SD (per 1 mmol/ L increase)	2.98 (2.23~3.98)	2.72 (2.01~3.68)	2.24 (1.60~3.13)	<0.001
Max-G (per 1 mmol/L increase)	2.45 (1.92~3.12)	2.28 (1.78~2.92)	1.92 (1.50~2.46)	<0.001

3.4 Interactive risk analysis of glycemic variability and HbA1c

Interaction terms (MAGE×HbA1c) were introduced into Model 3 to analyze the interaction between the two factors on DVT and MI (Table 4). Results showed that MAGE and HbA1c had significant interaction effects on both DVT and MI (both Pinteraction<0.05): For DVT: The OR of the interaction term was 1.32 (95% CI: 1.08~1.61, P=0.008), indicating that the risk effect of MAGE on DVT increased with the elevation of HbA1c level; For MI: The OR of the interaction term was 1.45 (95% CI: 1.12~1.88, P=0.005), suggesting that the higher the HbA1c level, the closer the association between MAGE and MI.

To further verify this interaction effect, patients were divided into three groups according to HbA1c levels (<7%, 7%~9%, >9%) for stratified analysis (Table 5). Results showed that with the elevation of HbA1c level, the OR values of DVT and MI risks corresponding to each 1 mmol/L increase in MAGE gradually increased: For DVT: OR=1.58 (1.12~2.23) in the HbA1c<7% group, OR=2.07 (1.56~2.75) in the HbA1c 7%~9% group, OR=3.02 (2.15~4.23) in the HbA1c>9% group, trend test P<0.001; For MI: OR=1.87 (1.19~2.93) in the HbA1c<7% group, OR=2.45 (1.70~3.54) in the HbA1c

7%~9% group, OR=3.61 (2.32~5.62) in the HbA1c>9% group, trend test P<0.001.

This result indicates that patients with poor long-term glycemic control (HbA1c>9%) are more sensitive to postoperative glycemic variability, and their risks of DVT and MI are significantly higher than those with good long-term glycemic control when glycemic variability increases.

Table 5. Interaction analysis of glycemic variability (MAGE) and HbA1c (OR, 95% CI)

Outcome	Main effect (MAGE per 1 mmol/L increase)	Interaction term (MAGE×HbA1c)	Pinteraction
DVT	2.13 (1.68~2.70)	1.32 (1.08~1.61)	0.008
MI	2.57 (1.81~3.65)	1.45 (1.12~1.88)	0.005

Table 6. Stratified analysis of the association between glycemic variability (MAGE) and DVT, MI by HbA1c level (OR, 95% CI)

Outcome	HbA1c<7% (n=289)	HbA1c 7%~9% (n=392)	HbA1c>9% (n=145)	Ptrend
DVT	1.58 (1.12~2.23)	2.07 (1.56~2.75)	3.02 (2.15~4.23)	<0.001
MI	1.87 (1.19~2.93)	2.45 (1.70~3.54)	3.61 (2.32~5.62)	<0.001

3.5 Sensitivity analysis

The following sensitivity analyses were conducted to verify the robustness of the results:

3.5.1 Excluding blood glucose values within 24 hours after surgery

After excluding blood glucose monitoring data within 24 hours after surgery (to avoid the impact of anesthesia and immediate surgical stress), MAGE and blood glucose SD were recalculated, and multivariate logistic regression was repeated. Results showed that each 1 mmol/L increase in MAGE was associated with a DVT risk OR=2.05 (95% CI: 1.59~2.64, P<0.001) and an MI risk OR=2.48 (95% CI: 1.73~3.55, P<0.001), which were close to the original results (Model 3) with no statistically significant difference (P>0.05).

3.5.2 Adjusting for postoperative infection

After further adjusting for postoperative infection (n=68 cases, 8.2%) on the basis of Model 3, results showed that the OR of MAGE with DVT was 2.09 (1.64~2.66, P<0.001) and with MI was 2.51 (1.76~3.58, P<0.001), and the significant association remained, suggesting that postoperative infection did not significantly affect the association between glycemic variability and complications.

The above sensitivity analyses indicate that the results of this study have good robustness.

4. Discussion

This study retrospectively analyzed 826 diabetic patients undergoing orthopedic surgery, and systematically explored the association of postoperative glycemic variability with DVT and MI, as well as its interactive risk with HbA1c for the first time. The main findings are as follows: (1) Postoperative glycemic variability (especially MAGE) in diabetic patients is an independent risk factor for DVT and MI within 30 days after orthopedic surgery — each 1 mmol/L increase in MAGE is associated with 2.13-fold and 2.57-fold higher risks of DVT and MI, respectively; (2) There is a significant interaction between glycemic variability and long-term glycemic control (HbA1c)—the hazard of glycemic variability is more significant in patients with HbA1c>9%, with each 1 mmol/L increase in MAGE associated with 3.02-fold and 3.61-fold higher risks of DVT and MI, respectively; (3) Sensitivity analysis confirmed that the above associations remain robust after excluding immediate surgical stress or adjusting for postoperative infection. These findings provide important clinical insights for postoperative glycemic management and complication prevention in diabetic patients undergoing orthopedic surgery.

4.1 Potential mechanisms of glycemic variability increasing DVT and MI risks

The reason why glycemic variability can significantly increase the risks of DVT and MI in diabetic patients after orthopedic surgery may be realized through the following mechanisms: First, glycemic variability exacerbates vascular endothelial dysfunction. Diabetic patients already have endothelial cell apoptosis, reduced nitric oxide (NO) synthesis, and enhanced oxidative stress induced by long-term hyperglycemia [13]; short-term postoperative glycemic variability further activates the oxidative stress pathway — when blood glucose rises sharply, the mitochondrial respiratory chain produces a large amount of reactive oxygen species (ROS), which inhibits the activity of endothelial nitric oxide synthase (eNOS) and reduces NO release; when blood glucose drops sharply, cell energy metabolism is disordered, exacerbating ischemic and

hypoxic damage to endothelial cells [14]. Damaged vascular endothelium cannot normally inhibit platelet activation and coagulation factor activation; instead, it promotes the expression of vascular adhesion molecules (e.g., VCAM-1, ICAM-1), leading to platelet aggregation and fibrin deposition, and ultimately increasing the risk of DVT [15]. This mechanism is consistent with the strong association between glycemic variability (especially MAGE) and DVT in this study.

Second, glycemic variability induces myocardial ischemic damage. Orthopedic surgery trauma leads to sympathetic nerve excitement and increased catecholamine release, which itself increases myocardial oxygen consumption; glycemic variability further aggravates myocardial metabolic disorders — under hyperglycemia, advanced glycation end products (AGEs) accumulate in myocardial cells, inhibiting the activity of myocardial energy metabolism enzymes; under hypoglycemia, anaerobic glycolysis in myocardial cells is enhanced, leading to lactic acid accumulation and aggravated myocardial cell acidosis [16]. For diabetic patients with coronary artery disease (23.5% of patients in this study had coronary heart disease), this metabolic disorder significantly reduces myocardial ischemia tolerance, inducing coronary artery spasm or plaque rupture, and ultimately leading to MI [17]. In addition, glycemic variability also aggravates myocardial damage by activating inflammatory responses (e.g., increasing IL-6, TNF-α), which also explains why MI is more sensitive to glycemic variability (OR=2.57) than DVT (OR=2.13) [18].

4.2 Interaction between glycemic variability and HbA1c: "Dual hit" effect

The core finding of this study is the interaction between glycemic variability and HbA1c—patients with poor long-term glycemic control are more sensitive to short-term glycemic variability. The mechanism of this "dual hit" effect may be that long-term hyperglycemia (HbA1c>9%) has already caused vascular wall remodeling (e.g., atherosclerosis, vascular fibrosis) and coagulation abnormalities (e.g., increased coagulation factors VII and VIII) [19], putting vascular endothelium in a "pre-damaged" state; at this time, superimposed with short-term postoperative glycemic variability, the compensatory capacity of endothelial cells is further exceeded, leading to a "synergistic" increase in the risks of thrombosis and myocardial ischemia [20]. For example, an in vitro study on type 2 diabetic patients found that under a high-glucose environment (HbA1c>9%), the apoptosis rate of endothelial cells induced by glycemic variability is 2.3 times that under a normal glucose environment, and platelet adhesion capacity is significantly enhanced [21], which is consistent with the result in this study that the risk effect of glycemic variability in the HbA1c>9% group is significantly higher than that in other groups.

The clinical significance of this interaction is that it suggests that glycemic management for diabetic orthopedic patients should "balance long-term and short-term": for patients with HbA1c<7%, MAGE can be controlled within 4 mmol/L after surgery; for patients with HbA1c>9%, MAGE needs to be controlled below 3 mmol/L to effectively reduce the risk of complications. Previous guidelines have mostly emphasized the preoperative HbA1c control target (e.g., <8%), but this study shows that even if HbA1c does not meet the standard, strict control of postoperative glycemic variability can significantly reduce the risk, providing a new basis for clinical stratified management.

4.3 Comparison with previous studies and advantages

Previous studies on postoperative complications in diabetic patients undergoing orthopedic surgery have mostly focused on absolute blood glucose values (e.g., fasting blood glucose, HbA1c). For example, Wang et al. [22] found that postoperative fasting blood glucose>8 mmol/L increases the risk of DVT (OR=1.89), but did not analyze the impact of glycemic variability. In recent years, a few studies have begun to pay attention to the association between glycemic variability and postoperative complications in orthopedic surgery. For example, Li et al. [23] studied 320 diabetic patients undergoing TKA and found that MAGE>4 mmol/L is a risk factor for postoperative DVT (OR=2.01), but the sample size of this study is small, and it did not analyze the association with MI or interactive risks. This study supplements the existing evidence in the following aspects: (1) The larger sample size (826 cases) covers three common major orthopedic surgeries (THA, TKA, spinal fusion), making the results more representative; (2) It is the first to analyze the interaction between glycemic variability and HbA1c, clarifying the risk differences under different long-term glycemic control levels; (3) Multiple glycemic variability indices (MAGE, SD, Max-G) and sensitivity analyses are used, resulting in higher robustness of the results.

Compared with studies on non-orthopedic surgery populations, this study also has unique value. For example, Zhang et al. [24] found that MAGE is associated with MI risk after cardiovascular surgery in diabetic patients (OR=2.23), but orthopedic surgery is characterized by more severe trauma stress and longer postoperative immobilization, which further exacerbates the association between glycemic variability and thrombosis risk—the OR of MAGE with MI in this study is 2.57, higher than that in the cardiovascular surgery study, suggesting that the hazard of glycemic variability after orthopedic surgery may be more significant and requires stricter control.

4.4 Clinical recommendations

Based on the results of this study, we put forward the following clinical recommendations:

4.4.1 Strengthen postoperative blood glucose monitoring and variability control

Diabetic patients undergoing orthopedic surgery should have their blood glucose monitored every 4 hours within 72 hours after surgery (including fasting and postprandial periods), with MAGE as the core monitoring index. The target values are: MAGE<4 mmol/L for patients with HbA1c<7%; MAGE<3.5 mmol/L for patients with HbA1c 7%~9%; MAGE<3 mmol/L for patients with HbA1c>9%. For patients with large glycemic variability, continuous glucose monitoring (CGM) can be used to assess the variability in real time to avoid sharp rises and falls in blood glucose.

4.4.2 Optimize hypoglycemic regimens

Postoperative hypoglycemic regimens should prioritize drugs that can stably control blood glucose, such as the basal-bolus insulin regimen (long-acting insulin + rapid-acting insulin), and avoid drugs that are prone to causing hypoglycemia (e.g., sulfonylureas) [25]. For patients with HbA1c>9%, insulin therapy can be adjusted 1~2 weeks before surgery to reduce the "pre-damage" of blood vessels caused by long-term hyperglycemia and lay a foundation for controlling postoperative glycemic variability.

4.4.3 Stratified prevention of complications

Complication prevention strategies should be formulated according to HbA1c levels and glycemic variability: for patients with HbA1c>9% and MAGE>3 mmol/L, in addition to routine LMWH anticoagulation after surgery, the anticoagulation course can be extended to 14 days (routine is 7~10 days), and myocardial ischemia monitoring (e.g., daily ECG, monitoring cTnI within 3 days after surgery) should be strengthened to identify MI risks early.

4.5 Study limitations

This study is a single-center retrospective study, which may have selection bias (e.g., excluding patients with incomplete data); fingerstick blood glucose is used for blood glucose monitoring, which is less accurate than CGM although it can reflect short-term variability; the follow-up time is only 30 days after surgery, so the impact of glycemic variability on long-term complications (e.g., cardiovascular events within 1 year) cannot be evaluated; potential confounders such as postoperative rehabilitation exercise and nutritional support are not included, which may indirectly affect the association between glycemic variability and complications by influencing glycemic variability. In the future, multi-center prospective studies are needed to evaluate glycemic variability using CGM and extend the follow-up time to further verify the conclusions of this study.

5. Conclusion

Postoperative glycemic variability (especially MAGE) is an independent DVT/MI risk factor in diabetic orthopedic patients, with significant interaction with HbA1c (higher risks in HbA1c>9% patients). Clinicians should strengthen variability management and formulate individualized regimens based on long-term glycemic control.

6. Acknowledgments

The authors would like to thank the Institutional Review Board of the Seventh Affiliated Hospital of Sun Yat-sen University for approving the study protocol. The authors declare no competing financial or non-financial interests. No funding was received for this study.

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