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Association between preoperative hyperglycemia and adverse cardiac events after non-cardiac surgery: a multicenter cohort study

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Background: We conducted a multicenter cohort study to evaluate whether preoperative acute hyperglycemia is associated with postoperative adverse cardiac events.

Methods: Data from 10 hospitals were converted to the Observational Medical Outcomes Partnership Common Data Model and analyzed. We extracted the records of 318 119 adult patients who underwent non-cardiac surgery and had available blood glucose measurements less than 24 hours before surgery. We defined acute hyperglycemia as at least one fasting blood glucose measurement > 140 mg/dl or random blood glucose level measurement > 180 mg/dl < 24 hours before surgery. Risk of adverse cardiac events during the first year after surgery was analyzed.

Results: After 1:2 propensity score matching, 40 340 patients with acute hyperglycemia and 70 770 patients without hyperglycemia were enrolled. Acute hyperglycemia was associated with an increased risk of adverse cardiac events (hazard ratio [HR]: 1.26, 95% CI [1.16–1.36], P < 0.001). In the subgroup analyses, the young age group (≤ 65 years) had a significantly higher risk (HR: 1.61, 95% CI [1.40–1.85]) than the older age group (HR: 1.13, 95% CI [1.03–1.25]; P for interaction < 0.001). A greater adverse cardiac events risk was observed in patients without hypertension (HR: 1.37, 95% CI [1.24–1.52]) but not in those with hypertension (HR: 1.09, 95% CI [0.96–1.22]; P for interaction = 0.003).

Conclusions: Preoperative acute hyperglycemia was associated with adverse cardiac events during one year of follow up. Further investigation is warranted to determine whether acute glycemic control before non-cardiac surgery could prevent perioperative cardiac complications.

Keywords: Adverse cardiac event; Cardiac event; Cardiovascular disease; Hyperglycemia; Postoperative complications; Surgery.

Introduction

Cardiac complications are a significant concern in patients undergoing non-cardiac surgery because they increase the associated morbidity, mortality, and healthcare costs [1,2]. A recent study categorized heart failure, arrhythmias, acute pulmonary embolism,

cardiac arrest, myocardial infarction, and coronary artery revascularization as perioperative adverse cardiac events and found that such events occurred in 3.9% of patients after non-cardiac surgery, significantly increasing 30-day mortality [3]. The occurrence of these cardiac events is a multifactorial process, with acute hyperglycemia during the preoperative period a potential modifiable risk factor [4].

Hyperglycemia, in both diabetic and non-diabetic patients, is widely recognized as a predictor of poor outcomes including myocardial infarction, stroke, and critical illness in various clinical settings [5–7]. Several reports indicate that persistent or intermittent hyperglycemia is common in patients undergoing non-cardiac surgery (prevalence, 20%–40%), and control of hyperglycemia has a significant effect on postoperative complications and mortality [4,7–9]. However, the relationship between preoperative hyperglycemia and adverse cardiac events after non-cardiac surgery remains unclear due to the small number of related large-scale observational studies. Further research, including prospective studies, is needed to establish a more definitive understanding of this relationship.

Given these limitations, we aimed to investigate the association between preoperative hyperglycemia and adverse cardiac events after non-cardiac surgery. We hypothesized that hyperglycemia in the preoperative period would be associated with an increased risk of postoperative adverse cardiac events, independent of other established risk factors such as age, comorbidities, and surgical complexity. To test that hypothesis, we conducted a multicenter cohort study involving a diverse population of patients undergoing non-cardiac surgery. The primary endpoint of this study was the occurrence of adverse cardiac events within one year after surgery. To enhance the specificity of our findings, we excluded patients who experienced adverse cardiac events or mortality within the first seven days postoperatively. This exclusion was based on the assumption that early postoperative events were more likely to be attributable to intraoperative factors, such as hemodynamic instability, surgical stress, or anesthesia-related complications, than to preoperative glycemic status. Because our study focuses on preoperative hyperglycemia as the exposure of interest, we could not adequately adjust for intraoperative variables. Therefore, excluding early adverse cardiac events ensures that our findings primarily reflect the relationship between preoperative hyperglycemia and long-term cardiovascular risk. By analyzing data from multiple centers, we provide a comprehensive understanding of the long-term effects of preoperative hyperglycemia on postoperative cardiac outcomes.

Materials and Methods

Data sources

We used the electronic medical records (EMR) databases from 10 hospitals in Korea, comprising of data on 12 024 817 patients. Patient-level EMR data were standardized, de-identified into the standard vocabulary of the Observational Medical Outcomes Partnership Common Data Model [10], and stored at the associated hospital. The participating hospitals were Ajou University Medical Center (January 1994–February 2022; 2 873 443 patients), Kyung Hee University Hospital (January 2008–February 2022; 1 168 640 patients), Kangdong Sacred Heart Hospital (January 2005–October 2021; 1 101 850 patients), Gyeongsang National University Hospital (October 2009–April 2022; 626 663 patients), Ewha Womans University Medical Center (January 2001–December 2021; 1 667 671 patients), Kangwon National University Hospital (January 2003–January 2022; 567 439 patients), Soonchunhyang University Bucheon Hospital (February 2001–May 2021; 1 301 117 patients), Soonchunhyang University Cheonan Hospital (May 2006–May 2021; 987 701 patients), Soonchunhyang University Gumi Hospital (July 2007–May 2021; 632 252 patients), and Soonchunhyang University Seoul Hospital (May 2003–May 2021; 1 098 041 patients). This study was approved by the Institutional Review Board at Samsung Medical Center (AJIRB-MED-MDB-21-662), and the need for individual written informed consent was waived. The other nine hospitals are affiliated with the Research Border-free Zone of Korea and accept the approval of the organizing center for studies using de-identified Common Data Model data. Patient-level raw data remained within the associated hospital, and the authors had access only to aggregated statistics provided by the hospitals. The authors did not access or review individual patient-level data. Therefore, requirements for patient-level data sharing are not applicable. This study complied with the principles of the Declaration of Helsinki (2013) and was compiled using the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Study design

We conducted a second-stage participant data meta-analysis using data from 10 hospitals. The study uses individual-level patient data without pooling, performing the same statistical analysis separately at each participating site and combining the resulting statistics in a meta-analysis [11].

To form a study cohort, we extracted the records of adult patients (> 18 years) who underwent surgery before August 2018,

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had medical records for more than 180 days before surgery, and had at least one available blood glucose measurement recorded less than 24 hours prior to surgery. Patients were excluded from this study if they died or had an adverse cardiac event within seven days of surgery. Fig. 1 presents a flowchart of the study design. The specific surgical procedures included in this study are listed in Supplementary Table 1.

We divided the patients into two groups in each hospital according to hyperglycemia. We used the propensity score matching (PSM) method with variable ratio matching up to 1:2. If two possible normoglycemic patients were within the caliper (0.2) of hyperglycemia, we performed 1:2 matching; otherwise, we conducted 1:1 matching [12]. We conducted a stratified Cox regression analysis in the matched population to calculate the hazard ratio (HR) of adverse cardiac events within one year. In addition, we used data from the 10 institutions to obtain aggregated point estimates, 95% CIs, and P values based on the meta-analysis methodology.

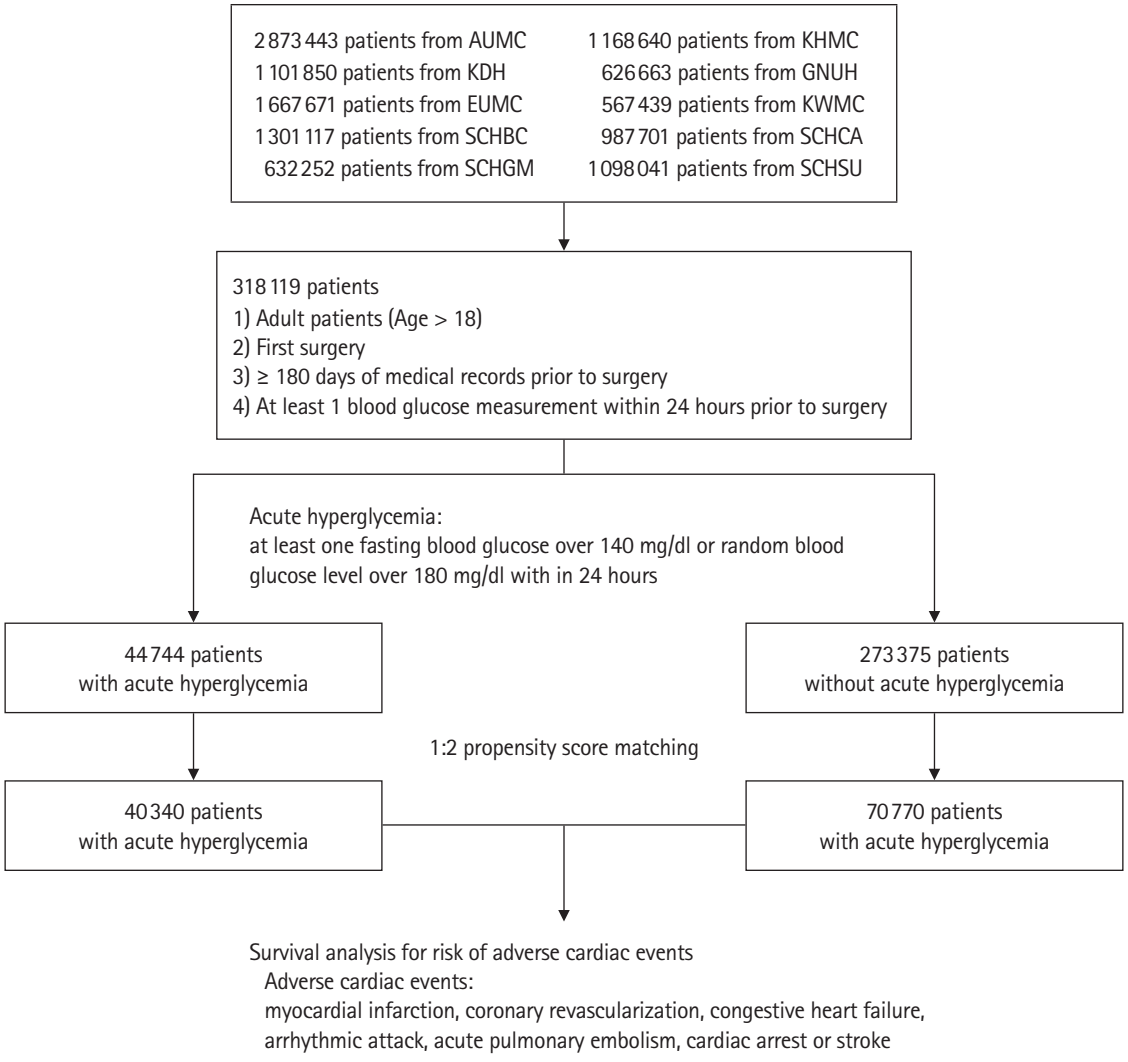

Fig. 1. Study flowchart of patients with and without adverse cardiac events after non-cardiac surgery. We began with de-identified data for 12 024 817 patients in Korea's standardized EMR database and extracted the records of 318 119 adult patients (> 18 years) who underwent surgery, had available medical records for more than 180 days before surgery, and had at least one blood glucose measurement from less than 24 hours prior to surgery. After 1:2 PSM, 40 340 patients with hyperglycemia and 70 770 with normoglycemia were matched. EMR: electronic medical records, PSM: propensity core matching, AUMC: Ajou University Medical Center, KHMC: Kyung Hee University Hospital, KDH: Kangdong Sacred Heart Hospital, GNUH: Gyeongsang National University Hospital, EUMC: Ewha Womans University Medical Center, KWMC: Kangwon National University Hospital, SCHBC: Soonchunhyang University Bucheon Hospital, SCHCA: Soonchunhyang University Cheonan Hospital, SCHGM: Soonchunhyang University Gumi Hospital, SCHSU: Soonchunhyang University Seoul Hospital.

Definitions

We defined acute hyperglycemia as a record of at least one fasting blood glucose measurement > 140 mg/dl or a random blood glucose level measurement > 180 mg/dl < 24 hours before surgery. These threshold values were established based on the 2012 guidelines for the management of hyperglycemia in hospitalized patients, as recommended by the American Diabetes Association and the American Association of Clinical Endocrinology [13].

Adverse cardiac events were defined as a composite of heart failure, arrhythmic attack, acute pulmonary embolism, cardiac arrest, myocardial infarction, coronary revascularization, and stroke within 30 days of surgery [1]. An arrhythmic attack was defined as rapid atrial fibrillation, ventricular tachycardia, or bradycardia that required medical intervention, such as electrical shock, temporary cardiac pacing, or two or more consecutive administrations of anti-arrhythmic agents. Cardiac arrest was defined as a diagnosis of cardiac arrest or a record of cardiopulmonary resuscitation. Pulmonary embolism was defined as the presence of a diagnostic code and an elevated d-dimer level. Coronary revascularization was confirmed by surgical records for coronary angiography using stent placement or coronary artery bypass graft surgery. Myocardial infarction was defined by the presence of an associated diagnostic code. Details on heart failure and stroke were obtained from the diagnostic codes, but only the first recorded diagnosis of each condition was included. The primary endpoint was adverse cardiac event(s) after non-cardiac surgery.

The PSM covariates were sex; age; comorbid diabetes, chronic kidney disease, stroke, coronary artery disease, heart failure, arrhythmia, peripheral artery disease, aortic disease, or valvular heart disease; current alcohol and smoking use; cancer grouped by organ; Diabetes Complications Severity Index [14]; and Romano's adaptation of the Charlson Comorbidity Index [15].

In our main analysis, age was grouped in five-year intervals. The disease covariate was binarized based on diagnosis of a specific International Classification of Diseases code in the preceding 365 days. Comorbidity was quantified using Romano's adaptation of the Charlson Comorbidity Index. The risk of each surgical procedure was classified according to the European Society of Cardiology/European Society of Anesthesiology guidelines on non-cardiac surgery [16].

Sensitivity and subgroup analyses

To assess the robustness of our findings, we conducted sensitivity and subgroup analyses. For sensitivity analyses, we reconducted the main analysis with different PSM ratios (1:1, 1:2) and calipers (0.1, 0.2). For subgroup analyses, we selected items based on proven association with surgical outcomes according to previous studies and perioperative guidelines [17]. The variables clinically relevant to perioperative outcomes were emergency operation status and surgical risk, categorized according to the European Society of Cardiology/European Society of Anesthesiology guidelines on non-cardiac surgery [16]. We also performed subgroup analyses based on comorbidities (diabetes, hypertension, and chronic kidney disease) and by sex, age (≤ 65 years and > 65 years), and uncontrolled HbA1c (> 7%). In the subgroup analyses, the variables that divided the subgroup were excluded from the PSM.

Statistical analysis

For baseline characteristics, we calculated means for continuous variables and percentages for categorical variables. To validate the appropriateness of PSM for each hospital, we used a PSM plot to examine the overlap between the hyperglycemia and normoglycemia groups after matching. Changes in the absolute standardized difference (ASD) of covariates between the two groups at each hospital before and after matching were depicted using a covariate balance plot [18]. After PSM, we regarded an ASD of 0.1 as balanced and calculated HRs with 95% CIs using stratified Cox survival analysis. The PSM incorporated a comprehensive set of baseline variables deemed most likely to influence both treatment assignment and outcomes. Key demographic and clinical covariates (age, sex, and comorbid conditions) were included alongside the newly added variables of healthcare utilization metrics and lifestyle factors. Specifically, we added outpatient visits, hospitalizations, and emergency department visits in the preceding year as proxies for overall health status and disease severity, reasoning that patients with frequent healthcare encounters might have more severe or poorly controlled conditions than those with fewer healthcare encounters. Smoking status was included given its well-known effects on cardiovascular and overall health outcomes, and history of cancer was incorporated as an indicator of significant comorbidity.

We applied the Benjamini-Hochberg false discovery rate procedure to address the multiple comparison issue for all pairs of subgroups [19]. In the meta-analysis, we conducted statistical tests of heterogeneity using χ^2 and I^2 statistics. Because I^2 is less than 50% in the main analysis, we used a fixed-effects model for subsequent meta-analysis.

To test for interactions between subgroup variables and outcome variables, we adopted a single-variable meta-regression. A meta-regression is a method that considers confounding covariates when conducting a meta-analysis. In this study, we conducted

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Table 1. Baseline Characteristics of Patients in the AUMC Cohort before and after PSM

Characteristic	Before PSM adjustment			After PSM adjustment		
	Hyperglycemia (%)	Normoglycemia (%)	ASD	Hyperglycemia (%)	Normoglycemia (%)	ASD
Age	61.3	53.8	0.47	60.9	61.4	0.04
Sex (F)	45.7	49.9	0.23	47	46.1	0.03
Chronic kidney disease	5.1	4.3	0.04	5.5	5.6	−0.01
Diabetes mellitus without complications	26.9	16	0.27	25.9	27.4	−0.03
Stroke	1.4	1.2	0.026	1.4	1.3	0.009
Coronary artery disease	3.2	2	0.072	3.1	3	0.007
Heart failure	2	1.7	0.025	2	2.1	0.005
Arrythmia	0.8	0.7	0.004	0.9	0.9	0.002
Peripheral artery disease	0.5	0.4	0.014	0.6	0.6	0.005
Aortic disease	0.4	0.3	0.027	0.4	0.4	0.003
Valvular heart disease	0.6	0.5	0.014	0.6	0.6	0.005
Current drinker	18	18.6	0.015	17.9	18.7	0.022
Current smoker	11.3	9.2	0.068	10.9	10.6	0.009
Malignant neoplasm of liver	6.4	1.6	0.24	4	4.1	0
Malignant tumor of stomach	4	0.7	0.22	2.2	2.2	0
Charlson index - Romano adaptation	2.69	1.56	0.42	2.38	2.35	−0.01
Diabetes Comorbidity Severity Index	0.42	0.35	0.08	0.43	0.45	−0.01

Values are presented as mean or percentage. After PSM, we observed balanced characteristics between the hyperglycemia and normoglycemia groups (ASD < 0.1). AUMC: Ajou University Medical Center, PSM: propensity score matching, ASD: absolute standardized difference.

meta-regressions with subgroup characteristics as a single variable. Then, we determined the significance of the subgroup variable based on the 'P value for interaction' and used it to test for interaction between the subgroup variable and the outcome.

All analyses were performed using R (version 4.1.0; R Foundation for Statistical Computing).

Results

We included 318 119 patients in this study. After 1:2 PSM, 40 340 patients with hyperglycemia and 70 770 with normoglycemia were matched. The baseline characteristics of the matched AUMC cohort are shown in Table 1 that reveals that the hyperglycemia group was predominantly male and had a greater incidence of comorbidities than the normoglycemia group. The baseline covariates became well-balanced after PSM (ASD < 0.1). The propensity score distribution according to the presence or absence of adverse cardiac events for each hospital is described in Fig. 2A. The improvements in balance between covariates in other cohorts are shown as changes in ASD in Fig. 2B.

The number of adverse cardiac events within one year was 1105 (2.7%) in patients with hyperglycemia versus 1554 (2.2%) in those with normoglycemia. The meta-analysis showed that hyperglycemia was associated with a greater risk of one-year adverse cardiac events (HR: 1.26, 95% CI [1.16–1.36]) compared to those with normoglycemia. The one-year adverse cardiac event risks for each cohort is presented in a forest plot in Fig. 3. Survival plots with the one-year adverse cardiac event risks in each cohort are shown in Fig. 4.

We tested our results using different matching ratios and calipers and consistently found a significantly higher risk of adverse cardiac events in the hyperglycemia group across all matching ratios and calipers. When using a 0.1 caliper, the result was HR 1.25 (95% CI [1.16–1.35]). When using a matching ratio of 1:1, the result was HR 1.16 (95% CI [1.07–1.27]). When using a 0.1 caliper and a matching ratio of 1:1, the result was HR 1.16 (95% CI [1.07–1.27]). The full analysis results with various matching ratios and calipers are presented in Supplementary Table 1.

The association between acute hyperglycemia and adverse cardiac events was analyzed separately by subgroup, and the P-value for interaction was significant for age (P < 0.001) and hypertension (P = 0.003). We found a significantly higher risk in the young (≤ 65 years) age group (HR: 1.61, 95% CI [1.40–1.85]) than in the older (> 65 years) age group (HR: 1.13, 95% CI [1.03–1.25]) and in those without hypertension (HR: 1.37, 95% CI [1.24–1.52]) vs. those with hypertension (HR: 1.09, 95% CI [0.96–1.22] P for interaction = 0.003). The detailed results of the subgroup analyses are given in Table 2. Detailed forest plots for each

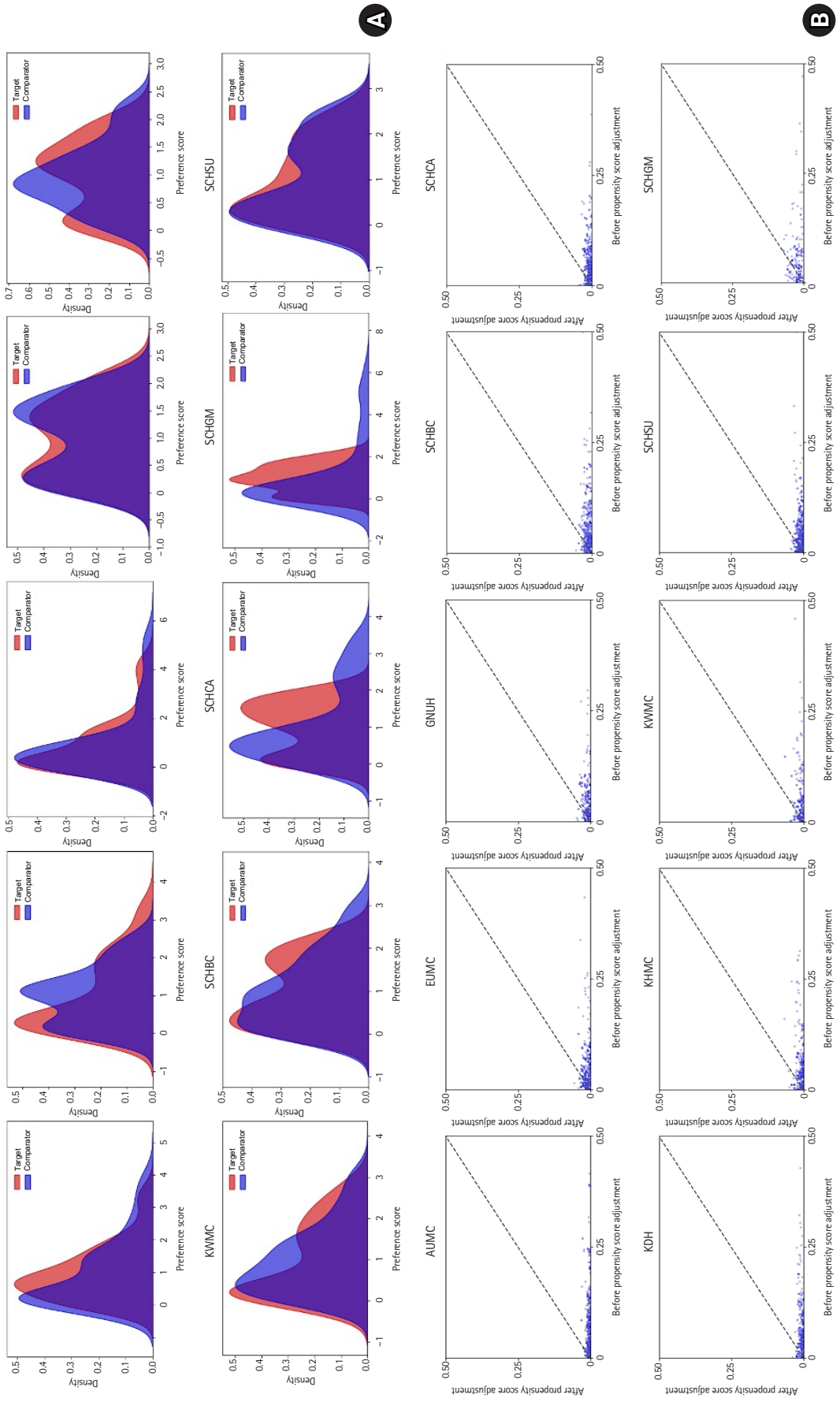

Fig. 2. (A) A graphical representation of the PSM used in this study. The x-axis of the plot represents the preference scores that estimate the likelihood of treatment based on observed characteristics. The y-axis represents density, indicating the concentration or distribution of data points. When the data points of the treated and control groups overlap, it suggests that individuals with similar propensity scores have been successfully matched. (B) Covariate balance plot before and after PSM across 10 hospitals. After PSM, we plotted the ASD of the covariates to validate the adequacy of matching, and most of the ASDs were < 0.1 that shows that matching was balanced and adequate. PSM: propensity score matching, ASD absolute standardized difference.

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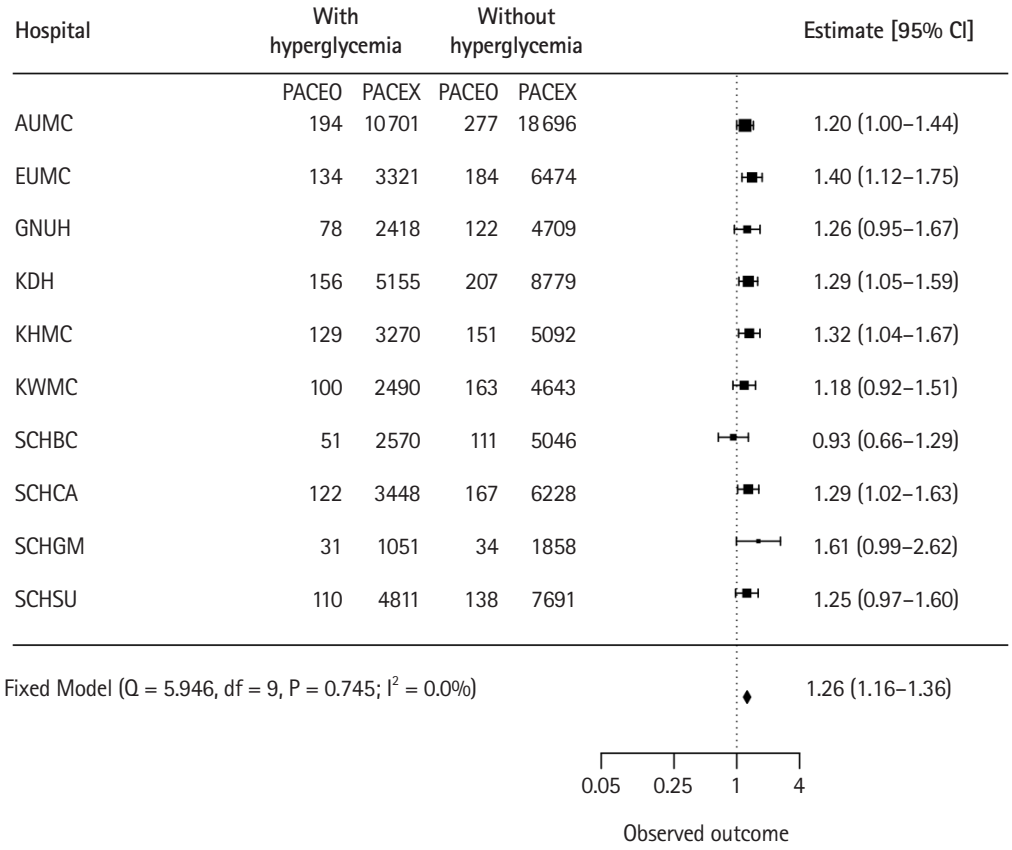

Fig. 3. Forest plot representing the meta-analysis results for the risk of adverse cardiac events within one year after non-cardiac surgery in patients with acute hyperglycemia across 10 hospitals. The HRs and 95% CIs are indicated by the diamond shapes for the combined effect estimate and by the squares for each individual study. The size of the square represents the weight of each study. The horizontal line represents the 95% CI, and the diamond shape represents the overall pooled effect estimate. The four numbers within each column represent the number of patients with acute hyperglycemia with the outcome and without it and the number of patients with normoglycemia with the outcome and without it. HR: hazard ratio, AUMC: Ajou University Medical Center, EUMC: Ewha Womans University Medical Center, GNUH: Gyeongsang National University Hospital, KDH: Kangdong Sacred Heart Hospital, KHMC: Kyung Hee University Hospital, KWMC: Kangwon National University Hospital, SCHBC: Soonchunhyang University Bucheon Hospital, SCHCA: Soonchunhyang University Cheonan Hospital, SCHGM: Soonchunhyang University Gumi Hospital, SCHSU: Soonchunhyang University Seoul Hospital.

subgroup can be found in Supplementary Fig. 1.

Discussion

Our study results reveal that patients with acute hyperglycemia, defined as a fasting glucose level > 140 mg/dl or random glucose level > 180 mg/dl within 24 hours pre-surgery, are at a higher risk of adverse cardiac events than their normoglycemic counterparts. The HR of 1.26 (95% CI [1.16–1.36]) suggests that acute hyperglycemia might independently elevate the risk of adverse cardiac events. These findings provide crucial insights into the role of acute hyperglycemia as a potential modifiable risk factor and highlight the importance of patient stratification during preoperative evaluations.

Our findings align with previous research showing that hyperglycemia is associated with an increased risk of cardiovascular complications in various clinical settings, including surgery [20,21]. Although much of the literature focuses on chronic hyperglycemia in diabetic patients, our study specifically examined the effects of acute hyperglycemia in a non-cardiac surgical context and extended the observation to one year postoperatively [22]. This approach highlights the long-term implications of even brief periods of preoperative hyperglycemia and emphasizes the need for careful glycemic management, particularly in patients without a history of diabetes or chronic hyperglycemia.

Diabetes and hyperglycemia are well-known contributors to cardiovascular complications, primarily through glucose toxicity and oxidative stress [23–26]. Diabetic patients are predisposed to conditions such as cardiomyopathy, and hyperglycemia—whether chronic or acute—has been associated with increased myocardial

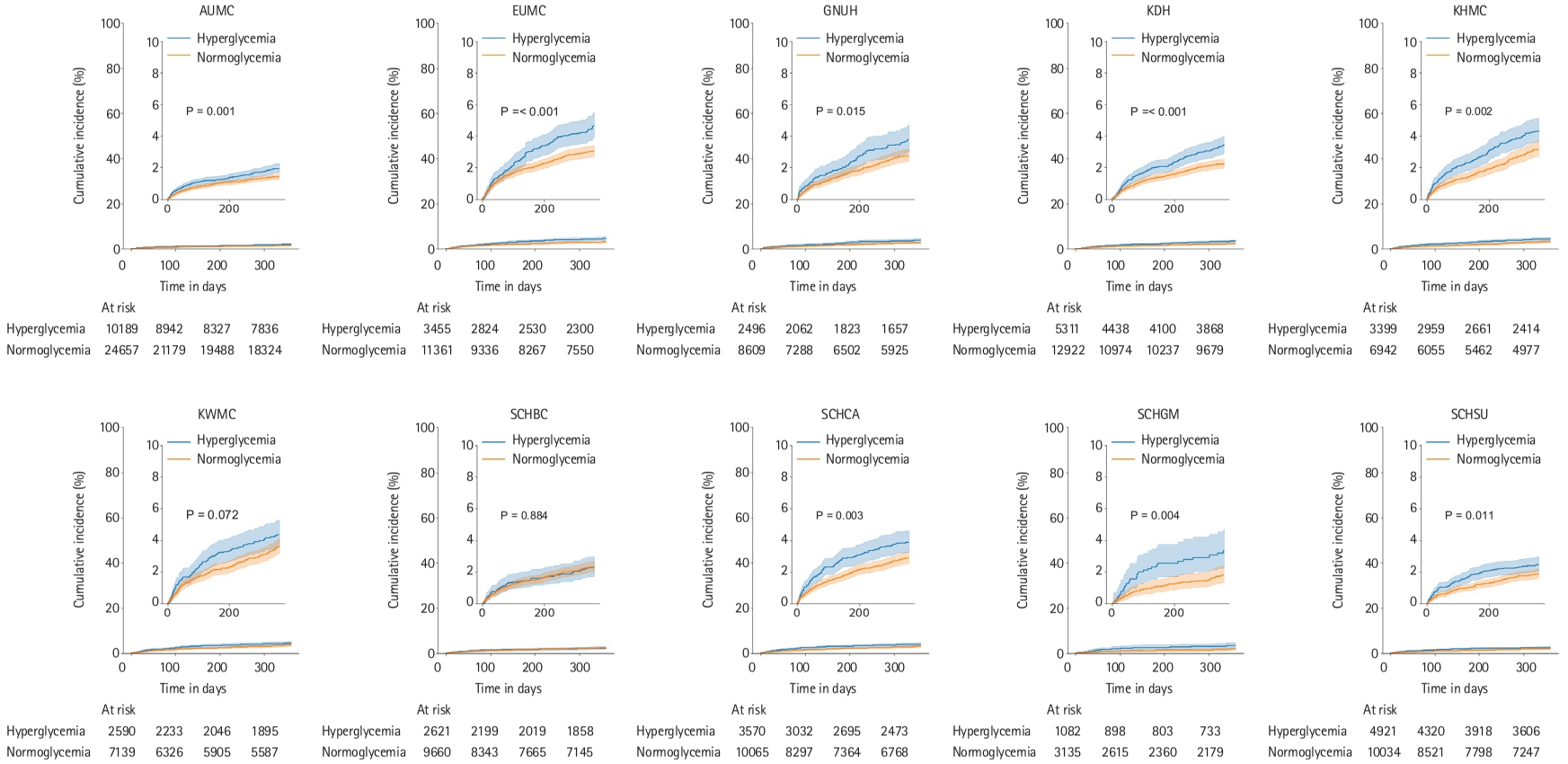

Fig. 4. This figure shows a one-year plot of survival across the 10 hospitals. Each KM plot shows the cumulative incidence of adverse cardiac events after non-cardiac surgery, defined as a composite of myocardial infarction, coronary revascularization, congestive heart failure, arrhythmic attack, acute pulmonary embolism, cardiac arrest, and stroke. The P value was calculated using the log-rank test. The insets show the same data on enlarged y-axes. KM: Kaplan Meier, EMR: electronic medical records, PSM: propensity core matching, AUMC: Ajou University Medical Center, KHMC: Kyung Hee University Hospital, KDH: Kangdong Sacred Heart Hospital, GNUH: Gyeongsang National University Hospital, EUMC: Ewha Womans University Medical Center, KWMC: Kangwon National University Hospital, SCHBC: Soonchunhyang University Bucheon Hospital, SCHCA: Soonchunhyang University Cheonan Hospital, SCHGM: Soonchunhyang University Gumi Hospital, SCHSU: Soonchunhyang University Seoul Hospital, PSM: propensity core matching, ASD: absolute standardized difference, HR: hazard ratio, KM: Kaplan Meier.

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Table 2. Subgroup Analyses by Demographics and Comorbidities

Subgroup analysis	HR	95% CI	P value	FDR	P value for difference
Demographics					
Sex					
M	1.25	1.20–1.39	< 0.001	< 0.001	0.862
F	1.28	1.14–1.43	< 0.001	< 0.001	
Age (yr)					
> 65	1.13	1.03–1.25	0.008	0.014	< 0.001
≤ 65	1.61	1.40–1.85	< 0.001	< 0.001	
Comorbidity					
Diabetes					
+	1.19	1.03–1.38	0.021	0.033	0.465
-	1.27	1.16–1.39	< 0.001	< 0.001	
Hypertension					
+	1.09	0.96–1.22	0.182	0.232	0.003
-	1.37	1.24–1.52	< 0.001	< 0.001	
Chronic kidney disease					
+	1.08	0.90–1.30	0.411	0.468	0.092
-	1.29	1.18–1.40	< 0.001	< 0.001	
HbA1c					
> 7%	1.13	0.96–1.30	0.169	0.222	0.221
≤ 7%	1.24	1.13–1.36	< 0.001	0	
Surgery status					
Emergency	1.48	1.21–1.81	< 0.001	< 0.001	0.072
Elective	1.21	1.11–1.32	< 0.001	< 0.001	
Surgical risk					
Low	1.31	1.18–1.46	< 0.001	< 0.001	0.146
Intermediate	1.23	1.08–1.39	0.002	0.004	
High	1.07	0.83–1.39	0.604	0.639	

The P value column in the table refers to the P value of the HR obtained from each individual study. P < 0.05 indicates that preoperative acute hyperglycemia had a significant effect on the perioperative adverse cardiac events rate in that subgroup. The 'FDR' column provides the P value after adjustment with the Benjamini–Hochberg false-discovery rate for multiple comparisons. The 'P value for difference' column provides the P value for the subgroup covariate obtained from the meta-regression analysis. A P value for difference < 0.05 indicates that the HR of the two subgroups differed with statistical significance due to the criterion for dividing the subgroups, such as differences in sex. HR: hazard ratio, FDR: false discovery rate.

injury and mortality [2,27,28]. Even transient episodes of hyperglycemia can aggravate complications by triggering oxidative stress that plays a significant role in myocardial injury and coronary microvascular dysfunction [2,27]. This cascade of events links elevated blood glucose levels to endothelial dysfunction, laying a basis for type 2 myocardial infarction [23–26]. The underlying mechanisms that explain these cardiac complications of glucose toxicity are complex and multifaceted. Hyperglycemia promotes the accumulation of advanced glycation end-products and disrupts the O-GlcNAcylation pathway, leading to adverse cellular outcomes such as cardiomyocyte hypertrophy, epigenetic modifications, mitochondrial dysfunction, apoptosis, fibrosis, and impaired calcium handling [23]. Together, these mechanisms contribute to the structural and functional deterioration of myocardial cells, adversely affecting cardiac function. Additionally, hyperglycemia-induced oxidative stress heightens inflammation and endothelial dysfunction, further contributing to the adverse cardiovascular outcomes observed in hyperglycemic patients.

The blood glucose thresholds used in this study (fasting glucose > 140 mg/dl, random glucose > 180 mg/dl) were based on the American Diabetes Association guidelines, but their universal applicability to all patient populations remains uncertain. Overly strict glucose control has been associated with increased in-hospital mortality in critically ill patients, raising concerns about individualized glycemic targets. Additionally, long-term diabetic patients can adapt to chronic hyperglycemia, and it is unclear whether they should be categorized using the same thresholds as non-diabetic patients. Although our findings suggest that preoperative acute hyperglycemia is associated with an increased risk of adverse cardiac events, further research is needed to determine

optimal perioperative glucose management strategies for different patient subgroups, including those with chronic diabetes or critical illness.

In our subgroup analyses, age and hypertension status were significant modifiers of the association between acute hyperglycemia and adverse cardiac events. Notably, younger patients (≤ 65 years) with acute hyperglycemia were at substantially greater risk than patients older than 65 years, suggesting that acute hyperglycemia might have a more pronounced effect in younger individuals. This elevated risk in younger patients can be attributed to several physiological and clinical factors. First, older patients often undergo long-term cardiovascular adaptations, such as vascular remodeling, myocardial hypertrophy, and autonomic regulation changes that could reduce their acute hemodynamic response to glucose fluctuations [29]. In contrast, younger individuals generally lack such adaptations and are more vulnerable to sudden glucose-induced endothelial dysfunction, oxidative stress, and platelet activation. Second, the difference in comorbidity burden could contribute to this finding. Older patients typically have multiple coexisting conditions, such as hypertension, chronic kidney disease, and atherosclerosis that independently increase their baseline risk for adverse cardiac events. As a result, the additional effect of acute hyperglycemia might be less pronounced in this group. Conversely, in younger individuals with fewer preexisting risk factors, the direct effects of acute hyperglycemia on cardiac stress, inflammation, and thrombogenicity could become more apparent, leading to a greater relative increase in the risk of adverse cardiac events [30]. Third, younger individuals might experience more pronounced hemodynamic responses to acute hyperglycemia, including greater sympathetic nervous system activation and fluctuations in vascular resistance, potentially exacerbating myocardial stress [31]. In contrast, hypertensive patients—who often exhibit arterial stiffness and chronic myocardial remodeling—might be somewhat protected from the hemodynamic swings associated with acute glucose fluctuations. That could explain why patients without hypertension had a significantly higher risk of adverse cardiac events when hyperglycemic (HR: 1.37, 95% CI [1.24–1.52]), whereas that association was not significant among hypertensive patients (HR: 1.09, 95% CI [0.96–1.22]). Given these findings, our results suggest that preoperative hyperglycemia should not be overlooked in younger and non-hypertensive individuals because they might be disproportionately affected by its cardiovascular consequences. Although old age (> 75 years) and hypertension are well-established risk factors for myocardial infarction and major adverse cardiovascular events after surgery [32], our study highlights the importance of glycemic control in younger patients and those without hypertension, who might otherwise be perceived as low-risk populations.

Our study does not establish causality, but the association we observed encourages consideration of blood glucose monitoring and management protocols for at-risk patients, especially younger and non-hypertensive individuals. Preoperative identification of acute hyperglycemia could help healthcare providers implement timely interventions, potentially reducing the risk of adverse cardiac events and improving long-term cardiovascular outcomes. Further studies are warranted to explore the potential benefits of glycemic control before surgery. Additionally, future research should investigate the molecular mechanisms through which hyperglycemia affects cardiac outcomes, including the roles of oxidative stress, inflammation, and endothelial dysfunction in the pathophysiology of hyperglycemia-induced cardiac injury.

This study has several limitations. First, as a retrospective analysis, it is inherently prone to selection bias. We relied on existing medical records and databases that could lack comprehensive data on certain patient variables. Although we used PSM to create balanced cohorts, unmeasured confounding factors could have influenced the outcomes. Second, our analysis focused solely on preoperative glucose levels, without considering intraoperative glucose fluctuations that could also affect perioperative cardiac complications. Acute hyperglycemia is a dynamic process, and its fluctuations throughout the perioperative period might have contributed to patient outcomes. However, due to the Common data model used in this study, we were unable to incorporate continuous glucose monitoring data or serial blood glucose measurements to evaluate the full spectrum of glucose variability. Future studies that incorporate real-time glucose monitoring could provide further insights into the effects of perioperative glycemic fluctuations on cardiovascular risk. Additionally, we did not investigate the effects of interventions to correct elevated glucose levels on adverse cardiac event outcomes. Future research should examine the effects of intraoperative hyperglycemia management and determine whether targeted glucose control interventions can reduce the risk of adverse cardiac events in this population to provide a more complete understanding of the relationship between acute hyperglycemia and cardiac outcomes.

In conclusion, this multicenter study demonstrated a significant association between preoperative acute hyperglycemia and the prevalence of adverse cardiac events in adult patients undergoing non-cardiac surgery. Our findings emphasize the importance of preoperative glycemic control to minimize cardiovascular complications. Further prospective studies investigating the association between blood glucose levels and adverse cardiac events are required.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Data Availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

Author Contributions

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Supplementary Materials

Supplementary Table 1. Types of surgical procedures.

Supplementary Fig. 1. Detailed forest plots for each subgroup.

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