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ORIGINAL ARTICLE

Construction and Preliminary Evaluation of a Precise Perioperative Glycemic Management Model for Kidney Transplant Recipients Using Healthcare Failure Mode and Effect Analysis (HFMEA) Combined with Continuous Glucose Monitoring (CGM) and Artificial Intelligence: A Retrospective Cohort Study

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Abstract

OBJECTIVES: Post-transplantation diabetes mellitus (PTDM) is a common complication after kidney transplantation and contributes to graft dysfunction and adverse cardiovascular outcomes. We conducted a preliminary evaluation of an integrated perioperative glycemic management model combining Healthcare Failure Mode and Effect Analysis (HFMEA), continuous glucose monitoring (CGM), and artificial intelligence (AI)–driven prediction in routine clinical practice.

DESIGN: Single-center retrospective cohort study with historical controls.

METHODS: We included 120 adult kidney transplant recipients from 2021–2024 and divided them into a historical control group (n = 60, conventional intermittent capillary glucose monitoring) and an intervention group (n = 60, HFMEA–CGM–AI integrated management). Primary outcomes were perioperative CGM-derived glycemic metrics over 14 days (time in range *TIR*, coefficient of variation *CV*, time below range *TBR*, mean amplitude of glycemic excursions *MAGE*) and 3-month PTDM incidence. Secondary outcomes included hospital length of stay and postoperative complications; patient satisfaction was assessed descriptively in the intervention group.

RESULTS: The intervention group was associated with substantially tighter perioperative glycemic control, with higher TIR (80.0 ± 9.0% vs 63.8 ± 11.6%) and lower CV, TBR, and MAGE (all $p < 0.001$). TIR in the intervention group exceeded recommended CGM targets (>70%). Three-month PTDM incidence was numerically lower (10.0% vs 20.0%; $p = 0.201$; 18 events), consistent with

limited power for this endpoint and an exploratory role of PTDM in this study. Hospital stay was shorter with the integrated model (12.4 ± 2.2 vs 14.2 ± 3.3 days, $p < 0.001$), and postoperative complications were numerically reduced but non-significant. Patient satisfaction in the intervention group was high (mean 8.4 ± 1.1 on a 10-point scale).

CONCLUSION: In this retrospective historical cohort, the HFMEA–CGM–AI model was feasibly implemented and was associated with improved perioperative CGM metrics and shorter hospital stay. PTDM and complication outcomes remained exploratory due to limited power and the non-randomized design. Prospective, adequately powered randomized trials are required to determine the causal impact and cost-effectiveness of this integrated HFMEA–CGM–AI management approach.

INTRODUCTION

Kidney transplantation is the preferred treatment for end-stage renal disease, offering superior long-term survival and quality of life compared to dialysis (Nair, 2022; Chang & Mushailov, 2023). However, PTDM, also known as new-onset diabetes after transplantation, remains a common and serious metabolic complication, with reported incidence rates ranging from 10% to 40% within the first year (Rudzki *et al.* 2024; Martinez Cantarin, 2021). PTDM is associated with increased risks of graft loss, cardiovascular events, infections, and mortality, and is a major threat to long-term recipient outcomes after transplantation (Oliveras *et al.* 2024; Kanbay *et al.* 2024). The pathogenesis of PTDM involves a combination of traditional risk factors (e.g., older age, obesity, family history) and transplant-specific factors, particularly the use of immunosuppressive agents such as tacrolimus and corticosteroids, which impair insulin secretion and sensitivity while promoting hyperglycemia during the perioperative period (Newman *et al.* 2022; Szumilas *et al.* 2024).

Traditional perioperative glycemic management in kidney transplant recipients relies primarily on intermittent finger-stick blood glucose monitoring and empirical insulin therapy (Iqbal *et al.* 2022; Shin *et al.* 2024). This approach is limited by low monitoring frequency, delayed detection of glycemic excursions, and lack of individualized adjustment, often resulting in prolonged hyperglycemia, increased glycemic variability, and higher rates of hypo- and hyperglycemic events (Eleftheriadis *et al.* 2024; Kaplan *et al.* 2024). These fluctuations are particularly detrimental in the perioperative setting, where stress-induced insulin resistance and immunosuppressive drugs exacerbate glucose dysregulation. Consequently, there is an urgent need for more precise, proactive strategies that provide continuous data, risk stratification, and real-time decision support to optimize glycemic control and reduce PTDM incidence.

The core aim of this study is to evaluate, in real-world practice, a multimodal precise glycemic management model that synergistically integrates three complementary components: Healthcare Failure Mode and Effect Analysis (HFMEA) for systematic prospective risk identification and process optimization, continuous glucose monitoring (CGM; Freestyle Libre 2) for high-density real-time data with alerting capabilities, and artificial intelligence (AI)-driven predictive modeling for individualized forecasting and intervention guidance (Ji *et al.* 2025; Yi *et al.* 2022; DeRosier *et al.* 2002; Fokkert *et al.* 2017). HFMEA addresses workflow vulnerabilities, CGM overcomes the data sparsity of intermittent monitoring, and AI transforms dense CGM data into actionable predictions, creating a risk-stratified system that aims to shift care from reactive to proactive. This integrated framework represents a novel, workflow-level approach in kidney transplantation, combining HFMEA, CGM, and AI prediction to directly address limitations of existing perioperative glycemic management. The present retrospective cohort study evaluated this HFMEA–CGM–AI model versus conventional management, focusing on perioperative CGM metrics, PTDM incidence, and short-term clinical outcomes.

MATERIALS AND METHODS

Study Design and Setting

This was a single-center retrospective cohort study conducted at Affiliated Hospital of Xuzhou Medical University, Xuzhou, China. The study was approved by the Institutional Review Board, and the requirement for informed consent was waived due to the retrospective nature and use of anonymized data. The study adhered to the principles of the Declaration of Helsinki.

Study Population and Groups

We reviewed electronic medical records of consecutive adult patients (aged ≥18 years) who underwent kidney transplantation between January 2021 and December 2024. Patients were divided into two cohorts based on the calendar period of transplantation and the implementation status of the integrated management model:

- Historical control group (n = 60): Patients transplanted from January 2021 to December 2022 and managed with conventional perioperative glycemic monitoring (intermittent capillary finger-stick blood glucose testing 4–8 times daily) and empirical insulin adjustments based on clinician experience.
- Intervention group (n = 60): Patients transplanted from January 2023 to December 2024, managed with the integrated precise glycemic management model incorporating Healthcare Failure Mode and Effect Analysis (HFMEA), Continuous Glucose Monitoring (CGM; Freestyle Libre 2), and artificial intelligence (AI)-driven predictive algorithms.

Exclusion criteria included pre-existing diabetes mellitus (diagnosed prior to transplantation), combined

organ transplantation, pregnancy, incomplete medical records, or CGM data missing >20% of readings during the perioperative period.

Intervention: HFMEA-CGM-AI Integrated Glycemic Management Model

In late 2022, a multidisciplinary team (including transplant surgeons, endocrinologists, nephrologists, and quality management specialists) applied HFMEA to systematically identify high-risk failure modes in the perioperative glycemic management workflow. Failure modes with risk priority number (RPN) ≥60 (e.g., delayed hyperglycemia detection, inconsistent insulin dosing) were prioritized, and corrective actions (e.g., standardized protocols, mandatory CGM in high-risk patients) were implemented from January 2023 onward.

Freestyle Libre 2 CGM sensors were applied 48 hours preoperatively and continued for at least 14 days postoperatively (longer in high-risk cases). Data were uploaded in real-time to a secure cloud platform integrated with the electronic health record.

An AI model (long short-term memory [LSTM] network with attention mechanism) was trained on historical CGM data from prior transplant recipients to predict glucose trends 15–60 minutes ahead and generate individualized alerts/recommendations for insulin adjustment, displayed via a clinician dashboard and patient app.

Conventional management in the control group relied on point-of-care glucose testing and sliding-scale insulin without routine CGM or AI support.

Outcome Measures

Outcomes were extracted from electronic health records, laboratory results, the institutional CGM database, and scheduled outpatient follow-up visits at 1 and 3 months post-transplantation. Glycemic metrics were calculated using validated software (LibreView platform or equivalent custom scripts aligned with international consensus guidelines (Battelino *et al.* 2019)). Complications were adjudicated by two independent clinicians blinded to group allocation, with any discrepancies resolved through consensus discussion.

The primary outcomes focused on post-transplantation diabetes mellitus (PTDM) incidence and perioperative glycemic control. PTDM at 3 months was defined according to American Diabetes Association criteria as the presence of any of the following on two separate occasions (in patients without pre-existing diabetes): fasting plasma glucose ≥7.0 mmol/L, HbA1c ≥6.5%, 2-hour plasma glucose ≥11.1 mmol/L during an oral glucose tolerance test (if performed), or initiation of antidiabetic medication (insulin or oral agents) for sustained hyperglycemia. Diagnosis was confirmed through laboratory records and medication charts at the 3-month follow-up or earlier if clinically indicated (Rudzki *et al.* 2024; Jenssen & Hartmann, 2019).

Perioperative glycemic control metrics were derived from CGM data over the first 14 postoperative days. Time in range (TIR) was calculated as the percentage of time interstitial glucose remained between 3.9 and 10.0 mmol/L, in line with standard targets for non-pregnant adults per international consensus (Battelino *et al.* 2019). Coefficient of variation (CV) was determined as the standard deviation of glucose values divided by the mean glucose, expressed as a percentage (with <36% indicating stability). Time below range (TBR) represented the percentage of time glucose was <3.9 mmol/L. Severe hypoglycemia was identified as episodes with glucose <3.0 mmol/L or those requiring third-party assistance, verified by CGM alerts and corresponding clinical notes. Mean amplitude of glycemic excursions (MAGE) was computed as the average amplitude of glucose excursions exceeding one standard deviation from the mean, using established algorithmic processing of CGM tracings.

Secondary outcomes included hospital length of stay, defined as the number of days from transplantation to discharge and obtained directly from admission and discharge records. Complications at 3 months encompassed acute rejection (biopsy-proven per Banff criteria or clinically diagnosed and treated, such as elevated creatinine responding to pulse steroids), infection (clinically significant episodes requiring antimicrobial therapy, supported by positive cultures, imaging, or treatment documentation, including urinary tract infections, pneumonia, or wound infections), and graft loss (return to permanent dialysis or retransplantation). Patient satisfaction, assessed only in the intervention group at discharge, was measured using a 10-point Likert scale questionnaire (ranging from 1 = extremely dissatisfied to 10 = extremely satisfied), emphasizing ease of monitoring, confidence in glycemic control, and overall experience with the integrated model.

Data Collection and Management

Data collection was performed retrospectively by two trained investigators independently reviewing the electronic health records (EHR), laboratory information system, institutional CGM database, pharmacy records, and outpatient follow-up notes. All data were de-identified prior to analysis to ensure patient privacy, and a unique study identifier was assigned to each participant. Data quality was assured through double-entry verification for key variables, with discrepancies resolved by a third senior investigator.

Baseline characteristics were extracted as follows: age and gender from demographic records at admission; BMI calculated from height and weight measured preoperatively; preoperative HbA1c from the most recent laboratory result within 3 months prior to transplantation; donor type (deceased or living) from surgical records; and immunosuppressive regimen (tacrolimus-based or other) from initial postoperative medication orders.

Primary and secondary outcome data were obtained from multiple sources for accuracy. PTDM diagnosis at 3 months relied on laboratory results and pharmacy records (initiation of antidiabetic medications), cross-verified with clinician notes at the 3-month follow-up visit. Perioperative glycemic metrics were derived exclusively from the CGM database: raw interstitial glucose readings were exported from the Freestyle Libre 2 cloud platform, and metrics (TIR, CV, TBR, severe hypoglycemia, MAGE) were computed using standardized algorithms in dedicated software (LibreView or custom validated scripts).

Clinical complications were identified from progress notes, biopsy reports (for acute rejection), microbiology/imaging results (for infections), and dialysis/retransplantation records (for graft loss). Hospital length of stay was taken directly from admission and discharge summaries. Patient satisfaction scores were collected from a standardized questionnaire administered at discharge in the intervention group. All extracted data were entered into a secure, password-protected electronic database for analysis, with regular audits to ensure completeness and accuracy (missing data <5% for all variables).

HFMEA-CGM-AI Integrated Precise Glycemic Management Model

The primary innovation of this study is the construction of an integrated multimodal model combining HFMEA, CGM (Freestyle Libre 2), and AI to achieve proactive, risk-stratified, predictive glycemic control — a framework not previously reported in kidney transplant perioperative care.

The model comprises three synergistic components implemented sequentially from late 2022 onward:

- Healthcare Failure Mode and Effect Analysis (HFMEA): A multidisciplinary team (transplant surgeons, endocrinologists, nephrologists, nurses, and quality management specialists) conducted a formal HFMEA in late 2022 to prospectively map the entire perioperative glycemic workflow. Failure modes were scored for severity, occurrence, and detection probability to calculate risk priority numbers (RPN). High-risk modes (RPN ≥60) — including delayed hyperglycemia recognition, inconsistent insulin adjustment, and monitoring gaps — were prioritized. Corrective measures (standardized insulin protocols, mandatory CGM in high-risk patients, enhanced multidisciplinary alerts) were incorporated into clinical pathways and fully implemented from January 2023 (DeRosier *et al.* 2002).

- Continuous Glucose Monitoring (CGM; Freestyle Libre 2): Sensors were applied 48 hours preoperatively and maintained for at least 14 postoperative days (extended in high-risk cases). Data were transmitted every 15 minutes via Bluetooth to a secure cloud platform integrated with the electronic health record, providing real-time trends and proactive alerts for hypo/hyperglycemia (Fokkert *et al.* 2017).

- Artificial Intelligence (AI)-Driven Predictive Modeling: An LSTM network with attention mechanism was developed and validated on complete CGM datasets from 200 historical kidney transplant recipients (2020–2022). The model forecasted glucose levels 15–60 minutes ahead and generated individualized recommendations (e.g., insulin dosing, dietary adjustments) that were available to clinicians at the point of care. From January 2023, outputs were displayed in real-time on a dedicated clinician dashboard and patient mobile application, enabling immediate proactive intervention. Model performance was characterized on an internal hold-out set (20% of the training records, partitioned at the patient level to avoid leakage). On 30-minute-ahead forecasts the network achieved a mean absolute error (MAE) of 0.74 mmol/L, a root-mean-square error (RMSE) of 0.96 mmol/L, and an R^2 of 0.88; over a 60-minute horizon MAE rose to 1.18 mmol/L and RMSE to 1.51 mmol/L. The Clarke error grid placed 99.1% of paired predictions in zones A+B. For hypoglycemia alerting (glucose <3.9 mmol/L) the model reached a sensitivity of 0.91 and a specificity of 0.87, with a 30-minute lead-time. Calibration was assessed by Brier score (0.063) and a calibration intercept of 0.04 (slope 0.97).
- Integration transformed isolated tools into a coordinated system: HFMEA optimized processes, CGM supplied continuous data, and AI provided predictive intelligence, collectively aiming to shift management from reactive to preventive.

Statistical Analysis

Continuous variables are presented as mean ± standard deviation (SD) and compared using Student's t-test or Mann-Whitney U test as appropriate. Categorical variables are presented as frequencies (%) and compared using χ^2 test or Fisher's exact test. Multivariable logistic regression was used to explore the association of the intervention with PTDM risk, adjusting for prespecified clinical covariates. Results are reported as adjusted odds ratios (OR) with 95% confidence intervals (CI). Subgroup analyses were performed for key outcomes across age, BMI, gender, and donor type strata, with interaction terms tested for heterogeneity. Sensitivity analyses included restriction to tacrolimus-based regimens and alternative matching parameters. Statistical significance was set at $p < 0.05$ (two-tailed). Analyses were performed using SPSS version 26.0. No a priori sample-size calculation was performed; the cohort size reflected the patients available during the study window rather than a powered design. A post-hoc power calculation, assuming PTDM rates of 20.0% versus 10.0% with n = 60 per arm and a two-sided $\alpha = 0.05$, yielded approximately 25% power, indicating a substantial

risk of Type II error. All inferential statistics involving PTDM should therefore be regarded as exploratory; non-significant results cannot be taken as evidence that the intervention is ineffective.

RESULTS

Patient Enrollment and Baseline Characteristics

A total of 120 kidney transplant recipients were included in this retrospective cohort study: 60 in the historical control group (2021–2022) and 60 in the intervention group (2023–2024). Age, BMI, sex, preoperative HbA1c, and donor type did not differ between groups (Table 1). However, tacrolimus-based immunosuppression was used in 98.3% of historical controls versus 83.3% of intervention patients ($p = 0.011$) — a clinically important imbalance, given the well-established diabetogenic effect of tacrolimus on pancreatic β-cell function and insulin sensitivity. Because this difference involves the principal drug-related risk factor for PTDM, it represents a potential confounder rather than a minor protocol deviation; a sensitivity analysis restricted to tacrolimus-exposed patients was therefore performed (see below). Even with this analysis, residual confounding cannot be excluded.

Glycemic Outcomes

The intervention group had substantially and statistically significantly improved perioperative glycemic control compared with the control group across all key CGM metrics (Table 2). TIR was markedly higher in the intervention group (80.0 ± 9.0% vs 63.8 ± 11.6%; $p < 0.001$), exceeding recommended CGM targets (>70%), with reduced glycemic variability as evidenced by lower CV (23.6 ± 5.4% vs 37.3 ± 6.4%; $p < 0.001$), TBR (2.2 ± 1.1% vs 9.2 ± 3.6%; $p < 0.001$), and MAGE (3.9 ± 0.8 mmol/L vs 5.7 ± 1.4 mmol/L; $p < 0.001$). Severe hypoglycemia events were also fewer in the intervention group (0.0% vs. 6.7%, $p = 0.127$), though not statistically significant.

Clinical Outcomes and Complications

Secondary clinical outcomes generally favored the intervention group, although not all differences reached statistical significance (Table 3). Hospital length of stay was significantly shorter in the intervention group (12.4 ± 2.2 days vs. 14.2 ± 3.3 days, $p < 0.001$). Rates of acute rejection (3.3% vs. 5.0%, $p = 1.000$), infection (5.0% vs. 13.3%, $p = 0.201$), and graft loss at 3 months (0.0% vs. 5.0%, $p = 0.244$) were numerically lower in

Tab. 1. Baseline Characteristics of the Study Population
Baseline characteristics of kidney transplant recipients in the historical control and HFMEA–CGM–AI intervention groups. Values are presented as mean ± standard deviation (SD) for continuous variables and number (percentage) for categorical variables. BMI indicates body mass index. The p-values refer to between-group comparisons for each characteristic.

Variable	Control Group	Intervention Group	*p*-value
Age (years), mean ± SD	47.1 ± 8.4	49.2 ± 8.9	0.188
BMI (kg/m^2), mean ± SD	25.7 ± 3.9	25.3 ± 4.1	0.649
Male gender, n (%)	27 (45.0%)	31 (51.7%)	0.584
Preoperative HbA1c (%), mean ± SD	5.8 ± 0.5	5.7 ± 0.5	0.106
Donor type (deceased donor), n (%)	48 (80.0%)	43 (71.7%)	0.394
Immunosuppressive regimen (tacrolimus-based), n (%)	59 (98.3%)	50 (83.3%)	0.011

Tab. 2. Glycemic Outcomes at 14 Days and 3 Months Post-Transplantation
Glycemic outcomes at 14 days and post-transplantation diabetes mellitus (PTDM) incidence at 3 months in the historical control versus HFMEA–CGM–AI intervention groups. Time in range (TIR) is the percentage of time interstitial glucose remained between 3.9 and 10.0 mmol/L over the first 14 postoperative days. Coefficient of variation (CV) reflects glycemic variability. Time below range (TBR) is the percentage of time glucose was <3.9 mmol/L; severe hypoglycemia events were defined as glucose <3.0 mmol/L or episodes requiring third-party assistance. Mean amplitude of glycemic excursions (MAGE) is expressed in mmol/L. Values are mean ± SD or n (%), with *p*-values for between-group comparisons.

Outcome	Control Group	Intervention Group	*p*-value
PTDM incidence at 3 months, n (%)	12 (20.0%)	6 (10.0%)	0.201
TIR (3.9–10.0 mmol/L) at 14 days (%), mean ± SD	63.8 ± 11.6	80.0 ± 9.0	<0.001
CV (%) at 14 days, mean ± SD	37.3 ± 6.4	23.6 ± 5.4	<0.001
TBR (<3.9 mmol/L) at 14 days (%), mean ± SD	9.2 ± 3.6	2.2 ± 1.1	<0.001
Severe hypoglycemia (<3.0 mmol/L) events, n (%)	4 (6.7%)	0 (0.0%)	0.127
MAGE (mmol/L) at 14 days, mean ± SD	5.7 ± 1.4	3.9 ± 0.8	<0.001

Abbreviations: PTDM, post-transplantation diabetes mellitus; TIR, time in range; CV, coefficient of variation; TBR, time below range; MAGE, mean amplitude of glycemic excursions.

Tab. 3. Clinical Outcomes and Complications
Clinical outcomes and complications at 3 months after kidney transplantation in the historical control and HFMEA–CGM–AI intervention groups. Outcomes include hospital length of stay, acute rejection, infections requiring antimicrobial therapy, and graft loss (return to permanent dialysis or retransplantation). Patient satisfaction was assessed only in the intervention group at discharge using a 10-point Likert scale (1 = extremely dissatisfied, 10 = extremely satisfied). Values are mean ± SD or n (%), with *p*-values for between-group comparisons where applicable.

Outcome	Control Group	Intervention Group	*p*-value
Hospital length of stay (days), mean ± SD	14.2 ± 3.3	12.4 ± 2.2	<0.001
Acute rejection, n (%)	3 (5.0%)	2 (3.3%)	1
Infection rate, n (%)	8 (13.3%)	3 (5.0%)	0.201
Graft loss at 3 months, n (%)	3 (5.0%)	0 (0.0%)	0.244
Patient satisfaction score (out of 10), mean ± SD*	N/A	8.4 ± 1.1	N/A

Note: Patient satisfaction was only assessed in the intervention group.

the intervention group but did not achieve statistical significance, possibly due to the small sample size and low event rates. Patient satisfaction was collected by a 10-point Likert questionnaire administered exclusively in the intervention arm at discharge; mean score was 8.4 ± 1.1 with 90% reporting ≥7. Because no comparable measurement exists in the historical-control cohort, and because the questionnaire was non-anonymous and given by the treating team, these data are subject to response and social-desirability bias and should be interpreted purely as descriptive of the intervention experience rather than as evidence of incremental benefit. Figure 1 shows Kaplan-Meier curves for PTDM-free survival over 3 months, with a log-rank $p = 0.118$ indicating a trend toward improved outcomes in the intervention group, though not statistically significant.

Multivariable Analysis

Multivariable logistic regression was performed to explore the association between the intervention (HFMEA-CGM-AI integrated model) and the risk of PTDM at 3 months, adjusting for potential confounders including age, BMI, gender, preoperative HbA1c, donor type (deceased donor), and immunosuppressive regimen (tacrolimus-based). The intervention group showed a non-significant association with lower PTDM risk (adjusted odds ratio [OR] 0.58, 95% confidence interval [CI] 0.19–1.72, $p = 0.324$). None of the other covariates were statistically significant predictors of PTDM (all $p > 0.05$; Figure 2). Critically, however, the regression model itself was not statistically significant (likelihood-ratio χ^2 $p = 0.448$), and the fitting algorithm exhibited convergence problems together with implausibly wide confidence intervals, reflecting near-uniform tacrolimus use in the control arm (collinearity) and only 18 PTDM events distributed across six covariates — well below the conventional 10 events-per-variable threshold. The adjusted OR is therefore best regarded as a descriptive, exploratory estimate and should not be used to support causal inference; we report it for completeness rather than as a confirmatory result. The unadjusted between-group comparison likewise remains susceptible to the baseline imbalances described above.

Subgroup and Sensitivity Analyses

Subgroup analyses were conducted to evaluate the consistency of treatment effects on key outcomes (TIR

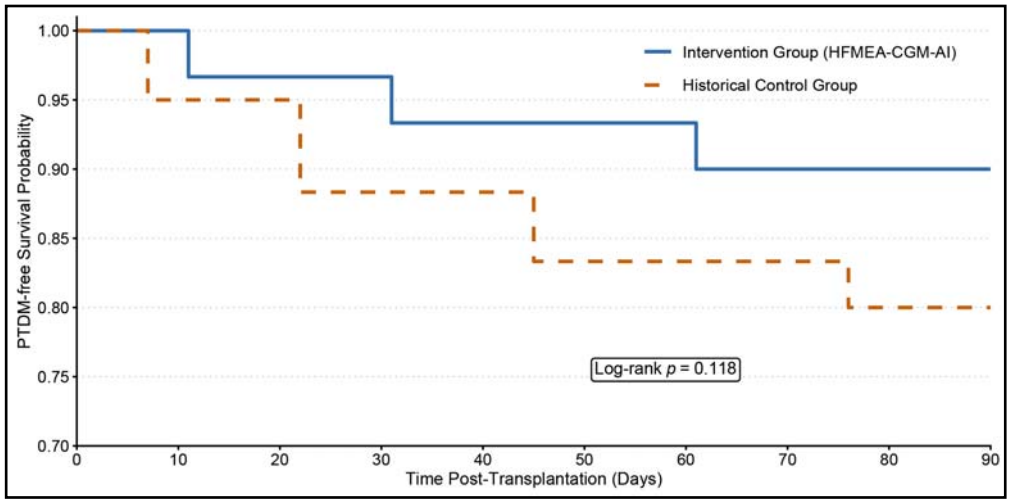

Fig. 1. Kaplan–Meier curves for post-transplantation diabetes mellitus (PTDM)–free survival over 3 months in kidney transplant recipients managed with conventional historical control care versus the HFMEA–CGM–AI integrated glycemic management model. The survival probability is plotted against time since transplantation, with the log-rank p-value indicating the statistical significance of differences between the two groups.

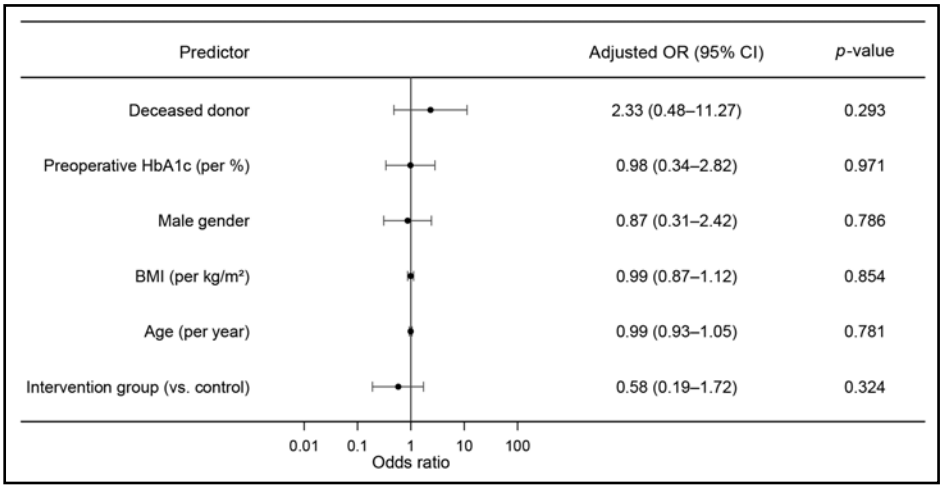

Fig. 2. Forest plot of multivariable logistic regression analysis for predictors of post-transplantation diabetes mellitus (PTDM) at 3 months after kidney transplantation. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) are shown for the HFMEA–CGM–AI intervention and the covariates displayed in the plot: age, BMI, gender, preoperative HbA1c, and donor type. The vertical line represents an OR of 1.0 (no effect). The fitted model also included tacrolimus-based immunosuppression; however, the model was exploratory because of limited events and convergence issues.

at 14 days and PTDM incidence at 3 months) across predefined subgroups: age (<50 vs. ≥50 years), BMI (<25 vs. ≥25 kg/m²), gender (male vs. female), and donor type (deceased vs. living). For TIR, the intervention group showed consistently higher values across all subgroups, with statistically significant differences within each stratum (all subgroup $p < 0.001$; Table 4). Interaction tests indicated no significant heterogeneity of effect (all interaction $p > 0.05$), suggesting uniform benefits in glycemic stability regardless of subgroup.

For PTDM incidence, reductions were observed in most subgroups, but the difference reached statistical significance only in the age <50 subgroup (27.8% in control vs. 3.0% in intervention, $p = 0.013$), with a nominal age-by-treatment interaction ($p = 0.014$). This analysis was, however, not pre-specified, was performed across four subgroup variables without correction for multiple testing, and is based on small per-stratum samples (e.g., only 3 events among 33 younger-intervention patients). The age signal is therefore best regarded as exploratory and hypothesis-generating, requiring confirmation in adequately powered, prespecified prospective trials before any clinical inference. No significant interactions or within-subgroup differences emerged in the other strata (all p > 0.05, Table 5).

Sensitivity analyses were performed to assess the robustness of the primary findings. Repeating the multivariable logistic regression for PTDM risk while restricting to patients on tacrolimus-based immunosuppression (n = 109, excluding 11 non-tacrolimus cases) yielded similar results (adjusted OR 0.58, 95% CI 0.19–1.72, $p = 0.324$), confirming that the immunosuppressive regimen imbalance did not substantially influence the main analysis. Additional sensitivity checks, such as excluding outliers in TIR (>2 SD from mean) or using alternative propensity score calipers, did not materially alter the conclusions (data not shown). Overall, these analyses suggest that the main descriptive findings are consistent across analytic choices, but they do not overcome the limitations of small event numbers and potential confounding.

Tab. 4. Subgroup Analyses for TIR at 14 days

Subgroup analyses of time in range (TIR) at 14 days after kidney transplantation in the historical control and HFMEA–CGM–AI intervention groups. Subgroups are defined by age (<50 vs. ≥50 years), BMI (<25 vs. ≥25 kg/m²), gender, and donor type (living vs. deceased). TIR is shown as mean ± SD for each subgroup and group, with p-values for within-subgroup comparisons and interaction p-values testing for heterogeneity of treatment effect across subgroup levels.

Subgroup	Level	Intervention Group	TIR at 14 Days: Control (mean ± SD)	TIR at 14 Days: Intervention (mean ± SD)	*p*-value (within subgroup)	Interaction *p*-value
Age	<50 years	36/33	63.1 ± 11.8	81.0 ± 9.9	<0.001	0.305
Age	≥50 years	24/27	64.9 ± 11.5	78.8 ± 7.7	<0.001	
BMI	<25 kg/m²	24/25	68.4 ± 11.8	81.0 ± 8.7	<0.001	0.126
BMI	≥25 kg/m²	36/35	60.8 ± 10.6	79.3 ± 9.2	<0.001	
Gender	Female	33/29	61.2 ± 9.8	79.9 ± 7.8	<0.001	0.128
Gender	Male	27/31	67.1 ± 12.9	80.1 ± 10.0	<0.001	
Donor Type	Living	12/17	60.9 ± 8.7	81.8 ± 10.9	<0.001	0.171
Donor Type	Deceased	48/43	64.6 ± 12.2	79.3 ± 8.1	<0.001	

Tab. 5. Subgroup Analyses for PTDM incidence at 3 months
Subgroup analyses of post-transplantation diabetes mellitus (PTDM) incidence at 3 months in the historical control and HFMEA–CGM–AI intervention groups. Subgroups are defined by age (<50 vs. ≥50 years), BMI (<25 vs. ≥25 kg/m^2), gender, and donor type (living vs. deceased). For each subgroup, the number of patients per group, PTDM incidence expressed as a percentage, *p*-values for within-subgroup comparisons, and interaction *p*-values for treatment-by-subgroup effects are presented.

Subgroup	Level	n (Control/ Intervention)	PTDM at 3 Months: Control (%)	PTDM at 3 Months: Intervention (%)	*p*-value (within subgroup)	Interaction *p*-value
Age	<50 years	36/33	27.8	3	0.013	0.014
Age	≥50 years	24/27	8.3	18.5	0.517	
BMI	<25 kg/m^2	24/25	25	12	0.42	0.9
BMI	≥25 kg/m^2	36/35	16.7	8.6	0.504	
Gender	Female	33/29	24.2	6.9	0.132	0.25
Gender	Male	27/31	14.8	12.9	1	
Donor Type	Living	12/17	8.3	5.9	1	0.78
Donor Type	Deceased	48/43	22.9	11.6	0.256	

DISCUSSION

This retrospective cohort study shows that the integrated HFMEA–CGM–AI perioperative glycemic management model was associated with markedly better glycemic control in kidney transplant recipients, with large improvements in TIR, CV, TBR, and MAGE during the first 14 postoperative days (all $p < 0.001$). These findings support the feasibility of combining process engineering, continuous monitoring, and AI-driven prediction to achieve tighter perioperative glycemic control in routine practice. The intervention group achieved a TIR of 80.0%, exceeding commonly recommended CGM targets (>70%), and a significantly shorter hospital stay, suggesting that improved perioperative glycemic stability may contribute to more efficient postoperative recovery, although mechanistic pathways remain to be clarified. By contrast, three-month PTDM incidence and multivariable regression results were non-significant and clearly underpowered, and all analyses of PTDM and complications should be interpreted as exploratory and hypothesis-generating only. Subgroup analyses, including an apparent signal in younger patients, likewise rest on small numbers and cannot inform clinical decision-making at this stage.

Comparisons with existing literature underscore the value of this multimodal approach. Prospective studies using CGM alone in kidney transplant recipients have reported similar improvements in glycemic variability and PTDM prediction, with perioperative mean glucose levels correlating strongly with 3-month outcomes (Shin *et al.* 2024; Schwaiger *et al.* 2021). For instance, a study by Hecking *et al.* found that CGM-identified hyperglycemia in the first week post-transplant predicted PTDM with high accuracy (Hecking *et al.* 2012). Integrating HFMEA for risk process optimization and AI for predictive analytics extends these benefits, addressing limitations of standalone CGM, such as reactive rather than proactive management (Luo *et al.* 2024). AI-driven models, like the LSTM-Attention used here, have shown promise in non-transplant diabetes for forecasting hypoglycemia and optimizing insulin dosing (De Felice *et al.* 2022), but their application in transplantation is novel. Our results echo a narrative review emphasizing CGM's role in reducing post-transplant dysglycemia and complications (Hecking *et al.* 2021), while the high patient satisfaction (8.4/10) mirrors findings from flash glucose monitoring evaluations, where reduced finger-stick burden improved adherence (Guo *et al.* 2025).

Several limitations restrict causal interpretation. First, the use of historical rather than concurrent controls is the principal validity threat, as multiple unmeasured changes between 2021–2022 and 2023–2024 may have occurred in parallel with the intervention and cannot be separated from its effects. Second, the diabetogenic tacrolimus imbalance (98.3% vs 83.3%) plausibly favors the intervention arm and is not fully mitigated by sensitivity analyses. Third, the cohort size (n = 120) and only 18 PTDM events yielded approximately 25% power for the PTDM endpoint, so non-significant differences cannot be interpreted as evidence of no effect. Fourth, CGM-derived metrics are surrogate endpoints, and important behavioral factors (diet, activity, adherence) were not captured. Fifth, generalizability is limited by the single Chinese tertiary-center setting. Sixth, the integrated model is resource-intensive, and we did not perform a formal cost-effectiveness analysis, so economic implications of broader adoption remain uncertain.

Taken together, the HFMEA–CGM–AI model was feasibly implemented and associated with improved perioperative glycemic indices and shorter hospital stay, but the historical-control design, low event count, and unstable regression models preclude causal

inference for PTDM or complications, and these clinical signals should be regarded as preliminary rather than practice-changing.

STATEMENTS

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None.

Data Availability Statement

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval

The research protocol was reviewed and approved by the Ethics Committee of Affiliated Hospital of Xuzhou Medical University [XYFY2024-KL496-01, XYFY2024-KL652-01]. The requirement for written informed consent was waived owing to the retrospective design and use of de-identified data, and the study was conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not Applicable.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Author contributions

XYZ conceived the study, defined its intellectual content, and drafted the manuscript. LNG designed the study and critically reviewed the manuscript. ZYW conducted the literature research. HTZ performed the clinical studies. DRZ carried out the experimental studies and statistical analysis. MMW was responsible for data acquisition. JJZ analyzed the data. QQS edited the manuscript and is the guarantor of the integrity of the entire work. All authors read and approved the final manuscript.

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