Surgical Site Infections and Inflammatory Reaction after Cardiac Surgery, Bedside Artificial Pancreas vs. Conventional Insulin Therapy: A Propensity Score-Matched Analysis

Tasuku Fujii, Takahiro Hirai, Shogo Suzuki, Kimitoshi Nishiwaki

Department of Anesthesiology, Nagoya University Hospital, Nagoya, Japan

Mailing address: 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Corresponding author: Tasuku Fujii

Department of Anesthesiology, Nagoya University Hospital, Nagoya, Japan

Mailing address: 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Email: plus9@med.nagoya-u.ac.jp

TEL: +81527442340

FAX: +81527442342

Conflict of interest: None

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Acknowledgments

The authors thank Editage (http://www.editage.jp/) for providing professional editing services.

＜**Abstract**＞

Objectives

Perioperative hyperglycemia is associated with poor postoperative recovery, including compromised immune function and increased risk of infection. A closed-loop glycemic control system (artificial pancreas) has demonstrated safe perioperative strict glycemic control without hypoglycemia risk. We hypothesized that the artificial pancreas would reduce surgical site infections and postoperative inflammatory reactions. Our study aimed to assess the effect of the artificial pancreas on surgical site infections and C-reactive protein levels after cardiac surgery.

Design

A single-center retrospective, propensity score-matched analysis

Setting

A university hospital

Participants

In total, 295 patients who underwent cardiovascular surgery with cardiopulmonary bypass were included.

Interventions

Patients were divided into two groups: artificial pancreas (target blood glucose: 120–150 mg/dL) and intravenous insulin infusion (conventional insulin therapy, target blood glucose: <200 mg/dL).

Measurements and Main Results

The difference in the incidence of surgical site infections and C-reactive protein levels between the two groups was assessed. After 1:1 propensity score-matching based on their covariates, 101 matched patients were selected from each group. The incidence of

surgical site infections was reduced by 3%, 5% (conventional insulin therapy), and 2% (artificial pancreas), but the reduction was not statistically significant (P=0.45). The postoperative maximum C-reactive protein level was significantly lower in the artificial pancreas group than in the conventional insulin therapy group (14.53 (5.64) mg/dL vs. 16.57 (5.58) mg/dL; P=0.01).

Conclusions

The artificial pancreas did not demonstrate a significant reduction in the incidence of surgical site infections. However, the artificial pancreas was safe and suppressed postoperative inflammation compared with conventional insulin therapy.

Key Words:

artificial pancreas; cardiac surgery; glycemic control; insulin therapy; perioperative hyperglycemia; postoperative inflammation; surgical site infection

Introduction

Perioperative hyperglycemia induced by surgical stress is common in patients with or without diabetes and is associated with poor postoperative recovery, including compromised immune function and increased risk of infection.[1–4] Some studies have suggested that normal perioperative glycemic control improves surgical outcomes and reduces postoperative mortality and morbidity.[5,6] Some guidelines also recommend an optimal target blood glucose range below 180–200 mg/dL to reduce surgical site infections (SSIs).[7–9] SSIs are one of the serious complications known to occur after cardiac surgery. The incidence of SSIs has been reported to be 1–10% and is associated with an increase in the mortality rate, reaching 25% in some cases.[10–11] In cardiac surgery, cardiopulmonary bypass (CPB) is a significant risk factor for postoperative hyperglycemia,[12] and postoperative strict glycemic control improves surgical outcomes;[13] however, strict glycemic control with insulin carries a risk of hypoglycemia.[14] Additionally, postoperative hypoglycemia is associated with morbidity and mortality in cardiac surgery patients.[15]

Recent studies have demonstrated that a closed-loop glycemic control system can achieve strict perioperative glycemic control safely, with no hypoglycemia events.[16–22] Therefore, after cardiovascular surgery with CPB, we routinely use a bedside closed-loop glycemic control device, termed the artificial pancreas, to maintain set blood glucose levels using an automatic infusion of insulin and glucose. The primary objective of this study was to test the hypothesis that the incidence of SSIs would be different in patients who underwent CPB and were treated with the bedside artificial pancreas or conventional insulin therapy. The secondary objective was to compare

inflammatory responses between the two groups using C-reactive protein (CRP) as a biomarker of inflammation. Therefore, our study aimed to assess the effect of the artificial pancreas on SSIs and CRP levels after cardiac surgery.

Methods

Study Design and Ethical Approvals

This was a single-center, retrospective study whose design was approved by our hospital's ethics committee (ref: 2020–0462). Written informed consent was not obtained due to the opt-out option provided during the recruitment of all participants who underwent cardiac surgery between July 2018 and September 2020.

Enrollment of Patients

Patients who underwent cardiovascular surgery with CPB and were transferred to the surgical intensive care unit (ICU) were included in the study. Patients who underwent an emergency operation or cardiovascular surgery without CPB were excluded. Additionally, patients who underwent cardiovascular surgery due to infection (i.e., infective endocarditis, infected aortic aneurysm) were excluded. Those who underwent heart transplantation and ventricular assist device surgery, thoracoabdominal aortic aneurysm replacement, or pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension were also excluded. Based on these inclusion and exclusion criteria, 295 patients were analyzed. The study included diabetic or non-diabetic patients.

In our institution, intraoperative glycemic control is determined by each anesthesiologist. Since October 2019, postoperative glycemic treatment with a closed-loop glycemic control device (artificial pancreas) has been administered after cardiac surgery with CPB in the surgical ICU. The patients were divided into two groups: those treated with the closed-loop glycemic control device (artificial pancreas) from October 2019 to September 2020 and those who received conventional insulin therapy to

maintain blood glucose levels using insulin infusion (conventional insulin therapy) from July 2018 to September 2019. All patients received cephalosporin antibiotics immediately before the surgery until 48 h after the surgery to prevent SSIs.

Postoperative Glycemic Control Method

The bedside artificial pancreas, a closed-loop glycemic control system (STG-55; Nikkiso Co. LMT, Tokyo, Japan), consists of a blood glucose measurement unit and an insulin or glucose injection unit. Blood is continuously collected from an intravenous catheter (less than approximately 2 mL/h), and the blood glucose level is continuously measured using the glucose oxidase enzyme electrode method. Automatic infusion of insulin and glucose is controlled by a management algorithm according to the blood glucose level and the change in the blood glucose level per minute. Insulin infusion rate = IA/100 × [BG(t) – ID] + IB/100 × [ΔBG(t)] + IC. Glucose infusion rate = GA × [GD – BG(t)] – GB × ΔBG(t) + GC. BG(t) is the current blood glucose level, and ΔBG(t) is the blood glucose level change. As proportional coefficients, IA was set to 10 (mUnit·mL/g^2/min) and GA to 0.5 (dL/kg/min). As differential coefficients for ΔBG(t), IB was set to 100 (mUnit·mL/g^2) and GB to 0.5 (dL/kg). As fixed coefficients, IC was set to 0.225 (mUnit/kg/min) and GC to 0 (mg/kg/min). ID was set to 150 (mg/dL) and GD to 120 (mg/dL) as target blood glucose levels (120–150 mg/dL). This glycemic control with the aid of the artificial pancreas was performed for 16–24 h after surgery. After the use of the artificial pancreas, blood glucose was controlled with conventional insulin therapy. Data regarding blood glucose, insulin dose, and glucose dose were recorded in the artificial pancreas system every minute.

By contrast, conventional insulin therapy was a glycemic control method of

continuous and/or bolus intravenous insulin infusion when the blood glucose levels exceeded 200 mg/dL after admission to the surgical ICU. We maintained the blood glucose level below 200 mg/dL by adjusting the insulin dose.

Outcome Measurements

Primary Outcome

The primary outcome was the incidence of SSIs for each of the two glycemic control methods: artificial pancreas vs. conventional insulin therapy. SSIs were broadly defined as the presence of signs of infection at the surgical site within 30 days after surgery (i.e., local pain, redness, swelling, secretion, purulent discharge, sternal osteomyelitis, or mediastinitis).

Secondary Outcomes

As a well-known blood test marker of the inflammatory acute phase response, baseline CRP level (before surgery), postoperative maximum CRP level (within 7 days after surgery), and postoperative 7-day CRP levels were evaluated and compared between the two groups. Additionally, the secondary outcome was the incidence of hypoglycemia as a major complication of insulin therapy. Hypoglycemia was defined as a blood glucose level below 70 mg/dL. Secondary outcomes also included the length of ICU stay, length of hospital stay, postoperative 30-day mortality, and postoperative acute kidney injury (AKI). AKI was defined as an elevated serum creatinine level of ≥0.3 mg/dL or ≥1.5 multiplied by the preoperative baseline value, based on the Kidney Disease Improving Global Outcomes criteria.[23] We also evaluated the use of insulin and glucose from the minute-by-minute data recorded in the artificial pancreas.

Moreover, in the subgroup analysis of the diabetic and non-diabetic groups, the

incidence of SSIs, postoperative maximum CRP level, and postoperative 7-day CRP levels were evaluated between the two glycemic control methods.

All of the patients' data were acquired from electronic medical records, electronic anesthesia charts, and the artificial pancreas. The electronic medical records were documented by surgeons or nurses who were blinded to the study information. The electronic anesthesia records and artificial pancreas data were automatically documented.

Statistical Analyses

A sample size of 88 participants in each group was calculated to provide an 80% power (two-sided α of 0.05) to test for an expected 3/35 (8.5%) to 0/20 (0%) incidence of SSIs, based on the subgroup data in a previous study.[21] Therefore, we sought to include more than 100 participants in each group to account for an expected 10% decline in propensity matching.

Baseline and intraoperative characteristics of the patients were compared using Student's t-test, the Mann–Whitney U test, or Fisher's exact test. Patients treated with the artificial pancreas were individually matched (1:1) with patients who were not treated with the artificial pancreas, based on the similarity of the propensity score calculated using a logistic regression model. Their covariates included age, sex, body mass index, operation time, CPB time, blood transfusion, intraoperative fluid balance, surgical procedure type (valve surgery, coronary surgery, aortic surgery, or complex surgery), and those with or without diabetes mellitus. The caliper distance for matching was defined as 0.1 of the pooled logit score standard deviation (SD). The primary outcome, the incidence of SSI between the groups, was statistically analyzed using

Fisher's exact test. As the secondary outcomes, CRP levels at each point were analyzed with Student's t-test. In addition, the incidence of hypoglycemia, AKI, and postoperative 30-day mortality were analyzed using Fisher's exact test, while the lengths of ICU stay and hospital stay were analyzed using Mann–Whitney U tests. Categorical variables were expressed as numeric values (proportion) and continuous variables as means (SD) or medians [interquartile range]. P values of <0.05 were considered statistically significant. All statistical analyses were performed using R software, version 3.5.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

In this study, 501 patients were enrolled. After applying the inclusion and exclusion criteria, 295 patients were included in the study and were divided into two groups: 113 patients who received the closed-loop glycemic control system (artificial pancreas) and 182 patients who received conventional insulin therapy without the artificial pancreas. Propensity score matching revealed 101 patients in each group, based on their covariates (Fig 1). There were no significant differences between the two groups based on their baseline and perioperative characteristics (Table 1).

Regarding the primary outcome measure (incidence of SSIs), there were 2/101 patients (2%) in the artificial pancreas vs. 5/101 (5%) in conventional insulin therapy who had SSIs. The difference in SSIs between the two groups was 3%; however, the difference was not statistically significant ($P = 0.45$) (Table 2).

The postoperative maximum CRP level was significantly lower in the artificial pancreas group than in the conventional insulin therapy group, both before propensity matching [14.58 (5.60) mg/dL vs. 16.18 (6.01) mg/dL; $P = 0.02$] and after matching [14.53 (5.64) mg/dL vs. 16.59 (5.59) mg/dL; $P = 0.01$], (Table 2). There was no difference in the number of postoperative days at which the CRP level was the highest in both groups, 3 [(3–3)] vs. 3 [2–3] days for the artificial pancreas vs. conventional insulin therapy groups, respectively ($P = 0.48$). Baseline and postoperative 7-day CRP levels before and after propensity matching are shown in Table 2. Fig 2 shows the highest CRP value within 7 days after surgery.

Hypoglycemia (a secondary outcome) did not occur in patients in the artificial pancreas group but occurred in 3/182 (2%) patients in the conventional insulin therapy group (Table 3). Postoperative AKI decreased from 24/101 (24%) in the conventional

insulin therapy group to 15/101 (15%) in the artificial pancreas group, although the difference was not statistically significant ($P = 0.15$) (Table 3). The other secondary outcomes, namely, lengths of ICU stay and hospital stay, and postoperative 30-day mortality, were not significantly different between the two groups. Additionally, based on the minute-by-minute artificial pancreas data, insulin was automatically administered to all 113 patients to maintain their blood glucose levels within the target range of 120–150 mg/dL.

Regarding the secondary outcome, the results of subgroup analysis on the diabetic or non-diabetic groups are shown in Table 4. The incidence of SSIs was not significantly different in each group. In the non-diabetic group, the artificial pancreas significantly reduced the postoperative maximum CRP levels compared to conventional insulin therapy [14.42 (5.37) mg/dL vs. 16.65 (5.90) mg/dL; $P = 0.01$].

Discussion

In this study, we retrospectively compared the incidence of SSIs and postoperative inflammatory reactions of the bedside closed-loop glycemic control system (artificial pancreas) with conventional insulin therapy. The artificial pancreas (target blood glucose range: 120–150 mg/dL) did not demonstrate a statistically significant reduction in the incidence of SSIs compared to conventional insulin therapy (target blood glucose levels: < 200 mg/dL). Notably, the artificial pancreas could suppress the increase in CRP levels more than conventional insulin therapy. Furthermore, automatic insulin infusion was required to control blood glucose levels at 120–150 mg/dL in all patients who received artificial pancreas treatment. Nevertheless, the present study findings demonstrate that the closed-loop glycemic control system artificial pancreas was safe, with no hypoglycemic events. Our results suggest that the closed-loop glycemic control system artificial pancreas may be safe and effective for suppressing postoperative inflammatory responses after cardiac surgery with CPB.

Shin et al. have suggested that the same artificial pancreas used in our study reduced postoperative surgical site complications, including infection and dehiscence, in their subgroup analysis.[21] They performed a subgroup analysis focusing on isolated coronary artery bypass grafts (with the use of CPB not described). However, their study did not show a significant reduction in SSIs, with 0/20 (0%) in the artificial pancreas (target blood glucose levels < 140 mg/dL) group vs. 3/25 (8%) in the conventional insulin therapy (target range of 125–175 mg/dL) group.[21] Based on their subgroup analysis results, our study focused primarily on the incidence of SSIs as a major postoperative complication, with a larger sample size. In our study, the artificial pancreas reduced SSI incidence by 3% compared with conventional insulin therapy,

although the difference was not significant. There may have been no statistical difference in the incidence of SSIs between the two glycemic control methods because the incidence of SSIs with conventional insulin therapy was lower than expected. Therefore, this study might be considered a pilot study that demonstrated a reduction in the incidence of SSIs after cardiac surgery. Further studies with larger sample sizes or multicenter trials are required.

Tamura et al. found in an observational study that included 36 patients in each group (artificial pancreas vs. conventional glucose control) that the same closed-loop glycemic control system used in our study with a wide target blood glucose range of 110–180 mg/dL, suppresses the maximal postoperative CRP level after cardiac surgery.[22] However, in their study, there were 24 cases (67%) involving cardiac surgery with CPB in the artificial pancreas group vs. 31 cases (86%) in the conventional insulin therapy ($P = 0.09$) group, and the analysis was not adjusted for patient background characteristics. [22] By contrast, our propensity-matched analysis was performed to reduce bias with larger sample size. Our findings revealed that postoperative glycemic control with the artificial pancreas suppressed the inflammatory response after cardiac surgery with CPB, which is a significant risk factor for postoperative hyperglycemia.

In our subgroup analysis on the diabetic or non-diabetic groups, the artificial pancreas significantly reduced the postoperative maximum CRP levels only in the non-diabetic group. In the diabetic group, the difference may not have been significant due to the small sample size (22 cases in artificial pancreas vs. 21 cases in conventional insulin therapy) or the varying diabetic control status within the group. However, some reports have suggested that perioperative hyperglycemia was associated with worse postoperative adverse events in the non-diabetic group than in the diabetic group[24] and

different perioperative glycemic control strategies between the two groups.[25] Therefore, further research with a larger sample size and more diverse group of patients is needed.

van den Berghe et al. demonstrated that intensive insulin therapy with a target blood glucose range of 80–110 mg/dL led to lower morbidity and mortality rates than a target blood glucose range of 180–200 mg/dL.[26] However, many intensive insulin therapy studies did not show significant benefits for surgical outcomes; rather, the studies found a high risk of hypoglycemia. The optimal postoperative blood glucose levels that are safe and reduce mortality and morbidity remain controversial. In this study, the artificial pancreas targeted a blood glucose range of 120–150 mg/dL. This study confirmed the safety of the closed-loop glycemic control device artificial pancreas for maintaining the target blood glucose level, with no adverse events such as hypoglycemia. Further research should be safely conducted to assess the optimal blood glucose levels, e.g., intensive insulin therapy (blood glucose range 80–110 mg/dL).

In addition, Egi et al. demonstrated that the variability of blood glucose levels is associated with patient outcomes, such as ICU stay and hospital mortality.[27] Our study findings suggest that the artificial pancreas can suppress fluctuations in blood glucose levels. Strictly controlling glucose level variability using this artificial pancreas may also have a significant impact on patient outcomes.

There were several limitations in this study. First, this was a retrospective and observational study in which patients were not randomized to the glycemic control methods. While we have found no significant differences in patient characteristics between the two groups, further randomized controlled trials are required. To obtain comparable groups with minimal bias, we used a propensity score-matching approach. Second, these data were collected from patients who underwent cardiac surgery with

CPB at a single center; consequently, the sample size may be too small to compare the glycemic control methods effectively. Therefore, the generalizability of these findings remains controversial. Third, although the subgroup analysis on the diabetic and diabetic groups was performed, the diabetes control status was not compared in this study. Patients with poor preoperative glycemic control are at risk of perioperative complications. In our study, a subgroup analysis on preoperative glycemic control status was not possible due to the very small sample size; only four patients had a hemoglobin A1c level greater than 9% (poor control of diabetes). Patients with a higher body mass index and poor glycemic control may have results different from the findings presented in this study. Therefore, future studies are needed to determine for which group of patients postoperative glycemic control with an artificial pancreas is most effective or ineffective. Fourth, this study did not control intraoperative blood glucose levels. Intraoperative hyperglycemia in cardiac surgery is associated with worse clinical outcomes.[28] Further studies are needed to evaluate whether intraoperative use of this artificial pancreas affects clinical outcomes. Finally, all patients, with and without diabetes, in the artificial pancreas group received glycemic control using the artificial pancreas until 24 h postoperatively. However, the Society of Thoracic Surgeons practice guidelines recommend that blood glucose levels be maintained below 180 mg/dL for at least 24 h postoperatively.[9] Furthermore, McConnell et al. demonstrated that the mean blood glucose level at 48 h postoperatively was associated with SSIs.[29] Strict glycemic control using the artificial pancreas for a long period may effectively improve surgical outcomes, especially the incidence of SSIs. In addition, the optimal perioperative blood glucose level remains unclear. Further studies using this safe closed-loop glycemic control system in varying clinical situations are required.

In conclusion, the findings suggest that the incidence of SSIs was not significantly different in patients who received CPB and were treated with the bedside closed-loop glycemic control system artificial pancreas, with a target blood glucose range of 120–150 mg/dL, compared to those who received conventional insulin therapy. However, the present study findings suggest that the artificial pancreas is safe and can suppress postoperative inflammation compared with conventional insulin therapy, which adheres to a target blood glucose level below 200 mg/dL.

References

1. Peacock TS. Perioperative Hyperglycemia: A Literature Review. AORN J 2019;109:80–86.

2. Ramos M, Khalpey Z, Lipsitz S, et al. Relationship of perioperative hyperglycemia and postoperative infections in patients who undergo general and vascular surgery. Ann Surg 2008;248:585–591.

3. Kwon S, Thompson R, Dellinger P, et al. Importance of perioperative glycemic control in general surgery: a report from the Surgical Care and Outcomes Assessment Program. Ann Surg 2013;257:8–14.

4. Hanazaki K, Maeda H, Okabayashi T. Relationship between peri-operative glycemic control and postoperative infections. World J Gastroenterol 2009;15:4122–4125.

5. Vogt AP, Bally L. Perioperative glucose management: Current status and future directions. Best Pract Res Clin Anaesthesiol 2020;34:213–224.

6. Tsai LL, Jensen HA, Thourani VH. Intensive Glycemic Control in Cardiac Surgery. Curr Diab Rep 2016;16:25.

7. Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention Guideline for the Prevention of Surgical Site Infection, 2017. JAMA Surg 2017;152:784–791.

8. Ban KA, Minei JP, Laronga C, et al. American College of Surgeons and Surgical Infection Society: Surgical Site Infection Guidelines, 2016 Update. J Am Coll Surg 2017;224:59–74.

9. Lazar HL, McDonnell M, Chipkin SR, et al. Society of Thoracic Surgeons Blood Glucose Guideline Task Force: The Society of Thoracic Surgeons practice guideline series: Blood glucose management during adult cardiac surgery. Ann Thorac Surg

2009;87:663–669.

10. Cardiothoracic Interdisciplinary Research Network. National survey of variations in practice in the prevention of surgical site infections in adult cardiac surgery, United Kingdom and Republic of Ireland. J Hosp Infect 2020;106:812–819.

11. Andrade LS, Siliprandi EMO, Karsburg LL, et al. Surgical Site Infection Prevention Bundle in Cardiac Surgery. Arq Bras Cardiol 2019;112:769–774.

12. Knapik P, Nadziakiewicz P, Urbanska E, et al. Cardiopulmonary bypass increases postoperative glycemia and insulin consumption after coronary surgery. Ann Thorac Surg 2009;87:1859–1865.

13. Siddiqui KM, Asghar MA, Khan MF, et al. Perioperative glycemic control and its outcome in patients following open heart surgery. Ann Card Anaesth 2019;22:260–264.

14. Stamou SC, Nussbaum M, Carew JD, et al. Hypoglycemia with intensive insulin therapy after cardiac surgery: predisposing factors and association with mortality. J Thorac Cardiovasc Surg 2011;142:166–173.

15. Johnston LE, Kirby JL, Downs EA, et al. Postoperative Hypoglycemia Is Associated With Worse Outcomes After Cardiac Operations. Ann Thorac Surg 2017;103:526–532.

16. Okabayashi T, Nishimori I, Yamashita K, et al. Continuous postoperative blood glucose monitoring and control by artificial pancreas in patients having pancreatic resection: a prospective randomized clinical trial. Arch Surg 2009;144:933–937.

17. Hanazaki K, Maeda H, Okabayashi T. Tight perioperative glycemic control using an artifi cial endocrine pancreas. Surg Today 2010;40:1–7.

18. Yatabe T, Yamazaki R, Kitagawa H, et al. The evaluation of the ability of closed-loop glycemic control device to maintain the blood glucose concentration in intensive care unit patients. Crit Care Med 2011;39:575–578.

19. Tsukamoto Y, Okabayashi T, Hanazaki K. Progressive artificial endocrine pancreas: the era of novel perioperative blood glucose control for surgery. Surg Today 2011;41:1344–1351.

20. Hanazaki K, Munekage M, Kitagawa H, et al. Current topics in glycemic control by wearable artificial pancreas or bedside artificial pancreas with closed-loop system. J Artif Organs 2016;19:209–218.

21. Shin U, Naoko H, Michinori T, et al. Utility of bedside artificial pancreas for postoperative glycemic control in cardiac surgery. J Artif Organs (in press).

22. Tamura T, Yatabe T, Namikawa T, et al. Glucose control using a closed-loop device decreases inflammation after cardiovascular surgery without increasing hypoglycemia risk. J Artif Organs 2019;22:154–159.

23. Kellum JA, Lameire N; KDIGO AKI Guideline Work Group. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care 2013;17:204.

24. Kotagal M, Symons RG, Hirsch IB, et al. Perioperative hyperglycemia and risk of adverse events among patients with and without diabetes. Ann Surg 2015;261:97–103.

25. Nair BG, Neradilek MB, Newman SF, et al. Association between acute phase perioperative glucose parameters and postoperative outcomes in diabetic and non-diabetic patients undergoing non-cardiac surgery. Am J Surg 2019;218:302–310.

26. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. N Engl J Med 2001;345:1359–1367.

27. Egi M, Bellomo R, Stachowski E, et al. Variability of blood glucose concentration and short-term mortality in critically ill patients. Anesthesiology 2006;105:244–252.

28. Rassias AJ. Intraoperative management of hyperglycemia in the cardiac surgical

patient. Semin Thorac Cardiovasc Surg 2006;18:330–338.

29. McConnell YJ, Johnson PM, Porter GA. Surgical site infections following colorectal surgery in patients with diabetes: association with postoperative hyperglycemia. J Gastrointest Surg 2009;13:508–515.

Table 1

Baseline Characteristics and Intraoperative Data from Each Group Before and After Propensity Score-Matching

	Before matching			*After matching*		
	Artificial pancreas *n* = 113	Conventional insulin therapy *n* = 182	*P*-value	Artificial pancreas *n* = 101	Conventional insulin therapy *n* = 101	*P*-value
Age, years	70 [60–75]	69.5 [61–77]	0.86	70 [60–75]	71 [61–76]	0.65
Sex, Male/Female	76/37	120/62	0.90	68/33	70/31	0.88
BMI, kg/m^2	22.7 (3.5)	22.9 (3.6)	0.66	22.7 (3.2)	23.0 (3.4)	0.49
Diabetes	25 (22%)	53 (29%)	0.22	22 (22%)	21 (21%)	1.00
Surgical procedure			0.13			1.00
Valve	54 (48%)	89 (49%)		53 (53%)	54 (54%)	
Coronary	21 (19%)	44 (24%)		21 (21%)	21 (21%)	
Aorta	18 (16%)	33 (18%)		18 (18%)	18 (18%)	
Other procedures	5 (4%)	7 (4%)		4 (4%)	4 (4%)	
Complex operation time, min	15(13%)	9 (5%)		5 (5%)	4 (4%)	
CPB time, min	415 (91)	402 (110)	0.29	405 (85)	412 (120)	0.60
	169 (59)	163 (66)	0.47	163 (55)	168 (73)	0.60

Blood transfusion	84 (74%)	123 (68%)	0.24	73 (72%)	73 (72%)	1.00
Intraoperative fluid balance, mL	2574 (1551)	2446 (1434)	0.47	2502 (1492)	2469 (1531)	0.88

Values are presented as mean (± standard deviation), median [interquartile range], or number (proportion, %) of patients.

BMI, body mass index; CPB, cardiopulmonary bypass.

Table 2

Surgical Site Infections and Inflammatory Reaction in Each Group Before and After Propensity Score-Matching

	Before matching			*After matching*		
	Artificial pancreas *n* = 113	Conventional insulin therapy *n* = 182	*P*-value	Artificial pancreas *n* = 101	Conventional insulin therapy *n* = 101	*P*-value
SSIs	2 (2%)	9 (5%)	0.21	2 (2%)	5 (5%)	0.45
Maximum CRP, mg/dL	14.58 (5.60)	16.18 (6.01)	0.02*	14.53 (5.64)	16.59 (5.59)	0.01*
CRP highest day	3 [3–3]	3 [2–3]	0.58	3 [3–3]	3 [2–3]	0.48
Baseline CRP, mg/dL	0.24 (0.38)	0.20 (0.28)	0.39	0.24 (0.40)	0.19 (0.25)	0.28
POD7 CRP, mg/dL	5.46 (3.46)	6.27 (3.99)	0.08	5.43 (3.47)	6.54 (3.94)	0.04*

Values are presented as mean (± standard deviation) or number (proportion, %) of patients.

* $P < 0.05$.

SSIs, surgical site infections; CRP, C-reactive protein; POD, postoperative day.

Table 3

Secondary Outcomes in Each Group Before and After Propensity Score-Matching

	Before matching			*After matching*		
	Artificial pancreas *n* = 113	Conventional insulin therapy *n* = 182	*P*-value	Artificial pancreas *n* = 101	Conventional insulin therapy *n* = 101	*P*-value
Hypoglycemia	0 (0%)	3 (2%)	0.29	0 (0%)	1 (1%)	1.00
AKI	18 (16%)	41 (23%)	0 .18	15 (15%)	24 (24%)	0.15
Hospital stay, days	16 [13–23]	17 [14–22]	0.26	16 [13–22]	17 [14–23]	0.22
ICU stay, days	3 [2–4]	3 [2–4]	0.18	3 [2–4]	3 [2–4]	0.45
Intubation time, hours	8 [6–14]	8.5 [6–15]	0.35	7.5 [6–12]	8.5 [6–15.5]	0.18
30-day mortality	0 (0%)	2 (1%)	0.53	0 (%)	0 (%)	-
Use of insulin	113 (100%)	71 (39%)	0.01*	101 (100%)	37 (37%)	0.01*

Values are presented as median [interquartile range] or number (proportion, %) of patients.

* P <0.05.

AKI, acute kidney injury, ICU, intensive care unit.

Table 4

Subgroup Analysis on the Diabetic and Non-diabetic groups, Surgical Site Infections and Inflammatory Reaction in Two Glycemic Control Methods

	Diabetes (n = 43)			*Non-diabetes (n = 159)*		
	Artificial pancreas *n* = 22	Conventional insulin therapy *n* = 21	*P*-value	Artificial pancreas *n* = 79	Conventional insulin therapy *n* = 80	*P*-value
SSIs	0 (0%)	1 (5%)	0.49	2 (3%)	4 (5%)	0.68
Baseline CRP, mg/dL	0.16 (0.17)	0.27 (0.40)	0.21	0.26 (0.44)	0.17 (0.18)	0.08
Maximum CRP, mg/dL	14.92 (6.64)	16.37 (4.30)	0.40	14.42 (5.37)	16.65 (5.90)	0.01*
POD7 CRP, mg/dL	5.00 (3.02)	6.25 (3.76)	0.24	5.55 (3.59)	6.61 (4.01)	0.08

Values are presented as mean (± standard deviation) or number (proportion, %) of patients.

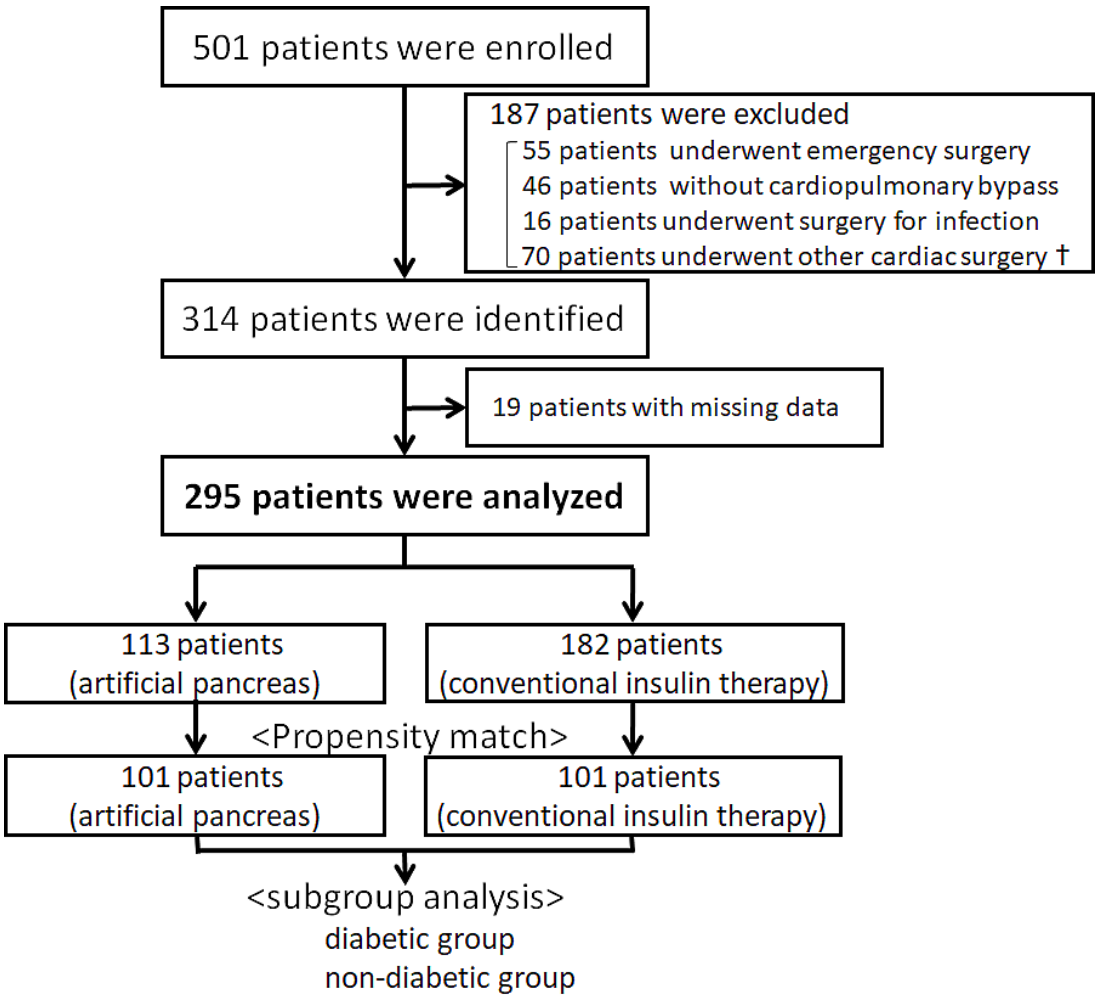
* $P < 0.05$.

SSIs, surgical site infections; CRP, C-reactive protein; POD, postoperative day.

Figures

Figure 1

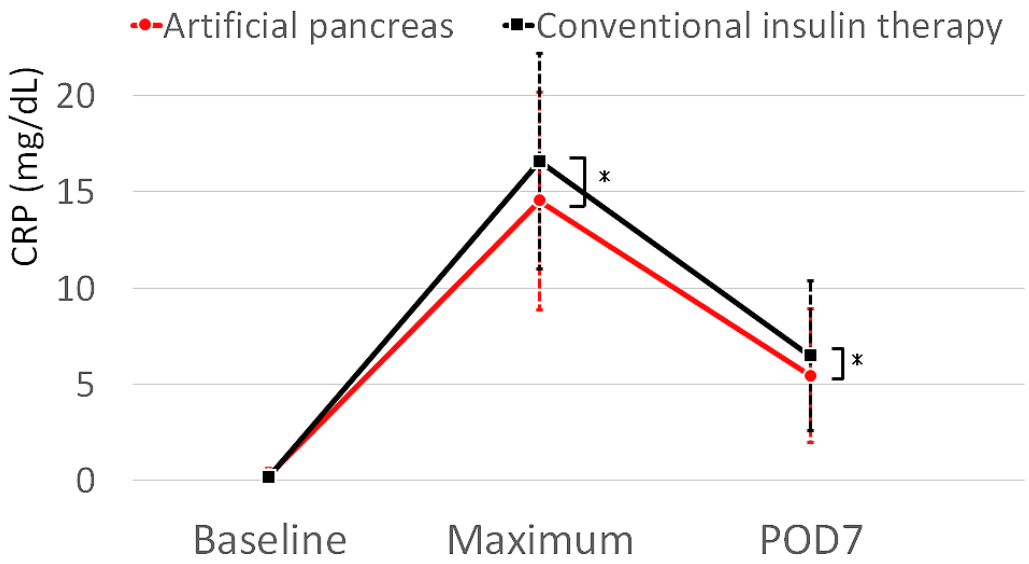
Flow diagram of the selection of the study population.



† Other cardiovascular surgery: heart transplantation and ventricular assist device surgery, thoracoabdominal aortic aneurysm replacement, or pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension.

Figure 2

Postoperative inflammation, C-reactive protein



Baseline indicates before surgery, POD7 indicates postoperative day 7, and maximum indicates the highest CRP value within 7 days after surgery. Values are presented as mean, and error bars represent standard deviations.

* P <0.05. CRP, C-reactive protein; POD, postoperative day.