ORIGINAL

Effect of glucose load on metabolism in patients with type 2 diabetes during elective surgery using remifentanil-induced anesthesia : a randomized controlled trial

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Abstract : This study aimed to explore the effect of intraoperative glucose load on metabolism in patients with type 2 diabetes anesthetized with remifentanil. A total of 30 patients were enrolled and randomly allocated to one of two groups : no glucose or low-dose glucose (0.1 g/kg/h for 1 hour followed by 0.05 g/kg/h for 1 hour). Glucose, adrenocorticotropic hormone, 3-methylhistidine, insulin, cortisol, free fatty acid, ketone bodies, and creatinine were measured at several points before, during, and after general anesthesia. Glucose levels in the low-dose glucose group increased significantly at 1 and 2 hours after glucose infusion compared to their preanesthetic levels and to those in the no glucose group. Two patients in the low-dose glucose group had blood glucose levels exceeding 11.1 mmol/L. Free fatty acids, ketone bodies, and 3-methylhistidine/creatinine did not differ significantly between groups. Ketone body levels were significantly higher at 1 hour than preanesthetic levels in both groups ; after 1 hour, however, they did not change in the no glucose group but significantly decreased in the low-dose glucose group. Intraoperative low-dose glucose load may suppress ketogenesis, but clinicians must consider the risk of causing hyperglycemia in patients with type 2 diabetes undergoing remifentanil-induced anesthesia.
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Keywords **:** *Catabolism, Remifentanil, Type 2 diabetes*

INTRODUCTION

Surgical stress responses, such as the release of catecholamines and stress hormones, impair glucose tolerance (1-4). Therefore, hyperglycemia can occur during surgery. Hyperglycemia causes various adverse events such as wound infection, sepsis, ischemia/infarction, hemodynamic compromise, arrhythmia, nephropathy, and neuropathy through tissue effects such as endothelial dysfunction, increased pro-inflammatory cytokines, platelet activation, procoagulation/antifibrinolysis, and mitochondrial dysfunction (5). Furthermore, perioperative hyperglycemia has been reported as an independent risk factor for mortality (6, 7). Therefore, appropriate perioperative glycemic control is important for improving surgical prognosis.

Due to the potential to cause intraoperative hyperglycemia, using a glucose-containing solution during surgery is risky. However, insufficient glucose administration during surgery can cause lipid and/or protein catabolism to compensate for energy deficiency, and prolonged preoperative fasting can also induce catabolism. If these conditions persist, ketoacidosis, loss of skeletal muscle mass, delayed wound healing, and other conditions may occur. However, if surgical stress is sufficiently controlled, it may be possible to administer a sufficient amount of glucose intraoperatively to prevent catabolism without causing hyperglycemia.

Several studies have reported that remifentanil suppresses stress hormone secretion (8-10) and that an adequate intraoperative glucose load suppresses only lipid catabolism or both lipid and protein catabolism without inducing hyperglycemia in patients receiving remifentanil anesthesia (11-13). However, these studies on remifentanil did not evaluate patients with diabetes, and only a limited number of studies have examined how intraoperative glucose administration affects metabolic responses in patients with diabetes. Therefore, it is unclear whether an adequate intraoperative glucose load can suppress lipid or protein catabolism, or both, without causing hyperglycemia in patients with diabetes, similar to what has been shown in non-diabetic patients. In this study, we examined how intraoperative glucose administration affects metabolic responses in diabetic patients undergoing surgery under remifentanil anesthesia.

MATERIALS AND METHODS

Participants

Patients diagnosed with type 2 diabetes mellitus awaiting elective surgical procedures at Tokushima University Hospital, Japan, from August 2013 to September 2016 were eligible. Patients were included if they had American Society of Anesthesiologists Physical Status 1 or 2, had diabetes with a glycated hemoglobin (HbA1c) level less than 53 mmol/mol, received only oral antidiabetic or only diet therapy, and underwent scheduled surgery lasting more than 2 hours without using a tourniquet or laparoscopy. Patients were excluded if they were aged < 20 or > 65 years, were obese (body mass index (BMI) > 30 kg/m2) or emaciated (BMI < 17 kg/m2), had renal, liver, neurologic, or thyroid disease, or were receiving steroids or insulin. Randomization allocated eligible patients to either the 0G group, which received no glucose (n = 15), or the LG group, which received a low glucose dose (n = 15).

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Ethics

This study was approved by the Ethics Committee of Tokushima University Hospital (No. 1688 ; 2-50-1, Kuramoto, Tokushima City, Tokushima, Japan). The study was registered with the University Hospital Medical Information Network Center (http://www.umin.ac.jp/english/) (ID : UMIN000010145). Written informed consent was obtained from all participants.

Procedures

Patients were permitted to have meals until midnight on the day prior to surgery. Patients undergoing surgery in the morning were administered 250 ml (200 kcal) of Alginate Water® (Nestlé Japan Ltd., Tokyo, Japan), while those undergoing in the afternoon were administered 500 ml (400 kcal) at least 2 hours before entering the operating room. No patients were premedicated. Once in the operating room, each patient was monitored with an electrocardiograph, a sphygmomanometer, and a pulse oximeter. Following catheter placement in the patient's left or right forearm using a 20G catheter, glucose-free bicarbonate Ringer's solution was infused. General anesthesia was induced after preoxygenation using thiamylal (3 mg/kg) and remifentanil (0.25–0.5 μg/kg/min) intravenously, and maintained with sevoflurane (end-tidal ≥ 1.0%) in combination with remifentanil (0.2–0.5 μg/kg/min). Muscle relaxation was achieved using rocuronium bromide (0.7 mg/kg) administered prior to endotracheal intubation, followed intermittently (0.1–0.2 mg/kg) as needed.

Figure 1 illustrates the study protocol. Following endotracheal intubation, an S/5 compact monitor (GE Healthcare, Helsinki, Finland) was connected to the heat and moisture exchanger to measure the respiratory quotient (RQ), oxygen consumption (VO_2), carbon dioxide output (VCO_2), and energy expenditure (EE). The tidal volume was set at 7 ml/kg, respiratory rate at 10/min, and O_2/air mixture at FiO_2 0.5. The monitor required approximately 20 min to output these data in a stable manner. We defined the point in time when RQ and EE were stably measured as Time 0. Normal saline was administered to patients in the 0G group at 0.4 ml/kg/h for the first hour starting at Time 0, followed by 0.2 ml/kg/h for the second hour. In contrast, the LG group received a 25% glucose solution at the same rates, corresponding to an effective glucose dose of 0.1 g/kg/h initially and 0.05 g/kg/h subsequently. All patients were infused with bicarbonate Ringer's solution at 10 ml/kg/h for the initial hour and 5 ml/kg/h for the subsequent hour, with modifications to the administration rate occurring 2 h after Time 0, according to the patient's hemodynamics. After 2 h from Time 0, neither group received further glucose.

Measurements

Blood samples were obtained and labeled as follows : before induction of anesthesia (Base), 1 h after Time 0 (1H), 2 h after Time 0 (2H), at the end of surgery (End), and the next morning (Next) (Figure 1). About 12 ml of blood was subjected to centrifugation at 150 g for 10 minutes at 4 °C (Table Top cooling centrifuge 2800, Kubota, Tokyo, Japan), and both plasma and serum were preserved at –20 °C until they were analyzed. An additional 2 ml of blood sample was obtained at Base and stored at 4 °C to measure HbA1c. Whole blood levels of HbA1c, plasma levels of glucose, adrenocorticotropic hormone (ACTH), and 3-methylhistidine (3-MH), and serum levels of insulin, cortisol, free fatty acid (FFA), ketone bodies, and creatinine (Cr) were analyzed by SRL Inc. (Tokyo, Japan). Blood glucose was also measured in the operating room with a bedside glucose monitoring device (Medisafe Fit, Terumo, Tokyo, Japan). If blood glucose levels were > 13.9 mmol/L, 2 U of insulin were administered intravenously. The RQ, VO_2, VCO_2, and EE values were recorded every 30 min from Time 0 through the end of the operation. FFA and ketone body levels were used as indicators of lipid catabolism. The 3MH/Cr ratio, which is obtained by correcting the 3-MH level according to muscle mass, was used as an indicator of protein catabolism. Glucose and insulin levels were used as indicators of glucose metabolism, while ACTH and cortisol levels were used as indicators of the stress reaction, and RQ was used as an indicator of the energy source consumed.

Randomization and blinding

A computer-generated distribution (QuickCalcs, GraphPad Inc., La Jolla, CA, USA) was used to randomly allocate patients

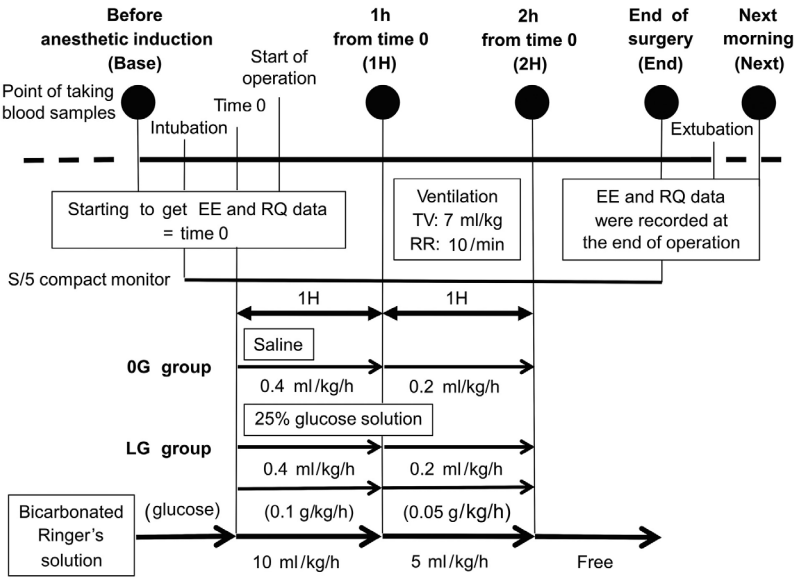

Figure 1. Study protocol. EE, energy expenditure ; RQ, respiratory quotient ; TV, tidal volume ; RR, respiratory rate.

into the two groups. An anesthesiologist who was not engaged in intraoperative data collection prepared the saline or glucose syringes to ensure that patients, surgeons, and data-collecting anesthesiologists remained blinded to group assignment.

Statistical analysis

In the present study, the primary endpoint was ketone body levels. A previous study demonstrated that, in patients who did not receive intraoperative glucose, ketone body levels rose from approximately 200 ± 150 μmol/L at anesthesia induction to about 450 ± 250 μmol/L by the end of surgery (14). Expecting a mean intraoperative difference of 200 ± 170 μmol/L between groups, at least 12 participants per group were needed to obtain 80% statistical power with an alpha of 0.05 for ketone body measurements. Considering the possibility of patient exclusions, we recruited a total of 30 patients (15 in each group). Normal distribution of the data was examined using the Shapiro–Wilk test. Parametric data were evaluated using repeated measures analysis of variance to compare time points within each group, with Bonferroni correction applied for multiple comparisons. Comparisons of parametric data between the groups at the same time points were performed with unpaired t-tests. In contrast, nonparametric data were analyzed using the Friedman test to assess differences between time points within each group. The Mann–Whitney rank-sum test was used to compare nonparametric data from the two groups at the same time point. Nominal variables were assessed with the chi-squared test. Statistical significance was determined at $P < 0.05$. All statistical analyses were performed using SPSS version 20 (IBM Corp., Armonk, NY, USA).

RESULTS

Of the 32 patients who were determined to be eligible, two declined to participate. The remaining 30 patients were randomly allocated into two equal groups. As summarized in Tables 1 and 2, the 0G and LG groups showed no notable differences in characteristics of the patients or surgical procedure types.

Figure 2 shows the plasma ACTH and serum cortisol levels of both groups at each study time point. In the 0G group, plasma ACTH levels at 1H, 2H, End, and Next were significantly lower than those at Base (1H vs. Base : $p = 0.008$, 2H

Table 1. Baseline demographic and clinical characteristics of surgical patients in the no glucose (0G) and low-dose glucose (LG) groups

	0G group (n = 15)	LG group (n = 15)
Male, n (%)	9 (60.0)	8 (53.3)
Age (years)	64.5 ± 5.6	65.5 ± 5.7
Height (cm)	161.5 ± 8.5	159.4 ± 10.6
Weight (kg)	62.4 ± 10.3	66.8 ± 14.5
BMI (kg/m^2)	23.8 ± 2.5	26.0 ± 3.1
Operation time (min)	168.6 ± 76.4	150.0 ± 50.4
Blood loss (ml)	100 (10–350 [0–470])	27 (0–45 [0–250])
HbA1c (mmol/mol)	47.2 ± 6.5	46.1 ± 4.2

Values are presented as the number (%), mean ± standard deviation, or median (interquartile range [range]). BMI, body mass index ; HbA1c, glycated hemoglobin.

Table 2. Types of surgical procedures performed in the no glucose (0G) and low-dose glucose (LG) groups

0G group (n = 15)		LG group (n = 15)	
Total hip arthroplasty	2	Total hip arthroplasty	1
Revision of total hip arthroplasty	1	Cervical laminectomy	1
Cervical laminoplasty	1	Cervical laminoplasty	2
Lumbar laminectomy	2	Lumbar laminectomy	3
Lumbar disc hernia hysterectomy	1	Lumbar laminoplasty	1
Irrigation for post-operative wound infection	1	Submandibular gland tumor resection	1
Subcutaneous tumor resection	1	Dacryocystorhinostomy	1
Endoscopic sinus surgery	3	Endoscopic sinus surgery	2
Parotid gland tumor resection	1	Parotid gland tumor resection	2
Neck dissection	1	Tympanoplasty	1
Parathyroidectomy	1		

Values are presented as number of patients.

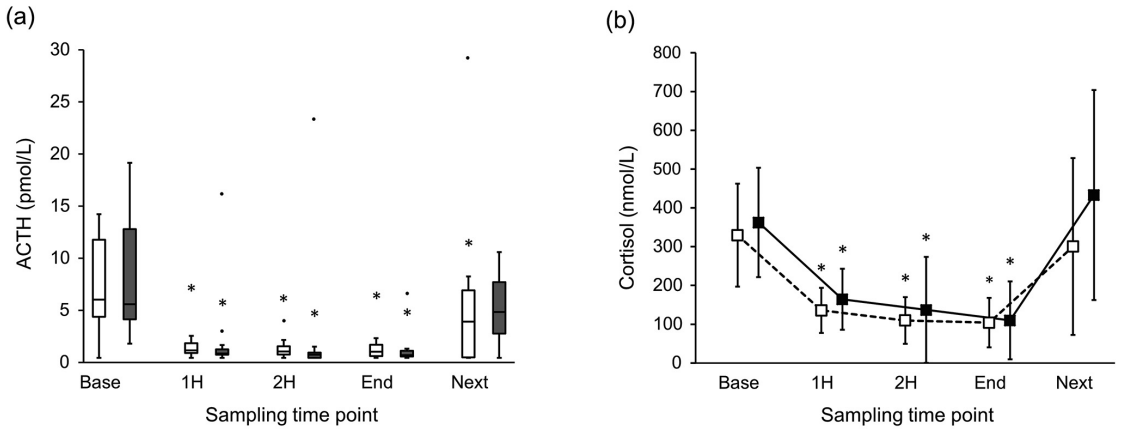

Figure 2. Plasma adrenocorticotropic hormone (ACTH) (a) and serum cortisol (b) levels of patients in the no glucose (0G) and low-dose glucose (LG) groups before anesthetic induction (Base), at 1 h (1H) and 2 h (2H) after saline or glucose infusion, at the end of surgery (End), and the next morning (Next). Values are presented as the median (horizontal bars), interquartile range (box), and range (whiskers) (a). Values are presented as the mean ± standard deviation (b). *$P < 0.05$ compared with Base. 0G group (□), LG group (■).

vs. Base : $p < 0.001$, End vs. Base : $p < 0.001$, and Next vs. Base : $p = 0.047$). In the LG group, plasma ACTH levels at 1H, 2H, and End were significantly lower than those at Base (1H vs. Base : $p = 0.047$, 2H vs. Base : $p < 0.001$, and End vs. Base : $p < 0.001$). Across all measured time points, the groups did not differ significantly. Serum cortisol levels at 1H, 2H, and End were significantly lower than those at Base in both groups (0G group : 1H vs. Base : $p < 0.001$, 2H vs. Base : $p < 0.001$, and End vs. Base : $p < 0.001$; LG group : 1H vs. Base : $p < 0.001$, 2H vs. Base : $p = 0.004$, and End vs. Base : $p < 0.001$). Across all measured time points, the groups did not differ significantly.

Figure 3 shows the plasma glucose and serum insulin levels at each study time point in both groups. While plasma glucose levels were unchanged in the 0G group during surgery, the LG group exhibited significant increases at 1H and 2H relative to baseline (1H vs. Base : $p < 0.001$ and 2H vs. Base : $p = 0.001$). Compared with the 0G group, the LG group exhibited significantly higher plasma glucose levels at 1H and 2H. ($p = 0.01$ and 0.025, respectively). The highest blood glucose level observed in the LG group was 12.5 mmol/L, with two patients showing values above 11.1 mmol/L. By contrast, the highest blood glucose level in the 0G group was 9.7 mmol/L, and none of the patients had values above 11.1 mmol/L. There were no cases of intraoperative hypoglycemia, and no patients required intravenous insulin in either group. Across all measured time points, serum insulin levels were comparable to baseline in both groups, but a significant between-group difference was observed at 1H, with lower levels in the 0G group ($p = 0.045$).

Figure 4 shows the serum FFA and ketone body levels at each study time point for both groups. In both groups, serum FFA concentrations did not differ significantly from baseline at any time point, and no significant between-group differences were observed at all measured time point. Serum ketone body levels increased significantly from baseline to 1H in both groups. (0G group : 1H vs. Base : $p = 0.003$; LG group : 1H vs. Base : $p = 0.001$). In the 0G group, ketone body levels did not change after 1H ; however, in the LG group, they significantly decreased (1H vs. 2H : $p = 0.027$; 1H vs. End : $p = 0.005$). Ketone body levels did not differ significantly between the two groups at any measured time point.

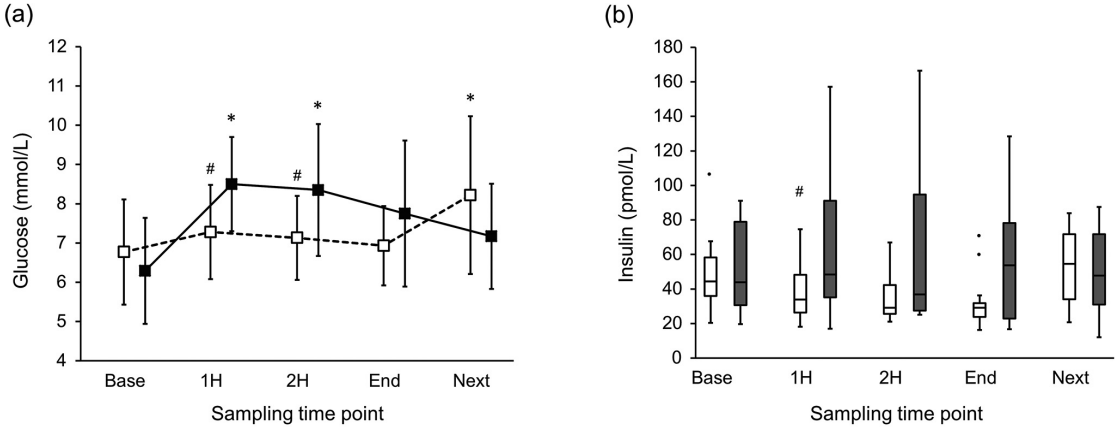

Figure 3. Plasma glucose (a) and serum insulin (b) levels of patients in the no glucose (0G) and low-dose glucose (LG) groups before anesthetic induction (Base), at 1 h (1H) and 2 h (2H) after saline or glucose infusion, at the end of surgery (End), and the next morning (Next). Values are presented as the mean ± standard deviation (a). Values are presented as the median (horizontal bars), interquartile range (box), and range (whiskers) (b). *P < 0.05 compared with Base. #P<0.05 compared with the LG group. 0G group (□), LG group (■).

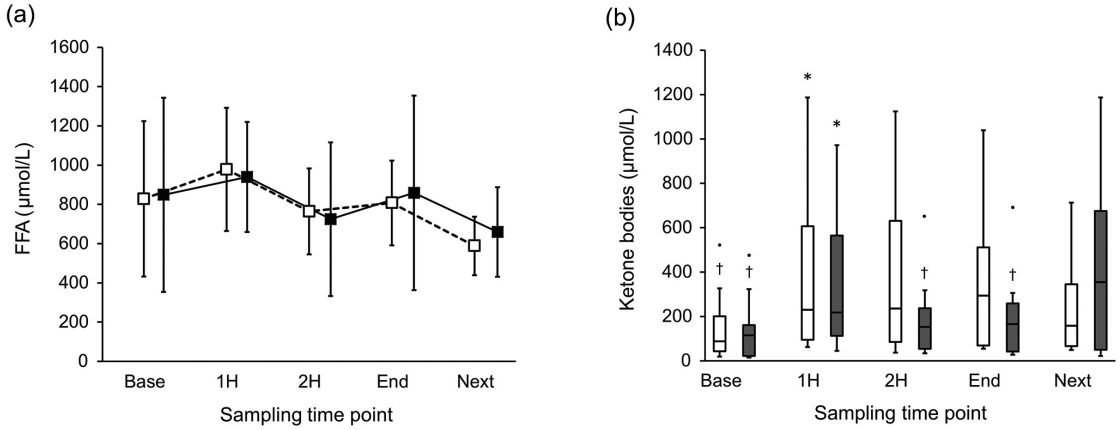

Figure 4. Serum free fatty acid (FFA) (a) and ketone body (b) levels of patients in the no glucose (0G) and low-dose glucose (LG) groups before anesthetic induction (Base), at 1 h (1H) and 2 h (2H) after saline or glucose infusion, at the end of surgery (End), and the next morning (Next). Values are presented as the mean ± standard deviation (a). Values are presented as the median (horizontal bars), interquartile range (box), and range (whiskers) (b). *P < 0.05 compared with Base. †P < 0.05 compared with 1H. 0G group (□), LG group (■).

No significant differences were found in the levels of plasma 3-MH, 3-MH/Cr ratio, serum Cr, EE (Figure 5a), RQ (Figure 5b), VO2, and VCO2.

DISCUSSION

The present study evaluated the metabolic effects of administering an intraoperative glucose load of approximately 1% in patients with type 2 diabetes anesthetized with remifentanil. Both ketone body and FFA levels did not differ significantly between the 0G and LG groups. These findings indicate the possibility that a low intraoperative dose of glucose did not attenuate lipid catabolism in patients with type 2 diabetes. These results differed from those of studies in non-diabetic patients, in which intraoperative glucose load suppressed lipid and/or protein catabolism (11-13).

In the present study, there were no significant differences in ketone body levels between the two groups, but ketone body levels did change with time : ketone body levels increased significantly from Base to 1H in both groups. In the 0G group, no change after 1H was observed ; in contrast, ketone body levels decreased significantly after 1H in the LG group, and there was little variation in the values. This trend in ketone values is similar to the results of a previous study (11), in which an intraoperative glucose load of approximately 1% for non-diabetic patients was shown to attenuate lipid catabolism. In addition, a study of glucose load in patients with diabetes anesthetized with remifentanil during surgery found that a low intraoperative dose of glucose administered for approximately 3 h significantly reduced levels of acetoacetic acid and total ketone bodies (15). We postulate that an adequate intraoperative glucose load during surgery still requires time, likely a few hours, to produce demonstrable suppression of lipid catabolism in patients with type 2 diabetes.

Similar to the results of previous studies (11), insulin levels were maintained during glucose loading in the LG group and tended to decrease in the 0G group. No significant difference was observed over time, but this may be due to variation in diabetic conditions and characteristics among the individual patients who comprised the 0G group, such as insulin secretory capacity and insulin resistance.

Previous studies on non-diabetic patients reported that a low intraoperative dose of glucose did not cause hyperglycemia (11-13). In contrast, in the present study of type 2 diabetic patients, although none of the patients received intravenous insulin, two patients in the LG group exhibited hyperglycemia exceeding 11.1 mmol/L (individual values are 11.9 mmol/L and 12.5 mmol/L), while zero of the 15 patients in the 0G group exhibited blood glucose levels exceeding 11.1 mmol/L (maximum level 9.7 mmol/L).

In the present study, remifentanil-induced anesthesia suppressed the secretion of ACTH and cortisol, both of which are stress hormones, in patients with diabetes, as in previous studies (8-13). Therefore, our results suggest that intraoperative glucose load in patients with type 2 diabetes may cause hyperglycemia even if the stress response is sufficiently suppressed and the glucose load is low. Furthermore, 2 of 15 patients (13%) in our study experienced hyperglycemia, even though the patients recruited for our study had relatively mild diabetes and underwent only mildly to moderately invasive surgery. Therefore, when performing intraoperative glucose load in patients with type 2 diabetes, blood glucose levels should be measured during surgery regardless of the severity of diabetes or the degree of surgical invasiveness.

In the present study, there were no significant differences in 3-MH/Cr ratios. This finding is consistent with previous studies conducted in both diabetic and non-diabetic patients (11, 13, 15). However, Sawada *et al*. reported that in non-diabetic patients who received no glucose during major surgery, the 3-MH/Cr ratio measured 6 h after anesthetic induction was significantly greater than that at induction (12). This discrepancy in results may be attributable to the degree of surgical invasiveness, duration of surgical procedure, and/or dose of glucose loading.

Preoperative mental stress, long-term fasting, cessation of antidiabetic drugs, and surgical invasiveness may cause acute metabolic failure such as diabetic ketoacidosis and hyperosmolar hyperglycemic state during the perioperative period in patients with diabetes. In the present study, no laboratory data indicated onset of either condition (16). Preoperative oral rehydration and adequately controlled surgical stress may have contributed to the prevention of these conditions. However, further investigation is needed, as the risk of developing these diseases in connection with anesthesia has not yet been investigated in patients with type 1 diabetes and severe type 2 diabetes.

Volatile anesthetics suppress insulin secretion. We reported that isoflurane inhibited to close adenosine triphosphate-sensitive potassium (K_{ATP}) channels in pancreatic β-cells and impaired insulin secretion and glucose utilization, while propofol did not affect K_{ATP} channels or suppress insulin secretion (17,

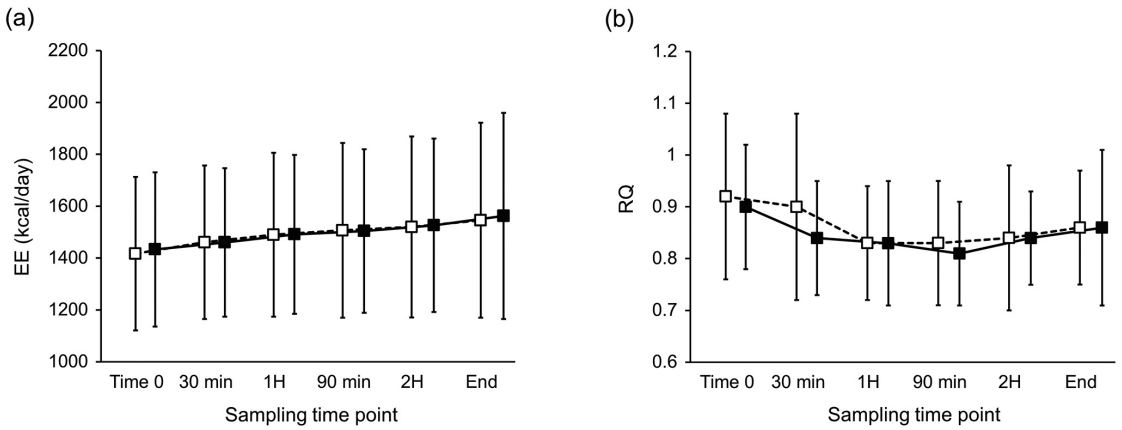

Figure 5. Energy expenditure (EE) (a) and respiratory quotient (RQ) (b) levels of patients in the no glucose (0G) and low-dose glucose (LG) groups from the time of stabilization (Time 0) to the end of surgery (End). Values are presented as the mean ± standard deviation. 0G group (□), LG group (■).

18). Kitamura *et al*. also reported that sevoflurane decreased insulin secretion by opening K_{ATP} channels (19). In addition, a study on patients with diabetes who underwent gynecological surgery demonstrated increased blood glucose levels when anesthesia was maintained with volatile anesthetics instead of intravenous anesthetics (20) ; in the present study, volatile anesthetics were used to maintain anesthesia and some patients experienced hyperglycemia, which may suggest that use of intravenous anesthetics could reduce the likelihood of hyperglycemia in patients with diabetes, especially when glucose loading is performed during surgery.

An optimal blood glucose level that does not adversely affect prognosis in patients with diabetes undergoing surgery has not been determined. However, several studies have investigated the relationship between blood glucose levels during intensive care unit (ICU) stays and hospital or ICU mortality in patients with diabetes. Egi *et al*. reported that ICU mortality increased as mean blood glucose levels increased for non-diabetic patients but not diabetic patients (21). Krinsley *et al*. reported that hospital mortality increased with increasing mean blood glucose levels in both non-diabetic and diabetic patients, but in non-diabetic patients, mortality increased significantly when mean blood glucose level ≥ 7.8 mmol/L, whereas in patients with diabetes, mortality increased significantly when the mean blood glucose level ≥ 10.0 mmol/L (22). In addition, Wernly *et al*. reported that in patients with diabetes, only hypoglycemia not hyperglycemia was associated with increased intra-ICU mortality (23). Intensive insulin therapy was more likely to cause hypoglycemia in patients with diabetes compared to patients without (24). Considering these reports, patients with diabetes may have a higher upper threshold of harmful blood glucose levels than patients without diabetes ; therefore, to avoid causing hypoglycemia, a higher blood glucose level should be maintained in patients with diabetes.

In the present study, there were no significant differences in EE and RQ levels between the groups, similar to previous studies of non-diabetic patients (11, 13). However, these parameters may change based on factors such as increased surgical invasiveness, longer surgery time, and more severe diabetes.

Our study had several limitations. First, the data were collected approximately a decade ago. However, the physiological mechanisms evaluated in this study, including the metabolic response to intraoperative glucose administration and ketone body suppression under remifentanil-induced anesthesia, remain applicable to current anesthetic practice. As the aim of this study was to provide mechanistic insight into perioperative metabolic regulation in patients with type 2 diabetes, rather than to propose a specific clinical protocol, we believe that the findings continue to have relevance in contemporary settings. Second, surgical invasiveness may have differed between the groups because patients underwent different types of surgery. However, both groups demonstrated equal suppression of the stress hormones cortisol and ACTH, which suggests that the differences in surgical procedures had little to no effect on the findings. Third, we based the amount and rate of glucose administration on the protocols of previous studies that did not involve patients with altered glucose metabolism (11, 14) ; thus, the amount of glucose administered during surgery in the present study may not have been appropriate for patients with diabetes. Although marked hyperglycemia was not observed in the present study, given that the patients had diabetes, increasing the frequency of blood glucose measurements might have been preferable in order to detect hyperglycemia at an earlier stage. Few studies have examined the relationship between intraoperative glucose load and metabolism in patients with diabetes. Additional investigation is needed into optimal dosages and administration rates of intraoperative glucose that may be able to control lipid and/or protein catabolism without causing hyperglycemia.

In conclusion, the results of our study indicated that a low intraoperative dose of glucose in patients with type 2 diabetes anesthetized with remifentanil and sevoflurane caused hyperglycemia and did not result in a significant difference between the two groups in their ability to suppress ketogenesis, but a decrease in ketogenesis was observed over time. These results suggest that although low intraoperative doses of glucose in patients with type 2 diabetes may have a positive effect on the suppression of ketogenesis, the risk of hyperglycemia should always be considered, regardless of the glucose load and degree to which surgical stress is suppressed.

COMPETING INTERESTS

All authors declare no competing interests.

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We used ChatGPT (GPT-5, OpenAI, San Francisco) exclusively for improving the clarity and accuracy of our English text. We thoroughly reviewed and verified the accuracy of the suggestions provided by the artificial intelligence before incorporation. All statements related to the hypotheses, interpretations, results, conclusions, limitations, and implications of the study represent our own original ideas and work.

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REFERENCES

1. Bower WF, Lee PY, Kong APS, Jiang JY, Underwood MJ, Chan JCN, van Hasselt CA : Peri-operative hyperglycemia : a consideration for general surgery? Am J Surg 199 : 240-248, 2010
2. Marik PE, Bellomo R : Stress hyperglycemia : an essential survival response! Crit Care 17 : 305, 2013
3. Bosarge PL, Kerby JD : Stress-induced hyperglycemia : is it harmful following trauma? Adv Surg 47 : 287-297, 2013
4. Desborough JP : The stress response to trauma and surgery. Br J Anaesth 85 : 109-117, 2000
5. Dungan KM, Braithwaite SS, Preiser JC : Stress hyperglycaemia. Lancet 373 : 1798-1807, 2009
6. McGirt MJ, Woodworth GF, Brooke BS, Coon AL, Jain S, Buck D, Huang J, Clatterbuck RE, Tamargo RJ, Perler BA : Hyperglycemia independently increases the risk of perioperative stroke, myocardial infarction, and death after carotid endarterectomy. Neurosurgery 58 : 1066-1073, 2006
7. Doenst T, Wijeysundera D, Karkouti K, Zechner C, Maganti M, Rao V, Borger MA : Hyperglycemia during cardiopulmonary bypass is an independent risk factor for mortality in patients undergoing cardiac surgery. J Thorac Cardiovasc Surg 130 : 1144-1150, 2005
8. Winterhalter M, Brandl K, Rahe-Meyer N, Osthaus A, Hecker H, Hagl C, Adams HA, Piepenbrock S : Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanil infusion to intermittent fentanyl. Eur J Anaesthesiol 25 : 326-335, 2008

9. Shinoda T, Murakami W, Takamichi Y, Iizuka H, Tanaka M, Kuwasako Y : Effect of remifentanil infusion rate on stress response in orthopedic surgery using a tourniquet application. BMC Anesthesiol 13 : 14, 2013
10. Taniguchi H, Sasaki T, Fujita H, Takano O, Hayashi T, Cho H, Yoshikawa T, Tsuburaya A : The effect of intraoperative use of high-dose remifentanil on postoperative insulin resistance and muscle protein catabolism : a randomized controlled study. Int J Med Sci 10 : 1099-1107, 2013
11. Kambe N, Tanaka K, Kakuta N, Kawanishi R, Tsutsumi YM : The influence of glucose load on metabolism during minor surgery using remifentanil-induced anesthesia. Acta Anaesthesiol Scand 58 : 948-954, 2014
12. Sawada A, Kamada Y, Hayashi H, Ichinose H, Sumita S, Yamakage M : Effect of intraoperative glucose infusion on catabolism of adipose tissue and muscle protein in patients anesthetized with remifentanil in combination with sevoflurane during major surgery : a randomized controlled multicenter trial. Anesth Analg 123 : 869-876, 2016
13. Fukuta K, Kasai A, Niki N, Ishikawa Y, Kawanishi R, Kakuta N, Sakai Y, Tsutsumi YM, Tanaka K : The effect of 1% glucose loading on metabolism in the elderly patients during remifentanil-induced anesthesia : a randomized controlled trial. BMC Anesthesiol 20 : 143, 2020
14. Yamasaki K, Inagaki Y, Mochida S, Funaki K, Takahashi S, Sakamoto S : Effect of intraoperative acetated Ringer's solution with 1% glucose on glucose and protein metabolism. J Anesth 24 : 426-431, 2010
15. Hasegawa-Moriyama M, Nakahara M, Saito T, Yamada T, Mukaihara K, Masuda M, Matsunaga A, Kanmura Y : The effect of glucose load on catabolism during remifentanil-based anesthesia in patients with diabetes mellitus : a prospective randomized trial. Open J Anesthesiol 5 : 155-162, 2015
16. Kitabchi AE, Miles JM, Umpierrez GE, Fisher JN : Hyperglycemic crises in adult patients with diabetes. Diabetes Care 32 : 1335-1343, 2009
17. Tanaka K, Kawano T, Tomino T, Kawano H, Okada T, Oshita S, Takahashi A, Nakaya Y : Mechanisms of impaired glucose tolerance and insulin secretion during isoflurane anesthesia. Anesthesiology 111 : 1044-1051, 2009
18. Tanaka K, Kawano T, Tsutsumi YM, Kinoshita M, Kakuta N, Hirose K, Kimura M, Oshita S : Differential effects of propofol and isoflurane on glucose utilization and insulin secretion. Life Sci 88 : 96-103, 2011
19. Kitamura T, Sato K, Kawamura G, Yamada Y : The involvement of adenosine triphosphate-sensitive potassium channels in the different effects of sevoflurane and propofol om glucose metabolism in fed rats. Anesth Analg 114 : 110-116, 2012
20. Behdad S, Mortazavizadeh A, Ayatollahi V, Khadiv Z, Khalilzadeh S : The effects of propofol and isoflurane on blood glucose during abdominal hysterectomy in diabetic patients. Diabetes Metab J 38 : 311-316, 2014
21. Egi M, Bellomo R, Stachowski E, French CJ, Hart GK, Hegarty C, Bailey M : Blood glucose concentration and outcome of critical illness : the impact of diabetes. Crit Care Med 36 : 2249-2255, 2008
22. Krinsley JS : Glycemic control, diabetic status, and mortality in a heterogeneous population of critically ill patients before and during the era of intensive glycemic management : six and one-half years experience at a university-affiliated community hospital. Semin Thorac Cardiovasc Surg 18 : 317-325, 2006
23. Wernly B, Jirak P, Lichtenauer M, Franz M, Kabisch B, Schulze PC, Braun K, Muessig J, Masyuk M, Paulweber B, Lauten A, Hoppe UC, Kelm M, Jung C : Hypoglycemia but not hyperglycemia is associated with mortality in critically ill patients with diabetes. Med Princ Pract 28 : 186-192, 2019
24. Krinsley J, Schultz MJ, Spronk PE, van Braam Houckgeest F, van der Sluijs JP, Mélot C, Preiser JC : Mild hypoglycemia is strongly associated with increased intensive care unit length of stay. Ann Intensive Care 1 : 49, 2011