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Impact of intraoperative hyperglycaemia on renal dysfunction after off-pump coronary artery bypass

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Abstract

OBJECTIVES: Acute kidney injury (AKI) is one of the most frequently occurring complications after off-pump coronary artery bypass graft (OPCAB). Hyperglycaemia is a major, potentially modifiable risk factor of adverse outcome after cardiac surgery known to aggravate organ damage. The aim of this study was to address the association between intraoperative glucose concentration and postoperative AKI in patients who underwent OPCAB.

METHODS: The medical records of 880 consecutive patients were retrospectively reviewed. Patients were divided into three groups according to the time-weighted average of intraoperative glucose concentrations (<110, 110–150 and >150 mg/dl), and the incidence of AKI (increase of serum creatinine to >2.0 mg/dl and 2 × most recent preoperative value or a new requirement for dialysis) was compared. Multivariate logistic regression analysis was performed to identify independent risk factors for postoperative AKI.

RESULTS: The incidence of AKI was higher in patients with a glucose level >150 mg/dl than in patients with a glucose level = 110–150 mg/dl [8% (20 of 251) vs 3% (14 of 453), $P = 0.004$]. On multivariate analysis, glucose >150 mg/dl (odds ratio [OR], 2.78; 95% confidence interval [CI], 1.12–6.86, $P = 0.027$), coefficient of variation of glucose (OR, 1.04; 95% CI, 1.01–1.07, $P = 0.027$) and preoperative serum creatinine >1.4 mg/dl (OR, 8.81; 95% CI, 3.90–19.9, $P < 0.001$) were identified as independent risk factors for postoperative AKI.

CONCLUSIONS: Intraoperative glucose concentration >150 mg/dl and increased variability of glucose were independently associated with AKI after OPCAB. Tight intraoperative glycaemic control (<110 mg/dl) does not seem to provide additional benefit in terms of AKI.

Keywords: Acute kidney injury • Hyperglycaemia • Coronary artery bypass • Off pump

INTRODUCTION

Acute kidney injury (AKI) is a frequent complication after cardiac surgery, which is known to have an adverse influence on the patients' outcome [1]. Multiple pathophysiological factors are thought to be involved in the development of AKI, including inflammatory response, embolic events and decreased renal perfusion [2]. Since a substantial part of these factors is related to the use of cardiopulmonary bypass (CPB), off-pump coronary artery bypass surgery (OPCAB) was considered to be advantageous. As yet, definite evidence in favour of OPCAB is lacking and AKI still remains a serious and frequent morbidity after OPCAB [3].

Hyperglycaemia *per se*, regardless of the presence of diabetes mellitus (DM), is one of the major risk factors associated with poor prognosis in cardiac surgical patients [4–6]. As it is a modifiable risk factor, numerous studies have highlighted the importance of strict glycaemic control and its influence on outcome, including renal dysfunction [7–10]. In the current literature, however, recommendations regarding perioperative glycaemic control mostly stem from studies performed in the intensive care units (ICUs) [7–9]. A limited number of studies have focused on the intraoperative period, and no study has specifically investigated the renal outcome primarily. Accordingly, uncertainty exists whether the same recommendations can be applied to different cardiac surgical settings and morbidity endpoints.

During CPB, glucose homeostasis is invariably altered with hypothermia, glucose-containing cardioplegic solutions, inflammatory response and insulin resistance, and these aspects indicate that recommendations regarding glycaemic control need to be surgery specific and cannot be generalized, particularly to cardiac surgeries without CPB. As expected, intraoperative glucose homeostasis was less disturbed in OPCAB compared with its on-pump counterpart [11]. Yet, no comprehensive data exist regarding the relationship between intraoperative blood glucose concentration and postoperative AKI in OPCAB.

The aim of this study was to evaluate the impact of intraoperative glucose concentrations on postoperative AKI in patients who underwent OPCAB.

MATERIALS AND METHODS

Patients and perioperative management

After approval of the Institutional Review Board, we retrospectively reviewed the electronic medical records of 900 consecutive patients who underwent elective, isolated OPCAB between 23 December 2006 and 16 February 2012 at the Cardiovascular Hospital of Yonsei University Health System. The need to obtain written consent from patients was waived by the Institutional Review Board. After careful examination of the clinical data, 20 patients were excluded due to incomplete medical records or conversion to an on-pump procedure.

All patients received standard perioperative care, as described previously [12]. In brief, standard monitoring included a pulmonary artery catheter and transoesophageal echocardiography. Anaesthesia consisted of sufentanil and sevoflurane. All surgical procedures were performed through a median sternotomy, and a cell salvage device was used intraoperatively. After the surgery, all patients were transferred to the ICU.

Data collection

Assessed preoperative variables included demographic data, DM, hypertension, cerebrovascular accident (CVA), chronic obstructive pulmonary disease, New York Heart Association functional classification (NYHA) and congestive heart failure (CHF; NYHA III or IV), left ventricular ejection fraction (LVEF), unstable angina, history of recent myocardial infarction (MI, within 1 month), chronic renal failure (serum creatinine >1.4 mg/dl), anaemia (haemoglobin <13 g/dl for male and <12 g/dl for female), medications and the corresponding EuroSCORE of each patient [13].

Assessed operative variables included the number of grafts performed, duration of the surgery, insulin requirement, fluid balance and transfusion requirement.

Postoperative AKI was defined on the basis of the current Society of Thoracic Surgeons (STS) definitions as one or more of the following: (i) increase of serum creatinine to >2.0 mg/dl, and 2 × most recent preoperative creatinine level, (ii) a new requirement for dialysis postoperatively [14]. Other assessed major morbidity endpoints were 30-day mortality, deep sternal wound infection, permanent stroke, haemostatic re-exploration, prolonged ventilator care >48 h and postoperative MI (an increase in troponin-T 10 times or greater over upper normal limit within 48 h occurring from a normal baseline value, or a newly developed Q-wave or left bundle branch block on electrocardiogram, or angiographically documented new graft or native coronary artery occlusion, or imaging evidence of new loss of viable myocardium or new regional wall motion abnormality) [15]. The lengths of ICU and hospital stay were also assessed.

Glucose variables and control

In all patients, intraoperative glycaemic control and measurements of serum glucose concentrations were performed as per a standard protocol of our institution. Maintaining intraoperative serum glucose concentrations within a target range of 100–180 mg/dl with intermittent doses of intravenous insulin (Humalog®, regular insulin, RI) or 50% dextrose in water (DW) was attempted. When the glucose concentration was >180 mg/dl, we administered 3 units of RI for every 50 mg/dl increment of glucose. When the glucose concentration was <100 mg/dl, we administered 5 ml of 50% DW for every 10 mg/dl decrement of glucose. Serum glucose concentration was rechecked 30 min after each treatment.

Intraoperative serum glucose concentrations were serially collected at least for the following six time points in all patients; before and after induction of anaesthesia, during composite Y-graft formation between a left internal mammary artery and a radial artery, at completion of coronary artery anastomoses, sternum closure and upon arrival in the ICU. The time-weighted average of the glucose concentrations (TWA-Glcs) for each patient was calculated as the area under the curve divided by the time from first to last measurement. Patients were then divided into three groups according to their TWA-Glc (<110, 110–150 and >150 mg/dl) [9, 16]. In addition, coefficient of variation of glucose as a measure of glucose variability was calculated as standard deviation of glucose × 100/mean of glucose. Serum glucose concentration was determined from arterial blood gas analyzer by the glucose oxidase method.

Study endpoint

The primary endpoint was to compare the incidence of postoperative AKI in relation to the distribution of the TWA-Glc (<110, 110–150 and >150 mg/dl). The secondary endpoint of this study was to evaluate the independent risk factors for postoperative AKI.

Statistical analysis

All analyses were performed with SPSS 15.0 (SPSS, Inc., Chicago, IL, USA). Intergroup comparisons were made with analysis of variance for continuous data with normal distribution, Kruskal–Wallis test for discrete, ordinal data and continuous data without normal distribution and χ^2 test or Fisher's exact test for categorical variables. Fisher's exact test was used when there were >20% of cells with an expected value of <5 in a contingency table. To identify independent predictors of a composite outcome, a logistic regression model was used. Potential confounding factors for analysis were selected on the basis of a literature review. The variables included demographic data (age, gender and body mass index), known risk factors with cardiac surgery (duration of the surgery, DM, hypertension, LVEF <35%, recent MI and preoperative serum creatinine >1.4 mg/dl). First, univariate logistic regression analysis was performed to identify significant predictors of composite outcome using variables. All of the variables that had a *P*-value of <0.1 in univariate logistic regression were further introduced to multivariate logistic regression analysis along with variables, including demographic data and known risk factors. Odds ratios (ORs) and associated 95% confidence interval (CI) were estimated. Continuous variables are shown as mean ± SD or median [interquartile range], and categorical variables are given as number (percentage). A *P*-value of <0.05 was considered significant.

RESULTS

Eight hundred and eighty patients were divided into three groups according to their TWA-Glc (<110 mg/dl; *n* = 176, 110–150 mg/dl;

Table 1: Preoperative characteristics

	TWA-Glc <110 mg/dl (*N* = 176)	TWA-Glc=110–150 mg/dl (*N* = 453)	TWA-Glc >150 mg/dl (*N* = 251)	*P*-value
Gender (M/F)	133/43	310/143	154/97[a]	0.008
Age (year)	66 ± 10	65 ± 9	66 ± 8	0.440
Body mass index (kg/m^2)	24.6 ± 4.3	24.5 ± 2.9	24.4 ± 3.5	0.833
Diabetes	31 (18)	126 (28)[a]	205 (82)[a,b]	<0.001
Hypertension	113 (64)	308 (68)	189 (75)[a]	0.034
History of cerebrovascular accident	31 (18)	47 (10)[a]	27 (11)	0.034
Chronic obstructive pulmonary disease	3 (2)	10 (2)	2 (1)	0.401
Congestive heart failure	13 (8)	38 (9)	28 (12)	0.360
Unstable angina	64 (36)	136 (30)	79 (32)	0.307
Myocardial infarction within 1 month	39 (22)	83 (18)	38 (15)	0.179
Preoperative ejection fraction <35%	14 (8)	22 (5)	19 (8)	0.221
Preoperative serum creatinine >1.4 mg/dl	15 (9)	39 (9)	26 (10)	0.710
Anaemia	73 (42)	155 (34)	96 (38)	0.204
EuroSCORE	3 [2–5.5]	3 [2–5]	4 [2–5]	0.400
Preoperative medications				
Aspirin	137 (79)	381 (84)	212 (85)	0.220
Clopidogrel	118 (68)	340 (75)	175 (70)	0.129
Beta-blocker	100 (58)	295 (65)	174 (65)[a]	0.043
Calcium channel blocker	78 (45)	211 (47)	126 (50)	0.505
Angiotension-converting enzyme inhibitor	56 (32)	131 (29)	86 (34)	0.301

Values are mean ± SD or median [IQR] or number of patients (percentage).
TWA-Glc: time-weighted average of intraoperative serum glucose concentrations; Anaemia: haemoglobin <13 g/dl for male and <12 g/dl for female.
[a]*P* < 0.05 vs TWA-Glc <110 mg/dl.
[b]*P* < 0.05 vs TWA-Glc = 110–150 mg/dl.

Table 2: Operative data

	TWA-Glc <110 mg/dl (*N* = 176)	TWA-Glc=110–150 mg/dl (*N* = 453)	TWA-Glc >150 mg/dl (*N* = 251)	*P*-value
Duration of the surgery (min)	306 ± 57	308 ± 49	316 ± 53	0.087
Number of grafts	3 [3–4]	3 [3–4]	3 [3–4]	0.056
Coefficient of variation of glucose	11.9 [8.5–19.4]	13.8 [8.9–18.7]	14.2 [9.6–20.1]	0.227
Intraoperative use of insulin	12 (7)	35 (8)	19 (8)	0.943
Insulin dose (U)	4 [3.5–5]	5 [4–5.5]	4 [3–5]	0.371
Intraoperative crystalloid (ml)	2349 ± 960	2497 ± 1091	2429 ± 956	0.277
Intraoperative colloid (ml)	1027 ± 370	1020 ± 421	1013 ± 391	0.938
Urine output (ml)	570 [343–950]	530 [320–820]	520 [335–765]	0.281
Number of patients required transfusion	43 (26)	108 (24)	62 (25)	0.938
Salvaged blood (ml)	160 [120–240]	166 [120–250]	150 [120–240]	0.695

Values are mean ± SD or median [IQR] or number of patients (percentage).
TWA-Glc: time-weighted average of intraoperative serum glucose concentrations.

n = 453 and >150 mg/dl; *n* = 251). Sixteen patients had at least one episode of intraoperative hypoglycaemia (glucose concentration <65 mg/dl), and none of the patients had TWA-Glc of <65 mg/dl.

Patients' characteristics and operative data

Patients' characteristics are listed in Table 1 and were all similar among the groups, except the following. The proportion of female patients was higher in the TWA-Glc >150 mg/dl group than the TWA-Glc <110 mg/dl group (*P* = 0.006). Significantly more patients in the TWA-Glc >150 mg/dl group had DM compared with those in the TWA-Glc <110 mg/dl and TWA-Glc = 110–150 mg/dl groups (*P* < 0.001). In addition, significantly more patients in the TWA-Glc = 110–150 mg/dl group had DM compared with those in the TWA-Glc <110 mg/dl group (*P* = 0.024). History of hypertension was more frequent in the TWA-Glc >150 mg/dl group than the TWA-Glc <110 mg/dl group (*P* = 0.039). More patients in the TWA-Glc <110 mg/dl group had a history of CVA compared with those in the TWA-Glc = 110–150 mg/dl group (*P* = 0.039). The number of patients receiving β-blockers was significantly higher in the TWA-Glc >150 mg/dl group compared with the Glc <110 mg/dl group (*P* = 0.039). The mean haemoglobin A1c (HbA1c) of the patients with DM was 7.3 ± 1.5%. HbA1c was significantly higher in the TWA-Glc >150 mg/dl group (7.6 ± 1.6%) compared with those of the TWA-Glc <110 mg/dl (6.6 ± 1.2%, *P* = 0.006) and TWA-Glc = 110–150 mg/dl groups (6.8 ± 1.2%, *P* = 0.006).

Table 3: Comparison of postoperative outcomes

	TWA-Glc <110 mg/dl (*N* = 176)	TWA-Glc = 110–150 mg/dl (*N* = 453)	TWA-Glc >150 mg/dl (*N* = 251)	*P*-value
Renal dysfunction	7 (4)	14 (3)	20 (8)[a]	0.012
New requirement for dialysis	6 (3)	10 (2)	11 (4)	0.265
Postoperative myocardial infarction	2 (1)	6 (1)	3 (1)	1.000
Permernant stroke	1 (1)	3 (1)	4 (2)	0.462
Haemostatic reoperation	4 (1)	2 (1)	6 (2)	0.287
Wound infection	7 (4)	5 (1)	11 (4)[a]	0.014
Prolonged intubation over 48 h	5 (3)	12 (3)	8 (3)	0.919
Mortality	1 (1)	3 (1)	3 (1)	0.785
Duration of ICU stay (day)	3 [3–4]	3 [3–4]	3 [3–4]	0.142
Duration of hospitalization (day)	10 [9–15]	10 [9–13]	11 [9–15]	0.060

Values are median [IQR] or number of patients (percentage).
TWA-Glc: time-weighted average of intraoperative serum glucose concentrations.
[a]*P* < 0.05 vs TWA-Glc = 110–150 mg/dl.

Operative data are listed in Table 2 and were all similar among the groups.

Postoperative outcomes

Postoperative outcome variables are listed in Table 3. The incidence of AKI was significantly higher in patients of the TWA-Glc >150 mg/dl group compared with those of the TWA-Glc = 110–150 mg/dl group (8 vs 3%, *P* = 0.012). Patients in the TWA-Glc <110 mg/dl and TWA-Glc = 110–150 mg/dl groups showed similar incidences of AKI. The incidence of new requirement for dialysis was similar among the three groups. Significantly more patients in the TWA-Glc >150 mg/dl group developed deep sternal wound infection compared with those in the TWA-Glc = 110–150 mg/dl group (4 vs 1%, *P* = 0.015). Other outcome variables including the lengths of ICU and hospital stay were similar among the groups.

Risk factors of acute kidney injury

In univariate logistic regression analysis, TWA-Glc >150 mg/dl (OR, 2.72; 95% CI, 1.35–5.47, *P* = 0.005), coefficient of variation of glucose (OR, 1.05; 95% CI, 1.02–1.08; *P* < 0.001), age (OR, 1.06; 95% CI, 1.02–1.11, *P* = 0.006), DM (OR, 4.76; 95% CI, 2.30–9.83; *P* < 0.001), hypertension (OR, 2.68; 95% CI, 1.11–6.45; *P* = 0.028), anaemia (OR, 3.95; 95% CI, 2.02–7.74; *P* < 0.001), CHF (OR, 2.96; 95% CI, 1.30–6.74; *P* = 0.010), history of CVA (OR, 2.18; 95% CI, 1.01–4.70; *P* = 0.048) and preoperative serum creatinine >1.4 mg/dl (OR, 12.4; 95% CI, 6.35–24.1; *P* < 0.001) were identified as risk factors of AKI. After multivariate logistic regression analysis, TWA-Glc >150 mg/dl (OR, 2.78; 95% CI, 1.12–6.86; *P* = 0.027), coefficient of variation of glucose (OR, 1.04; 95% CI, 1.01–1.07; *P* = 0.027) and preoperative serum creatinine >1.4 mg/dl (OR, 8.81; 95% CI, 3.90–19.9; *P* < 0.001) remained as independent risk factors of AKI after OPCAB (Table 4).

Table 4: Multivariate logistic regression analysis for independent risk factors of a postoperative acute kidney injury

	OR	95% CI	P-value
TWA-Glc >150 mg/dl	2.78	1.12–6.86	0.027
CV of glucose	1.04	1.01–1.07	0.027
Age	1.04	0.99–1.10	0.127
Diabetes	2.11	0.83–5.36	0.115
Hypertension	1.22	0.45–3.29	0.693
Anaemia	1.34	0.60–2.99	0.472
Preoperative Cr >1.4 mg/dl	8.81	3.90–19.9	<0.001
Congestive heart failure	1.40	0.54–3.63	0.485
History of CVA	1.63	0.66–4.05	0.293

TWA-Glc: time-weighted average of intraoperative serum glucose concentrations; CV: coefficient of variation; Anaemia: haemoglobin <13 g/dl for male and <12 g/dl for female; Cr: serum creatinine; CVA: cerebrovascular accident.

DISCUSSION

In this study, evaluating the relationship between intraoperative blood glucose concentrations and AKI after OPCAB, TWA-Glc >150 mg/dl and high glycaemic variability were identified as independent risk factors of AKI along with the presence of preoperative chronic renal failure.

Hyperglycaemia is well known to aggravate kidney injury by the following multiple mechanisms. Hyperglycaemia can increase oxidative stress and results in amplification of ischaemia-reperfusion injury [17]. Celluar glucose overload also induces mitochondrial dysfunction and kidney injury [18]. Inflammation is an important factor for the development of kidney injury, and hyperglycaemia was reported to increase inflammatory cytokines such as interleukin-6, tumour necrosis factor-α and interleukin-18 [19]. In addition, endothelial dysfunction induced by hyperglycaemia can contribute to the pathogenesis of kidney injury [20].

Being a potentially modifiable risk factor, Van den Berghe *et al.* [7] first investigated the effects of intensive insulin therapy in the surgical ICU, and they reported that tight glycaemic control (80–110 mg/dl) reduced mortality and the incidence of renal impairment compared with conventional glycaemic control (180–200 mg/dl). A subsequent study by the same authors in the medical ICU also showed reduced incidence of renal impairment [8]. In a more detailed secondary analysis of these two studies regarding

the kidney, the incidence of renal impairment was found to be lowest in patients with glucose <110 mg/dl and highest in those with glucose >150 mg/dl [9]. However, subsequent studies to re-affirm the effect of tight glycaemic control have demonstrated conflicting results. Two recent trials examining the outcome of tight glycaemic control (80–110 mg/dl) vs conventional protocol (140–180 mg/dl) in the ICU were prematurely aborted for safety issues related to the increased incidence of severe hypoglycaemia in patients who received intensive insulin therapy [21, 22]. A recent meta-analysis also showed no significant benefit in terms of need for renal replacement therapy either with very tight (≤110 mg/dl) or moderately tight (≤150 mg/dl) glycaemic control in patients requiring ICU care [23].

In the surgical setting, although evidence is limited, sustained hyperglycaemia during the intraoperative period has also been observed to influence the outcome including renal dysfunction after cardiac surgery with CPB [4–6]. In contrast to the results of the previous studies in the ICU setting, however, a somewhat higher glucose level (>200 mg/dl) has been shown to be associated with poor prognosis [4, 6]. Moreover, Duncan *et al.* [6] reported no improved renal dysfunction with the glucose level of near normoglycaemia (<140 mg/dl) compared with the glucose level >200 mg/dl. These conflicting results may be attributable to the facts that none of these studies investigated postoperative renal dysfunction primarily, and different definitions of renal morbidity were used complicating comparisons between the studies.

By avoiding CPB, reducing the inflammatory response and nephrotoxins theoretically could result in less risk of postoperative renal dysfunction. However, OPCAB is also a major surgical procedure with a significant stress response. Moreover, displacement of the heart during the coronary anastomoses can impair ventricular filling, and the resultant low cardiac output makes the patients undergoing OPCAB prone to renal hypoperfusion. Accordingly, OPCAB carries a significant risk of postoperative kidney injury. As the current study first addressed the above-mentioned issues in OPCAB, we could observe that an intraoperative TWA-Glc >150 mg/dl was associated with the increased incidence of postoperative renal dysfunction following OPCAB, regardless of the presence of DM, while strict normoglycaemia <110 mg/dl provided neither harm nor added benefit. Although significanlty more patients of TWA-Glc >150 mg/dl had DM, it did not remain an idependent risk factor for adverse outcome after multivariate regression analysis. As expected, the cut-off glucose level associated with outcome of the current study is inconsistent with the results of previous studies involving cardiac surgeries using CPB.

Plausible explanations for the inconsistency are as follows. First, factors involved in disturbed glucose homeostasis during cardiac surgeries using CPB and OPCAB are different, which include CPB-related factors such as hypothermia, insulin resistance and administration of glucose-containing cardioplegic solutions. Secondly, assessed renal morbidities in previous studies were mainly postoperative renal replacement therapy [4, 6]. Control of hyperglycaemia to a certain level, e.g. ≤150 mg/dl, might be beneficial for a milder form of kidney injury as shown in the secondary analysis of the Leuven study [9]. Even a transient, small increase in the postoperative serum creatinine level was also associated with poor long-term outcome [1]. In the current study, there was no difference in postoperative renal replacement therapy among different intraoperative glycaemic profiles. It can be speculated that hyperglycaemia alone has limited influence on the development of severe kidney injury. A larger, prospective trial is needed to clarify this issue. Finally, in addition to high mean glucose concentrations, glycaemic variability may influence the development of postoperative renal dysfunction. Acute glucose fluctuation has been shown to enhance apoptosis and oxidative stress [24], and recent evidence suggests that increased glycaemic variability is associated with poor outcome in the critically ill [25]. In the current study, high glycaemic variability was also an independent risk factor for postoperative renal dysfunction, along with increased mean of glucose concentrations. Increased glycaemic variability may predispose the patients with similar mean glucose level to episodes of hypo- or hyperglycaemia or, conversely, increased/decreased mean glucose level with minimal glycaemic variability may reflect sustained hyperglycaemia/hypoglycaemia. Thus, comparing relevant glucose concentrations between the studies possessing different levels of glycaemic variability should be done cautiously. Continuous insulin infusion instead of intermittent bolus administration may be advantageous in terms of glycaemic variability, which would theoretically decrease the risk of developing episodes of concealed dangerous hypoglycaemia, yet it remains to be proven.

The limitations of this study are as follows. Although all the data including the glucose levels were collected prospectively and comprehensive inclusion of possible confounding risk factors for postoperative renal dysfunction encompassing intraoperative haemodynamic variables was done, this was a retrospective study subject to the limitations inherent to such an analysis. Thus, it is unclear whether hyperglycaemia of >150 mg/dl is a risk factor for postoperative renal dysfunction or merely an indicator of severity of illness or stress response. In addition, patients' characteristics including gender, history of diabetes, hypertension, preoperative beta-blocker medication and CVA were different between the groups. The interaction between the variables, for example, diabetes and intraoperative hyperglycaemia, could result in these differences; however, the inhomogeneity among the groups may also reflect selection bias. Finally, we did not calculate the time-weighted average and coefficient of variation of glucose concentrations because of irregular and wide intervals of the measurements. Glycaemic profile in the ICU may be an important confounding factor in this study.

In conclusion, intraoperative TWA-Glc >150 mg/dl and high glycaemic variability were independent risk factors of renal dysfunction after OPCAB. Tight normoglycaemic intraoperative TWA-Glc (<110 mg/dl) was not associated with either harm or benefit in terms of renal morbidity compared with TWA-Glc between 110 and 150 mg/dl, which merits further investigation.

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eComment. Intraoperative glycaemic control in cardiac surgical patients

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We read with great interest the article by Song and coworkers [1]. We would like to congratulate the authors on their well-designed study with an important message that intraoperative hyperglycaemia >150 mg/dl and high glycaemic variability were independent risk factors of renal dysfunction after off-pump coronary artery bypass surgery, but would also like to add some comments.

Intraoperative hyperglycaemia, which occurs frequently in cardiac surgical patients with and without diabetes, has been shown to be associated with increased morbidity and mortality. These patients are exposed to significant adverse consequences including surgical site infection, neurologic, renal, and cardiac complications as well as longer intensive care unit and hospital stay. In recent years, glycaemic control during coronary artery bypass surgery and all cardiac surgical procedures has been the focus of interest. However, an optimal value for glycaemic control has yet to be fully elucidated. Moreover, there are clear potential adverse consequences of tight glycaemic control such as hypoglycaemia [2].

In cardiac surgical patients, a number of observational studies have specifically investigated the effect of intraoperative glycaemic control on outcomes. These studies have suggested an association between greater glycaemic control and improved outcomes. While prospective randomized trials have been promising, the results have been less robust [2-4].

Successful glycaemic control requires a multidisciplinary approach, which includes representation from nursing, anesthesiology, pharmacy, surgery, and endocrinology. All studies have shown that maintaining serum glucose levels <180 mg/dl reduces morbidity and mortality, while the effects of more aggressive control on clinical outcomes are less clearly defined [2].

Recently, Lazar and colleagues [3] performed a prospective, randomized trial in diabetic patients undergoing coronary artery bypass surgery to determine whether tight glycaemic control (90-120 mg/dl) would result in more optimal clinical outcomes than a more moderate glycaemic control (121-180 mg/dl). In their study, patients with tight glycaemic control had a higher incidence of hypoglycaemic events, but this did not result in any clinical sequelae. Moreover, tight glycaemic control did not result in any significant improvement in clinical outcomes that could not be achieved with more moderate control.

In a prospective randomized controlled study, Desai and colleagues [4] demonstrated that maintenance of blood glucose in a liberal range (121-180 mg/dl) after coronary artery bypass surgery led to similar outcomes compared with a strict target range (90-120 mg/dl) and was superior in glucose control and target range management. On the basis of the results of this study, a target blood glucose range of 121-180 mg/dl was recommended for patients after coronary artery bypass surgery, as advocated by the Society of Thoracic Surgeons [2,4].

Although we agree that the optimal range for glycaemic control in cardiac surgical patients is 120-180, we should all remember that the exact value for optimal glycaemic control is still unknown and the subject of numerous studies.

Conflict of interest: none declared

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