Original Article

Morning or Afternoon Scheduling for Elective Coronary Artery Bypass Surgery: Influence of Longer Fasting Periods from Metabolic and Hemodynamic Perspectives

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ABSTRACT

Background: Prolonged preoperative fasting may worsen postoperative outcomes. Cardiac surgery has higher perioperative risk, and longer fasting periods may be not well-tolerated. We analysed the postoperative metabolic and hemodynamic variables in patients undergoing elective coronary artery bypass grafting (CABG) according to their morning or afternoon schedule.

Methods: Single-centre retrospective study at University teaching hospital (1-year data collection from electronic medical records). Using a mixed-effects linear regression model adjusted for several covariates, we compared metabolic (lactatemia, pH, and base deficit [BD]) and haemodynamic values (patients on vasoactive support, and vasoactive inotropic score [VIS]) at 7 prespecified time-points (admission to intensive care, and 1st, 3rd, 6th, 12th, 18th, and 24th postoperative hours).

Results: 339 patients ($n = 176$ morning, $n = 163$ afternoon) were included. Arterial lactatemia and BD were similar (overall $P = 0.11$ and $P = 0.84$, respectively), while pH was significantly lower in the morning group (overall $P < 0.05$; mean difference 0.01). Postoperative urine output, fluid balance, mean arterial pressure, and central venous pressure were similar ($P = 0.59$, $P = 0.96$, $P = 0.58$ and $P = 0.53$, respectively). A subgroup analysis of patients with diabetes ($n = 54$ morning, $n = 45$ afternoon) confirmed the same findings. The VIS values and the proportion of patients on vasoactive support was higher in the morning cases at the 18th ($P = 0.002$ and p=0.04, respectively) and 24th postoperative hours ($P = 0.003$ and $P = 0.04$, respectively). Mean intensive care length of stay was 1.94 ± 1.36 days versus 2.48 ± 2.72 days for the afternoon and morning cases, respectively ($P = 0.02$).

Conclusions: Patients undergoing elective CABG showed similar or better metabolic and hemodynamic profiles when scheduled for afternoon surgery.

Keywords: Acidosis, base excess, cardiac surgery, intensive care, lactates, preoperative fasting

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INTRODUCTION

The enhanced recovery after surgery (ERAS) programs have been implemented for a few decades,[1] and after initial challenges, the benefits of these programs have been clearly demonstrated, including in the

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cardiac surgery setting.[2] Among the ERAS bundles, avoidance of prolonged preoperative fasting is a mainstay.[3,4] Better patient outcomes have been shown using shorter preoperative fasting periods, especially in patients undergoing major surgery, with several possible physiological mechanisms.[3,5] The ERAS programs have also introduced preoperative carbohydrate drinks being given a couple of hours before surgery[6]; together with a shorter fasting preoperative period, this approach has demonstrated benefits at multiple levels.[7]

However, in real-world practice at institutions where such ERAS programs are not running, patients scheduled for elective surgery are usually fasted for at least 6 to 8 h preoperatively to lower the risks of pulmonary aspiration during anesthesia induction.[8] Further, several studies have demonstrated that the real-world fasting duration is much longer and approaches or even exceeds 12 h.[9,10] For instance, a study in older adults undergoing elective surgery under spinal anesthesia demonstrated that fasting times are far longer than recommended, and are significantly higher in cases scheduled in the afternoon (12.7 and 15.5 h for liquids and food, respectively) as compared to morning ones (9.5 and 12 h, respectively). Notably, afternoon cases showed more frequent electrocardiogram changes and lower body temperature.[11] To a variable extent, it has been shown that such prolonged preoperative fasting may increase the incidence of adverse effects (i.e., as intraoperative hemodynamic instability, postoperative delirium, or patient discomfort), resulting in longer length of stay (LOS).[12]

Cardiac surgery is not an exception to the issue of prolonged fasting; in fact, in this setting, the decision on the timing regarding preoperative fasting is even more complex. As cardiac surgery cases are long by definition, the schedule is usually divided into morning or afternoon cases. Nonetheless, inversion of the morning and afternoon cases may frequently happen as a result of unforeseen factors, such as temporary unavailability of requested blood products or changes from elective to urgent schedule due to new-onset complications (e.g., acute chest pain overnight). Hence, it is common practice to fast patients from midnight, regardless of the operating room schedule. Consequently, patients undergoing cardiac surgery in the afternoon may experience prolonged fasting periods that could be longer than 12 hours. Considering these patients' comorbidities, including a relatively high incidence of diabetes and metabolic alterations, the impact of prolonged fasting may have a deleterious metabolic impact in the postoperative period. However, the evidence in this regard remains conflicting, and it is unclear whether cases scheduled in the afternoon have an increased perioperative risk. For instance, Ranucci *et al*.[26] reported higher morbidity and 30-day mortality in the afternoon cases, which showed also higher lactate values at intensive care unit (ICU) admission. Conversely, another study showed lower major adverse cardiac events in the afternoon as compared to the morning group in patients undergoing aortic valve replacement.[13] Finally, several other studies demonstrated no evidence that time of surgery influences mortality and myocardial injury.[14-16]

We previously demonstrated no clinically significant differences in the first 24 h between patients undergoing on- or off-pump coronary artery bypass grafting (ONCABG or OPCABG, respectively) from metabolic, hemodynamic, and respiratory profiles.[17,18] Using the same database, we evaluated metabolic differences during the initial 24 h after ICU admission dividing patients into two groups according to surgical timing. We primarily hypothesized that afternoon cases would have worse postoperative metabolic profiles and greater incidence of postoperative acidosis as compared to the morning ones. We also planned to evaluate the subgroup of patients with diabetes, with the hypothesis that this group may have had a greater impact from prolonged fasting.

MATERIALS AND METHODS

We conducted a retrospective single-centre study using a database of patients receiving cardiac surgery with ONCABG or OPCABG at the Oxford University Hospitals NHS Trust (Oxford, UK). The local ethics committee waived the need for informed consent as the data were collected retrospectively and with an anonymized approach. We collected data on adult patients electively scheduled for isolated coronary artery bypass grafting (CABG) and admitted postoperatively to the cardiothoracic ICU over 1 year, starting from the time of introduction of an electronic medical records (EMRs) system.

We excluded patients undergoing nonelective cardiac surgery, those readmitted to theater in the first postoperative day or those requiring preoperative organ support (i.e., the presence of intra-aortic balloon pump, infusion of vasoactive pharmacological drugs, renal replacement therapy, or non-invasive ventilation), and patients with at least moderate liver disease. Patients received ONCABG or OPCABG according to the surgeons' preferences (two surgeons used both techniques, whereas others were used to performing only ONCABG).

Data were extracted and stored in an Excel file with a password for data protection. The results of the comparison of postoperative metabolic, hemodynamic, and respiratory effects have been previously published.[17,18] As mentioned, in the present study, we analyzed the population of patients undergoing CABG according to the timing of their operations, dividing patients into "morning" and "afternoon" groups, regardless of the surgical technique for grafting. The length of the fasting period was not recorded. Patients did not receive supplementation with carbohydrate loading or of any other kind. We further performed a subgroup analysis focusing on patients with past medical histories of diabetes with the hypothesis that metabolic repercussions of prolonged fasting would have been greater in this group of patients.

Database organization

Baseline data were collected in various fields:

- *Demographic information*: height, weight, body mass index (BMI), age, sex.
- *Preoperative conditions*: comorbidities (EuroScore II, diabetes, hypercholesterolemia, hypertension, smoking history, creatinine), and left and right ventricular (LV and RV) function with LV systolic function classified as (A) normal (ejection fraction [EF] >55%), (B) mildly impaired (EF: 46% to 55%), (C) moderately impaired (EF: 36% to 45%), or (D) severely impaired (EF <35%).
- *Results of arterial blood gas (ABG) at anesthesia induction*: lactate and chloride (both in mmol/L), as well as pH and base deficit (BD) (both as absolute values).
- *Surgical specifics*: number of coronary grafts performed.

At the time of the study, we had no EMR systems accounting the intraoperative management; hence, we could not truthfully report such data. At our institution, propofol or midazolam were used for the induction, whereas volatile agents (isoflurane) were the preferred method for the maintenance of cardiac anesthesia (propofol infusion was used more rarely), and the sole opioid used at the time of this study was fentanyl (administered in boluses); pancuronium was the muscle relaxant of choice. Intraoperative warming was achieved with both a heating system for intravenous fluids and a warming mattress under the patient.

We recorded several variables after ICU admission: ABG with lactate, BD, pH (alpha-stat method), and chloride levels; $PaCO_2$; central venous pressure (CVP), mean arterial pressure (MAP), and hemodynamic support; fluid administration, urine output, and hourly fluid balance; and administration of sodium bicarbonates and diuretics. We collected this set of variables starting at ICU admission and at six subsequent time points (1st, 3rd, 6th, 12th, 18th, and 24th postoperative hours) using the closest available value recorded in the EMRs. Regarding the postoperative pharmacological cardiovascular support, we analyzed at each time point the number of patients requiring any vasoactive support and also the mean vasoactive inotropic score (VIS) using the following formula[19,20]:

$$VIS = (100 \times \text{norepinephrine } [\mu g \cdot kg^{-1} \cdot min^{-1}]) + (100 \times \text{epinephrine } [\mu g \cdot kg^{-1}\, min^{-1}]) + (\text{dopamine } [\mu g \cdot kg^{-1} \cdot min^{-1}]) + (\text{dobutamine } [\mu g \cdot kg^{-1} \cdot min^{-1}]) + (50 \times \text{levosimendan } [\mu g \cdot kg^{-1} \cdot min^{-1}]) + (10 \times \text{milrinone } [\mu g \cdot kg^{-1} \cdot min^{-1}]) + (10.000 \times \text{vasopressin [units} \cdot kg^{-1} \cdot min^{-1}])$$

Finally, we collected data on the LOS and ICU mortality.

Statistical analysis

The statistical analysis was performed using Stata Release 14. We compared baseline variables according to the timing of surgery with Student's *t*-test for continuous variables, presenting the results as mean with a 95% confidence interval (CI) or standard deviation and *P* value.

The categorical parameters are reported as percentages and CIs, and between-group comparisons were performed with the Chi-square test with Yates' correction. Temporal changes of continuous parameters that were recorded at multiple time points during the first 24 postoperative hours were compared using mixed effects linear regression models (using time as a random effect for clustering of repeated measures). We used separate models, one for each parameter of interest, and we adjusted all models for all available covariates and the baseline data of the parameter analyzed. The parameters added as covariates included baseline data and comorbidities, preoperative ABG values, and MAP, CVP, and vasoactive drug doses at all time points. For the pH, we also added to the model the values of chloride levels gathered from ABG. At least one covariate was missing in 27% of the included patients. As these were missing at random, and to avoid a reduction in model efficiency, missing values were imputed using multiple imputations by chained equations, and the missing values were mainly for BMI, number of grafts, or one comorbidity. Twenty imputed datasets were created. We used the mi package of Stata Release 14 for performing multiple imputations.

RESULTS

Our database was comprised 363 patients who had undergone isolated CABG, and 24 patients were excluded (*n* = 14, emergency surgery; *n* = 3, preoperative use of intra-aortic balloon pump; *n* = 2, early reoperation due to suspected bleeding; *n* = 4, mini-invasive surgical approach; *n* = 1, history of dialysis), leaving 339 patients for analysis. Of these, 176 (51.9%) were operated in the morning, and the remaining 163 (48.2%) were scheduled in the afternoon. There was no difference in the proportion of patients undergoing OPCABG between morning and afternoon cases (114/176 vs. 101/163, $P = 0.65$). The characteristics of the two groups were similar, although a higher number of grafts were performed in the morning cases (2.9 [2.8, 3.0]) versus in the afternoon (2.7 [2.5, 2.8]) [$P = 0.03$, Table 1].

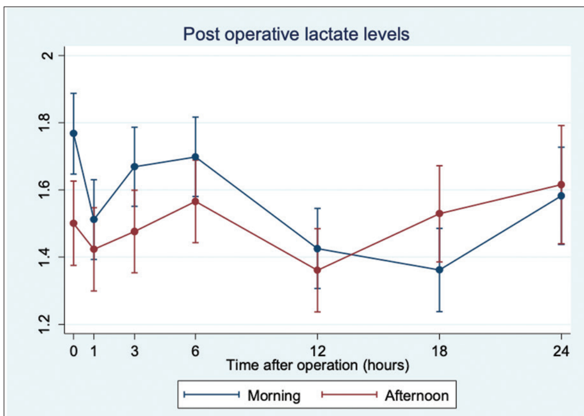
Lactate (Figure 1, including differences between time points) and BD (Figure 2, including differences between time points) were comparable between groups ($P = 0.11$ and $P = 0.84$, respectively). The pH was lower in the afternoon group in the overall comparison ($P = 0.0046$, Figure 3, including differences between time points).

Postoperative urine output and fluid balance were similar between groups ($P = 0.59$ and $P = 0.96$, respectively) and are provided as Supplemental Material. The exclusion of patients with missing covariate information from the mixed effects linear regression models produced similar results.

With regard to hemodynamics, we found similar MAP and CVP values when comparing the morning and afternoon cases, both overall and in all single time points ($P = 0.58$ and $P = 0.53$, respectively; Supplemental Material). The percentage of patients requiring vasoactive support calculated on the overall population was similar between groups until the 12th postoperative hour but significantly higher in the morning cases at the 18th and 24th postoperative hours [$P = 0.04$ in both cases, Table 2]. Similarly, we found significantly higher VIS values in the morning group at the same time points (18th postoperative hour, $P = 0.003$; 24th postoperative hour, $P = 0.003$; Table 3).

The mean LOS was 1.94 ± 1.36 days versus 2.48 ± 2.72 days for the afternoon and morning cases, respectively ($P = 0.02$). We observed similar mortality in the two groups: two patients died after being operated on as morning cases (1.1%) and the other two after being operated on as afternoon cases (1.2%, $P = 1.00$). No significant differences were found regarding postoperative myocardial infarction, use of renal replacement therapy, or stroke.

Regarding the subgroup of patients with diabetes ($n = 54$ in morning cases, $n = 45$ in afternoon cases), the



Lactate levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	1.77 (1.65, 1.89)	1.50 (1.38, 1.63)	-0.27 (-0.44, -0.09)	0.111
1st postoperative hour	1.51 (1.39, 1.63)	1.42 (1.30, 1.55)	-0.09 (-0.26, 0.08)	
3rd postoperative hour	1.67 (1.55, 1.79)	1.48 (1.35, 1.60)	-0.19 (-0.36, -0.02)	
6th postoperative hour	1.70 (1.58, 1.82)	1.57 (1.44, 1.69)	-0.13 (-0.30, 0.04)	
12th postoperative hour	1.43 (1.31, 1.54)	1.36 (1.24, 1.48)	-0.06 (-0.24, 0.11)	
18th postoperative hour	1.36 (1.24, 1.49)	1.53 (1.39, 1.67)	0.17 (-0.02, 0.36)	
24th postoperative hour	1.58 (1.44, 1.73)	1.62 (1.44, 1.79)	0.03 (-0.20, 0.26)	

Figure 1: Arterial lactate values over the first 24 h at seven postoperative time points starting from the time of admission to the intensive care unit. Data are presented with a 95% confidence interval in two cardiac surgery populations according to morning or afternoon schedule. Results are from mixed effects linear regression models

Table 1: Characteristics of patients separated by schedule

	Morning (n=176)	Afternoon (n=163)	P
Age (years)	66.5 (65.1, 68.0)	66.6 (65.1, 68.1)	0.95
Males	83.0% (80.1, 85.0)	87.1% (85.0, 89.0)	0.28
Height (cm)	170.7 (169.4, 171.9)	173.0 (171.6, 174.4)	0.17
Weight (kg)	85.6 (83.4, 87.8)	85.0 (82.3, 87.7)	0.71
BMI (kg/m^2)	28.9 (28.2, 29.6)	28.9 (28.2, 29.6)	0.99
Hypertension	75.4% (72.9, 77.9)	72.4% (69.7, 75.1)	0.38
Creatinine (μmol/L)	88.4 (83.6, 93.2)	90.1 (85.4, 94.7)	0.61
Diabetes	30.6% (28.0, 33.3)	27.5% (24.9, 30.2)	0.40
Hypercholesterolemia	85.3% (83.0, 87.5)	78.0% (75.1, 90.8)	0.12
Actual smoker	18.5% (16.2, 21.0)	19.3% (17.0, 21.9)	0.86
Ex-smoker	48.3% (45.3, 51.4)	51.3% (48.3, 54.4)	0.37
Good RV systolic function	96.0% (94.8, 97.0)	97.5% (96.5, 98.4)	0.43
Good LV systolic function	86.9% (84.9, 88.8)	88.3% (86.3, 90.1)	0.70
Logistic Euroscore	4.2 (3.5, 5.0)	4.0 (3.3, 4.6)	0.59
Number of grafts performed	2.9 (2.8, 3.0)	2.7 (2.5, 2.8)	0.03
Preoperative lactate (mmol/L)	1.4 (1.3, 1.5)	1.2 (1.2, 1.3)	0.08
Preoperative base	0.1 (−0.2, 0.4)	−0.1 (−0.4, 0.3)	0.45
Preoperative pH	7.4 (7.4, 7.4)	7.4 (7.4, 7.4)	0.30
Preoperative chloride (mmol/L)	108.5 (108.0, 109.1)	108.3 (107.7, 108.9)	0.65

Table 2: Percentage of patients requiring inotropic and/or vasopressor support over the first 24 h after intensive care unit admission in patients undergoing elective coronary artery bypass grafting

	Morning (n=176)	Afternoon (n=163)	P
At ICU admission	33 (18.7%)	30 (18.4%)	0.93
1st postoperative hour	43 (24.4%)	38 (23.3%)	0.97
3rd postoperative hour	49 (27.8%)	44 (26.9%)	0.96
6th postoperative hour	50 (28.4%)	43 (26.3%)	0.77
12th postoperative hour	63 (35.7%)	43 (26.3%)	0.52
18th postoperative hour	50 (28.4%)	24 (14.7%)	0.035
24th postoperative hour	35 (19.8%)	18 (11.0%)	0.037

results were mostly overlapping with the entire analysis. Lactate ($P = 0.69$), BD ($P = 0.45$), pH (0.30), MAP ($P = 0.86$), CVP ($P = 0.28$), urine output ($P = 0.61$), and fluid balance ($P = 0.54$) were all not different between morning and afternoon cases as shown in the Supplemental Material.

DISCUSSION

In this single-center retrospective study, we investigated whether the schedule of patients undergoing cardiac surgery for elective CABG had an influence on the postoperative course of metabolic and hemodynamic parameters. Patients' characteristics were well balanced at baseline before ICU arrival apart from a slightly higher number of grafts performed in the morning cases.

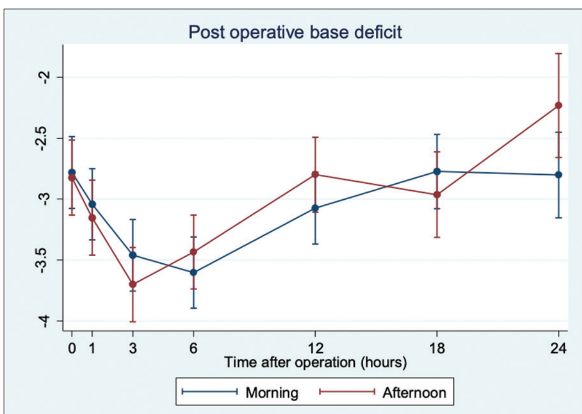
Our preliminary hypothesis was that patients undergoing surgery in the morning would have had better metabolic and hemodynamic postoperative courses as compared to patients scheduled in the afternoon. Indeed, the latter were exposed to prolonged fasting periods, which theoretically may have negatively influenced the perioperative courses. In contrast with our hypothesis, we found no differences in most of the outcomes investigated. Metabolic parameters were similar between groups with the only exception being significantly lower pH in the afternoon cases with an average difference of − 0.01, which could be of doubtful clinical meaning. Further, we planned a subgroup analysis focusing on patients with diabetes as we thought this group of patients would have been more susceptible to the negative influence of prolonged fasting.[21,22] However, even in this subgroup analysis involving a population at greater risk we found no difference in all the metabolic variables, including pH.

We also explored the hemodynamic consequences as patients with prolonged fasting may be more hypovolemic and may experience a greater response to surgical stress. Overall, we also found that the values of MAP and CVP were comparable between groups. Interestingly, we found no differences in the percentage of patients requiring

Table 3: Vasoactive inotropic score (VIS) over the first 24 h after intensive care unit admission in patients undergoing elective coronary artery bypass grafting

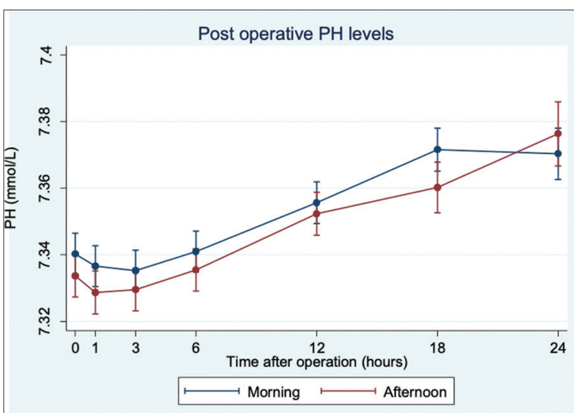
VIS score	Morning (*n*=176)	Afternoon (*n*=163)	*P*
At ICU admission	0.9±2.6	0.7±1.9	0.40
1st postoperative hour	1.1±2.6	0.8±1.9	0.32
3rd postoperative hour	1.5±3.3	1.2±2.7	0.29
6th postoperative hour	1.8±3.9	1.2±2.8	0.17
12th postoperative hour	1.9±4.0	1.3±2.7	0.14
18th postoperative hour	1.9±4.1	0.8±2.0	0.002
24th postoperative hour	1.3±3.9	0.4±1.3	0.003

VIS formula = (100 × norepinephrine [µg·kg^{-1}·min^{-1}]) + (100 × epinephrine [µg·kg^{-1}·min^{-1}]) + (dopamine [µg·kg^{-1}·min^{-1}]) + (dobutamine [µg·kg^{-1}·min^{-1}]) + (50 × levosimendan [µg·kg^{-1}·min^{-1}]) + (10 × milrinone [µg·kg^{-1}·min^{-1}]) + (10.000 × vasopressin [units·kg^{-1}·min^{-1}])



Base deficit levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	-2.78 (-3.08, -2.49)	-2.82 (-3.13, -2.52)	-0.04 (-0.47, 0.39)	0.846
1st postoperative hour	-3.04 (-3.33, -2.75)	-3.15 (-3.46, -2.84)	-0.11 (-0.54, 0.32)	
3rd postoperative hour	-3.46 (-3.75, -3.17)	-3.70 (-4.00, -3.39)	-0.24 (-0.67, 0.19)	
6th postoperative hour	-3.60 (-3.89, -3.31)	-3.43 (-3.74, -3.13)	0.17 (-0.26, 0.59)	
12th postoperative hour	-3.07 (-3.37, -2.78)	-2.80 (-3.11, -2.49)	0.27 (-0.16, 0.70)	
18th postoperative hour	-2.77 (-3.08, -2.47)	-2.96 (-3.31, -2.61)	-0.19 (-0.66, 0.28)	
24th postoperative hour	-2.80 (-3.15, -2.45)	-2.23 (-2.66, -1.81)	0.57 (0.01, 1.12)	

Figure 2: Base deficit values over the first 24 hours at seven postoperative time points starting from the time of admission to the intensive care unit. Data are presented with a 95% confidence interval in two cardiac surgery populations according to morning or afternoon schedule. Results are from mixed effects linear regression models



PH levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	7.34 (7.33, 7.35)	7.33 (7.33, 7.34)	-0.01 (-0.02, 0.00)	0.046
1st postoperative hour	7.34 (7.33, 7.34)	7.33 (7.32, 7.34)	-0.01 (-0.02, 0.00)	
3rd postoperative hour	7.34 (7.33, 7.34)	7.33 (7.32, 7.34)	-0.01 (-0.01, 0.00)	
6th postoperative hour	7.34 (7.33, 7.35)	7.34 (7.33, 7.34)	-0.01 (-0.01, 0.00)	
12th postoperative hour	7.36 (7.35, 7.36)	7.35 (7.35, 7.36)	0.00 (-0.01, 0.01)	
18th postoperative hour	7.37 (7.37, 7.38)	7.36 (7.35, 7.37)	-0.01 (-0.02, 0.00)	
24th postoperative hour	7.37 (7.36, 7.38)	7.38 (7.37, 7.39)	0.01 (-0.01, 0.02)	

Figure 3: pH values over the first 24 hours at seven postoperative time points starting from the time of admission to the intensive care unit. Data are presented with a 95% confidence interval in two cardiac surgery populations according to morning or afternoon schedule. Results are from mixed effects linear regression models

vasoactive support until the 12th postoperative hour, but beyond this time point, we found a greater number of patients receiving vasoactive support in the morning cases (18th and 24th postoperative hours). This result seems to exclude a negative influence from scheduling in the afternoon because of the longer fasting time. However, although significant, it is difficult to exclude the potential influence of human factors such as the attitude to be more cautious in weaning of vasoactive drugs during night-time. Another significant difference was a significantly shorter ICU LOS by around half a day for the cases scheduled in the afternoon. We think that this result is potentially biased by two potential confounders. First, it is well accepted that patients are usually discharged to the cardiac surgery ward in the late morning (by midday) to make space for new cardiac surgery cases and once a bed is free in the ward after home discharge, patients arriving late in the afternoon and having an uncomplicated postoperative period had shorter LOS being discharged even before 24 hours of ICU LOS. As the second factor potentially influencing the ICU discharge, it is common practice to schedule the more complex cases as first on the list (morning); however, it must be noted that in our study the Logistic Euro score was similar between groups as it was the prevalence of good left and right ventricular systolic function distribution and other comorbidities. Mortality and postoperative complications were similar between groups.

Overall, our results suggest that being scheduled for elective cardiac surgery and being exposed to prolonged fasting seems safe and does not influence the postoperative course in the ICU, nor prevent early discharge to the surgical ward.

Our results are in the same direction as recent evidence. In a meta-analysis of over 18,000 patients undergoing isolated aortic valve replacement or isolated CABG, Fudulu *et al*. demonstrated no evidence that the time of surgery influences mortality and myocardial injury. Moreover, the authors confirmed the same findings from another large dataset (UK National Adult Cardiac Surgery Audit) of over 91,000 patients.[14] In a propensity score matching with 269 paired patients undergoing elective aortic valve replacement with or without CABG, Michaud *et al*. showed that the timing of cardiac surgery did not influence the primary composite endpoint (occurrence of 30-day death, low cardiac output syndrome, myocardial infarction, and stroke) nor the tolerance to ischemia and reperfusion injury.[15] Similar results have been reported by Hijazi *et al*., with no difference in mortality and low cardiac output syndrome in a population of almost 10,000 patients, including more complex surgical cases[16] Also, Nemeth *et al*. reported similar results with no difference in perioperative mortality and major morbidity between well-matched morning and afternoon patients undergoing either CABG or aortic valve replacement. Interestingly, in this study, the authors also evaluated the subgroup of patients with diabetes, and they reported no difference in most postoperative outcomes in this subgroup of patients at potentially greater risk.[23]

However, it must be noted that there is also evidence in the opposite direction. A large propensity-score matching study with 630 paired patients showed no differences in the short term according to operating room scheduling but also demonstrated a significant three-fold increase (hazard ratio 3.44, 95% CI: 1.33–10.49) in the incidence of acute myocardial infarction at 1-year follow-up.[24] Another propensity-score matching analysis published recently by Ranucci *et al*. with 800 paired patients reported significantly a higher major morbidity rate for afternoon cases (13% as compared to 8.8% in the morning) and higher 30-day mortality (4.1% versus 2.3%, respectively), and such results remained significant after correction for EuroScore and operating surgeon with an odds ratio of 1.6 (95% CI: 1.16–2.23).[25] Interestingly, the latter study showed higher values of lactates at ICU admission for the afternoon cases as compared to the morning ones, a finding different from our study. Finally, another propensity score study showed lower major adverse cardiac events in the afternoon surgery group as compared to the morning group in patients undergoing aortic valve replacement in the 500 days following surgery.[13] Considering the above findings, it seems clear that more research is needed to clarify this aspect, bearing in mind that most of the available evidence relies on retrospective studies (with or without propensity-score matching).

Strengths and limitations

A strength of our study was the collection of large sample size; moreover, we collected reliable information using the EMRs system, and the advanced statistical analysis allowed the clustering of data at different time points and adjustment for a large number of baseline variables and several other covariates.

However, our study has a significant number of limitations. First, it remains a single-center study conducted at an academic hospital and hence could be influenced by local practice. For instance, our findings would not be applicable to patients undergoing cardiac surgery in the afternoon who have been allowed a light breakfast around 6.00 am. Second, our study is not randomized and by definition, the retrospective data collection and analysis is subject to biases. However, the use of EMRs minimized the risk of bias due to subjective measurements. Third, we found a small difference in the number of grafts performed between groups (a difference of 0.2, higher in the morning cases), which may be explained by the tendency to schedule the more complex surgical cases (greater coronary artery territory disease) in the morning. In this regard, we did not evaluate the postoperative course of troponin nor the follow-up on myocardial function. However, all other baseline characteristics were balanced in the two groups. Fourth, we could not perform a sample size calculation due to the retrospective design. In this regard, our study is reported in line with the STROBE guidelines,[26] and the 95% CIs were reasonably small, supporting a fair power in our analysis. Even if the sample size is relatively large and the 95% CI small, readers should keep in mind that we analyzed a low-risk population; hence, some analyses may possibly be underpowered and our results do not necessarily apply to cardiac surgery patients at higher preoperative risk. Fifth, we had no data on continuous cardiac output monitoring, as the preferred monitoring in ICU was performed with transoesophageal echocardiography but details on the assessment were not always available. Therefore, our hemodynamic interpretation is very limited, being related to the comparison of MAP and CVP. Sixth, no EMR system was implemented for the intraoperative variables; hence, the intraoperative data were not analyzed. Seventh, we had missing information on 27% of the total population; however, in most cases, this was limited to one covariate of minor importance. To keep the efficiency of the models, we performed a multiple imputation approach using chained equations. Eighth, we did not investigate the impact of the circadian rhythm on patients' outcomes after cardiac surgery; we do not have data in this regard and its influence is still controversial, with opposite findings reported in the literature[13,24].

CONCLUSIONS

In a cohort of elective CABG patients, afternoon cases resulted in similar or even better metabolic and hemodynamic profiles when compared to morning cases. The metabolic and hemodynamic improvements are of unlikely clinical meaning. Because our study included low-risk elective CABG patients, our conclusion that afternoon scheduling does not negatively influence metabolic or hemodynamic profiles in the early postoperative period remains confined to this low-risk population.

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Declaration of Generative AI and AI-assisted technologies in the writing process

Statement: During the preparation of this work, the authors did not use any AI or AI-assisted technologies in the writing process, nor for any other purpose.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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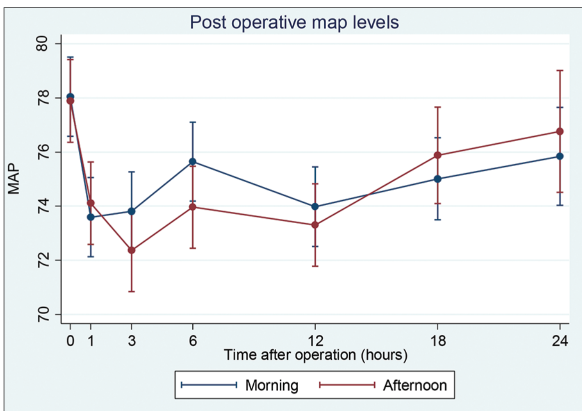
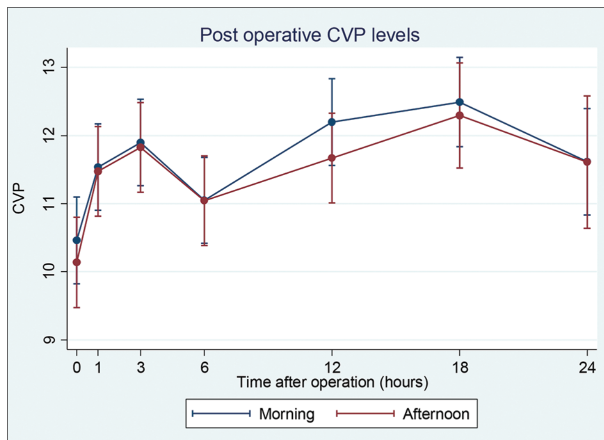
Supplemental Material 1: Characteristics of the patients included in the study and separated according to the schedule of the operation

	Morning (*n*=176)	Afternoon (*n*=163)	*P*
Age (years)	66.5 (65.1, 68.0)	66.6 (65.1, 68.1)	0.95
Males	83.0% (80.1, 85.0)	87.1% (85.0, 89.0)	0.28
Height (cm)	170.7 (169.4, 171.9)	173.0 (171.6, 174.4)	0.17
Weight (kg)	85.6 (83.4, 87.8)	85.0 (82.3, 87.7)	0.71
BMI (kg/m^2)	28.9 (28.2, 29.6)	28.9 (28.2, 29.6)	0.99
Hypertension	75.4% (72.9, 77.9)	72.4% (69.7, 75.1)	0.38
Creatinine (μmol/L)	88.4 (83.6, 93.2)	90.1 (85.4, 94.7)	0.61
Diabetes	30.6% (28.0, 33.3)	27.5% (24.9, 30.2)	0.40
Hypercholesterolemia	85.3% (83.0, 87.5)	78.0% (75.1, 90.8)	0.12
Actual smoker	18.5% (16.2, 21.0)	19.3% (17.0, 21.9)	0.86
Ex-smoker	48.3% (45.3, 51.4)	51.3% (48.3, 54.4)	0.37
Good RV systolic function	96.0% (94.8, 97.0)	97.5% (96.5, 98.4)	0.43
Good LV systolic function	86.9% (84.9, 88.8)	88.3% (86.3, 90.1)	0.70
Logistic Euroscore	4.2 (3.5, 5.0)	4.0 (3.3, 4.6)	0.59
Number of grafts performed	2.9 (2.8, 3.0)	2.7 (2.5, 2.8)	0.03
Preoperative lactate (mmol/L)	1.4 (1.3, 1.5)	1.2 (1.2, 1.3)	0.08
Preoperative base	0.1 (−0.2, 0.4)	−0.1 (−0.4, 0.3)	0.45
Preoperative pH	7.4 (7.4, 7.4)	7.4 (7.4, 7.4)	0.30
Preoperative chloride (mmol/L)	108.5 (108.0, 109.1)	108.3 (107.7, 108.9)	0.65

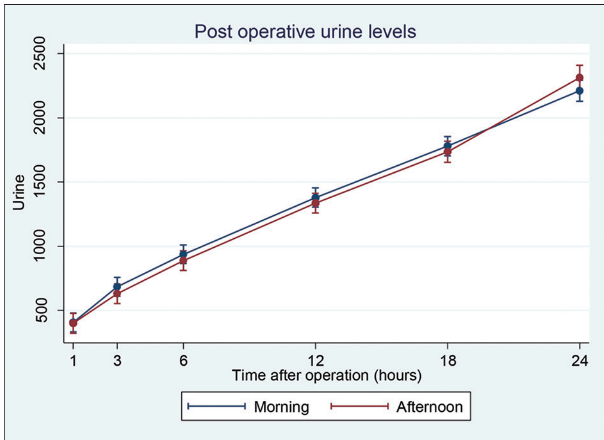
SUPPLEMENTAL MATERIAL 2



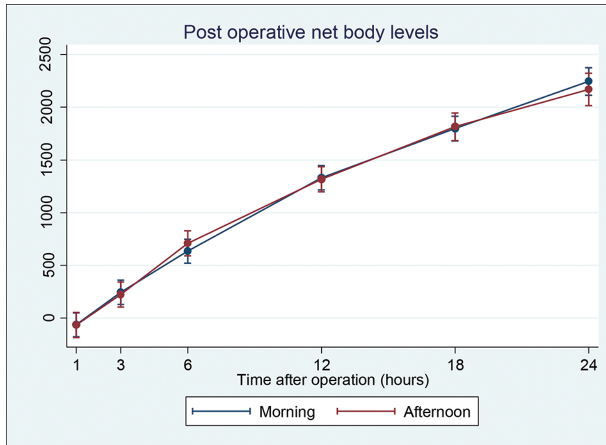
MAP levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	78.04 (76.58, 79.51)	77.89 (76.36, 79.41)	-0.16 (-2.28, 1.96)	0.584
1st postoperative hour	73.59 (72.13, 75.05)	74.10 (72.58, 75.63)	0.51 (-1.61, 2.64)	
3rd postoperative hour	73.80 (72.34, 75.26)	72.36 (70.85, 73.87)	-1.44 (-3.56, 0.67)	
6th postoperative hour	75.65 (74.19, 77.11)	73.96 (72.45, 75.47)	-1.69 (-3.80, 0.43)	
12th postoperative hour	73.98 (72.51, 75.44)	73.30 (71.78, 74.82)	-0.68 (-2.80, 1.45)	
18th postoperative hour	75.01 (73.49, 76.52)	75.87 (74.09, 77.66)	0.86 (-1.49, 3.21)	
24th postoperative hour	75.84 (74.03, 77.65)	76.76 (74.51, 79.01)	0.92 (-1.97, 3.82)	



CVP levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	10.46 (9.82, 11.09)	10.14 (9.47, 10.80)	-0.32 (-1.24, 0.60)	0.532
1st postoperative hour	11.54 (10.90, 12.17)	11.48 (10.81, 12.14)	-0.06 (-0.98, 0.86)	
3rd postoperative hour	11.90 (11.27, 12.53)	11.82 (11.17, 12.48)	-0.07 (-0.99, 0.84)	
6th postoperative hour	11.05 (10.42, 11.68)	11.04 (10.39, 11.70)	-0.01 (-0.92, 0.91)	
12th postoperative hour	12.20 (11.56, 12.84)	11.67 (11.01, 12.33)	-0.53 (-1.45, 0.39)	
18th postoperative hour	12.49 (11.83, 13.15)	12.30 (11.52, 13.07)	-0.19 (-1.21, 0.82)	
24th postoperative hour	11.61 (10.83, 12.40)	11.61 (10.64, 12.58)	-0.01 (-1.26, 1.25)	

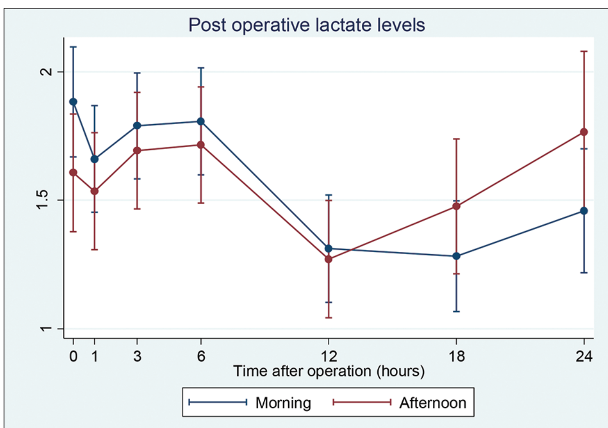


Urine levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
1st postoperative hour	407.36 (333.60, 481.12)	399.63 (322.74, 476.52)	-7.73 (-115.67, 100.21)	0.590
3rd postoperative hour	682.99 (609.35, 756.63)	629.44 (552.71, 706.18)	-53.54 (-161.32, 54.23)	
6th postoperative hour	937.80 (864.08, 1011.51)	888.01 (811.29, 964.72)	-49.79 (-157.58, 58.00)	
12th postoperative hour	1379.66 (1305.79, 1453.53)	1336.00 (1259.16, 1412.85)	-43.66 (-151.69, 64.37)	
18th postoperative hour	1780.23 (1705.33, 1855.13)	1735.00 (1652.16, 1817.84)	-45.23 (-158.28, 67.83)	
24th postoperative hour	2211.67 (2130.07, 2293.27)	2314.85 (2220.55, 2409.16)	103.18 (-22.51, 228.86)	

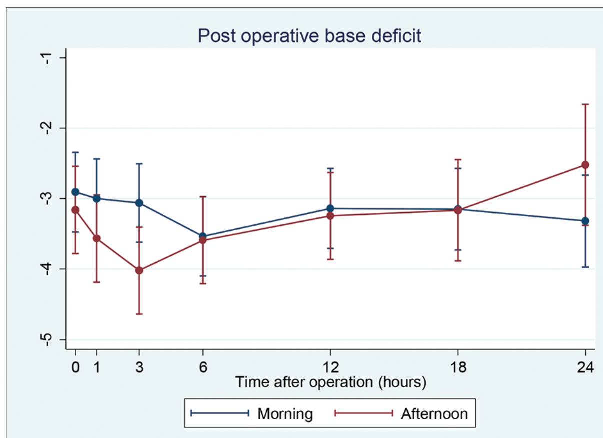


Net body levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
1st postoperative hour	-62.92 (-176.77, 50.93)	-63.25 (-181.89, 55.39)	-0.34 (-166.55, 165.88)	0.964
3rd postoperative hour	245.91 (132.31, 359.50)	225.64 (107.33, 343.95)	-20.26 (-186.12, 145.60)	
6th postoperative hour	636.36 (522.61, 750.11)	710.74 (592.47, 829.01)	74.39 (-91.50, 240.27)	
12th postoperative hour	1331.23 (1217.16, 1445.30)	1318.75 (1200.22, 1437.29)	-12.48 (-178.86, 153.91)	
18th postoperative hour	1797.84 (1681.56, 1914.11)	1815.02 (1683.83, 1946.21)	17.18 (-159.87, 194.24)	
24th postoperative hour	2245.24 (2114.83, 2375.65)	2169.68 (2014.99, 2324.36)	-75.57 (-278.96, 127.83)	

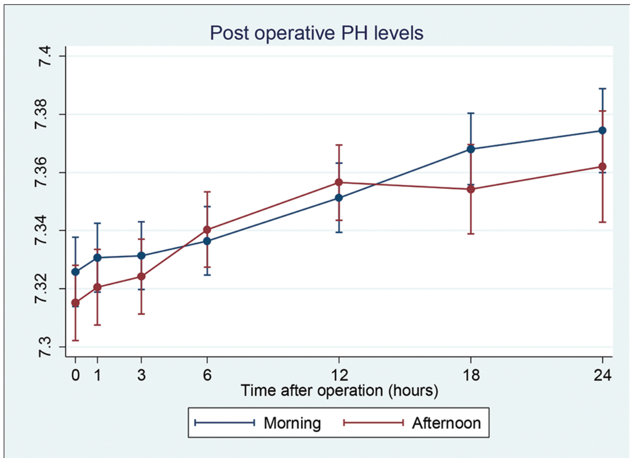
SUPPLEMENTAL MATERIAL 3: ANALYSIS PERFORMED IN THE SUBPOPULATION WITH DIABETES AS COMORBIDITY (N=54 IN MORNING CASES, N=45 IN AFTERNOON CASES)



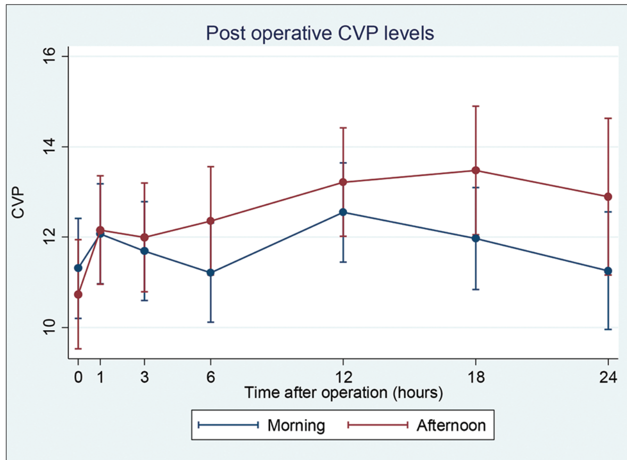
Lactate levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	1.88 (1.67, 2.10)	1.61 (1.38, 1.84)	-0.28 (-0.60, 0.05)	0.689
1st postoperative hour	1.66 (1.45, 1.87)	1.54 (1.31, 1.76)	-0.13 (-0.44, 0.19)	
3rd postoperative hour	1.79 (1.58, 2.00)	1.69 (1.47, 1.92)	-0.10 (-0.41, 0.22)	
6th postoperative hour	1.81 (1.60, 2.02)	1.72 (1.49, 1.94)	-0.09 (-0.41, 0.23)	
12th postoperative hour	1.31 (1.10, 1.52)	1.27 (1.04, 1.50)	-0.04 (-0.36, 0.28)	
18th postoperative hour	1.28 (1.07, 1.50)	1.48 (1.21, 1.74)	0.19 (-0.15, 0.54)	
24th postoperative hour	1.46 (1.22, 1.70)	1.77 (1.45, 2.08)	0.31 (-0.10, 0.71)	



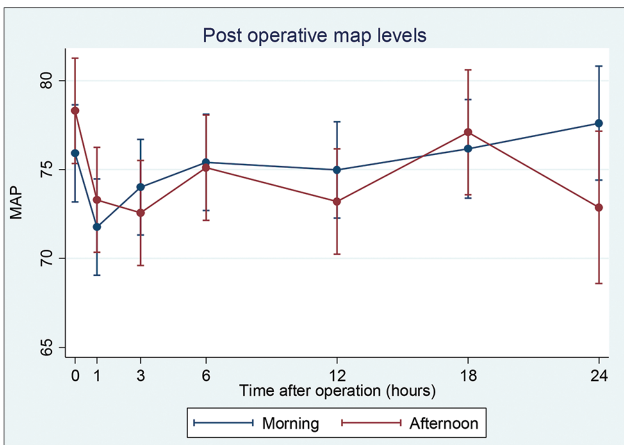
Base deficit levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	-2.91 (-3.47, -2.34)	-3.16 (-3.78, -2.54)	-0.25 (-1.11, 0.61)	0.447
1st postoperative hour	-3.00 (-3.56, -2.44)	-3.57 (-4.19, -2.95)	-0.57 (-1.43, 0.30)	
3rd postoperative hour	-3.06 (-3.62, -2.50)	-4.02 (-4.64, -3.40)	-0.96 (-1.82, -0.10)	
6th postoperative hour	-3.53 (-4.10, -2.97)	-3.59 (-4.21, -2.97)	-0.06 (-0.92, 0.80)	
12th postoperative hour	-3.14 (-3.70, -2.57)	-3.25 (-3.86, -2.63)	-0.11 (-0.97, 0.76)	
18th postoperative hour	-3.15 (-3.73, -2.57)	-3.16 (-3.88, -2.44)	-0.01 (-0.96, 0.93)	
24th postoperative hour	-3.32 (-3.97, -2.66)	-2.52 (-3.38, -1.66)	0.80 (-0.31, 1.90)	



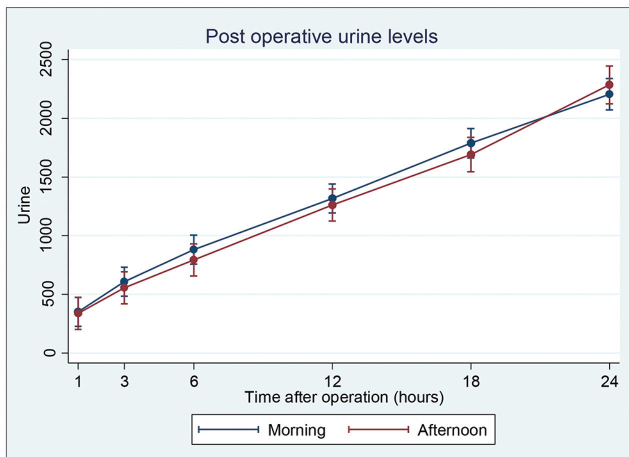
PH levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	7.33 (7.31, 7.34)	7.32 (7.30, 7.33)	-0.01 (-0.03, 0.01)	0.299
1st postoperative hour	7.33 (7.32, 7.34)	7.32 (7.31, 7.33)	-0.01 (-0.03, 0.01)	
3rd postoperative hour	7.33 (7.32, 7.34)	7.32 (7.31, 7.34)	-0.01 (-0.02, 0.01)	
6th postoperative hour	7.34 (7.32, 7.35)	7.34 (7.33, 7.35)	0.00 (-0.01, 0.02)	
12th postoperative hour	7.35 (7.34, 7.36)	7.36 (7.34, 7.37)	0.01 (-0.01, 0.02)	
18th postoperative hour	7.37 (7.36, 7.38)	7.35 (7.34, 7.37)	-0.01 (-0.03, 0.01)	
24th postoperative hour	7.37 (7.36, 7.39)	7.36 (7.34, 7.38)	-0.01 (-0.04, 0.01)	



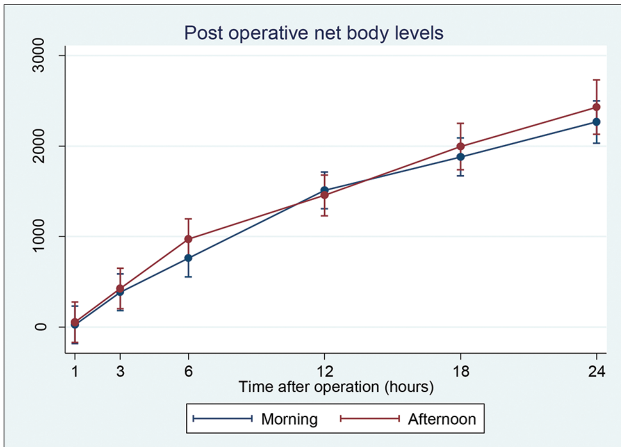
CVP levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	11.31 (10.21, 12.42)	10.74 (9.53, 11.94)	-0.57 (-2.24, 1.09)	0.278
1st postoperative hour	12.07 (10.97, 13.18)	12.16 (10.96, 13.36)	0.09 (-1.58, 1.75)	
3rd postoperative hour	11.69 (10.60, 12.78)	11.99 (10.79, 13.20)	0.30 (-1.36, 1.96)	
6th postoperative hour	11.22 (10.12, 12.32)	12.36 (11.16, 13.56)	1.15 (-0.52, 2.81)	
12th postoperative hour	12.55 (11.45, 13.64)	13.22 (12.02, 14.42)	0.67 (-0.99, 2.33)	
18th postoperative hour	11.97 (10.85, 13.10)	13.48 (12.06, 14.90)	1.51 (-0.33, 3.35)	
24th postoperative hour	11.26 (9.95, 12.56)	12.89 (11.16, 14.63)	1.64 (-0.56, 3.83)	



MAP levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
ICU admission	75.92 (73.19, 78.64)	78.30 (75.34, 81.27)	2.39 (-1.72, 6.50)	0.858
1st postoperative hour	71.77 (69.06, 74.48)	73.30 (70.34, 76.26)	1.53 (-2.58, 5.64)	
3rd postoperative hour	74.02 (71.33, 76.71)	72.56 (69.60, 75.52)	-1.45 (-5.54, 2.63)	
6th postoperative hour	75.41 (72.70, 78.13)	75.11 (72.14, 78.07)	-0.30 (-4.41, 3.80)	
12th postoperative hour	74.99 (72.28, 77.70)	73.21 (70.24, 76.18)	-1.78 (-5.87, 2.31)	
18th postoperative hour	76.18 (73.41, 78.95)	77.11 (73.60, 80.63)	0.93 (-3.62, 5.48)	
24th postoperative hour	77.62 (74.41, 80.82)	72.87 (68.59, 77.16)	-4.74 (-10.17, 0.68)	



Urine levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
1st postoperative hour	350.06 (226.34, 473.77)	337.92 (201.81, 474.03)	-12.14 (-203.80, 179.52)	0.607
3rd postoperative hour	607.14 (484.11, 730.18)	554.31 (418.07, 690.55)	-52.84 (-244.16, 138.49)	
6th postoperative hour	880.61 (757.09, 1004.14)	791.65 (655.53, 927.76)	-88.97 (-280.50, 102.56)	
12th postoperative hour	1316.48 (1193.21, 1439.76)	1261.48 (1125.24, 1397.73)	-55.00 (-246.36, 136.36)	
18th postoperative hour	1787.25 (1662.67, 1911.84)	1690.93 (1544.47, 1837.40)	-96.32 (-295.67, 103.02)	
24th postoperative hour	2204.78 (2071.91, 2337.64)	2284.59 (2122.86, 2446.32)	79.81 (-136.53, 296.16)	



Net body levels	Morning Mean (95% CI)	Afternoon Mean (95% CI)	Difference (95% CI)	Overall p-value
1st postoperative hour	25.59 (-179.80, 230.98)	53.42 (-170.71, 277.55)	27.83 (-286.98, 342.64)	0.543
3rd postoperative hour	384.37 (181.22, 587.52)	427.07 (202.53, 651.61)	42.70 (-270.92, 356.31)	
6th postoperative hour	761.57 (556.93, 966.20)	972.84 (748.68, 1197.00)	211.27 (-102.95, 525.49)	
12th postoperative hour	1511.14 (1307.34, 1714.93)	1455.39 (1230.87, 1679.90)	-55.75 (-369.29, 257.79)	
18th postoperative hour	1881.43 (1673.47, 2089.40)	1994.68 (1738.52, 2250.83)	113.25 (-225.75, 452.24)	
24th postoperative hour	2267.27 (2033.95, 2500.60)	2431.51 (2130.30, 2732.71)	164.23 (-226.31, 554.77)	