Accuracy of blood glucose measurements using the NOVA StatStrip® glucometer during cardiac surgery: a prospective observational study

Précision des mesures de la glycémie prises avec le glucomètre StatStrip® de NOVA pendant une chirurgie cardiaque : une étude observationnelle prospective

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Abstract

Purpose The Nova StatStrip® Glucose Hospital Meter System (Nova Biomedical, Waltham, MA, USA) is United States Food and Drug Administration approved for point-of-care use in critically ill patients, but its use during cardiac surgery has not been evaluated. In this study, we compare glucose values obtained during cardiac surgery by StatStrip® with values obtained by a blood gas analyzer.

Methods Blood glucose concentrations were analyzed in 121 patients by the StatStrip point-of-care test (POCT) glucose monitor and the GEM® Premier™ 3000 blood gas analyzer (Instrumentation Laboratory Company, Bedford MA, USA). Arterial blood samples were taken at baseline (before surgery), before cardiopulmonary bypass (CPB), during early and late CPB, and 30 min after CPB. Accuracy of the StatStrip glucometer was analyzed using the Clinical and Laboratory Standards Institute (CLSI) POCT12-A3 criteria (criterion 1; 95% of samples should

be $\pm 0.66 \text{ mMol}\cdot\text{L}^{-1}$ of reference glucose values $< 5.5 \text{ mMol}\cdot\text{L}^{-1}$ and $\pm 12.5\%$ for reference glucose values $> 5.5 \text{ mMol}\cdot\text{L}^{-1}$, criterion 2; 98% of samples should be $\pm 0.83 \text{ mMol}\cdot\text{L}^{-1}$ of reference glucose values $< 4.1 \text{ mMol}\cdot\text{L}^{-1}$ or 20% of the reference glucose for values $> 4.1 \text{ mMol}\cdot\text{L}^{-1}$).

Results The accuracy of StatStrip glucose measurements at baseline (99%, 100%) and before CPB (95%, 98%), but not during (early: 84%, 97%; late: 83%, 96%) and after (92%, 100%) CPB, satisfied the CLSI POCT12-A3 criteria.

Conclusion Arterial blood glucose measurement by StatStrip was accurate before CPB, but lacked accuracy during and after CPB. Glucose values should be interpreted with caution when intensive glucose control protocols are being used during cardiac surgery.

Trial registration ClinicalTrials.gov (NCT02729064); registered 5 April, 2016.

Résumé

Objectif Le glucomètre hospitalier StatStrip® de Nova (Nova Biomedical, Waltham, MA, É.-U.) est approuvé par la FDA (Food and Drug Administration) américaine pour une utilisation au chevet chez les patients en état critique, mais son utilisation n'a pas été évaluée en chirurgie cardiaque. Dans cette étude, nous avons comparé les valeurs glycémiques obtenues par le lecteur StatStrip® et les valeurs obtenues par un analyseur des gaz du sang pendant une chirurgie cardiaque.

Méthode Les concentrations glycémiques de 121 patients ont été analysées en utilisant le moniteur glycémique StatStrip et l'analyseur de gaz sanguins GEM® Premier™ 3000 (Instrumentation Laboratory Company, Bedford, MA,

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É.-U.). Des échantillons de sang artériel ont été prélevés avant la chirurgie, avant la circulation extracorporelle (CEC), au début et à la fin de la CEC et 30 min après la CEC. La précision du glucomètre StatStrip a été analysée à l'aide des critères de l'Institut des normes cliniques et de laboratoire (Clinical and Laboratory Standards Institute (CLSI)) POCT12-A3 (1^{er} critère; 95 % des échantillons doivent être à l'intérieur de $\pm 0,66 \text{ mMol}\cdot\text{L}^{-1}$ des valeurs glycémiques de référence $< 5,5 \text{ mMol}\cdot\text{L}^{-1}$ et $\pm 12,5 \%$ pour les valeurs glycémiques de référence $> 5,5 \text{ mMol}\cdot\text{L}^{-1}$, 2^{ème} critère; 98 % des échantillons doivent être à l'intérieur de $\pm 0,83 \text{ mMol}\cdot\text{L}^{-1}$ des valeurs glycémiques de référence $< 4,1 \text{ mMol}\cdot\text{L}^{-1}$ ou 20 % du taux glycémique de référence pour les valeurs $> 4,1 \text{ mMol}\cdot\text{L}^{-1}$).

Résultats La précision des mesures glycémiques prises par le StatStrip avant l'opération (99 %, 100 %) et avant la CEC (95 %, 98 %), mais non durant (début : 84 %, 97 %; fin : 83 %, 96 %) et après (92 %, 100 %) la CEC, respectait les critères POCT12-A3 du CLSI. <0

Conclusion La mesure de la glycémie artérielle réalisée avec le StatStrip était précise avant la CEC mais a manqué de précision pendant et après la CEC. Les valeurs glycémiques devraient donc être interprétées avec prudence lorsque des protocoles intensifs de contrôle glycémique sont utilisés pendant une chirurgie cardiaque.

Enregistrement de l'étude ClinicalTrials.gov (NCT02729064); enregistrée le 5 avril 2016.

It is well recognized that acute changes in glycemic control (i.e., increased or decreased circulating glucose concentrations) are associated with poor outcome after surgery.¹ Accurate, precise, and timely measurement of blood glucose is therefore an important element of modern perioperative care.

Glucose values can be assessed using laboratory serum and plasma glucose analysis, as well as by whole blood and capillary glucose measurement using blood gas analyzers (BGA) or other glucometers. Glucose analysis in the laboratory (i.e., the gold standard)² may not provide results fast enough to promptly and effectively treat hypo- or hyperglycemic episodes in the operating room. Hence, perioperatively, glycemia is routinely assessed by point-of-care test (POCT) devices such as glucometers and BGA.

In 2014, the StatStrip® Glucose Hospital Meter System (Nova Biomedical, Waltham, MA, USA), the predominantly used POCT glucometer in North America (70% of POCT glucometer sales in 2018), received United States Food and Drug Administration (FDA) approval for POCT in the critically ill.³ While its accuracy in the

intensive care unit appears to be well documented, its use during major surgery has not been evaluated.

The purpose of this study was to assess the accuracy of the Nova StatStrip device in testing glucose levels in patients undergoing open-heart surgery requiring cardiopulmonary bypass (CPB). We hypothesized that arterial whole blood samples analyzed with this glucometer would meet the accuracy criteria as defined by the Clinical and Laboratory Standards Institute (CLSI) POCT12-A3 guideline⁴ and/or the consensus-based Parkes error grid⁵ of the International Organization for Standardization (ISO15197:2013), which was originally developed for patients with type-1 diabetes mellitus requiring subcutaneous insulin therapy.⁶

Methods

This study was a *post hoc* exploratory study of blood samples that were obtained and analyzed from participants in a prospective randomized-controlled trial of intranasal insulin in surgical patients (ClinicalTrials.gov NCT02729064; registered on 5 April, 2016). The primary aim of the original trial was to study the effect of two intranasal doses of insulin (40 IU and 80 IU) on glycemic control during cardiac surgery requiring CPB.⁷ This sub-study was conducted at the Royal Victoria Hospital (McGill University Health Center MUHC, Montreal, Quebec, Canada) between 21 September 2016 and 14 March 2018.

Patients

All patients gave written informed consent, and the study was approved by our institutional ethics review board on 1 September, 2016. We enrolled patients (> 18 yr old) undergoing elective cardiac surgery requiring CPB. The exclusion criteria included procedures with anticipated deep hypothermic circulatory arrest, planned use of drugs that effect glycemia during the first two hours of surgery (e.g., insulin, steroids, epinephrine), allergy to insulin, acromegaly, Cushing's syndrome, hyperthyroidism, pheochromocytoma, pregnancy, and a baseline blood glucose $< 3.9 \text{ mMol}\cdot\text{L}^{-1}$.⁷

Before surgery, we recorded the patients' age, sex, height, weight, body mass index, Euroscore-II,⁸ hematocrit, plasma creatinine, left ventricular ejection function, and comorbidities.

Anesthetic care

Oral hypoglycemic drugs were discontinued 12 hr before surgery, and a subcutaneous sliding scale insulin regimen

was used in patients at risk of hyperglycemia ($> 10 \text{ mMol}\cdot\text{L}^{-1}$) or hypoglycemia ($< 4 \text{ mMol}\cdot\text{L}^{-1}$). Anesthetic care included the use of standard anesthesia monitors⁹ that were supplemented by central venous or pulmonary artery catheters and transesophageal echocardiography. Midazolam, propofol, sufentanil, sevoflurane, and a depolarizing or non-depolarizing muscle relaxant were given during induction and maintenance of anesthesia. The inhaled oxygen concentration was adjusted to 50%–100% based on the surgical procedure and the patients' blood oxygen saturation. Normal saline solution and/or Ringer's lactate were used as intravenous fluids. Systolic blood pressure (BP) was maintained at 100 mmHg before and after CPB with the mean arterial pressure during CPB maintained at 50–70 mmHg using norepinephrine ($1\text{--}10 \mu\text{g}\cdot\text{kg}^{-1}\cdot\text{hr}^{-1}$) as needed. Body temperature (BT) was maintained at $32\text{--}36^\circ$ during CPB. Red blood cells were administered when the hematocrit was $< 25\%$. Before CPB, heparin $400 \text{ IU}\cdot\text{kg}^{-1}$ was administered intravenously followed by additional doses, if necessary, to maintain an activated clotting time (ACT) of $> 480 \text{ sec}$. Protamine was administered on a 1:1 ratio after separation from CPB. Cardioplegia solution was free of glucose and mannitol and consisted of high-dose ($100 \text{ mEq}\cdot\text{L}^{-1}$) potassium to induce and maintain cardiac arrest.

Blood glucose was measured every ten to 30 min during surgery to clarify whether intranasal insulin affected glucose values.⁷ When the blood glucose measured by BGA was $< 4.0 \text{ mMol}\cdot\text{L}^{-1}$, 10ml of 20% dextrose with phosphate $30 \text{ mMol}\cdot\text{L}^{-1}$ was administered and a continuous dextrose infusion was started at $20 \text{ mL}\cdot\text{hr}^{-1}$. When the blood glucose concentration was $> 10.0 \text{ mMol}\cdot\text{L}^{-1}$, an insulin infusion of $2 \text{ units}\cdot\text{hr}^{-1}$ was initiated to maintain the blood glucose between 4.0 and $10.0 \text{ mMol}\cdot\text{L}^{-1}$.

We also recorded the duration of anesthesia, surgery, CPB, and aortic cross clamping.

Glucose measurement protocol

Arterial whole blood samples were drawn from a catheter placed in either the radial, femoral, or brachial artery. Glucose concentrations were collected in a 3-mL syringe (without any additives) and analyzed by the StatStrip glucometer with additional blood collected in a 3-mL lithium heparin blood gas syringe (or a regular syringe during heparinization) for analysis in a GEM® Premier™ 3000® (Instrumentation Laboratory Company, Bedford, MA, USA) blood gas analyzer. Blood glucose analyses were performed within two minutes of blood collection.

Samples were collected at five time-points: baseline (before surgery), pre-CPB (before CPB after heparinization), during early CPB (30 min after

establishing full CPB; CPB1), during late CPB (one to two hours after establishing full CPB; CPB2), and post-CPB (30 min after separation of CPB and the administration of protamine).

The following data were recorded at the five above time-points: arterial pH, pO_2 , pCO_2 , lactate, hematocrit, ACT, (BT, nasal, and bladder), BP (systolic, diastolic, and mean), heart rate (HR), and catecholamine infusion rate.

Study outcomes

The primary outcome was the accuracy of blood glucose values obtained by the StatStrip glucometer, which was defined by the criteria specified by the POCT12-A3 guideline⁴ of the CLSI and/or criteria established by the ISO 15197:2013.⁶

The two CLSI POCT12-A3 criteria, both of which needed to be met, were as follows⁴: criterion 1: 95% of samples should be within $\pm 0.66 \text{ mMol}\cdot\text{L}^{-1}$ of reference glucose values $< 5.5 \text{ mMol}\cdot\text{L}^{-1}$ and $\pm 12.5\%$ for reference glucose values $> 5.5 \text{ mMol}\cdot\text{L}^{-1}$; and criterion 2: 98% of samples should be within $\pm 0.83 \text{ mMol}\cdot\text{L}^{-1}$ of reference glucose values $< 4.1 \text{ mMol}\cdot\text{L}^{-1}$ or 20% of the reference glucose for values $> 4.1 \text{ mMol}\cdot\text{L}^{-1}$ (Table 4) (Fig. 2). We estimated that a minimum of 100 samples would be needed to determine the accuracy. When 98 of 100 samples meet the criterion, the 95% confidential interval (CI) is 93 to 100%, and when 95 of 100 samples meet the criterion, the 95% CI is 89 to 98% consistent with the ISO 15197:2013.⁶ Clinical accuracy was acceptable when 99% of samples were within zones A and B on the Parkes error grid.^{5,10} The Parkes error grid is divided into five risk zones.⁵ The five risk zones were illustrated in Figure 3 and described in Table 1. In agreement with previous protocols, arterial blood glucose values measured by BGA were considered the reference.^{11,12}

When samples did not meet the above criteria, an additional *post hoc* exploratory analysis was performed to determine whether clinical variables, laboratory or hemodynamic parameters, and heparinization were associated with the discrepancy of glucose values

Table 1 Five risk zones on the Parkes error grid

Zone A	no effect on clinical action
Zone B	altered clinical action with little or no effect on clinical outcome
Zone C	altered clinical action likely to impact clinical outcome
Zone D	altered clinical action that could have significant medical risk
Zone E	altered clinical action that could have dangerous consequences

These zones are also illustrated in Fig. 2

obtained by the two methods and the accuracy of the StatStrip glucose measurements.

Statistical analysis

Preoperative, surgical, and laboratory data are summarized using descriptive statistics. Categorical variables are described as counts and percentages. All data were tested for normality using the Kolmogorov–Smirnov test. Continuous variables with normal distribution are presented as mean (standard deviation) and variables with skewed distribution as median [interquartile range (IQR)].

The differences between laboratory and hemodynamic data at five time-points were compared using the Friedman test. Patients with missing data were excluded.

Accuracy was analyzed using the criteria defined by the CLSI POCT12-A3 guideline⁴ for hospital POCT glucometers and by ISO 15197:2013 Parkes error grid for self-monitoring blood glucose glucometers used for patients with type 1 diabetes mellitus.

The Spearman's rank correlation was used to determine whether BT, laboratory (arterial pH, pO₂, pCO₂, lactate, Hematocrit, ACT) and hemodynamic parameters (mean BP, catecholamine infusion rate) were related to the difference of glucose values obtained by the two methods. The Mann–Whitney U test was used to determine whether blood transfusion and heparinization had an influence on the absolute difference of glucose values obtained by the two methods.

A logistic regression model was used for all samples to assess the relationship between accuracy defined by the CLSI POCT12-A3 criteria—i.e., whether each point-of-care glucose value is within $\pm 0.66 \text{ mMol}\cdot\text{L}^{-1}$ of reference glucose values $< 5.5 \text{ mMol}\cdot\text{L}^{-1}$ and $\pm 12.5\%$ for reference glucose values $> 5.5 \text{ mMol}\cdot\text{L}^{-1}$ (criterion 1 in CLSI POCT12-A3) and possible factors. Considering the Spearman's rank correlation and the Mann–Whitney U test, possible factors were put into the logistic regression model. Because multi-collinearity among covariates can

give spurious results, backward stepwise procedures were performed to identify independently associated variables, and odds ratios were calculated.

When significant continuous variables were detected, the areas under the receiver operating characteristic (ROC) curves were calculated. The area under the curve (AUC) is a measure of the parameter's accuracy (AUC = 0.5, no better than chance and no prediction possible; AUC = 1.0, best possible prediction). The optimal hematocrit cut-off point for StatStrip glucometer usage was defined by the Youden index [maximum (sensitivity + specificity – 1)].

Sample size

According to the CLSI POCT12-A3 guidelines, a minimum of 100 samples are needed to determine accuracy in a given patient population. Assuming that approximately 20% of patients would have missing data, we intended to analyze a minimum of 120 patients. To evaluate whether the data set was suitable for accurately characterizing the relationship between two measurement procedures, we calculated the Spearman correlation after data collection.⁴

All tests used for statistical analysis were two-sided and *P* values < 0.05 were considered statistically significant. Data were analyzed in SPSS version 23 (SPSS Inc, Chicago, IL, USA).

Results

We assessed 167 patients and interviewed 148 patients, of which 18 refused to participate and five met the exclusion criteria. Four of the remaining 125 consenting subjects were excluded (two where surgeries were rescheduled, and two where CPB was not used). Samples from 121 patients were analyzed (Fig. 1) (Table 2).

The median [IQR] blood glucose values obtained by StatStrip and BGA and the median difference in blood

Fig. 1 Patient flow diagram.
CPB = cardiopulmonary bypass

Table 2 Patient characteristics

Age (yr), mean (SD)	68	(10)
Female sex <i>n</i> (%)	30	(25)
Height (cm), median [IQR]	170	[165–175]
Weight (kg), median [IQR]	79	[70–90]
BMI (kg·m ⁻²), median [IQR]	27	[24–31]
Euroscore-II, median [IQR]	1.3	[0.9–2.2]
Hct (%), median [IQR]	41	[39–44]
Cr (mMol·L ⁻¹), median [IQR]	82	[66–93]
LVEF (%), median [IQR]	60	[45–60]
HL <i>n</i> (%)	87	(72)
DM <i>n</i> (%)	45	(37)
PVD <i>n</i> (%)	17	(14)
Smoker <i>n</i> (%)	17	(14)
OSAS <i>n</i> (%)	10	(8)
COPD <i>n</i> (%)	23	(19)
Surgical procedure		
CABG <i>n</i> (%)	75	(62)
Valve <i>n</i> (%)	19	(16)
CABG + valve <i>n</i> (%)	21	(18)
Others <i>n</i> (%)	6	(4)
Anesthesia time (min), median [IQR]	269	[225–314]
Surgical time (min), median [IQR]	187	[138–229]
CPB time (min), median [IQR]	90	[57–112]
Cross clamp time (min), median [IQR]	74	[47–95]
Intraoperative transfusion <i>n</i> (%)	74	(61)

BMI = body mass index; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CPB = cardiopulmonary bypass; Cr = creatinine; DM = diabetes mellitus; Hct = hematocrit; HL = hyperlipidemia; HT = hypertension; IQR = interquartile range; LVEF = left ventricular ejection fraction; OSAS = obstructive sleep apnea syndrome; PVD = peripheral vascular disease; SD = standard deviation

values obtained by the two methods are shown in Table 3. The laboratory and hemodynamic data at five time-points are also shown in Table 3.

The relationship between StatStrip and reference glucose values in the context of POCT12-A3 criteria are shown in Fig. 2. The number and percentage of the samples that met CLSI criteria 1 and 2 are shown in Table 4.

The accuracy of the StatStrip glucose measurements at baseline and pre-CPB satisfied CLSI POCT12-A3 criteria while its accuracy during and post-CPB did not. The plotted Parkes error grid results are shown in Fig. 3. All samples at all time-points were within zones A and B (i.e., all samples met the ISO 15197:2013 clinical criteria).

Differences between the blood glucose values measured by the two methods correlated with the PaO₂, lactate, hematocrit, ACT, and the norepinephrine infusion rate (Table 5). While heparinization was associated with a

higher absolute difference ($P < 0.001$), blood transfusion was not ($P = 0.45$).

Four variables (i.e., PaO₂, lactate, hematocrit, and heparinization) were put into the logistic regression model considering the above results. For each 1% increase in hematocrit values, the odds ratio (OR) of meeting the CLSI POCT12-3A2013 criterion 1 increased by approximately 10% (OR, 1.10; 95% CI, 1.05 to 1.14; $P < 0.001$), while heparinization was associated with less accuracy (OR, 0.08; 95% CI, 0.02 to 0.43; $P = 0.003$). In contrast, PaO₂ (OR, 1.27 for a 100 mmHg increase in PaO₂; 95% CI, 0.89 to 1.81; $P = 0.19$) and lactate (OR, 1.23 for each 1.0 mMol·L⁻¹ lactate increase; 95% CI, 0.62 to 2.46; $P = 0.54$) did not significantly influence accuracy.

Analysis of the hematocrit ROC revealed a cut-off point of 31.5%. Thirty-five (15%) of the 239 samples with a hematocrit below 31.5% and only 14 (5%) of 305 samples with a hematocrit $> 31.5\%$ failed to satisfy CLSI POCT12-A3 accuracy criterion 1 (Fig. 4) (Table 6).

The Spearman correlation between blood glucose values was $r = 0.97$ (95% CI, 0.96 to 0.97; $P < 0.001$)

Discussion

The results of this study show that arterial blood glucose analysis by the StatStrip glucometer during open-heart surgery does not meet CLSI POCT12-A3 accuracy criteria. Changes in the patients' hematocrit and heparinization significantly influenced accuracy during and after CPB. In contrast, blood glucose measurements consistently met the ISO 15197:2013 criteria established for subcutaneous insulin therapy in diabetic patients.

Blood glucose measurements in the acute critical care setting performed by older point-of-care devices have to be interpreted with caution, mainly because they do not correct for hematocrit^{2,13,14} or other interferences such as BT,² pH (2), PaO₂^{2,15} tissue perfusion,¹⁶ hypoglycemia,^{16,17} and various medications.^{2,14,16}

For example, blood glucose analyses by Accu-check® (Roche Pharmaceuticals, Basel, Switzerland) in surgical patients proved to be inaccurate according to the criteria developed for the safe use of subcutaneous insulin (ISO 15197:2013).^{6,18}

Although the advent of newer technologies has provided more reliable results in the critically ill,^{19,20} no studies have addressed the limitations and accuracy of glucometers during operations that are associated with the most profound alterations of glucose homeostasis, such as cardiac procedures and CPB. Hence, not unexpectedly, there are no clear recommendations by the FDA regarding specific glucometer safety requirements for patients warranting intravenous insulin therapy perioperatively.

Table 3 Arterial blood analysis and hemodynamic parameter

	Baseline	Pre-CPB	During CPB1	During CPB2	Post-CPB	<i>P</i> value
Statstrip BS (mMol·L ⁻¹)	6.0 [5.6–7.1]	5.9 [5.4–7.3]	6.8 [5.9–8.1]	7.7 [6.4–8.8] ^{*†‡}	8.3 [6.9–9.7] ^{*†‡}	<0.001
ABG BS (mMol·L ⁻¹)	5.9 [5.5–7.3]	5.8 [5.4–7.0]	6.4 [5.5–7.4]	7.4 [6.9–9.7] ^{*†‡}	8.2 [7.0–9.6] ^{*†‡}	<0.001
pH	7.41 [7.39–7.44]	7.40 [7.37–7.43]	7.40 [7.37–7.42]	7.37 [7.34–7.39] [*]	7.35 [7.32–7.41] [*]	<0.001
pO ₂ (mmHg)	208 [129–305]	363 [239–441] [*]	235 [205–277]	218 [190–241]	309 [210–400]	<0.001
pCO ₂ (mmHg)	43 [39–48]	42 [38–47]	41 [38–43]	42 [39–43]	39 [37–43]	0.06
Lactate (mMol·L ⁻¹)	0.9 [0.6–1.1]	0.8 [0.7–1.0]	0.9 [0.7–1.3]	1.1 [0.8–1.3] [*]	1.5 [1.2–2.5] [*]	<0.001
Hct (%)	44 [41–47]	40 [36–42] [*]	29 [27–32] [*]	30 [27–33] [*]	30 [27–32] [*]	<0.001
ACT (sec)	150 [141–160]	659 [562–834] [*]	610 [538–692] [*]	543 [498–591] [*]	123 [116–129]	<0.001
BT nasal (°C)	NA	35.6 [35.2–36.0]	35.6 [34.0–36.2]	35.7 [34.2–36.3]	36 [35.7–36.1]	0.17
BT bladder (°C)	NA	36.1 [35.9–36.4]	35.8 [34.8–36.2]	35.1 [34.3–36.3] [†]	36 [35.8–36.2]	<0.001
Systolic BP (mmHg)	132 [118–152]	102 [92–109] [*]	NA	NA	104 [98–112] [*]	<0.001
Diastolic BP (mmHg)	66 [58–77]	53 [48–58] [*]	NA	NA	53 [49–60] [*]	<0.001
Mean BP (mmHg)	87 [79–99]	69 [64–75] [*]	63 [58–70] [*]	65 [60–70] [*]	71 [66–76] [*]	<0.001
HR (bpm)	65 [60–75]	62 [53–73]	NA	NA	80 [70–90] [*]	<0.001
Epinephrine (mg·kg ⁻¹ ·hr ⁻¹)	0 [0–0]	0 [0–0]	0 [0–0]	0 [0–0]	2 [0–4] [*]	<0.001
Norepinephrine (mg·kg ⁻¹ ·hr ⁻¹)	0 [0–0]	0 [0–4]	0 [0–4]	1 [0–4] [*]	4 [4–8] [*]	<0.001

Data were analyzed using the Friedman test to generate the *P* values. The values are represented as median [interquartile range]

Post hoc pairwise comparison ^{*}*P* < 0.05 vs baseline, [†]*P* < 0.05 vs before CPB, [‡]*P* < 0.05 vs before CPB. ACT = activating clotting time; BT = body temperature; BP = blood pressure; Hct = hematocrit; HR = heart rate; Lac = lactate; NA = not applicable

Fig. 2 Scatter plot of the difference of glucose values (StatStrip® glucometer minus reference glucose) and reference glucose value. A = baseline; B = before CPB; C = early CPB; D = late CPB; E = post-CPB. Dashed lines represent CLSI POCT12-A3 error criteria 1: ± 0.66 mMol·L⁻¹ of reference glucose value (for reference glucose

values < 5.5 mMol·L⁻¹) and $\pm 12.5\%$ (reference glucose > 5.5 mMol·L⁻¹) and criteria 2: 0.83 mMol·L⁻¹ (reference glucose < 4.1 mMol·L⁻¹) or 20% (reference glucose > 4.1 mMol·L⁻¹). CPB = cardiopulmonary bypass CLSI POCT12-A3 = Clinical and Laboratory Standards Institute Point-of-Care testing 12-A3

Recently, the use of StatStrip glucometer in patients undergoing a variety of non-cardiac surgical procedures showed 100% accuracy of capillary and arterial glucose values based on ISO15197:2013 criteria (i.e., all values

were within zones A and B on the Parkes error grid for type-1 diabetes mellitus).¹⁰ Nevertheless, neither capillary nor arterial blood glucose results met the CLSI POCT12-

Table 4 Blood glucose data meeting the criteria defined by the Clinical and Laboratory Standards Institute Point-of-Care testing 12-A3 guideline

		Criterion 1		Criterion 2	
		Reference glucose (R) -mMol·L ⁻¹	Statstrip® glucose mMol·L ⁻¹	Reference glucose (R) -mMol·L ⁻¹	Statstrip® glucose mMol·L ⁻¹
		< 5.5	$R \pm 0.66$	< 4.1	$R \pm 0.83$
		> 5.5	$R \pm R \times 0.125$	> 4.1	$R \pm R \times 0.2$
Time point	<i>n</i>	Meeting to criterion 1; <i>n</i> (%; 95% CI)		Meeting to criterion 2; <i>n</i> (%; 95% CI)	
Baseline	121	120 (99; 96 to 100)		121 (100; 98 to 100)	
Pre-CPB	104	99 (95; 89 to 98)		102 (98; 93 to 100)	
CPB1	111	93 (84; 76 to 90)		108 (97; 92 to 100)	
CPB2	102	85 (83; 75 to 90)		98 (96; 90 to 99)	
Post-CPB	106	98 (92; 86 to 97)		106 (100; 97 to 100)	

Criterion 1: 95% of samples should be ± 0.66 mMol·L⁻¹ of reference glucose values < 5.5 mMol·L⁻¹ and $\pm 12.5\%$ for reference glucose values > 5.5 mMol·L⁻¹

Criterion 2: 98% of samples should be ± 0.83 mMol·L⁻¹ of reference glucose values < 4.1 mMol·L⁻¹ or 20% of the reference glucose for values > 4.1 mMol·L⁻¹

R = reference glucose; CI = confidential interval; CPB = cardiopulmonary bypass

Fig. 3 Error grid analysis for arterial glucose obtained by StatStrip® and reference glucose values as shown by the Parkes error grid for type 1 diabetes mellitus. A = baseline; B = before CPB; C = early

CPB; D = late CPB; E = post-CPB. To meet ISO 15197:2013 accuracy guidelines, 99% of values must fall within zone A or zone B. CPB = cardiopulmonary bypass; POC = point-of-care

Table 5 Correlation between difference of glucose values obtained by the two methods and variables

	R	P value
Age (yr)	0.00	0.99
BMI (kg·m ⁻²)	0.04	0.31
pH	-0.06	0.14
PaCO ₂ (mmHg)	-0.02	0.59
PaCO ₂ (mmHg)	-0.15	<0.001
Lac (mMol·L ⁻¹)	-0.10	0.02
Hct (%)	-0.27	<0.001
ACT (sec)	0.18	<0.001
BT nasal (°C)	0.04	0.43
BT bladder (°C)	0.02	0.67
mean BP (mmHg)	0.01	0.94
Epinephrine (mg·kg ⁻¹ ·hr ⁻¹)	0.05	0.29
Norepinephrine (mg·kg ⁻¹ ·hr ⁻¹)	0.11	0.02

Data are determined by Spearman's rank correlation

ACT = activating clotting time; BMI = body mass index; BP = blood pressure; BT = body temperature; Hct = hematocrit

Fig. 4 Receiver operating characteristic curves for hematocrit. The optimal cut-off value for predicting the inaccuracy of blood glucose value obtained by StatStrip® in hematocrit was 31.5%. (AUC = 0.73; 95% CI, 0.66 to 0.78; $P < 0.001$). AUC = area under the curve; CI = confidence interval

A3 guidelines as required for intensive insulin protocols aimed at stricter glycemic control.¹⁰

These observations are in agreement with the present findings that the use of StatStrip glucometers is safe for the titration of subcutaneous insulin administration, but not for more intensive glycemic control during cardiac surgery and CPB.

A secondary objective of the present study was to detect clinical and laboratory variables that may contribute to

Table 6 Estimated sensitivity and specificity for meeting to CLSI POCT criteria regarding hematocrit between 20 and 45

Hct	A: Sensitivity	B: 1 - Specificity	A - B
21.5	0.993	1.000	-0.007
22.5	0.991	1.000	-0.009
23.5	0.982	0.984	-0.002
24.5	0.971	0.984	-0.013
25.5	0.943	0.887	0.056
26.5	0.916	0.823	0.094
27.5	0.867	0.661	0.205
28.5	0.812	0.548	0.264
29.5	0.767	0.452	0.315
30.5	0.704	0.403	0.300
31.5	0.654	0.290	0.364
32.5	0.602	0.242	0.360
33.5	0.536	0.194	0.343
34.5	0.500	0.177	0.323
35.5	0.448	0.113	0.335
36.5	0.421	0.097	0.324
37.5	0.398	0.097	0.301
38.5	0.373	0.081	0.293
39.5	0.335	0.081	0.254
40.5	0.303	0.048	0.255
41.5	0.251	0.048	0.203
42.5	0.219	0.032	0.187
43.5	0.181	0.032	0.149
44.5	0.149	0.032	0.117

CLSI = Clinical and Laboratory Standards Institute; Hct = hematocrit; POCT = StatStrip point-of-care treatment. Youden index = maximum (sensitivity + specificity - 1) = maximum (A - B)

glucometer bias. A previous study reported weak, although statistically significant, effects of comorbidity, PaCO₂, and mean diastolic BP in the 15 min before sampling, while other parameters, including time of general anesthesia, diabetes status, biometrics, BT, HR, hematocrit, PaO₂, and pH did not have any significant relationship.¹⁰

In the present study, heparinization and hematocrit showed a significant influence on StatStrip glucometer accuracy, particularly at hematocrit values below the cut-off point of 31.5%.

The heparin dose given in our protocol (400 IU·kg⁻¹) typically leads to heparin plasma concentrations > 500 IU·dL⁻¹,²¹ which according to the FDA²² can interfere with the hematocrit adjusting technology of glucometers. Although such interference should not occur with a hematocrit of 20–60%,³ heparinization in our study was associated with significant bias during and after CPB.

The inaccuracy observed after separation from CPB and the administration of protamine suggests that even lower plasma heparin levels may have an impact.

The fact that more restrictive transfusion methods and lower levels of hemoglobin are becoming more acceptable during cardiac surgery²³ further emphasizes the importance of accurate point-of-care blood glucose measurements in anemic patients.

We acknowledge several limitations. We only studied adult patients undergoing cardiac surgery making the applicability of our findings to pediatric settings uncertain. Secondly, as no episode of hypoglycemia ($< 3.5 \text{ mMol}\cdot\text{L}^{-1}$) was recorded in our study subjects, our observations may not be applied to blood glucose values in the hypoglycemic range. Thirdly, only a few ACT values between 200 and 400 sec were analyzed (CPB requires > 480 sec). Hence, the influence of lower concentrations of heparin needs further study. Fourthly, because we tested only one glucometer model, our results are not generalizable to others. Finally, it is not possible to fully predict whether a sample size of 100 is adequate to evaluate the accuracy of a glucometer under the CLSI POCT12-A3 guidelines assuming a Spearman correlation $r > 0.95$. Hence, a larger sample size may be required.⁴

In conclusion, arterial blood glucose measurement by StatStrip was accurate before CPB but was no longer accurate during and after CPB, most likely due to the impact of heparinization and anemia. Values obtained using the StatStrip must be interpreted with caution during intensive glucose control in cardiac surgery.

Conflict of interest All authors declare that they have no financial or non-financial interests that may be relevant to the submitted work.

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