Suitability of Capillary Blood Glucose Analysis in Patients Receiving Vasopressors

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Notice to CNE enrollees:
A closed-book, multiple-choice examination following this article tests your understanding of the following objectives:

1. Identify the factors that can affect the accuracy of blood sugar testing.
2. Discuss what blood glucose testing method is acceptable to use for patients with less than 2, or more than 2 vasopressors.
3. Describe the potential consequences of using an inaccurate blood glucose testing method.

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Background Glycemic control in critically ill patients decreases infection and mortality. Patients receiving vasopressors have altered peripheral perfusion, which may affect accuracy of capillary blood glucose values measured with point-of-care devices.

Objectives To compare capillary and arterial glucose values measured via point-of-care testing (POCT) with arterial glucose values measured via clinical chemistry laboratory testing (CCLT) in patients after cardiothoracic surgery. To determine if vasopressors or diminished peripheral perfusion influence the accuracy of POCT values.

Methods In a prospective, convenience sample of 50 adult postoperative cardiothoracic patients receiving insulin and vasopressors, 162 samples were obtained simultaneously from capillary and arterial sites during insulin infusion and tested via both POCT and CCLT. Clarke error grid analysis and ISO 15197 were used to analyze level of agreement. Two-way analysis of variance was used to analyze differences in glucose values with respect to vasopressor use and peripheral perfusion.

Results An unacceptable level of agreement was found between the capillary POCT results and arterial CCLT results (only 88.3% of values fell in zone A, or within the ISO 15197 tolerance bands). Arterial POCT results showed acceptable (94.4%) agreement with CCLT results. Vasopressor use had a significant effect on the accuracy of arterial blood glucose values \((F=15.01; P<.001)\).

Conclusions Even when the more accurate POCT with arterial blood is used, blood glucose values are significantly less accurate in patients receiving more than 2 vasopressors than in patients receiving fewer vasopressors. CCLT may be safer for titrating insulin doses in these patients. (American Journal of Critical Care. 2013;22:423-430)
Glucose measurement by using a finger stick to obtain capillary samples is a way to minimize blood sampling from arterial catheters in patients receiving insulin infusions. Additionally, the capillary glucose check is beneficial as it is a task that can be safely delegated to a nursing care assistant. Capillary blood glucose measurements are accurate in normotensive patients and correlate well with measurements from samples tested in a clinical chemistry laboratory. However, in critically ill patients, altered blood pressure affects the accuracy of blood glucose values measured by using point-of-care testing (POCT). In addition, in patients receiving vasopressors, the blood pressure may be normalized (normotensive) by arterial measurement, but peripheral perfusion may be altered by the vasoconstrictor effects of the medication. Altered peripheral perfusion may affect the accuracy of capillary blood glucose measurements; however, actual best practice for patients after cardiac surgery is not known. One study of 50 postoperative cardiovascular surgery patients demonstrated high correlation in capillary glucose sampling, in comparison with arterial and venous sampling, whereas other studies have shown poor correlation in patients with cardiopulmonary resuscitation, shock states, presence of edema, and after major surgery. The small sample sizes in these studies and the conflicting results support the need for further study in populations with compromised peripheral perfusion.

The standard of practice for continuous insulin infusions in many intensive care units is hourly monitoring of blood glucose levels, particularly in the acute postoperative phase. Standard procedure, however, does not dictate method, and as a result either arterial or capillary blood samples or both may be collected. Samples from both finger sticks and arterial catheters may be obtained concomitantly for purposes of validation; however, such validation is not required and is a nurse-dependent variation in care. Patients are typically admitted to the cardiothoracic intensive care unit from the operating room already receiving insulin infusions and vasoactive medications. During early postoperative recovery, frequent titration of both insulin and vasopressor infusions occurs; however, studies to date have not consistently supported the accuracy of capillary blood glucose testing in this setting or the correlation of arterial with capillary blood glucose values in these critically ill patients. In order to answer the research question regarding accuracy and correlation in the setting of high doses of vasopressor drugs, early access to temporally related samples is required. The purpose of this study was to compare blood glucose measurements obtained from arterial measurement, but peripheral perfusion may be altered by the vasoconstrictor effects of the medication. Altered peripheral perfusion may affect the accuracy of capillary blood glucose measurements; however, actual best practice for patients after cardiac surgery is not known. One study of 50 postoperative cardiovascular surgery patients demonstrated high correlation in capillary glucose sampling, in comparison with arterial and venous sampling, whereas other studies have shown poor correlation in patients with cardiopulmonary resuscitation, shock states, presence of edema, and after major surgery. The small sample sizes in these studies and the conflicting results support the need for further study in populations with compromised peripheral perfusion.

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POCT of capillary and arterial blood samples with measurements made in the clinical chemistry laboratory on arterial blood samples from patients after cardiothoracic surgery, and to determine if use of vasopressor medications or peripheral perfusion influenced the POCT values.

Methods

Design, Setting and Sample
This prospective, case-controlled study was conducted in the 20-bed cardiothoracic intensive care unit (CTICU) at a large academic tertiary care hospital. The unit provides care for patients undergoing cardiac and thoracic surgery, including bypass grafting, valve surgery, heart and lung transplant, implantation of ventricular assist devices, and thoracic surgeries. A convenience sample of 50 adult postoperative cardiothoracic patients receiving insulin and vasopressors was prospectively enrolled. All participants provided informed consent, and the study was approved by the institutional review board.

Measures
Prospctive data collection of all study variables occurred for participants upon admission to the CTICU and each time thereafter that a basic metabolic panel was ordered while the patient was receiving a continuous insulin infusion. Variables assessed included the following: pharmacotherapy, vital signs, and blood samples obtained simultaneously from arterial and capillary sites. Samples were tested by using POCT and clinical chemistry laboratory testing (CCLT) as the “gold standard.” The samples sent to the clinical laboratory were run on a Beckman Coulter Unicel DxC 600/800 by using the oxygen consumption rate method.

Vasopressor medications included in the evaluation for this study were dopamine, epinephrine, norepinephrine, phenylephrine, and vasopressin. The quality of peripheral tissue perfusion was assessed by standard scales for pulse (0-4), capillary refill (<3 sec, >3 sec), color (pink-mottled), and temperature (hot-cold) of the extremity used for study samples. The scales used for these assessments in this study are a part of the usual care procedures for all nurses certified to care for patients in the CTICU. The competency-based orientation process accounts for reliability, interobserver variation, and intraobserver variation for these scales. The temperature of the extremities was categorized into 2 groups (cool or warm) on the basis of the distribution of the data and the lack of variability among participants across groups. The documented temperature of the extremities fell into 1 of these 2 categories for all participants. The categories were coded as 1 = cold or cool and 2 = warm or hot. These categories were used as the measure of peripheral tissue perfusion for comparison in the study.

Study Procedures
Demographics and medical history were abstracted from the medical record. Fifty adult (age ≥18 years) postoperative cardiothoracic patients receiving insulin and vasopressor infusions were enrolled and consented to participate in the study. Because samples were needed early in the postoperative recovery process and patients were sedated and therefore incapable of giving consent, we obtained ethical review and approval for a conditional waiver of consent and authorization. We collected the early matched samples, and these data were used only if the participant or legally authorized representative later gave consent for use of the samples.

Patients with a hematocrit of less than 20% or greater than 70% were excluded from the study because of reported inaccuracy of the glucometer (Abbott Precision PCx) in such patients. All participants were required to have undergone coronary artery bypass grafting, valve repair or replacement, lung transplant, or heart transplant and were receiving insulin as a part of standard care for blood glucose management after cardiothoracic surgery. The first blood sample was obtained at the immediate postoperative admission as per standard postoperative care orders. Results of blood glucose checks from capillary and arterial sources were recorded. The type and number of intravenous vasopressor medications and intravenous insulin administered were also recorded. Additional assessment data included the presence of edema, quality of capillary refill, and quality of pulse in the arm from which the blood samples were obtained. The test nurse was not blinded to the results; however, bias was limited by the objective nature of the data and the assessment strategy. The majority of variables were objective data (blood glucose values and the number of vasopressor medications used) with the exception of the perfusion assessment. The possibility for introduction of bias in the perfusion assessment was limited by the fact that nurses used a standardized assessment scale and evaluated all patients in the same manner. There was no “treatment group” per se; all patients had exactly the same assessment. In addition, nurses documented the same information in each patient’s record as was used for the research study.
Analysis

A descriptive, quantitative evaluation of all demographic variables was conducted to estimate the frequency and distribution of patients’ characteristics. Each patient had blood samples obtained simultaneously from arterial and capillary sites for the duration of the insulin infusion. This procedure resulted in all patients having 2 to 5 sets of blood samples. A total of 162 sets of blood glucose values were used in the analysis after missing values and outliers were removed. The “outliers” consisted of 3 samples with blood glucose values of 1002, 14, and 18 mg/dL. These values are inconsistent with the correlating capillary pOCT value taken from these same patients at the same time points. We therefore consider these values to be errors, and we eliminated those samples from the analysis.

Clarke error grid analysis (EGA) was performed to assess the level of agreement between both capillary and arterial blood glucose levels measured by using pOCT and arterial blood glucose levels measured by using CCLT. The error grid analysis has 5 zones of relative accuracy of estimation of blood glucose level. Zone A indicates a difference of less than 20% in the blood glucose values being compared. This zone represents acceptably equivalent values, and no difference would be expected with regard to clinical decision making in response to values that fall in this zone. Zone A is the only acceptable zone that has the same criteria as the International Standardization Organization (ISO) 15197 gold standard guideline. Zone B represents a difference of greater than 20% in glucose values but has minimal impact on the clinical treatment. Zone C indicates that the difference in glucose values would lead to overcorrection or unnecessary treatment of the acceptable blood glucose level and causes a change in the clinical action. Zone D indicates that the difference in glucose values has the risk of failure to detect or treat an error. Zone E indicates that the difference in glucose values causes erroneous treatment.

The ISO 15197 guideline states that measurements should be within 15 mg/dL of reference for glucose levels less than 75 mg/dL and within 20% for glucose levels of 75 mg/dL or higher. A blood glucose device is considered accurate if 95% of pairs satisfy these criteria. Results that fall outside the ISO 15197 tolerance bands are considered inaccurate.

Analysis of variance was used to evaluate the association between the differences in sets of blood glucose values within each time point, peripheral perfusion, and vasopressor use. The patients were classified into 2 groups according to medication use at the time of the blood sampling: 1-2 medications and 3-5 medications. The patients’ peripheral perfusion was classified as either cool or warm. The analyses were performed by using SAS statistical software version 9.2.

Results

Of 50 patients who agreed to participate in the study, 1 patient had incomplete data and could not be included in the final analysis. Among the 49 remaining participants, a total of 162 sets of blood glucose values were available for the final analysis. The mean age of participants was 61.3 years (SD, 13.9 years) and 82% (n = 40) were white. The mean body mass index (calculated as weight in kilograms divided by height in meters squared) for the sample was 28.8 (SD, 7.0), and 27% (n = 13) of the participants were smokers. The mean core body temperature was 37.2°C (SD, 0.9°C), and the mean number of vasopressor medications (dopamine, epinephrine, vasopressin, norepinephrine, or phenylephrine) that patients were receiving was 3.2 (SD, 1.0).

First, the level of agreement between the capillary blood glucose level measured by using the pOCT and the arterial blood glucose level measured by using CCLT was evaluated with respect to the Clarke EGA and ISO 15197 guideline. Only 88.3% of the capillary POCT values fell in zone A (Figure 1), and 88.3% were within the ISO 15197 tolerance bands. The capillary blood glucose level measured by using POCT was therefore considered inaccurate, as less than 95% of the values satisfy the criteria of the ISO clinical standards guideline. A systematic bias between the POCT and CCLT results was present, as was expected on the basis of previously reported research.

Next, Clarke EGA was used to evaluate the level of agreement in the arterial blood glucose levels.
measured by using POCT and the arterial blood glucose levels measured by using CCLT. Acceptable agreement between arterial blood glucose levels measured by POCT and those measured by CCLT was indicated, with 94.4% of values falling in zone A (Figure 2). The comparison performed by ISO 15197 guideline had the same results: 94.4% of the pairs of arterial blood glucose levels measured by using POCT and arterial blood glucose levels measured by using CCLT were within the tolerance bands.

Finally, analysis of variance was used to examine the relationship among use of vasopressor medications, peripheral perfusion scores, and the accuracy and reliability of blood glucose values obtained via arterial POCT. Patients receiving more vasopressors (>2 concomitant vasopressor medications) demonstrated a significant difference in the accuracy of arterial blood glucose measurements obtained via POCT as compared with patients receiving fewer vasopressors (0-2 vasopressor medications; \( F = 15.01; P = .001 \)). Figure 3 shows Clarke EGA with 90% of arterial POCT values falling in zone A in patients receiving more than 2 vasopressor medications. The accuracy of blood glucose levels obtained via arterial POCT is not significantly different in patients with decreased peripheral perfusion, categorized as cool, and patients with better perfusion, categorized as warm (\( F = 0.0; P = .98 \)).

In summary, blood glucose levels measured via arterial POCT are significantly less accurate in patients who are being treated with more vasopressors (see Table).

**Discussion**

In this study, we evaluated the accuracy of POCT blood glucose measurements of both capillary and arterial blood samples from patients receiving insulin after cardiothoracic surgery. Accuracy was determined by the level of agreement between blood glucose measurements obtained from capillary as well as arterial samples tested by using POCT in comparison with the gold standard measure, CCLT of an arterial sample. Two statistical approaches were used to verify level of agreement, the Clarke error grid analysis and the ISO 15197, the standard analysis used in the clinical chemistry laboratory, upon which guidelines for clinical acceptability in levels of agreement are based.

In addition and most importantly, we evaluated the relationship between both use of vasopressor medications and altered peripheral perfusion and the accuracy of blood glucose values measured via arterial POCT in patients receiving insulin after cardiothoracic surgery. Results showed that patients receiving more than 2 vasopressor infusions had significantly less accurate arterial blood glucose values than did patients receiving less than 2 vasopressors. Peripheral perfusion did not affect the accuracy of arterial POCT blood glucose values.

These findings play an important role in intensive care, particularly for patients undergoing cardiothoracic surgery. The importance of glycemic control for all patients undergoing cardiac surgery has been demonstrated in numerous studies.\(^{1,2,15}\) Having higher glucose levels (>180 mg/dL) during the perioperative
period is an independent predictor of mortality in diabetic and nondiabetic patients. Although glycemic control in critically ill patients decreases infection and mortality, tight glycemic control (<150 mg/dL) is associated with increased incidence of hypoglycemic events and increased mortality. These results led to the early discontinuation of research protocols for tight glycemic control. Glycemic control (glucose <180 mg/dL) is a class I recommendation in the 2011 ACCF/AHA guidelines. Despite this recommendation, the evidence for titration of insulin infusions following cardiothoracic surgery in patients who are subsequently receiving high doses of vasopressor medications is scant.

In populations of critically ill patients, altered blood pressure affects the accuracy of POCT blood glucose measurements. These studies have shown that POCT blood glucose measurements are accurate in normotensive patients and correlate well with measurements of arterial samples. However, after cardiothoracic surgery, patients are likely to be hypertensive and typically receive more than 2 vasopressor medications for short-term hemodynamic support. These patients may be normotensive by arterial blood pressure measurement, but because of the α- and β-adrenergic receptor agonist effects of the medication, may have resultant peripheral vasoconstriction. Our study supports the hypothesis that a relationship does exist between the accuracy of POCT blood glucose measurements and use of vasopressor medications.

Although other studies addressing this specific relationship have not been reported, our study results suggest that administration of more than 2 vasopressor medications affects the accuracy of POCT blood glucose measurements in postoperative cardiothoracic surgery patients. We evaluated the relationship between peripheral perfusion in postoperative cardiac surgery patients and the accuracy of POCT blood glucose analysis and found no significant difference in accuracy of blood glucose measurements in patients with decreased perfusion.

**Limitations**

A limitation of the study was the short stay in the intensive care unit for patients after cardiothoracic surgery in this study. We were likely to lose data capture opportunities for data collection after the first 4 to 8 hours, owing to the rapid discontinuation of vasopressor drugs. Because all patients did not have data beyond the second time period, we were not able to conduct a multiple repeated-measures analysis and therefore lacked the ability to have increased sensitivity in the statistical output beyond the second data collection point for each patient. For example, we could not evaluate the trends in warming and decreasing drug use on blood glucose values over time by using repeated-measures analysis because all patients did not have more than 2 time points of evaluation. In addition, patients were warmer than anticipated (higher core body temperature) in the immediate postoperative period, which may have minimized the effect of peripheral vasoconstriction. Last, the care nurse served as the investigator as well as the care nurse; therefore, patients with high doses of multiple inotropic agents may have required care that precluded regularly scheduled data collection.

**Implications for Clinical Practice**

Clinical practice recommendations based on these findings included the following:

- POCT using arterial blood samples was recommended to improve the efficiency and reduce the cost of obtaining frequent blood glucose measurements.
- POCT was only within acceptable limits of accuracy in patients receiving no more than 2 concomitant vasopressors.
- Use of a consistent blood source for testing was recommended to reduce unnecessary variation and improve safety in insulin dosing.

This study validated previous work showing a systematic bias in the use of capillary POCT as opposed to CCLT for management of patients’ insulin infusions. In addition, the arterial POCT results were within the 95% acceptable level of agreement with CCLT results. Those patients receiving 3 or more vasopressor medications had significant and unacceptable differences in blood glucose values as compared with CCLT results. Therefore the POCT device cannot be recommended for patients receiving 3 or more vasopressors.

Our research work group was interested in conducting this study because nurses had observed situ-

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<th>Zone</th>
<th>No. (%) of blood glucose values</th>
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<tr>
<td></td>
<td>0-2 Medications</td>
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<tr>
<td>A</td>
<td>126 (95.5)</td>
</tr>
<tr>
<td>B</td>
<td>6 (4.5)</td>
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<tr>
<td>C</td>
<td>0 (0.0)</td>
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ations when simultaneous testing in patients produced large variances in results. These differences were confirmed in the initial analysis of the accuracy of capillary blood glucose values. Because of the overall inaccuracy of capillary values, it was irrelevant to analyze further the effect of vasoconstrictors or peripheral perfusion. The recommendation to the clinical practice council supported the use of POCT with arterial blood to improve accuracy at the highest rate of precision and avoiding using capillary samples in these patients. In addition, our study shows that blood glucose measurements obtained via arterial pOCT in patients receiving more than 2 vasopressors are not reliable in cardiac surgery patients. Study results were disseminated at a patient safety conference for our entire health system, and the study team received a first place award for research to improve patient safety.

Current practice includes use of POCT testing with arterial blood samples for titration of insulin infusions in cardiac surgery patients. Our study results demonstrate inaccuracy in these values in patients receiving more than 2 vasopressors. These results must be verified in a larger sample of patients before we can recommend practice change. A quality improvement project to verify these results is planned.

Conclusions

Our findings show that capillary POCT resulted in unacceptable, low levels of agreement with the gold standard CCLT. Arterial POCT blood glucose measurements were within the 95% acceptable level of agreement with CCLT measurements, and arterial POCT is recommended for safe titration of insulin infusions in postoperative cardiothoracic patients. In patients receiving 3 or more vasopressor infusions, arterial POCT yielded significantly different results from CCLT and cannot be recommended for safe titration of insulin. Last, arterial POCT blood glucose measurements were not significantly different from CCLT measurements in patients with poor peripheral perfusion (cold) as compared with patients with normal peripheral perfusion (warm).

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1. Which of the following is a benefit of blood glucose (BG) measurement by using the finger-stick method?
   a. It is accurate in normotensive patients
   b. It can be delegated safely to nursing care assistant
   c. All of the above
   d. None of the above

2. Which of the following is not a current nursing practice?
   a. Hourly BG monitoring of patients with insulin infusion
   b. Nurses check BG via finger stick
   c. Nurses check BG using arterial sample
   d. Nurses check BG via clinical chemistry laboratory testing (CCLT)

3. Which of the following is the gold standard of BG testing?
   a. Capillary point-of-care testing (POCT)
   b. Arterial POCT
   c. Capillary CCLT
   d. Arterial CCLT

4. Which of the following is not a quality used to assess peripheral tissue perfusion in the study?
   a. Edema
   b. Pulse
   c. Capillary refill
   d. Temperature

5. Which of the following patients were excluded from the study?
   a. Patients with hematocrit less than 20%
   b. Patients with hematocrit greater than 70%
   c. All of the above
   d. None of the above

6. According to Clarke Error Grid Analysis, which of the following zones indicates the highest level of agreement between capillary and arterial blood glucose using POCT or CCLT?
   a. Zone A
   b. Zone B
   c. Zone C
   d. Zone D

7. Which of the following methods of checking blood glucose have an acceptable level of agreement in patients with 3 or fewer vasopressors?
   a. Capillary POCT and arterial POCT
   b. Capillary POCT and peripheral perfusion
   c. Capillary POCT and CCLT
   d. Arterial POCT and CCLT

8. Which of the following is not a recommendation of the study?
   a. Capillary POCT should not be used on postoperative cardiothoracic patients.
   b. Arterial POCT can be used on patients with less than 3 vasopressors.
   c. Capillary POCT can be used on normotensive patients.
   d. Arterial POCT can be used on postoperative patients with more than 3 vasopressors.

9. According to the study, what is the relationship between peripheral perfusion in postoperative cardiac surgery patients and accuracy of POCT?
   a. There is no significant difference in patients with decreased perfusion.
   b. There is no significant difference in patients with increased perfusion.
   c. There is a significant difference in patients with increased perfusion.
   d. There is a significant difference in patients with decreased perfusion.

10. Which of the following is not a major limitation of the study?
    a. Short stay of patients in intensive care unit
    b. Rapid discontinuation of vasopressors
    c. Ability to conduct multiple repeated measures analysis
    d. Patients were warmer than anticipated

11. In patients receiving more than 2 vasopressors, what does the study recommend?
    a. Check BG by CCLT.
    b. Check BG via arterial CCLT.
    c. Check BG via capillary POCT.
    d. Analyze peripheral perfusion.

12. According to the study, what is the relationship between arterial POCT BG measurements and peripheral perfusion?
    a. Arterial POCT is more accurate in patients with cold extremities.
    b. Arterial POCT is more accurate in patients with warm extremities.
    c. There is no significant difference in accuracy of BG measurements in patients with cold extremities as compared with those with warm extremities.
    d. There is a significant difference in accuracy of BG measurements in patients with cold extremities as compared with those with warm extremities.