Accuracy of Capillary and Arterial Whole Blood Glucose Measurements Using a Glucose Meter in Patients under General Anesthesia in the Operating Room

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ABSTRACT

Background: The aim of this study was to evaluate the use of a glucose meter with surgical patients under general anesthesia in the operating room.

Methods: Glucose measurements were performed intraoperatively on 368 paired capillary and arterial whole blood samples using a Nova StatStrip (Nova Biomedical, USA) glucose meter and compared with 368 reference arterial whole blood glucose measurements by blood gas analyzer in 196 patients. Primary outcomes were median bias (meter minus reference), percentage of glucose meter samples meeting accuracy criteria for subcutaneous insulin dosing as defined by Parkes error grid analysis for type 1 diabetes mellitus, and accuracy criteria for intravenous insulin infusion as defined by Clinical and Laboratory Standards Institute guidelines. Time under anesthesia, patient position, diabetes status, and other variables were studied to determine whether any affected glucose meter bias.

Results: Median bias (interquartile range) was −4 mg/dl (−9 to 0 mg/dl), which did not differ from median arterial meter bias of −5 mg/dl (−9 to −1 mg/dl; P = 0.32). All of the capillary and arterial glucose meter values met acceptability criteria for subcutaneous insulin dosing, whereas only 89% (327 of 368) of capillary and 93% (344 of 368) arterial glucose meter values met accuracy criteria for intravenous insulin infusion. Time, patient position, and diabetes status were not associated with meter bias.

Conclusions: Capillary and arterial blood glucose measured using the glucose meter are acceptable for intraoperative subcutaneous insulin dosing. Whole blood glucose on the meter did not meet accuracy guidelines established specifically for more intensive (e.g., intravenous insulin) glycemic control in the acute care environment. (Anesthesiology 2017; 127:466-74)

According to the Centers for Disease Control and Prevention, approximately 9.3% of the U.S. population has diabetes mellitus, with 27% of the population being undiagnosed.1 Although glycemic control for critically ill patients remain controversial,2–4 glycemic control using insulin in patient with diabetes mellitus undergoing surgery has become an increasingly common quality metric.5 Treatment of hyperglycemia requires monitoring of blood glucose, because even a single episode of severe hypoglycemia (glucose less than 40 mg/dl) may increase the risk of death in the hospital up to twofold.6 Guidelines recommend glucose monitoring for patients under general anesthesia if the patient receives insulin, the procedure is longer than 1 to 2 h, or if there is concern for hyperglycemia or hypoglycemia.7,8 Glucose monitoring can be performed using laboratory serum or plasma glucose analysis, whole blood glucose by blood gas analyzer, or whole blood glucose by glucose meter. Although laboratory and blood gas analysis methods require an arterial or venous blood specimen, most glucose meters can also analyze capillary (via fingerstick) blood. Glucose analysis by laboratory methods is more time consuming and expensive than glucose meter testing and may not provide timely results for dosing insulin or treating hyperglycemia or hypoglycemia in the operating room (OR).
The correlation between results from glucose meters and laboratory glucose measurements varies between meter technologies, and correlation in the hypoglycemic and hyperglycemic ranges is poor for some meters. Although newer technologies may provide more accuracy, there is still concern about the use of meters in the critically ill. Studies have demonstrated potentially dangerous discrepancies in capillary glucose measurement in patients on vasopressor therapy, patients in shock or with poor tissue perfusion, and in other critically ill patient populations. Consequently, no glucose meter is currently approved by the U.S. Food and Drug Administration (FDA) for use with capillary samples in critically ill hospitalized patients.

Although the FDA has not provided a definition of what constitutes “critically ill” for purposes of capillary glucose testing, previous studies have shown that factors expected to change rapidly during anesthesia and surgery can affect glucose meter accuracy. These factors include hematocrit, blood pressure, peripheral perfusion, temperature, anesthesia technique, medications, P O2, and pH. Vasopressor therapy has been associated with glucose meter outliers in the intensive care unit. Therefore, patients receiving vasopressors intraoperatively may also be at risk of glucose meter errors or outliers. Despite these concerns, very few studies of glucose meter accuracy in the OR have been performed.

The aim of this study was to assess the accuracy of a newer glucose meter technology (Nova StatStrip, Nova Biomedical Corp., USA) with hematocrit and interference correction in the OR with patients under general anesthesia. We hypothesized that capillary and arterial whole blood samples analyzed on the glucose meter would meet established accuracy criteria for safe and effective insulin dosing. We also studied the impact of patient position, time under general anesthesia (early vs. late paired measurements), diabetes status, and other clinical and laboratory variables on the relationship between glucose meter and reference glucose concentrations.

Materials and Methods

Patient Selection

Members of the Anesthesia Clinical Research Unit performed a manual scan of the following day’s surgical listing for all patients scheduled for thoracic, vascular, or neurologic surgery from August 2014 to March 2015 (N = 234 screened). Study participants had to be 18 yr or older, have a preoperative hemoglobin greater than 10 mg/dl, and speak English. A diagnosis of diabetes mellitus was neither an inclusion or exclusion criterion. Glucose testing was performed only on patients who had an arterial catheter placed. The decision to place an arterial catheter was at the discretion of the anesthesia provider at the time of surgery, and the anesthesia provider was not aware of the patient’s study participation. The study design was approved by the Mayo Clinic Institutional Review Board, Rochester, Minnesota, and written informed consent was obtained from all of the subjects.

Sample Collection and Glucose Analysis

Sample collection was performed by the Mayo Clinic Clinical Trials Research Unit, Rochester, Minnesota. Members of Clinical Trials Research Unit nursing staff came to the OR approximately 30 min after the arterial catheter placement and obtained the first set of samples. Each set included the following: (1) a capillary fingerstick sample tested on the glucose meter; (2) an arterial whole blood sample tested on the glucose meter; and (3) an arterial whole blood sample tested in the laboratory on a blood gas analyzer (Radiometer ABL90, Radiometer America, Inc., USA). The arterial whole blood used for samples (2) and (3) were from the same blood draw and were collected in a 3-ml lithium heparin blood gas syringe. The arterial glucose result from the laboratory blood gas analyzer was considered the reference value. Arterial blood samples were obtained within 10 min of capillary sampling, and laboratory blood glucose analysis was performed within 10 min of arterial whole blood collection. Staff from the Clinical Trials Research Unit obtained a second set of samples approximately 60 min after the first set. All of the patients were under general anesthesia at the time of both glucose sample collections. Capillary samples from patients in the lateral position were obtained from a finger on the lower ( dependent) hand. Staff from the Clinical Trials Research Unit were trained on glucose meter operation and capillary sampling according to manufacturer’s instructions and laboratory procedures. Blood gas analyzer testing was performed by trained technologists in the testing laboratory, and the blood gas data, including glucose, were available to providers for clinical use.

Perioperative Data

Subject data, including temperature, systolic and diastolic blood pressures, mean arterial pressure, heart rate, as well clinical variables and patient demographic information, were extracted using a customized, integrative relational research database that contains a near–real-time copy of clinical, administrative, and environmental exposure data from the Electronic Medical Record, Hospital Surgical Listing, and Mayo Clinic Life Sciences System databases. All of the intraoperative variables were electronically captured with 3-min resolution. Additional laboratory data (hemoglobin, pH, partial pressure of carbon dioxide [PCO2], and PO2) were obtained from the sample submitted for reference glucose determination on the blood gas analyzer or retrieved from clinical databases. Manual review of the data for fidelity was performed with removal of obvious errors resulting from measurement techniques.
Primary outcomes for the study were median bias and percentage of glucose meter samples meeting accuracy criteria for subcutaneous and intravenous insulin infusion. Median (interquartile range [IQR]) bias between capillary glucose meter and reference glucose concentration and median (IQR) bias between arterial glucose meter and reference glucose concentration were calculated (meter glucose minus reference glucose). Univariate linear regression with generalized estimating equation (GEE) analysis was used to assess for differences in median bias between capillary bias and arterial bias while accounting for the correlation between up to two observations per patient. To assess whether time under general anesthesia impacted glucose meter accuracy, linear regression with GEE was also used to determine whether glucose meter bias differed between samples collected early during surgery (within 30 min after arterial catheter placement) versus later during surgery (approximately 60 min after the initial capillary sample). We also performed linear regression with GEE to determine whether limb position during surgery (lateral vs. supine) affected capillary glucose bias.

Clinical concordance between glucose meter and reference glucose values for subcutaneous insulin dosing was assessed using the Parkes error grid for type 1 diabetes mellitus, developed by a consensus of endocrinologists to define glucose meter accuracy needed for safe and effective subcutaneous insulin dosing. The Parkes error grid displays the relationship between glucose meter and reference glucose by use of an error grid divided into five risk zones. Zone A represents no effect on clinical action (glucose meter and reference glucose value would lead to the same clinical action). Zone B represents altered clinical action with little or no effect on clinical outcome. Zone C represents altered clinical action likely to impact clinical outcome; zone D represents altered clinical action that could have significant medical risk; and zone E represents altered clinical action that could have dangerous consequences. Consistent with the ISO 15197:2013 guideline used by glucose meter manufacturers, we defined acceptable accuracy for subcutaneous insulin dosing as 99% of glucose meter values within zones A and B on the Parkes error grid. We defined accuracy requirements for more intensive glucose monitoring (e.g., that required for intravenous insulin dosing) using the Clinical and Laboratory Standards Institute (CLSI) POCT12-A3 guideline. CLSI POCT12-A3 is a consensus guideline developed to define accuracy requirements for acute care use of glucose meters (including intravenous insulin administration). It states that 95% of glucose meter results should be within ±12 mg/dl of reference glucose value for reference glucose values less than 100 mg/dl and ±12.5% for reference glucose of 100 mg/dl or more. In addition, the guidelines require that no more than 2% of results contain error exceeding ±15 mg/dl (for reference glucose less than 75 mg/dl) or 20% (for reference glucose of 75 mg/dl or more). CLSI POCT12-A3 guidelines suggest a minimum of 200 measurements from 100 samples be measured to determine accuracy in a given patient population. In previous studies we were able to differentiate glucose meter bias between capillary and arterial samples with 100 samples. We used the CLSI POCT12-A3 guidelines and previous experience to determine that 300 or more measurements from 150 or more patients would allow us to differentiate glucose meter bias in capillary and arterial samples.

Univariate linear regression with GEE was used to perform post hoc statistical analysis to determine whether clinical variables such as age, sex, diabetes status, disease severity (age-adjusted Charlson comorbidity index), body mass index, temperature, blood pressure (systolic, diastolic, and mean arterial), or heart rate impacted the relationship (bias) between either capillary or arterial glucose meter and reference glucose concentration (secondary outcomes). For age-adjusted Charlson comorbidity index, we compared glucose meter bias in patients with few comorbidities (index 0 to 3) with patients with more comorbidities (index 4 to 6). For blood pressure, the average systolic, diastolic, and mean arterial pressures in the 15 min before a capillary sampling (measurements were recorded every 3 min) were used to determine whether blood pressure impacted the accuracy of capillary or arterial glucose meter measurement. A similar approach was used for heart rate and temperature (average value within 15 min of capillary sampling). Before the study we planned the use of univariate analysis with GEE to determine whether laboratory variables including pH, hemoglobin, PO2, and PCO2 affected glucose meter bias (secondary outcomes). All of the tests were two sided, and P < 0.05 was considered statistically significant. SAS version 9.4M3 (SAS Institute, Inc., USA) was used for all of the analyses.

**Results**

**Participants**
A total of 235 subjects were assessed for study eligibility. Fifteen refused to participate, one had a starting hemoglobin less than 10 mg/dl, and one did not speak English. Of the 218 subjects who were consented, 22 subjects did not have at least one pair of capillary and arterial samples drawn (arms not accessible, arterial catheter not placed, or surgery cancelled) or were missing one or more glucose values for comparison. Thus, 196 patients had one or more complete sets of samples obtained for analysis. A total of 192 complete sets were obtained for analysis at the first blood draw (within 30 min of arterial catheter placement), whereas 176 complete second sample sets (approximately 1 h after first sample) were obtained. Characteristics of the participants studied and the surgical procedures, including positioning, fluid administration, and vasopressor use, are provided in table 1.
Median (IQR) bias among the 192 capillary samples collected within 30 min of arterial catheter placement was −4 mg/dl (−8 to −1 mg/dl), whereas median (IQR) capillary bias among the 176 samples collected approximately 60 min after the first sampling was −5 mg/dl (−10 to 0 mg/dl; P = 0.85, no difference in median bias between first and second collection). Thus, time under anesthesia (time in surgery) did not affect the accuracy of capillary sampling for glucose.

Impact of Clinical Variables on Capillary and Arterial Glucose Meter Measurement

We performed univariate linear regression with GEE to determine whether age, sex, diabetes status, disease severity as measured by age-adjusted Charlson comorbidity index, body mass index, blood pressure, or heart rate impacted the relationship between capillary or arterial whole blood glucose (meter glucose) and reference glucose concentration. Among clinical variables, only age-adjusted Charlson comorbidity index demonstrated a statistically significant relationship with capillary glucose meter bias (P = 0.04). However, the magnitude (slope estimate) of that effect was small (1.9 mg/dl increase in bias for patients with higher risk scores; table 2). Diabetes status did not impact either capillary or arterial glucose meter bias (table 2).

Impact of Laboratory Variables on Capillary and Arterial Glucose Meter Measurement

Among laboratory variables, only PCO2 significantly impacted the relationship between capillary glucose meter and reference glucose (P = 0.04). As with clinical variables, the magnitude (slope estimate) of these effects was small (1.5 mg/dl change in bias per 10-mmHg change in diastolic blood pressure; P = 0.03; table 2).

Impact of Human Error on Capillary and Arterial Glucose Meter Measurement

Parkes error grid analysis for type 1 diabetes mellitus was used to assess the clinical concordance of glucose meter values (both capillary and arterial) for subcutaneous insulin dosing. All of the capillary and arterial glucose meter values were within zones A and B of the Parkes error grid (i.e., 100% of meter results met accuracy criteria), with the majority falling into zone A (fig. 1).

Capillary glucose bias ranged from −44 to 19 mg/dl, whereas arterial glucose bias ranged from −45 to 15 mg/dl (fig. 2). A total of 327 (89%) of 368 capillary and 344 (93%) of 368 arterial glucose meter values met CLSI POCT12-A3 accuracy guidelines for intravenous insulin dosing (±12 mg/dl at reference glucose less than 100 mg/dl and ±12.5% at reference glucose of 100 mg/dl or more). Glucose meter “outlier” results, those exceeding 20% of the reference glucose value, were observed with 7 (2%) of 368 of both capillary and arterial glucose meter values.
Discussion

The use of glucose meters in critically ill patients remains controversial. A number of variables, including hematocrit, \( P_{O_2} \), \( P_{CO_2} \), pH, and medications, may interfere with or impact the accuracy of glucose meters.\(^9,29-31\) The accuracy of capillary (fingerstick) glucose measurement in critically ill patients is of even greater concern, because previous studies have demonstrated potentially dangerous discrepancies.
in capillary glucose measurement in patients on vasopressor therapy,
patients in shock, or with poor tissue perfusion, as well as other critically ill patient populations. Studies have also found that systematic (mean or median) glucose meter bias differs for capillary glucose meter samples compared with arterial or venous whole blood samples.

Many of the studies demonstrating limitations to glucose meters were performed with older glucose meter technologies that did not correct for hematocrit or other interferences. Newer meter technologies may provide more accurate glucose measurements when used on critically ill patients, although studies have not specifically addressed capillary sampling or the use of meters intraoperatively. One previous study specifically examined glucose measurements in the OR, although few patients were under anesthesia at the time of sample collection. Their data suggest that performance of glucose meters in the OR could be much worse than in the intensive care unit. That study compared glucose meter and central laboratory measurements that were collected within 5 min of each other, using both arterial and venous blood samples.

We found that median bias did not differ between capillary and arterial blood specimens tested using the blood glucose meter. Outliers (glucose meter value greater than 20% different from reference) were also rare with both capillary and arterial glucose meter samples. Thus, we observed improved accuracy of glucose meter measurement compared with previous reports, especially for capillary whole blood glucose. It is important to interpret studies of glucose meter accuracy in the context of the generation and type of meter technology used. For both capillary and arterial samples, 100% of values were within zones A and B on the Parkes error grid for type 1 diabetes mellitus, indicating excellent clinical concordance between glucose meter and reference glucose values for subcutaneous insulin dosing. We conclude that improved accuracy (reduced systematic bias and number/percentage of outliers) allows for safe subcutaneous insulin dosing in the OR using both capillary and arterial samples on the glucose meter.

The glucose meter accuracy required for more intensive glycemic control protocols remains controversial. We assessed glucose meter accuracy for more intensive glycemic control protocols using the CLSI POCT12-A3 guidelines. Although Parkes error grid analysis was developed to reflect accuracy required for self-monitoring of blood glucose

Table 2. Relationship between Clinical Variables and Capillary and Arterial Glucose Meter Bias (vs. Reference Glucose)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit Change</th>
<th>Capillary Glucose Meter Bias</th>
<th>Arterial Glucose Meter Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Slope Estimate (mg/dl) (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Sex</td>
<td>Male vs. female</td>
<td>−0.38 (−2.18 to 1.43)</td>
<td>0.68</td>
</tr>
<tr>
<td>Age</td>
<td>10 yr</td>
<td>−0.59 (−1.30 to 0.12)</td>
<td>0.11</td>
</tr>
<tr>
<td>Diabetes status</td>
<td>Diabetes vs. no diabetes</td>
<td>−0.58 (−4.61 to 3.44)</td>
<td>0.78</td>
</tr>
<tr>
<td>Charlson age-adjusted comorbidity index</td>
<td>Risk score 4–6 vs. 0–3</td>
<td>−1.90 (−3.68 to −0.11)</td>
<td>0.04*</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1 kg/m²</td>
<td>−0.05 (−0.17 to 0.06)</td>
<td>0.34</td>
</tr>
<tr>
<td>Mean systolic BP</td>
<td>10 mmHg</td>
<td>−0.82 (−1.71 to 0.06)</td>
<td>0.09</td>
</tr>
<tr>
<td>Mean diastolic BP</td>
<td>10 mmHg</td>
<td>−0.19 (−1.37 to 0.99)</td>
<td>0.75</td>
</tr>
<tr>
<td>Mean temperature</td>
<td>1ºC</td>
<td>0.96 (−3.60 to 5.53)</td>
<td>0.68</td>
</tr>
<tr>
<td>Mean heart rate</td>
<td>1 beat/min</td>
<td>−0.03 (−0.15 to 0.10)</td>
<td>0.67</td>
</tr>
</tbody>
</table>

Slope estimate is from univariate linear regression with generalized estimating equations and estimates magnitude of change in glucose meter bias per unit of variable (for continuous variables) or between groups (for categorical variables). Slope estimates include 95% CI.

Table 3. Relationship between Laboratory Variables and Capillary and Arterial Glucose Meter Bias (vs. Reference Glucose)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unit Change</th>
<th>Capillary Glucose Meter Bias</th>
<th>Arterial Glucose Meter Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Slope Estimate (mg/dl) (95% CI)</td>
<td>P Value</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>1 mg/dl</td>
<td>0.09 (−0.54 to 0.72)</td>
<td>0.77</td>
</tr>
<tr>
<td>pH</td>
<td>0.1 pH unit</td>
<td>1.55 (−0.13 to 3.23)</td>
<td>0.08</td>
</tr>
<tr>
<td>PO2</td>
<td>10 mmHg</td>
<td>0.05 (−0.03 to 0.12)</td>
<td>0.22</td>
</tr>
<tr>
<td>PCO2</td>
<td>10 mmHg</td>
<td>−1.54 (−2.85 to −0.22)</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

Slope estimate is from univariate linear regression with generalized estimating equations and estimates magnitude of change in glucose meter bias per unit of variable. Slope estimates include 95% CI.

*P < 0.05 indicates statistically significant relationship between variable and glucose meter bias.

BP = blood pressure.
Conclusions

The median bias for arterial whole blood glucose meter samples collected intraoperatively was −5 mg/dl, which did not differ from a median bias of −4 mg/dl for capillary glucose meter samples. In contrast to findings of previous studies that used older glucose meter technologies, we found that neither the systematic (median) bias nor the number/percentage of outlier results differed between capillary and
arterial glucose meter samples. One hundred percent of both capillary and arterial glucose values were within zones A and B on the Parkes error grid for type 1 diabetes mellitus, demonstrating that both capillary and arterial whole blood glucose can be used to safely dose subcutaneous insulin in the OR. Neither arterial nor capillary whole blood glucose met CSLI POCT12-A3 guidelines, suggesting that caution must be exercised when using glucose meter values for intravenous or more intensive glycemic control protocols.

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Competing Interests
Dr. Karon has received travel support from Nova Biomedical Corporation, Waltham, Massachusetts. The other authors declare no competing interests.

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References


