Glucose meter use in the intensive care unit: much ado about something

Brad S. Karon

Department of Laboratory Medicine and Pathology, Mayo Clinic

ARTICLE INFO

Corresponding autor:
Brad S. Karon
Department of Laboratory
Medicine and Pathology
Mayo Clinic
200 First Street SW
Rochester, MN 55905
Phone: 507-538-4921
Fax: 507-538-7060
E-mail: karon.bradley@mayo.edu

ABSTRACT

Glucose meters are a fast and convenient way to measure circulating blood glucose. Like many technologies in healthcare, the use of glucose meters within the hospital has evolved significantly over the last few decades. This change has been driven predominantly by changes in the approach to glycemic control for critically ill patients. Both glycemic control in the intensive care unit (ICU), and use of glucose meters to manage insulin dosing during glycemic control, are likely to remain controversial topics in the years to come. This review will elaborate on the evidence for and against use of glucose meters in the ICU to monitor glucose concentrations during glycemic control, and provide some tips for point of care programs on how to evaluate glucose monitors for this purpose.

INTRODUCTION

Glucose meters have been used in the hospital setting for decades. Traditionally glucose meters were used in the hospital to dose subcutaneous insulin for patients with diabetes when they were hospitalized. As even well-controlled diabetic patients will have their insulin needs, diet and caloric requirements change during periods of acute illness; glucose must be measured frequently (four or more times per day) before meals and/or insulin dosing in the hospital. Although most hospital laboratories offer a measurement of serum or plasma glucose, hospitals and healthcare systems find it both convenient and efficient to measure capillary whole blood glucose at the bedside in order to expedite insulin dosing. This can help insure that glucose values are taken before (rather than after) meals are consumed, as it is the preprandial blood sugar value that is most often used to dose insulin.

In 2001 Dr. Van den Berghe and colleagues changed the landscape of glucose control in the hospital by studying the impact of tight glycemic control (maintaining blood glucose between 80-110 mg/dL) among critically ill patients (both diabetic and non-diabetic) after cardiovascular surgery. Dr. Van den Berghe's original study sought to determine whether closely controlling glucose levels in patients in a surgical intensive care unit (ICU) would improve patient outcome. In the study 1500 patients were divided into two groups: one control group that received what was conventional treatment of hyperglycemia in the ICU at that time (subcutaneous or intravenous insulin to keep glucose levels less than 200 mg/dL), and an experimental group that received intravenous insulin to keep blood glucose at relatively normal levels of 80-110 mg/dL. The experimental group that received intravenous insulin to keep blood glucose relatively normal had much better health outcomes than the control group (mortality decreased 34%, renal failure 41%, bloodstream infections 46%)[1]. The outcomes were startling to critical care experts, and almost overnight changed the standard of care in critical care medicine from a relaxed attitude towards hyperglycemia in the ICU to vigilant glucose monitoring and insulin treatment to maintain normal or near-normal blood glucose levels.

Subsequent studies found that depending upon the patient population (medical vs. surgical ICU), ICU nutrition practices, and protocols to dose insulin and monitor glucose; intensive glycemic control was of either benefit in only some ICU patients or not beneficial at all[2-4]. Finally, in 2011 a multi-center trial called NICE-SUGAR was performed to determine what level of glycemic control was optimal in the ICU setting. Unlike the preliminary studies done by Dr. Van den Berghe, NICE-SUGAR did not compare "conventional treatment" to more rigorous management of glycemic control; as by that time some active management of glucose levels in the ICU was standard of care. Rather, NICE-SUGAR compared two different glucose management strategies—one aimed at controlling glucose levels among critically ill patients to near-normal levels (similar to the Van den Berghe strategy) and one that aimed for slightly higher (140-180 mg/dL) glucose levels. NICE-SUGAR, performed in over 40 medical centers, found that patients assigned to the higher (< 180 mg/dL) glucose target had significantly better health outcomes than those whose glucose target was near-normal (81-108 mg/dL)[5].

Among the reasons why more moderate glucose targets may be beneficial to critically ill patients, rates of hypoglycemia are most commonly cited. All studies of intensive glucose control in the ICU, including the original studies by Dr. Van den Berghe, found that rates of hypoglycemia are higher among patients whose glucose levels are controlled actively with intravenous insulin. In

fact, studies have shown that intravenous insulin therapy increases the rate of hypoglycemia among ICU patients on average 5-fold[4]. This is significant because even a single episode of hypoglycemia in the ICU may increase the odds of death in the hospital up to two-fold[6]. Thus the need to control glucose levels in the ICU must be balanced against the risk of hypoglycemia.

While the original study (showing the most positive outcomes) by Dr. Van den Berghe and colleagues used more accurate blood gas analyzers for all glucose measurements; the subsequent studies often used less accurate glucose meters for measurement of blood glucose. This has fueled considerable controversy over whether glucose meters, originally intended for use in diabetic patients to monitor glucose and dose subcutaneous insulin, are accurate enough to manage intravenous insulin in critically ill hospitalized patients[7, 8].

Traditionally, accuracy requirements for glucose meters were developed based upon the level of accuracy needed for safe and effective subcutaneous insulin dosing in the routine care of diabetes. These specifications are often visually displayed in an error grid, a tool developed by collecting the opinions of endocrinologists and other healthcare providers about the implications of various amounts of glucose measurement error on the safety and efficacy of subcutaneous insulin dosing. These error grid observations were codified in a set of guidelines issued by the International Organization for Standardization (ISO) and Clinical and Laboratory Standards Institute (CLSI) some years ago, and until recently used by some regulatory agencies as the measure of required glucose meter accuracy. One such commonly cited guideline, ISO 15197, required that 95% of glucose meter values fall within ± 15 mg/dL of the true or reference glucose value for serum glucose values < 75 mg/dL; and ± 20% of the reference value for serum glucose values ≥ 75 mg/dL[9].

Because glucose meter use in the hospital has changed as glycemic control strategies have changed, most experts now feel that the original ISO guideline is not appropriate as an accuracy guideline for hospital use glucose meters[7, 8]. To address these concerns, more stringent criteria for glucose meter accuracy have been proposed by both National Academy of Clinical Biochemistry (NACB) and CLSI. The guidelines are similar, and require 95% of glucose meter results to be within either ± 15 mg/dL (NACB) or ± 12 mg/dL (CLSI) of reference glucose for glucose values < 100 mg/dL, and within ± 15% (NACB) or 12.5% (CLSI) for glucose values ≥ 100 mg/dL[10, 11].

The case against glucose meter use in the ICU

Several studies have documented that some glucose meters have limited accuracy when used on critically ill patients such as those on intravenous insulin in the ICU. The degree to which glucose meters correlate with laboratory glucose measurement varies between glucose meter technologies[12]; and correlation in the hypoglycemic and hyperglycemic ranges is poor for some meters currently available[13, 14]. In addition, patients in the ICU are on multiple medications, and often have abnormal hematocrit and/or oxygen tension, all of which may affect the performance of some glucose meters[12, 15, 16]. Finally, target glucose concentrations are narrower for this patient population than they are for patients using handheld meters to dose subcutaneous insulin, logically suggesting that improved accuracy of glucose measurement might be required. A number of studies have examined glucose meter accuracy and its impact on insulin dosing in the context of glycemic control, and concluded that glucose meters could not be safely and effectively used to manage critically ill patients on intravenous insulin in the ICU[13, 17, 18].

Because studies examining glucose meter accuracy in the ICU have been relatively small studies

using different meters and reference methods, the larger question of the impact of glucose meter error on patient outcomes during glycemic control remains difficult to address. The primary manner this has been overcome is by utilizing simulation studies to model the effects of various levels of glucose meter error on insulin dosing decisions and glycemic control.

Boyd and Bruns first established the use of simulation modeling as a tool to examine the relationship between glucose meter performance (bias and precision) and insulin dosing errors[19]. The initial study was based upon glucose values and insulin doses used for conventional subcutaneous insulin dosing for diabetic patients. The authors used Monte Carlo simulation to relate glucose meter bias and imprecision to insulin dosing errors during conventional subcutaneous insulin dosing. They found that glucose meters available at that time had sufficient accuracy and precision to avoid large insulin dosing errors in the context of traditional subcutaneous insulin dosing regimens[19].

Another study, designed to specifically model glucose meter use during glycemic control in the ICU, was based upon 29,920 observed glucose values among patients on intravenous insulin therapy in 2 ICU units within one healthcare institution. As expected, most of the values were in a narrow range of glucose value (102-135 mg/dL), such that insulin dose would change with every 20 mg/dL glucose increment according to the insulin dosing protocol in use. The authors found that allowing 20% total error in glucose meter measurements (previous ISO 15197 criteria) allowed for rare large (3 or more insulin dosing categories) insulin dosing errors; those that are most likely to produce hypoglycemia[20]. Decreasing allowable error to 15% eliminated large insulin dosing errors; but still allowed for 2-5% of insulin dosing decisions to be in error by 2 insulin dosing categories. Reducing error tolerance to 10% further reduced

the rate of 2 category insulin dosing errors to less than 0.2%. The authors concluded that 20% glucose measurement error was not safe and effective for intravenous insulin dosing protocols that sought to maintain glucose values at normal or near-normal concentrations (tight glycemic control)[20].

After the publication of the NICE-SUGAR study, many institutions changed the glucose target values for ICU patients on intravenous insulin therapy to more moderate glucose values. To investigate whether glucose meter accuracy requirements for more moderate glycemic protocols differed from those suggested for tight glycemic control, the authors repeated the simulation studies using 25,948 observed glucose values in 1503 ICU patients on a moderate glycemic control protocol (110-150 mg/dL target value)[21]. Although the median glucose value was significantly higher among patients on moderate (134 mg/dL) compared to tight (116 mg/dL) glycemic control, most glucose values among patients on the moderate glycemic control protocol still fell into insulin dosing categories where insulin dose changed with every 20 mg/dL increment in glucose value. Rates of insulin dosing errors as a function of meter bias and precision were nearly identical to those predicted for the population of patients on tight glycemic control. This suggests that the observed relationship between glucose meter and insulin dosing errors can be generalize to insulin infusion protocols where insulin dose changes with every 20 mg/dL change in glucose value[21].

Simulation models suggest that 20% error is too much for glucose meters used to manage patients on intravenous insulin therapy. Because some studies of glucose meter accuracy in the ICU observed that glucose meter error exceeded 20% when used on critically ill patients[17, 21, 22], the simulation models have been used as evidence that glucose meters do not have the level of accuracy required for safe and effective

management of critically ill patients placed on intravenous insulin (glycemic control).

Only a small number of simulation studies have gone beyond relating glucose meter accuracy to insulin dosing errors; and attempted to relate meter error to the short-term patient outcomes such as rates of hypoglycemia, rates of hyperglycemia, or glycemic variability (rate and extent of change in glucose levels over time). One simulation model used a complex algorithm to predict the impact of glucose meter error over many days on rates of hypoglycemia, hyperglycemia and glycemic variability when glucose meter results were used to dose subcutaneous insulin in the context of diabetes self-management. The authors found that there was a threshold between 10-15% meter error that was predicted to result in increased incidences of hypoglycemia, hyperglycemia and increased glycemic variability[23]. One additional study used simulation modeling to assess the impact of both glucose measurement frequency and precision on predicted rates of hypoglycemia in the context of glycemic control in the hospital. Using hourly glucose monitoring to adjust insulin dose, the simulation model predicted that increasing imprecision above 10% CV would result in progressively increased rates of hypoglycemia (glucose < 60 mg/dL). The same simulation models suggested that using hourly glucose monitoring rates of hyperglycemia (> 160 mg/dL), time within intended target glucose range, and glycemic variability were all detrimentally affected when precision increased beyond 5-10% CV[24]. These studies differed in the type of insulin dosing modeled (subcutaneous vs. intravenous), glucose target ranges assumed, and frequency of glucose monitoring. However both raise concerns about the use of glucose meters to manage patients on intravenous insulin in the ICU. Both studies suggest a threshold effect of either glucose meter total error[23]or imprecision[24]; with a suggested minimum total error of 10-15% and

imprecision of < 5%. Because a number of previous studies demonstrated total error greater than 10-15% when glucose meters are used on ICU patients[13, 17, 21], this has fueled concern about their use in this context.

The case for using glucose meters in the ICU

While studies of glucose meter use among critically ill patients have demonstrated both systematic differences (generally positive bias)[17, 25, 26] and variability[13, 14, 18] between glucose meter and laboratory glucose values, a few studies have concluded that the use of glucose meters during glycemic control may be appropriate. One study used Parke's error grid analysis to assess the clinical impact of glucose meter errors when arterial, venous or capillary samples were used to dose glucose meters. These authors concluded that glucose meters may be appropriate for use in glycemic control protocols when arterial or venous (but not capillary) samples are used[26]. However it is not clear whether use of the Parke's error grid is appropriate for assessing the clinical impact of glucose meter errors in the context of intravenous insulin therapy during ICU glycemic control protocols. Another study also examined differences between glucose meter and laboratory glucose when either arterial, venous or capillary samples from critically ill patients were used. This study examined the number and magnitude of insulin dosing errors when glucose meter (compared to laboratory glucose) results were used to make insulin dosing decisions using the institutional glycemic control protocol (target glucose 80-110 mg/dL). This study found that errors in the measurement of both venous catheter and capillary glucose resulted in more frequent large (2 or more insulin dosing categories) dosing errors; whereas use of arterial catheter whole blood on the glucose meter resulted in predominantly one category dosing errors[25]. Finally one study used consensus error grid and Bland Altman

analysis to study whole blood glucose accuracy using several different devices; and found that by limiting sample type to arterial blood that some glucose meters were accurate enough to be used during glycemic control[27].

In assessing the appropriateness of glucose meter use in the ICU, choice of sample type is an essential consideration. A number of studies have demonstrated that capillary glucose can be highly inaccurate in patients in shock, or patients with edema or poor tissue perfusion [13, 28-30]. Several studies have also demonstrated systematic overestimation of glucose values when venous catheters are used to obtain venous whole blood for analysis on some glucose meter technologies[31-34]. Arterial whole blood is very likely the best sample choice for monitoring whole blood glucose in critically ill patients. In considering the evidence for and against use of glucose meters in the ICU, one should pay special attention to sample source as a potential cause for poor glucose meter performance.

Other investigators have studied whether other factors may be more important than glucose monitor accuracy in determining the effectiveness of a glycemic control protocol. One study compared use of a standardized insulin infusion protocol to physician-directed intravenous insulin dosing in a mixed medical/surgical ICU. Use of the standardized infusion protocol reduced the rate of hypoglycemia from 16% to 4%, and also reduced the frequency of dextrose rescue[22]. Patients using the standardized protocol reached target glucose faster and maintained blood glucose in the target range (81-110 mg/dL) longer. Glucose in this study was monitored using capillary samples on a glucose meter, perhaps the least desirable sample for critically ill patients. Even with this limitation, the study demonstrated that execution of a standardized infusion protocol can improve at least short-term outcomes (hypoglycemia, time in therapeutic range)[22]. Another study demonstrated

that by using an insulin infusion protocol that focused on velocity of glucose change (rather than absolute glucose levels), glucose meters could be used to maintain blood glucose in the range of 100-139 mg/dL with very little (0.3% of all glucose values < 60 mg/dL) hypoglycemia[35].

Another investigator has described a collaborative approach to establishing both glucose target ranges and insulin infusion algorithms based upon practice and nursing leader opinions about what could be safely accomplished. Using this approach they implemented an initial glycemic control protocol to keep glucose levels among critically ill patients below 140 mg/dL. They used hourly capillary glucose meter and/or laboratory serum/plasma glucose for all patients on intravenous insulin and observed a rate of severe hypoglycemia (glucose < 40 mg/dL) of 0.38%[36]. When staff in the ICU was comfortable with the "under 140" protocol, the target glucose range was decreased to 80-125 mg/dL with only a modest increase in severe hypoglycemia (0.92%). The authors concluded that by taking an incremental approach to glycemic control, starting with a higher target range and lowering the range only after staff demonstrated they could reliably execute the protocol, safe and effective glycemic control was possible using glucose meters for some monitoring[36].

A more common approach to improving outcomes during glycemic control is to use information technology solutions to computerize insulin doses based upon trended (rather than individual) glucose values. This approach mitigates the risk of hypoglycemia from a single aberrant glucose meter value. Using this approach one study demonstrated that rates of severe hypoglycemia were 4.25% when mostly capillary whole blood glucose meter values were used to dose insulin among 4588 critically ill patients managed on a glycemic control protocol with an 81-110 mg/dL target range[37]. These authors went on to investigate causes of hypoglycemia

among all incidents where glucose fell below 40 mg/dL. The authors found that ~ 70% of hypoglycemic episodes could be attributed to delay in obtaining glucose measurement; suggesting that human error (rather than measurement error) is responsible for the most insulin-induced hypoglycemia during traditional tight glycemic control protocols[37]. The same authors compared the computerized infusion protocol to a paper-based protocol and found that using a computerized protocol improved the time in therapeutic range, mean blood glucose level, and percent of blood glucose measurements below 70 mg/dL[38].

Finally a study over a one month period in three intensive care units at one institution found that using arterial whole blood to dose glucose meters, and relying upon consistent hourly glucose measurements performed by laboratory (rather than nursing) staff, rates of severe hypoglycemia were 1.4% despite a relatively low glucose target range of 80-130 mg/dL. In addition, 86% of severe hypoglycemic episodes observed were due to protocol violations (missed hourly glucose measurements or failure to change insulin infusion rate according to protocol instructions)[39]. When the glucose target range was changed to 110-150 mg/dL (with no change in glucose meter used or measurement frequency), no episodes of hypoglycemia were observed in 211 patients over one month[39]. A larger study (three months, 1503 patients) within the same ICU units found a rate of severe hypoglycemia of 0.25 %[21].

Collectively these studies highlight several key points that must be considered before determining the appropriateness of glucose meters for managing glycemic control in the ICU. The choice of sample type (arterial whole blood preferred) may be as or more important than the type of glucose monitor used for whole blood glucose measurement. Glucose meters have been used in effective glycemic control

protocols demonstrating both low rates of severe hypoglycemia and reliable glycemic control in the ICU. Elements of effective protocols are computerized (rather than paper-based) insulin dosing algorithms, collaboration and teamwork to determine the appropriate glucose target for a given hospital or ICU population, and use of frequent (often hourly) arterial whole blood sampling for all patients on intravenous insulin.

The FDA draft guidance on glucose meter accuracy

While many studies demonstrating poor performance of glucose meters in critically ill patients used older glucose meter technologies, newer technologies with improved accuracy have recently become available[40-43]. Some recent studies have demonstrated that newer glucose meter technologies can meet even the more stringent CLSI POCT12-A3 accuracy guidelines (± 12.5% for values above 100 mg/dL) when used in the intensive care unit[41, 42]. Meters that meet more stringent accuracy guidelines such as POCT12-A3 would be performing within the 10-15% total error allowance predicted to minimize large insulin dosing errors in the context of ICU glycemic control. With the improved performance of newer glucose meters, one might think that the issue of glucose meter accuracy in the ICU was close to resolution.

To add fuel to the ongoing controversy about glucose meter use in the ICU, the Food and Drug Administration (FDA) released draft guidelines suggesting that improved accuracy was necessary for any future glucose monitors intended for hospital use. While the guidelines are still in draft form at the time of this review, FDA draft guidance criteria suggested that 99% of glucose meter values should be within 10% of the reference or true glucose value[44]. There is concern among some that tightening accuracy criteria to this level could impede the development of new meters and monitors, without improving

the quality of care delivered in the ICU during glycemic control.

Tips for point of care programs

Amidst this cloud of confusion and controversy surrounding glucose meter use in the ICU, what is the point of care program to do? First and foremost, consider the entire glycemic control protocol in use within your institution, and the role that glucose meters play in the overall scheme of glycemic control. Eliminating the use of glucose meters in support of intravenous insulin protocols, without first considering alternatives and implications, would almost certainly have an adverse effect on patient care. Understand the effectiveness of the glycemic control protocol (rates of hypo and hyperglycemia, time within intended glucose range) as implemented, and the systematic issues that may be leading to adverse outcomes such as hypoglycemia. If the major issues are remembering to obtain glucose values in a timely manner to facilitate insulin dosing decisions, or communicating glucose results to providers in a timely manner, then changing glucose measurement devices (especially away from the bedside) would not be expected to improve outcome. If spurious glucose results have been observed in some ICU patients, determine whether common interferences (low hematocrit, some medications) in the ICU environment may be affecting the glucose meter technology in use. If user errors such as incorrect strip codes or under-dosing of strips are suspected; consider switching to a glucose meter technology that reduces the likelihood of these errors and examining training and competency systems.

Hospitals and point of care programs should also consider the sample type (capillary, arterial or venous whole blood) routinely used for bedside glucose measurements, before making a decision to switch technologies or glucose measurement devices. If capillary sampling is being used as the predominant sample type, switching to arterial whole blood may improve measurement accuracy without requiring large changes in workflow or testing processes. Finally, consider evaluating the accuracy of the device being used by comparing whole blood glucose meter values to laboratory serum or plasma glucose obtained from ICU patients. If the vast majority of glucose meter values are not within 15% of lab glucose values, then it is likely that more accurate glucose measurements are both possible and desirable.

CONCLUSION

Glucose meter use in the ICU environment will continue to be a controversial issue. Simulation models have provided the best evidence available to relate glucose meter accuracy to insulin dosing errors during glycemic control in the ICU. However they do not provide a way to measure the impact of glucose meter error on patient outcome. Studies directly relating glucose monitor accuracy to glycemic control outcome (mortality, infections, transfusions, etc) or effectiveness (hypoglycemia, hyperglycemia, time in therapeutic range) are needed to understand the level of glucose meter accuracy required for management of critically ill patients on intravenous insulin therapy.

REFERENCES

1. Van den Berghe G, Wouters P, Weekers F, Verwaest C, Bruyninckx F, Schietz M, et al. Intensive insulin therapy in critically ill patients. N Engl J Med. 2001;345:1359-67.

2. Reeds D. Near-normal glycemia for critically ill patients receiving nutritional support: Fact or folly. Curr Opin Gastroenterology. 2010;26:152-5.

3. Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters P, Milants I, et al. Intensive insulin therapy in the medical ICU. N Engl J Med. 2006;354:449-61.

4. Wiener B, Wiener D, Larson R. Benefits and risks of tight glucose control in critically ill adults. JAMA. 2008;300:933-44.

5. NICE-SUGAR Investigators. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360:1283-97.

6. Krinsley J, Grover A. Severe hypoglycemia in critically ill patients: Risk factors and outcomes. Crit Care Med. 2007;35:2262-7.

7. Dungan K, Chapman J, Braithwaite S, Buse J. Glucose measurement: Confounding issues in setting targets for inpatient management. Diabetes Care. 2007;30:403-9.

8. Scott M, Bruns D, Boyd J, Sacks D. Tight glucose control in the intensive care unit: Are glucose meters up to the task? Clin Chem. 2008;55:18-20.

9. International Organization for Standardization (ISO). In vitro diagnostic test systems-requirements for blood glucose monitoring systems for self-testing in managing diabetes mellitus. Report number ISO 15197: International Organization for Standardization; 2003.

10. National Academy of Clinical Biochemistry. Guidelines and recommendations for laboratory analysis in the diagnosis and management of diabetes mellitus. American Association for Clinical Chemistry and the American Diabetes Association. Washington, DC2011.

11. CLSI. Point of care blood glucose testing in acute and chronic care facilities: Approved guideline-third edition. CLSI Document POCT12- A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2013.

12. Karon B, Griesmann L, Scott R, Bryant S, DuBois J, Shirey T, et al. Evaluation of the impact of hematocrit and other interference on the accuracy of hospital-based glucose meters. Diabetes Technol Ther. 2008;10:111-20.

13. Kanji S, Buffie J, Hutton B, Bunting P, Singh A, McDonald K, et al. Reliability of point-of-care testing for glucose measurement in critically ill adults. Crit Care Med. 2005;33:2778-85.

14. Khan A, Vasquez Y, Gray J, Wians F, Kroll M. The variability of results between point-of-care testing glucose meters and the central laboratory analyzer. Arch Pathol Lab Med. 2006;130:1527-32.

15. Tang Z, Louie R, Lee J, Lee D, Miller E, GJ K. Oxygen effects on glucose meter measurements with glucose dehydrogenase- and oxidase-based strips for point-of-care testing. Crit Care Med. 2001;29:1062-70.

16. Watkinson P, Barber V, Amira E, James T, Taylor R, Young J. The effects of precision, haematocrit, pH, and oxygen tension on point-of-care glucose measurements in critically ill patients: A prospective study. Ann Clin Biochem. 2012;49:144-51.

17. Hoedemaekers C, Klein Gunnewiek J, Prinsen M, Willems J, Van der Hoeven J. Accuracy of bedside glucose measurement from three glucometers in critically ill patients. Crit Care Med. 2008;36:3062-66.

18. Vlasselaers D, Van Herpe T, Milants I, Eerdekens M, Wouters P, De Moor B, et al. Blood glucose measurements in arterial blood of intensive care unit patients submitted to tight glycemic control: Agreement between bedside tests. J Diabetes Sci Technol. 2008;2:932-8.

19. Boyd J, Bruns D. Quality specifications for glucose meters: Assessment by simulation modeling of errors in insulin dose. Clin Chem. 2001;47:209-14.

20. Karon B, Boyd J, Klee G. Glucose meter performance criteria for tight glycemic control estimated by simulation modeling. Clin Chem. 2010;56:1091-7.

21. Karon B, Boyd J, Klee G. Empiric validation of simulation models for estimating glucose meter performance criteria for moderate levels of glycemic control. Diabetes Tech Therap. 2013;15:996-1003.

22. Kanji S, Singh A, Meggison H, McIntyre L, Hebert P. Standardization of intravenous insulin therapy improves the efficiency and safety of blood glucose control in critically ill adults. Intensive Care Med. 2004;30:804-10.

23. Breton M, Kovatchev B. Impact of blood glucose self-monitoring errors on glucose variability, risk for hypoglycemia, and average gluocose control in type 1 diabetes: An in silico study. J Diabetes Sci Technol. 2010;4:562-70.

24. Boyd J, Bruns D. Effects of measurement frequency on analytical quality required for glucose measurement in intensive care units: Assessments by simulation models. Clin Chem. 2014;60:644-50.

25. Karon B, Gandhi G, Nuttall G, Bryant S, Schaff H, McMahon M, et al. Accuracy of Roche Accu-Chek Inform whole blood capillary, arterial, and venous glucose values in patients receiving intensive intravenous insulin therapy after cardiac surgery. Am J Clin Pathol. 2007;127:919-26.

26. Petersen J, Graves D, Tacker D, Okorodudu A, Mohammad A, Cardenas V. Comparison of POCT and central laboratory blood glucose results using arterial, capillary, and venous samples from micu patients on a tight glycemic control protocol. Clin Chim Acta. 2008;396:10-3.

27. Slater-Maclean L, Cembrowski G, Chin D, Shalapay C, Binette T, Hegadoren K, et al. Accuracy of glycemic measurements in the critically ill. Diabetes Tech Therap. 2008;10:169-77.

28. Atkin S, Dasmahapatra A, Jaker M, Chorost M, Reddy S. Fingerstick glucose determination in shock. Ann Intern Med. 1991;114:1020-24.

29. Desachy A, Vuagant A, Ghazali A, Baudin O, Longuet O, Calvat S, et al. Accuracy of bedside glucometry in critically ill patients: Influence of clinical characteristics and perfusion index. Mayo Clin Proc. 2008;83:400-5.

30. Sylvain H, Pokorny M, English S, Benson N, Whitley T, Ferenczy C, et al. Accuracy of fingerstick glucose values in shock patients. Am J Crit Care. 1995;4:44-8.

31. Karon B, Koch C, Wockenfus A, Brown J. Accuracy of whole blood glucose measurement when venous catheter blood samples are used on glucose meters. Diabetes Tech Therap. 2009;11:819-25.

32. Cook A, Laughlin D, Moore M, North D, Wilkins K, Wong G, et al. Differences in glucose values obtained from point-of-care glucose meters and laboratory analysis in critically ill patients. Am J Crit Care. 2009;18:65-71.

33. Shearer A, Boehmer M, Closs M, Dela Rosa R, Hamilton J, Horton K, et al. Comparison of glucose point-of-care values with laboratory values in critically ill patients. Am J Crit Care. 2009;18:224-30.

34. Boyd R, Leigh B, Stuart P. Capillary versus venous bedside blood glucose estimations. Emerg Med J. 2005;22:177-9.

35. Goldberg P, Siegel M, Sherwin R, Halickman J, Lee M, Bailey V, et al. Implementation of a safe and effective insulin infusion protocol in a medical intensive care unit. Diabetes Care. 2004;27:461-7.

36. Gerard S, Neary V, Apuzzo D, Giles M, Krinsley J. Implementing an intensive glucose management initiative: Strategies for success. Crit Care Nurs N Am. 2006;18:531-43.

37. Juneja R, Roudebush C, Nasraway S, Golas A, Jacobi J, Caroll J, et al. Computerized intensive insulin dosing can mitigate hypoglycemia and achieve tight glycemic control when glucose measurement is performed frequently and on time. Crit Care. 2009;13:R163.

38. Saur N, Kongable G, Holewinski S, O'Brien K, Nasraway S. Software-guided insulin dosing: Tight glycemic control and decreased glycemic derangements in critically ill patients. Mayo Clin Proc. 2013;88:920-9.

39. Patton V, Parsaik A, Brown J, Kudva Y, Vlahakis N, Basu A. Glucose control in mayo clinic intensive care units. J Diabetes Sci Technol. 2011;5:1420-6.

40. Chan P, Rozmanc M, Seiden-Ling I, Kwan J. Evaluation of a point-of-care glucose meter for heneral use in complex tertiary care facilities. Clin Biochem. 2009;42:1104-12.

41. Gijzen K, Moolenaar D, Weusten J, Pluim H, Demir A. Is there a suitable point-of-care glucose meter for tight glycemic control? Evaluation of one home-use and four hospital-use meters in an intensive care unit. Clin Chem Lab Med. 2012;50:1985-92.

42. Mitsios J, Ashby L, Haverstick D, Bruns D, Scott M. Analytical evaluation of a new glucose meter system in 15 different critical care settings. J Diabetes Sci Technol. 2013;7:1282-7.

43. Kost G, Tran N, Louie R, Gentile N, Abad V. Assessing the performance of handheld glucose testing for critical care. Diabetes Tech Therap. 2008;10:445-51.

44. Malone B. FDA moves on blood glucose meters. Clinical Laboratory News. 2014;40:1-7.