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ORIGINAL ARTICLE

Agreement of blood glucose levels between venous blood test and arterial blood glucometer in the ICU

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Abstract

Introduction: Glycaemic control has been associated with improvement in morbidity and mortality in critically ill patients. However, the method of measuring blood glucose is crucial for insulin adjustment. Arterial blood glucometers are used widely in intensive care units, but there is a limited evidence base.

Objective: To determine the correlation, accuracy, and agreement of blood glucose levels measured by the arterial blood glucometer versus standard venous blood glucose testing and identify the agreement of insulin dosage adjustment between the two methods.

Method: Forty-five pairs of arterial and venous blood samples were obtained from 15 haemodynamically stable, critically ill patients. Pearson's correlation coefficient and Clarke error grid analysis were used to identify the correlation and accuracy of the two methods, and Bland-Altman analysis to assess agreement. The Kappa statistic evaluated the agreement of insulin dosage adjustment between the two methods.

Results: The arterial blood glucometer showed good correlation (r = 0.973), excellent accuracy, and good agreement with the central laboratory measurement of venous blood glucose. Agreement of the dosage adjustment of insulin infusion in the two groups was almost perfect (Kappa = 0.942).

Conclusions: This study identified good correlation and excellent accuracy, and satisfactory agreement of blood glucose measured by the arterial glucometer and standard venous measurement. There was an almost perfect agreement of insulin dosage adjustment by arterial glucometer compared with venous blood. A glucometer for arterial blood glucose and insulin adjustment has evidence-based support.

Introduction

Stress-induced hyperglycaemia is a common complication in critically ill patients and is related to morbidity and mortality.[1] Recent clinical studies have shown that intensive blood glucose control improved the outcomes in critically ill patients, including infectious complications, multiple organ dysfunctions, critical polyneuropathy and myopathy, and possible mortality.[2-7] Studies have suggested the use of a standard protocol for regular insulin infusion to achieve the glycaemic goal. Those protocols consist of a range of blood glucose targets and specific infusion rates with the insulin adjusted hourly.

Nevertheless, the method used for measuring blood glucose is the key to insulin adjustment. There are several ways to measure blood glucose but central laboratory measurement of venous plasma glucose is recognised as the standard technique. Unfortunately, this method has a 15-30 minute turnaround time, which may delay adjustment of the insulin dosage and may impact achievement of glycaemic control in the critically ill setting. A glucometer is a point-of-care device for measuring blood glucose that requires less than 30 seconds to obtain the level of capillary blood glucose.[8] Unfortunately, the glucometer test requires painful fingertip pricking to obtain the capillary blood.

In addition, several studies have also shown that the blood glucose level from arterial blood, venous blood and capillary blood may be significantly different.[8] Several factors interfere with capillary blood glucose measurement in critically ill circumstances.[8-12]

In the critical care setting, arterial catheterisation is commonly performed for continuous blood pressure monitoring and for taking blood samples. Therefore, the arterial blood glucose level can be checked hourly by glucometer. However, a recent systematic review on the accuracy of the arterial blood glucometer showed inconclusive results because of the heterogeneity of glucometer devices, different sites of blood sampling, differences in blood glucose reference values, and finally no practical outcomes were determined.[13] Therefore, the objective of this study is to determine the correlation, accuracy, and agreement of blood glucose levels between central laboratory measurement of venous blood glucose and

arterial blood glucose measured by glucometer and to identify the agreement of insulin dosage adjustment based on the results of the blood glucose levels from these two methods.

Materials and Methods

Patients

The protocol of this prospective study was approved by the Faculty of Medicine, Prince of Songkla University Ethics Committee and Institutional Review Board and written informed consent was obtained from the patients or their next of kin.

The sample size was planned to have 80% statistical power to detect the hypothesis of a blood glucose difference of 5 mg/dl between the two determinations. Therefore, 45 pairs of tests were performed. The adult patients recruited into this study were admitted into the medical intensive care unit between January 2012 and June 2012 with complications from hyperglycaemia, a blood glucose level greater than 200 mg/dl, which required glycaemic control by the hospital continuous intravenous insulin infusion protocol (*table 1*), and had radial arterial catheterisation for continuous blood pressure monitoring. All patients were haemodynamically stable with or without inotropes or vasopressors.

Study protocol and blood glucose measurements

All eligible patients were on the hospital's standard protocol for regular insulin infusion. Each patient had three pairs of hourly blood samples from an artery and vein for blood glucose measurements. The venous blood samples were obtained from either the central venous catheter or a peripheral venous catheter by the double syringe technique. The initial 2 ml of venous blood in the first syringe was discarded to reduce interference from the anticoagulant inside the catheter. The consecutive 3 ml of venous blood from the second syringe was then sent immediately to the hospital central laboratory for the standard hexokinase/glucose-6-phosphate technique of blood glucose measurement. These blood glucose results were used as reference values. Arterial blood was immediately aspirated from the radial arterial catheter by the double syringe technique within one minute of venous sampling. The first 2 ml of the arterial sampling were discarded and the subsequent 1 ml of arterial blood was obtained for the glucometer measurement. The bedside arterial blood glucometer test was performed quickly within 30 seconds of arterial sampling. In this study, the ACCU-CHEK® Performa (Roche Diagnostics Company, Thailand) with a compatible reagent strip test was selected as the standard glucometer device. The blood glucose level from this test was applied for adjusting the insulin dosage according to the hospital protocol. The primary objective was to determine the correlation, accuracy, and agreement of blood glucose levels between the arterial blood measured by glucometer and the venous blood glucose measured by the standard technique in the central laboratory. The secondary objective was to identify the agreement of insulin dosage adjustment based on the results of the blood glucose levels from these two methods.

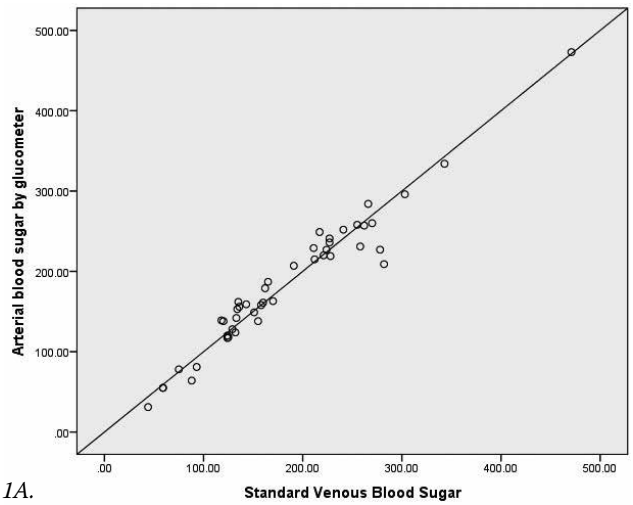
Statistical analysis

The blood glucose levels obtained from the two groups are represented by mean and standard error of mean (SEM). Pearson's correlation coefficient was calculated to determine the correlation of blood glucose between the two methods. The accuracy of the arterial blood glucometer compared with the standard central laboratory measurement of venous blood glucose was evaluated by the Clarke error grid analysis.[14] The bias and precision of blood glucose levels between the groups was then determined by a Bland-Altman plot with the limits of agreement range of bias ±1.96 standard deviation (SD).[15] The adjustment of insulin dosage based on the hourly blood glucose level, according to the hospital continuous insulin infusion protocol, was classified into increased rate, even rate, and decreased rate. The Kappa statistic was applied for the agreement analysis of the degree of insulin

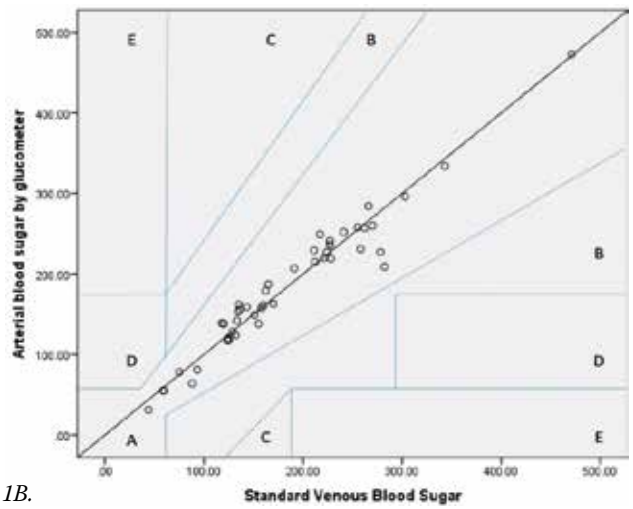
Table 1. Standard ICU protocol for insulin infusion

Initial dose of insulin infusion	
• Start insulin infusion protocol when blood glucose ≥ 200 mg/dl • Initial dose of insulin infusion = Initial blood glucose divided by 100 and round up to the nearest 0.5 unit/hour *For example: initial blood glucose is 325 mg/dl, then initial insulin infusion dose is 3.5 units/hour*	
Maintenance dose of insulin infusion	
Hourly blood glucose	**Insulin infusion dosage adjustment**
< 60 mg/dl	• Stop insulin infusion and inject 25 ml of 50% glucose intravenously, then repeat blood glucose in the next 15 minutes - If blood glucose < 60 mg/dl, repeat injection of 50% glucose intravenously and notify physician - If blood glucose > 100 mg/dl, restart insulin infusion at half the previous dose
60-100 mg/dl	• Stop insulin infusion for one hour and repeat blood glucose - If blood glucose > 100 mg/dl, restart insulin infusion at half the previous dose
101-180 mg/dl	Maintain insulin infusion dose
181-250 mg/dl	Increase insulin infusion dose by 0.5 unit/hour
251-300 mg/dl	Increase insulin infusion dose by 1 unit/hour
301-350 mg/dl	Increase insulin infusion dose by 1.5 unit/hour
351-400 mg/dl	Inject 5 units of regular insulin intravenously and increase insulin infusion dose by 2 units/hour
>400 mg/dl	Inject 10 units of regular insulin intravenously and increase insulin infusion dose by 2.5 units/hour If the blood glucose remains > 400 mg/dl during the following hour, notify physician

dosage adjustment by the hourly blood glucose level between the two groups. The Kappa agreement level was set according to the standard definition.[16]



1A.



1B.

Figure 1. Pearson's correlation coefficient (1A) and Clarke error grid (1B) of blood glucose between venous blood glucose and arterial glucometer

Results

Forty-five pairs of blood samples were collected for analysis from 15 critically ill patients of whom eight were male. The mean age ± SD was 52 ± 20.2 years. The underlying disease of diabetes mellitus was reported in five cases (33.33%) (*table 2*). Two episodes of moderate hypoglycaemia (venous blood glucose 41-70 mg/dl) were found; however, no emergency management was required. Most of the venous blood samples (42/45) were taken from a central venous catheter.

The mean ± SEM of the venous blood glucose measured by the standard technique and arterial blood glucose measured by glucometer were not statistically significantly different (183.98 ± 12.44 mg/dl vs. 183.98 ± 12.29 mg/dl, p = 1.0). Pearson's correlation coefficient of blood glucose levels between the two groups showed a 'very strongly positive correlation' with an r of 0.973 (*figure 1A*). According to the Clarke error grid analysis, 100% of the blood glucose measurements by arterial blood glucometer were in zone A, which indicated the results to be clinically accurate (*figure 1B*).

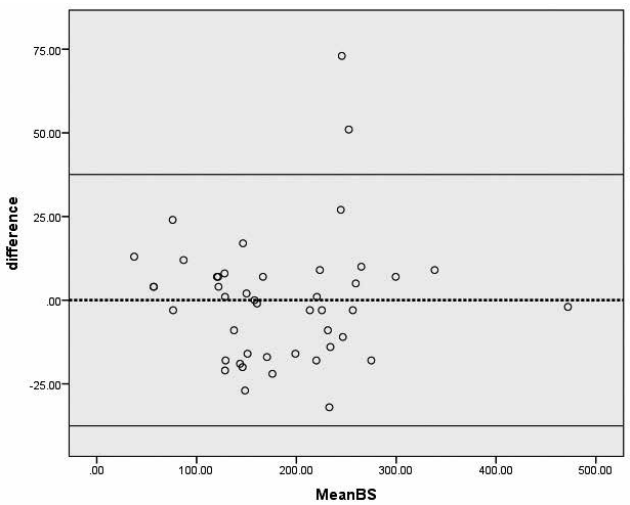


Figure 2. Bland-Altman agreement plot of blood glucose between venous blood glucose and arterial glucometer

Table 2. Sample characteristics for 15 patients

Characteristics	Value
Male sex, n (%)	8 (53.33%)
Age (mean ± SD), years	52 ± 20.2
APACHE-II score (mean ± SD)	15 ± 4.1
History of diabetes mellitus, n (%)	5 (33.33%)
Vasopressor/inotrope used, n (%)	3 (20%)
Causes for ICU admission, n (%) • Respiratory cause • Cardiovascular cause • Sepsis related cause • Neurological cause	 • 8 (53.33%) • 4 (26.67%) • 2 (13.33%) • 1 (6.67%)
Mean blood glucose ± SEM (mg/dl), (min,max) • Measured by venous plasma glucose • Measured by arterial blood glucometer • Mean blood glucose difference	 • 183.978 ± 12.44, (44,471) • 183.978 ± 12.29, (31,473) • 0.00 ± 2.86, (-73,32)

The Bland-Altman plot demonstrated strong agreement between the levels of venous blood glucose measured by the standard technique and arterial blood glucose measured by the glucometer. More than 95% of the cases were located in the range of the limits of agreement (*figure 2*). The mean difference and SD between the two tests were 0 and ± 19.17 mg/dl, respectively. The results indicated that the agreement between the blood glucose levels from the two determinations was satisfactory, but the precision of the arterial blood glucometer compared with the standard technique was unacceptable due to the significantly wide range of the limits of agreement of the mean blood glucose difference. However, the linear trend of the difference in blood glucose levels between the two groups to the mean of the blood glucose level difference by linear regression analysis showed no statistical significance (p = 0.729). This analysis indicated no proportional bias in the agreement between the blood glucose levels obtained by the two methods. Only two (4.44%) of the 45 pairs showed no agreement in the degree of insulin dosage adjustment when the blood glucose levels from arterial blood were measured by glucometer. The Kappa was 0.942, which indicated 'almost perfect agreement' between the two methods for adjustment of insulin dosage, based on hourly blood glucose levels (*table 3*).

Table 3. Kappa statistics to determine the agreement of insulin dosage adjustment by hourly blood glucose according to hospital continuous insulin infusion protocol

		Insulin dosage adjustment by arterial blood glucometer			
		Decreased rate	Even rate	Increased rate	Total
Insulin dosage adjustment by standard venous blood	Decreased rate	4	0	0	4
	Even rate	1	20	1	22
	Increased rate	0	0	19	19
	Total	5	20	20	45
Kappa statistic = 0.942 suggests almost perfect agreement.					

Discussion

The results of this study suggest strong correlation, excellent accuracy, and satisfactory agreement of blood glucose levels in haemodynamically stable, critically ill patients between the arterial blood glucose measured by a bedside point-of-care device and the standard laboratory hexokinase method in venous blood. In addition, there was an almost perfect agreement of continuous intravenous insulin dosage adjustment between the two groups.

The current study confirmed the findings of previous studies in which the arterial glucometer showed a strong agreement with the venous blood glucose, as determined by Bland-Altman analysis, gave a better correlation (r = 0.973), and higher clinical accuracy (100%), as shown by the Clarke error grid analysis.[17,18] These findings can be explained by the selection of a modern glucometer device, as in our study, which can overcome the interfering factors of the older devices used in previous studies.[8,19]

Nevertheless, two previous studies were against the use of an arterial blood glucometer and recommended either a blood gas analyser or the standard central laboratory measurement of plasma glucose to regulate glycaemic control in critically ill patients.[20,21] A central laboratory test of blood glucose from the radial artery is approximately 3.6 mg/dl (0.2 mmol/l) and 5.4-7.2 mg/dl (0.3-0.4 mmol/l) higher than the peripheral venous blood glucose and central venous blood glucose, respectively.[20,22] In addition, Posthouwer et al.[23] found a significant reduction in blood glucose over time after 10 minutes of blood sampling, which resulted in a discrepancy in blood glucose levels between the bedside glucometer and central laboratory measurements.

Although we could not record the exact turnaround time of the central laboratory measurements, our findings showed similar mean blood glucose levels between the central laboratory venous blood glucose and arterial blood glucometer (mean ± SEM = 0.00 ± 2.86 mg/dl), which possibly indicated that there was no time-dependent effect. Most of the venous blood samples in our study were taken from the central venous catheter. A difference in the blood glucose levels between the central and peripheral vein may not interfere with the outcome. Furthermore, those previous studies did not apply the Bland-Altman test to determine the agreement and precision. Several experts recommended that the Bland-Altman method be considered to determine the level of agreement between two medical devices or tests.[15,24-27]

Although the Bland-Altman plot in our study indicated satisfactory agreement of the arterial blood glucometer with the central laboratory venous blood glucose test, the application for the precision of the test remains inconclusive. The range for the limits of agreement of the blood glucose level was significantly wide and unacceptable (± 37.57 mg/dl). In addition, the calculated 95% CI for the limits of agreement was 11.26 mg/dl, which also indicated a sampling error and an inadequate number of samples to determine the precision of the arterial blood glucometer test.[27]

Our study offers evidence-based support for the current real-life clinical practice of insulin adjustment in an intensive care unit, as demonstrated by an almost perfect agreement (Kappa = 0.942) of insulin dosage adjustment by arterial glucometer, according to the hospital protocol.

In general, the definition of an acceptable variation of a new test from the standard test is ± 20%.[8] This study found only ± 11.29% variation from the standard venous blood glucose measurement which is in an acceptable boundary. The current worldwide glycaemic control protocol in critical illness essentially requires a fast and accurate blood glucose measurement; therefore, the arterial glucometer can be used instead of central laboratory venous blood measurement for adjusting insulin dosage because of the lower turnaround time, good accuracy, and acceptable variation.

Although the results of this study can be generally applied in the current real-life practice of an intensive care unit, there are some limitations. First, the majority of the blood glucose levels in this study were in the normoglycaemic range, so the accuracy and agreement of blood glucose at extreme hypoglycaemic and hyperglycaemic levels might need further confirmation. In addition, the precision of the arterial blood glucometer needs to be re-evaluated by a study with a larger sample size. Second, this study did not identify the interfering factors that may cause disagreement between the arterial glucometer and standard blood glucose measurement, for example the arterial pH, haematocrit level, and blood pressure. Some blood was discarded according to the blood sampling technique which may cause significant blood loss if more frequent testing is required. Also, this study did not mention the complications of arterial blood sampling such as air embolism, infection, thrombotic complication, and malfunction of the arterial pressure monitoring system.

Finally, although most pairs of blood glucose samples in our study correlated very well, some pairs showed remarkable differences. A wide blood glucose gap between the arterial glucometer and standard plasma glucose may affect a management decision. Nevertheless, we could not detect any adverse effects in this respect in our study, which could be because of the wide acceptable ranges of glucose levels of the unit glucose control protocol. Therefore, we suggest caution when using the arterial blood glucometer in tight and narrow ranges of the glucose management protocol. In addition, any exaggerated change of arterial blood glucose measured by glucometer should be repeated by a different measurement, such as central laboratory measurement or arterial blood gas analyser, before changing the management decision.

Conclusions

This study identified good correlation, good accuracy, and good agreement of blood glucose levels between the arterial blood measured by glucometer and the standard central laboratory method of measuring venous blood glucose. However, the precision of the arterial blood glucometer compared with the standard blood glucose measurement needs further evaluation. The almost prefect agreement of insulin dosage adjustment based on arterial glucometer testing was also confirmed. Therefore, this study verified the real-life practice in the intensive care unit of measuring blood glucose in arterial blood by glucometer rather than the standard method of testing venous blood.

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Disclosure

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References

1. Krinsley JS. Association between hyperglycemia and increased hospital mortality in a heterogeneous population of critically ill patients. Mayo Clin Proc. 2003;78:1471-8.
2. van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. N Engl J Med. 2001;345:1359-67.
3. Van den Berghe G, Wilmer A, Milants I, et al. Intensive insulin therapy in mixed medical/surgical intensive care units: benefit versus harm. Diabetes. 2006;55:3151-9.
4. Van den Berghe G, Schetz M, et al. Clinical review: Intensive insulin therapy in critically ill patients: NICE-SUGAR or Leuven blood glucose target? J Clin Endocrinol Metab. 2009;94:3163-70.
5. Krinsley JS. Effect of an intensive glucose management protocol on the mortality of critically ill adult patients. Mayo Clin Proc. 2004;79:992-1000.
6. Finfer S, Heritier S, Committee NSM, Committee SSE. The NICE-SUGAR (Normoglycaemia in Intensive Care Evaluation and Survival Using Glucose Algorithm Regulation) Study: statistical analysis plan. Crit Care Resusc. 2009;11:46-57.
7. Finfer S, Delaney A. Tight glycemic control in critically ill adults. JAMA. 2008;300:963-5.
8. Louie RF, Tang Z, Sutton DV, Lee JH, Kost GJ. Point-of-care glucose testing: effects of critical care variables, influence of reference instruments, and a modular glucose meter design. Arch Pathol Lab Med. 2000;124:257-66.
9. Tang Z, Du X, Louie RF, Kost GJ. Effects of pH on glucose measurements with handheld glucose meters and a portable glucose analyzer for point-of-care testing. Arch Pathol Lab Med. 2000;124:577-82.
10. Tang Z, Lee JH, Louie RF, Kost GJ. Effects of different hematocrit levels on glucose measurements with handheld meters for point-of-care testing. Arch Pathol Lab Med. 2000;124:1135-40.
11. Tang Z, Louie RF, Payes M, Chang KC, Kost GJ. Oxygen effects on glucose measurements with a reference analyzer and three handheld meters. Diabetes Technol Ther. 2000;2:349-62.
12. Kulkarni A, Saxena M, Price G, O'Leary MJ, Jacques T, Myburgh JA. Analysis of blood glucose measurements using capillary and arterial blood samples in intensive care patients. Intensive Care Med. 2005;31:142-5.
13. Inoue S, Egi M, Kotani J, Morita K. Accuracy of blood-glucose measurements using glucose meters and arterial blood gas analyzers in critically ill adult patients: systematic review. Crit Care. 2013;17:R48.
14. Clarke WL, Cox D, Gonder-Frederick LA, Carter W, Pohl SL. Evaluating clinical accuracy of systems for self-monitoring of blood glucose. Diabetes Care. 1987;10:622-8.
15. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet. 1986;1:307-10.
16. Sim J, Wright CC. The kappa statistic in reliability studies: use, interpretation, and sample size requirements. Phys Ther. 2005;85:257-68.
17. Corstjens AM, Ligtenberg JJ, van der Horst IC, et al. Accuracy and feasibility of point-of-care and continuous blood glucose analysis in critically ill ICU patients. Crit Care. 2006;10:R135.
18. Lacara T, Domagtoy C, Lickliter D, et al. Comparison of point-of-care and laboratory glucose analysis in critically ill patients. Am J Crit Care. 2007;16:336-46; quiz 47.
19. Kost GJ, Vu HT, Lee JH, et al. Multicenter study of oxygen-insensitive handheld glucose point-of-care testing in critical care/hospital/ambulatory patients in the United States and Canada. Crit Care Med. 1998;26:581-90.
20. Kanji S, Buffie J, Hutton B, et al. Reliability of point-of-care testing for glucose measurement in critically ill adults. Crit Care Med. 2005;33:2778-85.
21. Maser RE, Butler MA, DeCherney GS. Use of arterial blood with bedside glucose reflectance meters in an intensive care unit: are they accurate? Crit Care Med. 1994;22:595-9.
22. Finfer S, Wernerman J, Preiser JC, et al. Clinical review: Consensus recommendations on measurement of blood glucose and reporting glycemic control in critically ill adults. Crit Care. 2013;17:229.
23. Posthouwer D, de Graaf MJ, Frederiks M, et al. Time dependent decrease in blood glucose levels after sampling potentially affects intensive insulin therapy in the intensive care unit. Intensive Care Med. 2009;35:386-7.
24. Sedgwick P. Limits of agreement (Bland-Altman method). BMJ. 2013;346:f1630.
25. Bunce C. Correlation, agreement, and Bland-Altman analysis: statistical analysis of method comparison studies. Am J Ophthalmol. 2009;148:4-6.
26. Eken C. Bland-Altman analysis for determining agreement between two methods. J Emerg Med. 2009;36:307; author reply -8.
27. Hamilton C, Stamey J. Using Bland-Altman to assess agreement between two medical devices--don't forget the confidence intervals! J Clin Monit Comput. 2007;21:331-3.