Correlation between glucose concentrations in serum, plasma, and whole blood measured by a point-of-care glucometer and serum glucose concentration measured by an automated biochemical analyzer for canine and feline blood samples

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**Objective**—To investigate the correlation between glucose concentrations in serum, plasma, and whole blood measured by a point-of-care glucometer (POCG) and serum glucose concentration measured by a biochemical analyzer.

**Design**—Prospective clinical study.

**Samples**—96 blood samples from 80 dogs and 90 blood samples from 65 cats.

**Procedures**—Serum, plasma, and whole blood were obtained from each blood sample. The glucose concentrations in serum, plasma, and whole blood measured by a POCG were compared with the serum glucose concentration measured by a biochemical analyzer by use of the Lin concordance correlation coefficient ($\rho_c$) and Bland-Altman plots.

**Results**—For both canine and feline samples, glucose concentrations in serum and plasma measured by the POCG were more strongly correlated with the serum glucose concentration measured by the biochemical analyzer ($\rho_c$, 0.98 for both canine serum and plasma; $\rho_c$, 0.99 for both feline serum and plasma) than was that in whole blood ($\rho_c$, 0.62 for canine samples; $\rho_c$, 0.90 for feline samples). The mean difference between the glucose concentrations determined by the biochemical analyzer and the POCG in serum, plasma, and whole blood was 0.4, 0.3, and 31 mg/dL, respectively, for canine samples and 7, 6, and 32 mg/dL, respectively, for feline samples.

**Conclusions and Clinical Relevance**—Results indicated that use of a POCG to measure glucose concentrations in serum or plasma may increase the accuracy and reliability of diagnostic and treatment decisions associated with glucose homeostasis disorders in dogs and cats. (J Am Vet Med Assoc 2015;246:1327–1333)

Point-of-care glucometers are widely used in veterinary hospitals for quick, easy, and cost-effective measurement of blood glucose concentration in canine and feline patients. The use of POCGs is particularly important for serial measurement of blood glucose concentration in diabetic dogs and cats, in which insulin dose adjustments are required.1–3 Point-of-care glucometers are also commonly used to routinely monitor blood glucose concentration in hospitalized dogs and cats, especially patients with diseases associated with glucose homeostasis disorders such as liver disease, sepsis, neoplasia, hypoadrenocorticism, and insulinoma, and juvenile or neonatal animals that are weak, depressed, or neurologically unstable.

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**ABBREVIATION**

POCG  Point-of-care glucometer

Results of some studies4,5 indicate that use of a POCG for measurement of glucose concentration in whole blood samples produces unreliable results for dogs. Thus, use of a POCG to monitor blood glucose concentrations in hospitalized patients is limited by concerns that the results provided by the POCG might lead to erroneous clinical decisions.4 However, certain aspects of POCGs make their use preferable to that of an automated biochemical analyzer for measurement of glucose concentration. For example, results can be obtained within 1 minute, which is advantageous in emergency situations; only a small amount (0.6 µL) of blood is necessary to measure glucose concentration, which is helpful when monitoring patients that are very small or markedly anemic; and it is fairly inexpensive to use, which is beneficial when serial monitoring of serum or plasma glucose concentration by biochemical analysis is cost prohibitive.

In previous studies,4,5 glucose concentration was measured in whole blood by a POCG and in serum by...
Materials and Methods

Animals—The study was performed between April and October 2013 during periods allocated for research on one of the investigators (BST). Dogs and cats examined at the University of Pennsylvania Ryan Veterinary Hospital for reasons unrelated to the study that required collection of a blood sample for diagnostic purposes were eligible for enrollment. All study protocols were approved by the University of Pennsylvania Institutional Animal Care and Use Committee, and all blood samples were obtained from patients as part of a diagnostic plan developed by the attending clinicians with consent from the owners.

Sample size calculation—A 2-sided paired t test was used to perform a power calculation to determine the number of samples required to detect a difference of at least 15 mg/dL between the glucose concentration determined by the biochemical analyzer and that determined by the POCG. The calculation was made on the basis of the mean ± SD glucose concentration (117 ± 25 mg/dL) used to establish the reference interval for the biochemical analyzer. It was assumed that the SD of the glucose concentrations determined by the POCG would be similar to that of the glucose concentrations determined by the biochemical analyzer. Other assumptions included a power of 0.8, type I error rate of 0.05, correlation of 0.7, and a ratio of 1 between the POCG and biochemical analyzer results. The calculation resulted in a required sample size of 44 blood samples for both dogs and cats; however, additional samples from eligible animals were analyzed as they became available until the end of the allocated research time.

Experimental protocol—Immediately after each blood sample was obtained, a drop of whole blood was analyzed by a POCG that was designated specifically for the study, and the remainder of the sample was placed in a heparinized capillary tube, a nonheparinized capillary tube, and an evacuated glass blood collection tube or plastic microtainer. The capillary tubes were centrifuged within 3 minutes after collection and used to measure the PCV and obtain serum (nonheparinized tube) and plasma (heparinized tube) for measurement of glucose concentration by the POCG. Serum was harvested from the samples stored in the evacuated glass blood collection tubes or plastic microtainers within 15 minutes after collection, and the serum glucose concentration was determined by an automated biochemical analyzer.

POCG—The glucose concentration in all samples was measured with the same POCG by means of an enzymatic glucose dehydrogenase reaction and quantitative amperometric assay. Briefly, 0.6 μL of a sample
was applied directly to a glucose test strip, which was then inserted into the POCG, and results were generated in approximately 5 seconds. One investigator (BST) operated the POCG throughout the study. The POCG was operated in accordance with the manufacturer’s recommendations except that glucose concentrations were measured in serum and plasma as well as whole blood and venous rather than capillary blood samples were analyzed. The POCG was calibrated in accordance with the manufacturer’s instructions with manufacturer-provided control solution and calibration test strips at the onset of the study and each time a new box of 50 test strips was opened.

Biochemical analyzer—The biochemical analyzer measured the glucose concentration of each serum sample by use of an enzymatic hexokinase oxidase reaction, and results were detected colorimetrically.8 The analyzer required 10 µL of serum for analysis and generated results in approximately 5 minutes.8 It was operated by trained laboratory technologists. The reference range established by the laboratory for serum glucose concentration was 65 to 112 mg/dL for dogs and 67 to 168 mg/dL for cats, and serum glucose concentrations below or above those ranges were characterized as being consistent with hypoglycemia or hyperglycemia, respectively.

Statistical analysis—For each sample type (serum, plasma, and whole blood) and analyzer (biochemical analyzer and POCG), the distribution of the glucose concentration data was assessed for normality by means of the Shapiro-Wilks test. Descriptive data were generated. The respective differences between the glucose concentrations in serum, plasma, and whole blood measured by the POCG and the serum glucose concentration measured by the biochemical analyzer for a subset of 26 blood samples obtained from dogs and 25 blood samples obtained from cats that were characterized as being hyperglycemic (glucose concentration as determined by the biochemical analyzer, > 112 mg/dL for dogs and > 168 mg/dL for cats).

<table>
<thead>
<tr>
<th>Species</th>
<th>Sample analyzed by POCG</th>
<th>( \rho ) (95% confidence interval)</th>
<th>Bias correction factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>Serum</td>
<td>0.981 (0.97–0.99)</td>
<td>0.990</td>
</tr>
<tr>
<td></td>
<td>Plasma</td>
<td>0.984 (0.97–0.99)</td>
<td>0.995</td>
</tr>
<tr>
<td></td>
<td>Whole blood</td>
<td>0.656 (0.51–0.81)</td>
<td>0.711</td>
</tr>
<tr>
<td>Cat</td>
<td>Serum</td>
<td>0.988 (0.98–0.99)</td>
<td>0.996</td>
</tr>
<tr>
<td></td>
<td>Plasma</td>
<td>0.992 (0.990–0.998)</td>
<td>0.997</td>
</tr>
<tr>
<td></td>
<td>Whole blood</td>
<td>0.865 (0.79–0.94)</td>
<td>0.874</td>
</tr>
</tbody>
</table>

See Table 2 for key.

Figure 1—Box-and-whisker plots of the difference between the glucose concentration in whole blood, serum, and plasma measured by a POCG and the serum glucose concentration measured by an automated biochemical analyzer for 96 blood samples obtained from 80 dogs (A) and 90 blood samples obtained from 65 cats (B). For each plot, the solid line in the middle of each box represents the median, the top and bottom edges of the box delimit the interquartile range, the brackets represent the most extreme data point within 1.5 times the nearest quartile, and the circles represent outliers.
Linear regression analysis was used to evaluate the association of the PCV with the correlation between the whole blood glucose concentration measured by the POCG and the serum glucose concentration measured by the biochemical analyzer. For reporting purposes, the PCV reference range was 40% to 60% for dogs and 32% to 48% for cats, and anemia was defined as a PCV < 40% for dogs and < 32% for cats. All analyses were performed with a statistical software program, and values of \( P < 0.05 \) were considered significant.

**Results**

Ninety-six blood samples obtained from 80 client-owned dogs and 90 blood samples obtained from 65 client-owned cats were analyzed. For animals from which multiple blood samples were obtained, there was at least a 2-hour interval between sample collections. The glucose concentrations in serum, plasma, and whole blood measured by the POCG and the serum glucose concentration measured by the automated biochemical analyzer for both dogs and cats were summarized (Table 1). The serum...
glucose concentration measured by the biochemical analyzer was considered the gold standard for all samples.

For the 96 canine samples, the serum glucose concentration determined by the biochemical analyzer was within the reference range (65 to 112 mg/dL) for 70 (73%) samples and was > 112 mg/dL (hyperglycemia) for the remaining 26 (27%) samples. Twenty-three (24%) samples had a whole blood glucose concentration < 65 mg/dL when measured with the POCG (mean ± SD, 56 ± 6 mg/dL; median, 57 mg/dL; range, 45 to 64 mg/dL); however, none of those samples were classified as hypoglycemic (glucose concentration, < 65 mg/dL) on the basis of the serum glucose concentration measured by the biochemical analyzer. For the 90 feline samples, the serum glucose concentration determined by the biochemical analyzer was within the reference range (67 to 168 mg/dL) for 65 (72%) samples and was > 168 mg/dL (hyperglycemia) for the remaining 25 (28%) samples. Five (6%) samples had a whole blood glucose concentration < 67 mg/dL when measured with the POCG (mean ± SD, 55 ± 11 mg/dL; median, 62 mg/dL; range, 39 to 65 mg/dL); however, none of those samples were classified as hypoglycemic (glucose concentration, < 67 mg/dL) on the basis of the serum glucose concentration measured by the biochemical analyzer.

Results of the Lin concordance correlation analyses indicated that the serum glucose concentration measured by the biochemical analyzer was significantly (P < 0.001) correlated with the glucose concentration measured by the POCG, regardless of the sample (serum, plasma, or whole blood) analyzed (Table 2). However, the glucose concentrations in serum and plasma determined by the POCG were more strongly correlated with the serum glucose concentration determined by the biochemical analyzer than was the whole blood glucose concentration determined by the POCG. Similar results were obtained when the subset of 26 canine samples and 25 feline samples that were classified as hyperglycemic on the basis of the serum glucose concentration measured by the biochemical analyzer were assessed (Table 3), which suggested that the correlation between the results of the

Figure 3—Bland-Altman plots of the respective differences between glucose concentration in serum (A), plasma (B), and whole blood (C) measured by the POCG and the serum glucose concentration measured by the automated biochemical analyzer for 90 blood samples obtained from 65 cats. See Figure 2 for remainder of key.
POCG and biochemical analyzer did not vary as glucose concentration increased.

The respective differences between the glucose concentration in serum, plasma, and whole blood measured by the POCG and the serum glucose concentration measured by the biochemical analyzer for both canine and feline samples were summarized (Figure 1). The corresponding Bland-Altman plots for dogs (Figure 2) and cats (Figure 3) are provided. Similar to the Lin concordance correlation analyses, the Bland-Altman plots indicate that the glucose concentrations measured by the POCG in serum and plasma more closely agreed with the serum glucose concentration measured by the biochemical analyzer than did the whole blood glucose concentration measured by the POCG, as evidenced by the narrower 95% limits of agreement for the POCG results for serum and plasma, compared with the POCG results for whole blood.

For the 96 canine samples, the PCV was within the reference range (40% to 60%) for 67 (70%) samples and < 40% for the remaining 29 (30%) samples; none of the samples had a PCV > 60%. Results of linear regression indicated that the correlation between the whole blood glucose concentration measured by the POCG and the serum glucose concentration measured by the biochemical analyzer was significantly better for samples with a PCV < 40%, compared with that for samples with a PCV within the reference range, although the coefficient of determination for the analysis was only 0.48.

For the 90 feline samples, the PCV was within the reference range (32% to 48%) for 61 (68%) samples, was < 32% for 27 (30%) samples, and was > 48% for 2 (2%) samples. Results of the linear regression did not indicate an association between the PCV and the correlation between the whole blood glucose concentration measured by the POCG and the serum glucose concentration measured by the biochemical analyzer when the PCV was within or below the reference range. The small number of samples with a PCV above the reference range prevented a similar analysis with that group of samples.

**Discussion**

Results of the present study indicated that there was excellent correlation between serum glucose concentration measured by a biochemical analyzer (gold standard) and glucose concentrations measured by a POCG in serum and plasma, but not whole blood, for canine and feline samples. Accurate measurement of glucose concentration in hospitalized patients is of paramount importance for the timely diagnosis and treatment of many diseases and conditions, including diabetes mellitus. Measurement of glucose concentration by a POCG is appealing because POCGs are widely available, inexpensive, and easy to use and provide results rapidly. However, the use of POCGs in veterinary practice has been hampered because of inaccurate results, especially when whole blood is analyzed.5,9 Findings of the present study suggested that use of a POCG to measure glucose concentration in serum or plasma yielded accurate results, which could improve the accuracy, reliability, and speed of diagnostic and treatment decisions for hospitalized dogs and cats with abnormal glucose homeostasis.

Inaccurate measurement of glucose concentration can adversely affect treatment decisions.4,5 In a study4 in which the glucose concentration was measured in 110 whole blood samples obtained from 34 dogs with various POCGs, it was estimated that inaccurate glucose measurements would cause erroneous treatment decisions 8% to 67% of the time, depending on the POCG used. In another study10 in which a POCG was used to measure glucose concentration in serial whole blood samples obtained from diabetic dogs being treated with insulin, it was estimated that contradictory recommendations for insulin administration were often provided for the same dog on the basis of serial glucose measurements obtained on 2 consecutive days. These 2 studies4,10 highlight the possible unfortunate clinical outcomes associated with the use of a POCG to measure glucose concentration in whole blood samples. The findings of the present study suggested that use of a POCG to measure glucose concentration in serum or plasma instead of whole blood provided accurate results. Thus, the particular POCG used in this study might be useful for serial monitoring of serum or plasma glucose concentrations in patients with diabetes mellitus and enhance the accuracy of insulin dose adjustments for those patients; this may be particularly important for patients in which hypoglycemia is suspected. In the present study, all 23 canine and 5 feline samples that were misclassified as hypoglycemic on the basis of whole blood glucose concentration measured by the POCG were correctly classified as normoglycemic on the basis of the serum and plasma glucose concentrations measured by the POCG, when the serum glucose concentration measured by a biochemical analyzer was used as the gold standard.

Although serum glucose concentration measured with the biochemical analyzer was excellently correlated with the glucose concentration measured by the POCG in both serum and plasma, it was best correlated with the plasma glucose concentration measured by the POCG. Therefore, plasma might be the best sample for POCG measurement of glucose concentration, which means that heparinized capillary tubes would be preferred over nonheparinized capillary tubes for blood sample processing.

For both canine and feline samples, the correlation between serum glucose concentration measured by the biochemical analyzer and the glucose concentrations in serum and plasma measured by the POCG remained excellent, even for the subgroup of animals with hyperglycemia (glucose concentration, > 112 mg/dL for dogs and > 168 mg/dL for cats). However, samples with marked hyperglycemia (glucose concentration, > 300 mg/dL for dogs and > 500 mg/dL for cats) were not evaluated in the present study, and none of the samples in this study had marked hypoglycemia (glucose concentration, < 60 mg/dL for dogs and < 60 mg/dL for cats). Further research is warranted to investigate the correlation of glucose concentration measured by a biochemical analyzer or some other reference method and the glucose concentration measured by a POCG for dogs and cats with varying degrees of hypoglycemia and hyperglycemia.

Only the correlation between whole blood glucose concentration measured by the POCG and the serum
glucose concentration measured by the biochemical analyzer was evaluated for an association with PCV because the PCV was not expected to affect the glucose concentration measured by the POCG in serum and plasma samples. Results indicated that the correlation between the whole blood glucose concentration measured by the POCG and the serum glucose concentration measured by the biochemical analyzer was significantly better for canine samples with a PCV < 40%, compared with that for canine samples with a PCV within the reference range. However, the coefficient of determination was 0.48, which suggested that the PCV accounted for only 48% of the variation in the difference between the whole blood glucose concentration measured by the POCG and the serum glucose concentration measured by the biochemical analyzer. A similar association between PCV and the correlation between the whole blood glucose concentration measured by the POCGs and the serum glucose concentration measured by the biochemical analyzer was not observed in the feline samples. Results of other studies11–14 suggest that Hct significantly affects the measurement of whole blood glucose concentration by a POCG in dogs, cats, and humans. In human blood samples with a low Hct, the whole blood glucose concentration measured by a POCG is generally overestimated, compared with the serum glucose concentration measured by a biochemical analyzer.8 Although the mechanism for that finding is not fully understood, the viscosity of a blood sample is positively associated with its Hct and some investigators8 have hypothesized that the ability of plasma to reach the reaction surface of the POCG test strip is negatively associated with Hct such that the amount of plasma that reaches the reaction surface of the test strip for a sample with a low Hct is proportionately greater than the amount of plasma that reaches the reaction surface of the test strip for a sample with a higher Hct, and consequently, the glucose concentration measured by a POCG will be greater for the sample with a low Hct than that for the sample with a higher Hct. The reason that the glucose concentrations in serum and plasma measured by the POCG were more strongly correlated with the serum glucose concentration measured by the biochemical analyzer than was the whole blood glucose concentration measured by the POCG in the present study might have been associated with the removal of the RBCs from the serum and plasma. Additional studies are necessary to determine whether hemococoncentration or polycythemia affects the POCG measurement of glucose concentration in serum and plasma.

A limitation of the present study was the fact that only 1 POCG was evaluated. The results may have differed had other POCGs produced by the same manufacturer or other manufacturers been evaluated. Another limitation was that blood samples with marked hypoglycemia or hyperglycemia were not analyzed. Finally, the manufacturer of the POCG recommends that it only be used to evaluate fresh capillary blood samples. In the present study, fresh venous blood samples were analyzed, and it is unknown whether the type of blood sample (capillary vs venous) would affect measurement of the glucose concentration by the POCG.

In the present study, there was excellent correlation between serum glucose concentration measured by a biochemical analyzer and glucose concentrations measured by a POCG in serum and plasma, but not whole blood, for canine and feline blood samples. Use of the POCG to measure glucose concentrations in serum or plasma may increase the timeliness, accuracy, and reliability of diagnostic and treatment decisions associated with glucose homeostasis disorders in dogs and cats.

References