Clinical Impact of Prandial State, Exercise, and Site Preparation on the Equivalence of Alternative-Site Blood Glucose Testing

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OBJECTIVE — To determine whether clinically significant differences exist in fasting blood glucose (BG) at the forearm, palm, and thigh relative to the fingertip; to assess the impact of prandial status by comparing BG between alternative sites and the fingertip at several time intervals after carbohydrate intake; to assess the effects of moderate brief exercise on site-to-site differences in BG; to evaluate the impact of site preparation by local rubbing on alternative-site testing (AST) equivalence; and to determine levels of perceived pain and satisfaction associated with AST.

RESEARCH DESIGN AND METHODS — Fasting BG was measured using the One Touch Ultra (LifeScan, Milpitas, CA) at the fingertip, palm, thigh, and each forearm (with local rubbing) in 86 patients with type 2 diabetes. A 40-g carbohydrate meal was consumed and BG was again measured from each site at 60, 90, and 120 min postmeal, with an additional forearm test at 90 min without local rubbing. Patients then exercised for 15 min with repeat BG at each site. Differences in BG between sites were assessed using repeated-measures ANOVA and regression analyses.

RESULTS — Significant differences in BG at alternative sites were found 60 min postmeal ($P = 0.0003$) and postexercise ($P = 0.037$). Specifically, clinically significant differences (expressed as percent difference from the fingertip) at 60 min include $-8.8 \pm 10.8\%$ at the forearm and $-13.7 \pm 10.7\%$ at the thigh, and postexercise $+19.1 \pm 19.1\%$ at the forearm and $+15.6 \pm 22.6\%$ at the thigh. However, no significant differences were observed between sites in either the fasting state or at 90 and 120 min postmeal. The dynamic results suggest a time lag in equilibration of forearm and thigh BG during periods of rapid glucose change. Palm and fingertip BG test results were similar at all time points.

CONCLUSIONS — AST results are consistent with fingertip BG results in both the fasting state and 2 h postmeal; no benefit from site preparation by local rubbing was noted. However, testing at sites other than the hand cannot be recommended 1 h postmeal or immediately after exercise. AST is equivalent and appropriate for use at testing times commonly used in clinical practice.

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Self-monitoring of blood glucose (SMBG) is an essential component of intensive management of diabetes (1). Traditionally, fingertip capillary blood has been used for such monitoring. With technological advances available in some SMBG devices, the requirement of smaller blood samples, and the capillary action of the strip itself, alternative-site testing (AST) can now be performed at sites such as the forearm or thigh. As a result of these advances, increasing numbers of patients are considering testing at alternative sites to increase the frequency of testing while limiting the potential pain associated with fingertip testing. However, the validity and similarity of AST relative to fingertip blood glucose (BG) testing have been broadly debated. In particular, the reliability and reproducibility of postprandial BG results have been reported to demonstrate significant differences between samples obtained at the forearm and fingertip, even when the samples are collected simultaneously (2–7). Limited data have been reported regarding the specific impact of exercise or site preparation on the validity of AST.

The current study was performed *1*) to determine whether clinically significant differences exist in glucose values measured via capillary blood, with samples obtained simultaneously at the forearm, the base of the hand (palm), and the thigh, relative to samples obtained at the fingertip; *2*) to assess the impact of prandial status by comparing BG values between alternative sites and the finger at periodic intervals after carbohydrate intake; *3*) to determine whether clinically significant differences exist for glucose values measured at the forearm, palm, and thigh, as compared with the fingertip after moderate brief exercise; *4*) to assess the impact of site preparation (local rubbing) on the equivalence of the measured BG concentration at alternative sites; and *5*) to determine self-reported levels of pain and satisfaction associated with AST.

RESEARCH DESIGN AND METHODS

— A total of 87 adult subjects with type 2 diabetes participated in the study. All data were collected during a 2.5- to 3-h visit to the site. Informed consent was obtained from all patients before initiating any study procedures. A trained

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Abbreviations: AST, alternative-site testing; BG, blood glucose; SMBG, self-monitoring of blood glucose.
A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

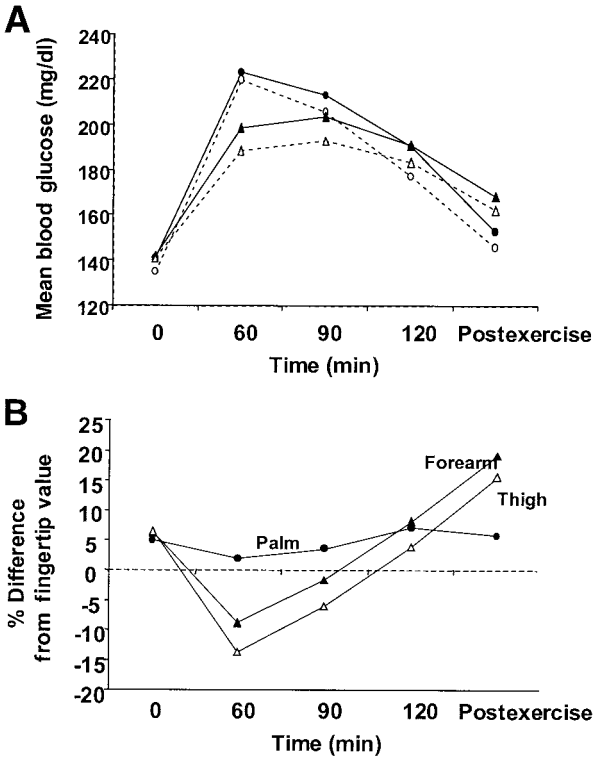

Figure 1—*Results from AST using the One Touch Ultra. Results are shown for mean BG in 86 subjects with type 2 diabetes before and after ingestion of a small meal (40 g carbohydrate) and after brief exercise* (A). *The percent difference in values obtained at the alternative sites (palm, forearm, and thigh) as compared with the fingertip are also shown* (B). ○, *finger;* ●, *palm;* △, *thigh;* ▲, *forearm.*

technician tested fasting (minimum of 4 h) BG using the One Touch Ultra (LifeScan, Milpitas, CA) twice on the fingertip and once on the palm (hypothenar eminence), thigh, and each forearm. Samples were collected after vigorous rubbing of the forearm and thigh testing sites using 10 strong back-and-forth motions in 5 s. A sample was obtained from the fingertip for determination of YSI glucose (YSI 2700 blood glucose analyzer; Yellow Springs Instruments, Yellow Springs, OH), hematocrit, Ultra glucose, and HbA_{1c}.

After baseline BG testing, each subject consumed a can of Ensure (8 fluid ounces, 40 g carbohydrate; Ross Products Division, Abbott Laboratories, North Chicago, IL) within 10 min. At 60, 90, and 120 min after the start of the meal, the study coordinator obtained BG results at the fingertip, palm, forearm, and thigh. In addition, at the 90-min sampling time, one forearm was sampled with no rubbing and the other forearm was sampled with vigorous rubbing.

After completion of postmeal BG measurements, the study coordinator recorded heart rate and blood pressure. Subjects then walked briskly at a rate of 2.5–3.5 miles per hour for 15 min on a treadmill to maintain a Borg rate of perceived exertion (RPE) of 3–5 (8). Immediately after the exercise, BG was again tested with the One Touch Ultra at each of the specific testing sites.

Subjects then completed a questionnaire that rated level of pain and satisfaction with fingertip and AST. This questionnaire contains numerical rating scales (ranging from 0 to 10, with 0 corresponding to no pain and 10 representing the worst pain) for level of perceived pain (9) and multiple-choice questions for likelihood of future use. Questions include likelihood of future testing at each site (always, most often, sometimes, rarely, or never) and likelihood of testing more frequently given the option of AST (very likely, likely, unlikely, or don't know).

Descriptive statistics were used to calculate frequencies (sex, insulin use, and questionnaire responses) and means (age, BMI, HbA_{1c}, duration of diabetes, and BG). BG concentrations are reported as average values when duplicate tests were performed. Repeated-measures ANOVA and correlation analyses were used to assess differences in BG concentrations between sites at each time point. Logistic regression was used to predict the probability of >10% forearm-fingertip and thigh-fingertip differences using the following independent variables: age, sex, BMI, HbA_{1c}, insulin use, and duration of diabetes. In addition, analyses at the 60-min time point evaluated change in BG between baseline and 60 min postmeal as a predictor of postprandial BG differences between sites, which was calculated as the difference in fingertip BG between the 60-min postmeal and baseline tests.

AST success rates were calculated for each site and represent the percent of total puncture attempts during the study that were successful (those that resulted in adequate blood samples for testing). The accuracy of the One Touch Ultra meter was assessed by Clarke error analysis, which compares results obtained simultaneously from two BG measurement devices and determines the clinical impact of observed differences (10). All statistical testing was performed at the 0.05 level of significance. The statistical analysis was performed independently by the authors using SAS version 8.0 software (SAS Institute, Cary, NC). The study protocol was developed solely by the study investigators and approved by the both the Protocol Review Committee and Institutional Review Board of Park Nicollet Health Services.

RESULTS — A total of 86 of the 87 patients enrolled were included in the data analysis. One patient was excluded due to failure to achieve the required 4-h fast at the time of enrollment. Four subjects were excluded from the exercise component due to elevated blood pressure readings at the time of the study. The study population included 55 men (64%) and 31 women (36%); the mean age (±SD) was 60 ± 9 years. Duration of type 2 diabetes was 9 ± 7 years, HbA_{1c} was 7.6 ± 1.7%, BMI was 31.1 ± 4.9 kg/m^2, and 24 (31%) of the subjects used insulin.

The One Touch Ultra testing system was found to be clinically accurate; all data points were in zones A and B, the two clinically acceptable regions of the Clarke error grid (10). When baseline fingerstick values were obtained simultaneously with both the Ultra and the YSI, 99% of data points were distributed within zone A of the Clarke error grid and 1% of the data points were in zone B.

The mean BG concentrations measured at each site at baseline, postmeal, and postexercise are shown in Fig. 1*A*. Mean (±SD) BG concentrations measured at each site for all time points are also shown in Table 1. Significant site dif-

Table 1—*BG concentrations (mg/dl) at each site and time point* (n = 86)

Site	Baseline	60 min postmeal*	90 min postmeal	120 min postmeal	After exercise†
Fingertip	135 ± 50	220 ± 62	205 ± 60	177 ± 54	145 ± 55
Palm	141 ± 52	223 ± 62	213 ± 64	190 ± 62	152 ± 57
Forearm	142 ± 50	199 ± 55	200 ± 59	191 ± 60	168 ± 53
Thigh	141 ± 51	189 ± 53	193 ± 60	183 ± 56	162 ± 50

Data are means ± SD. *Significant difference in BG across sites at 60 min postmeal ($P = 0.0003$); †significant difference in BG across sites after exercise ($P = 0.037$).

ferences in BG values were found 60 min postmeal and immediately postexercise ($P = 0.0003$ and 0.037, respectively). Specifically, clinically significant differences (expressed as % difference from the fingertip) at 60 min postmeal include −8.8 ± 10.8% at the forearm and −13.7 ± 10.7% at the thigh and at postexercise include +19.1 ± 19.1% at the forearm and +15.6 ± 22.6% at the thigh. However, BG values obtained simultaneously were not significantly different between sites in the fasting state or at the 90- and 120-min postmeal interval. Mean percent differences in BG concentrations at each site relative to the fingertip are shown in Fig. 1*B*.

Success rates of AST performed during the study are shown in Table 2. Puncture attempts were considered successful if they produced enough blood for BG testing. At each testing time, a maximum of three attempts per individual per site were made to obtain an adequate blood sample. Success rates for all sites exceeded 92%; the highest success rates were obtained at the fingertip.

At the 90-min time point, BG values obtained at the forearm with vigorous rubbing of the site (201 ± 58 mg/dl) were not significantly different from values obtained with no site preparation (202 ± 58 mg/dl). The mean (±SD) difference in BG concentration in the rubbed compared with the nonrubbed forearm was −1.5 ± 13 mg/dl (correlation coefficient = 0.975, $P < 0.0001$). In addition, rubbing did not significantly reduce the total number of puncture attempts required to obtain an adequate blood sample for testing (92 attempts after vigorous rubbing and 93 after no rubbing of the site).

Table 2—*AST success rates at each site*

Site	Successful attempts	Total attempts	Percent success*
Fingertip	508	517	98.3%
Palm	424	449	94.4%
Forearm	597	639	93.4%
Thigh	422	455	92.7%

Data are *n* or %. *Percent of total puncture attempts for all subjects ($n = 86$) that produced adequate blood samples across all five BG testing times.

Age, sex, BMI, insulin use, HbA_{1c}, and duration of diabetes were not found to be significant predictors of BG differences between sites. However, the magnitude of change in BG from the start of the meal to the BG test at 60 min postmeal (actual time 62.4 ± 2.5 min, range 55–70) was significantly correlated with fingertip-forearm ($r = 0.71$, $P < 0.0001$) and fingertip-thigh ($r = 0.78$, $P < 0.0001$) differences at the 60-min time point. The greater the change over the 60-min period, the larger the difference in BG between these alternative sites and the fingertip. The 60-min change remained a significant independent predictor of fingertip-forearm and fingertip-thigh differences, even after adjustment for the above covariates as well as for baseline BG.

Questionnaire results indicate that only five (5.8%) patients had tested at any site other than the fingertip before participating in the study. Although self-reported levels of pain were lower for alternative sites as compared with the fingertip, patients indicated that they will perform future BG testing at the fingertip more frequently than at other sites. This is perhaps due to familiarity and comfort with fingertip testing, and lack of previous experience with AST among most patients. However, given the option of testing at alternative sites, nearly half (48%) of patients expressed that they would be likely to test more frequently in the future. Patients' self-reported benefits of AST included protection of fingertips (50%), less pain (33%), and less blood (17%), whereas barriers were noted by patients to cause bruising (24%), lack of privacy (14%), and need for more blood (5%). Patient responses to questions regarding pain and future likelihood of testing at each site are detailed in Table 3.

CONCLUSIONS — The current study was performed to assess for clinically significant differences in SMBG results obtained at alternative sites and the fingertip. The study included testing at the most commonly used and clinically relevant testing times, with comparisons made in the fasting and postmeal state as well as before and after brief exercise. Our study presents evidence that AST, when performed by a skilled operator, provides BG test results similar to fingertip testing in both the fasting state and 2 h after meals. This study also confirms that significant differences in BG test results obtained at alternative sites can be anticipated at both the forearm and thigh during the early postmeal interval and after exercise. Consistent with other reports, the early postprandial increase in BG was significantly blunted when results were obtained from forearm (2–7) and thigh (2) samples, as compared with fingertip samples (Fig. 1*B*).

We found that in addition to the postprandial increase, the postexercise decrease in BG also produced a time lag in forearm and thigh results compared with fingertip BG results. Importantly, our findings suggest that BG values obtained at the palm were comparable to fingertip results under all testing conditions. These findings are consistent with those of Peled et al. (7), who reported that glucose levels at the palm were closely correlated with finger concentrations under all conditions tested. Given the results of our current study, clinicians can support the use of AST both in the fasting state and 2 h post meal. However, testing at sites other than the hand cannot be recommended in the early postmeal period nor can it be routinely advised during brief exercise.

The current study confirms earlier reports demonstrating clinically relevant differences in forearm and fingertip BG values when measured during times of rapid BG changes (2–7). Our study provides new and unique information in that regard, namely that such changes in BG can occur during even brief exercise and that the similarity of AST to fingertip testing during activity (at least at the forearm and thigh) cannot be reliably predicted.

AST testing may be particularly useful

Table 3—*Percentage of patients reporting low pain and high likelihood of future AST*

	Low pain* (n = 86)		Likely to use site† (n = 84)	
Site	Frequency	Percent	Frequency	Percent
Finger	30	35%	79	95%
Palm	39	45%	51	61%
Forearm	42	49%	53	63%
Thigh	38	44%	37	45%

Data are n or %. *Low pain is defined by a self-reported rating of 0 or 1 (scale 0–10); †questionnaire responses of "always," "most often," and "sometimes" qualify as "likely to use" the specified site.

for patients who incorporate frequent SMBG into their diabetes care regimen. Traditionally, such patients would test BG only in the fasting state using fingertip testing. However, postmeal testing can be valuable for optimizing glycemic control (11), particularly for patients who use rapid-acting insulin therapy. In addition, frequent testing traditionally has been encouraged during exercise. The findings of our study support that AST can be reliably used during the most common testing times, before and 2 h after meals. However, AST may be less useful in the early postmeal interval (such as is recommended for many women with gestational diabetes) or with brief exercise. As noted above, and suggested by other authors (2–7), each of these later circumstances is one during which more rapid change in BG may be observed.

Local manipulation of alternative sites has been advised by practitioners both to improve the success of AST and to limit variation in AST results. In our study, standard preparation of the forearm by vigorous rubbing did not significantly alter the measured BG concentration and did not significantly improve the ability to obtain an adequate blood sample. Indeed, success rates at alternative sites exceeded 92% at all times, regardless of site preparation. These current results support the previous findings of Jungheim and Koschinsky (3), who demonstrated that local rubbing of the forearm, while reducing variation in results for some patients, was not a predictably reliable method to decrease observed fingertip-forearm BG differences.

In a previous report, Szuts et al. (12) reported that postprandial BG values obtained simultaneously at the arm and finger did not differ significantly. These authors concluded that differences found with AST in other studies were likely explained by operational error related to the use of less precise devices. The findings of our study suggest that, with adequate training (as with the skilled operator used in this trial) and use of a consistent sampling technique, success with AST was excellent and results were reliably obtained. Our study used trained personnel for all testing to reduce this operational error and minimize individual variation in testing technique. In addition, our study is further strengthened by assessment of BG testing at the most clinically relevant intervals, before and 2 h after meals and with moderate activity. Uniquely, our study of AST assessed the impact of brief exercise on observed BG results. The current study also assessed site preparation, as performed by skilled technicians, on the measured BG results. Finally, this report provides additional and confirmatory evidence that periods of rapid glucose change are a critical determinant of AST reliability.

The current study is limited in that it assessed the impact of brief exercise and did not include additional BG testing for extended intervals postexercise. Postexercise testing at later time points may have provided additional information on site differences during times of continued change in BG observed in some patients. Such information would be of benefit for patients in whom risk of hypoglycemia remains significant during this later postexercise period.

Because BG testing was performed in 30- to 60-min intervals, the precise rate of change in BG could not be calculated in our study. Although BG generally becomes more stable 2 h postmeal than during the immediate postprandial period, as demonstrated in other AST studies (2,7), there are undoubtedly some individuals who experience greater BG changes in the late postmeal time period and rate of BG change would likely vary between individuals. Although our study was not designed to assess rate of BG fluctuations, the magnitude of postprandial BG change was a useful and significant predictor of site differences, and this is consistent with other studies assessing rapid change in BG and reliability of AST (2–7).

In addition, because all BG testing in our study was performed by a trained technician, it is not known whether our findings can be widely generalized to the greater patient population. Further studies using well-trained patient populations will be required to confirm our current results. And because our study included only subjects with type 2 diabetes, the applicability of these findings to patients with type 1 diabetes remains uncertain. However, prior studies of AST including patients with type 1 diabetes (2–7) have reported similar findings, and therefore, we anticipate that our findings are likely to be applicable to all patients with diabetes using frequent SMBG. Furthermore, all SMBG testing in this study was performed using only one BG monitoring device (the One Touch Ultra); however, studies using other devices have demonstrated similar results (3–7). Finally, because the meal component of this study included only a moderate carbohydrate load (40 g), it is not known how our results may have been affected by greater carbohydrate intake. However, our findings were similar to those of a study by Ellison et al. (2) in which patients were offered a meal choice of either 115 g or 143 g carbohydrate content.

In summary, the current study supports the theory that AST provides an equivalent measure of BG concentration at many of the currently used and clinically relevant testing times (in the fasting state before meals and 2 h postmeal). Although differences in AST results were observed 1 h postmeal, this is likely of limited importance except in circumstances in which early postprandial testing is to be used. Among alternative sites tested, the overall pattern of BG changes in the palm most closely paralleled the results obtained with fingertip testing, both after a meal and with exercise. Preparation of the site by vigorous rubbing before testing neither altered the measured BG concentration in the forearm nor significantly affected the success of testing. With appropriate instruction, AST can likely be used by many patients and may be expected to increase the likelihood of

higher testing frequency. If confirmed in larger clinical studies, AST very likely will enhance the willingness of individuals with diabetes to increase testing frequency and can be anticipated to make an important contribution to the intensive diabetes management efforts of many of these patients.

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