Accuracy of a Factory-Calibrated Continuous Glucose Monitor in Individuals With Diabetes on Hemodialysis

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OBJECTIVE

Continuous glucose monitoring (CGM) improves diabetes management, but its reliability in individuals on hemodialysis is poorly understood and potentially affected by interstitial and intravascular volume variations.

RESEARCH DESIGN AND METHODS

We assessed the accuracy of a factory-calibrated CGM by using venous blood glucose measurements (vBGM) during hemodialysis sessions and self-monitoring blood glucose (SMBG) at home.

RESULTS

Twenty participants completed the protocol. The mean absolute relative difference of the CGM was 13.8% and 14.4%, when calculated on SMBG ($n = 684$) and on vBGM ($n = 624$), and 98.7% and 100% of values in the Parkes error grid A/B zones, respectively. Throughout 181 days of CGM monitoring, the median time in range (70–180 mg/dL) was 38.5% (interquartile range 29.3–57.9), with 28.7% (7.8–40.6) of the time >250 mg/dL.

CONCLUSIONS

The overall performance of a factory-calibrated CGM appears reasonably accurate and clinically relevant for use in practice by individuals on hemodialysis and health professionals to improve diabetes management.

The management of diabetes in individuals on hemodialysis is complex due to physiologic changes in glucose and insulin homeostasis as well as limitations in the ability of the patient and clinician to obtain accurate information regarding glucose trends (1). Consequently, glucose levels in these individuals can be labile, with wide variability easily missed by both health care providers and individuals with diabetes relying only on self-monitoring blood glucose (SMBG) or HbA_{1c} (2) for effective glycemic management.

Continuous glucose monitoring (CGM) has been explored in this population (3); however, no studies have specifically assessed the accuracy of a factory-calibrated real-time CGM in the hemodialysis setting, which could potentially be affected by inter- and intraindividual variations in interstitial and intravascular volumes. Furthermore, a study recently reported improvement in glucose control in participants with diabetes on hemodialysis with automated closed-loop insulin delivery (4).

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Such therapeutic possibilities can only be advanced in day-to-day clinical practice with reliable factory-calibrated CGMs. Therefore, we present a prospective pilot study to assess the accuracy of a factory-calibrated CGM in outpatients on hemodialysis.

RESEARCH DESIGN AND METHODS

The study protocol was approved by the University of Virginia Institutional Review Board and registered at ClinicalTrials.gov NCT04094064. After signed informed consent, individuals with diabetes on thrice–weekly outpatient hemodialysis and a hematocrit >30% were recruited from four dialysis centers at the University of Virginia. The 10-day factory-calibrated Dexcom G6-Pro CGM (Dexcom, San Diego, CA) was placed by study staff on the subject's abdomen after completion of dialysis on day 1. Participants were required to obtain four to seven SMBG values per day at home while following usual care.

We assessed Dexcom G6-Pro accuracy comparing time-matched values (only CGM values between 40 mg/dL and 400 mg/dL are used, low and high codes are discarded) to *1*) blood glucose measurements from the venous line (vBGM) during hemodialysis sessions on days 4, 6, and 8 (iSTAT System, Abbott Laboratories, Chicago, IL) and *2*) SMBG values at home (ContourNext Glucometer, Ascencia Diabetes Care, Basel, Switzerland) (Supplemental Material). We determined the mean absolute relative difference (MARD). We analyzed the reliability with the Parkes error grid (PEG) (5) and surveillance error grid (SEG) (6). Glycemic outcomes and glucose management indicator (GMI) (7) were computed on CGM records.

The statistical analysis was done with MATLAB R2021a (MathWorks, Natick, MA) and GraphPad Prism 9.3.0 software (GraphPad Software, San Diego, CA).

Data and Resource Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

RESULTS

Participants

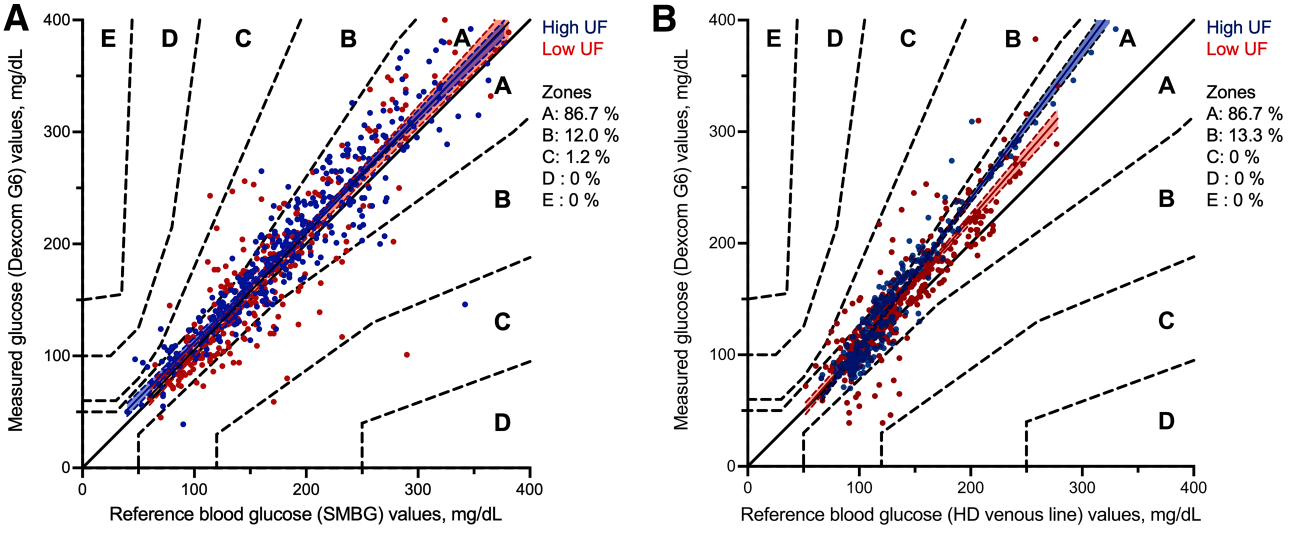
Between February 2020 and September 2021, 20 participants completed the protocol: 4 with type 1 diabetes, 15 with type 2 diabetes, and 1 with posttransplantation diabetes. They were predominantly male (70%), African American (55%), and insulin treated (85%). The mean ± SD age was 61.2 ± 11.6 years, and BMI was 31.5 ± 4.2 kg/m^2. Each participant completed three hemodialysis sessions with a mean duration of 3.9 ± 0.3 h per session and ultrafiltrate (UF) volume of 2.8 ± 0.6 L, and 12 participants were considered as having high UF (>2.5 L) volume.

Over the 10 days, the number of SMBG values collected was lower than expected, with a median (interquartile range [IQR]) of 37.5 (16–66) SMBG measurements per subject. In total, >181 days of glucose monitoring (median of 9.8 days per person) were collected, with 99.6% (90.1–100) time of active CGM. No adverse events related to wearing the CGM were reported. Three devices stopped working between 5 and 7 days.

Accuracy Assessment

The overall MARD was 13.8% (IQR 4.9–18.2) for CGM- to SMBG-matched pairs (n = 684) and 14.3% (IQR 5.0–19.7) for CGM- to vBGM-matched pairs (n = 624) during hemodialysis sessions. Not enough reference glucose measurements were collected in the hypoglycemic range to report accuracy metrics.

From PEG analysis (Fig. 1), Dexcom G6-Pro values showed clinical reliability, with 86.7% of all SMBG pairs and all vBGM pairs in zone A (clinically accurate



Glucose range	Matched pairs, n	MARD, %
Overall	684	13.8
< 70 mg/dL	13	NA
70-180 mg/dL	363	15.0
> 180 mg/dL	248	12.7

Glucose range	Matched pairs, n	MARD, %
Overall	624	14.3
< 70 mg/dL	6	NA
70-180 mg/dL	532	14.1
> 180 mg/dL	86	15.3

Figure 1—PEG analysis comparing reference blood glucose measurement with SMBG (*A*) (n = 684) and hemodialysis (HD) venous line (*B*) (n = 624). Blue points are matched pairs from participants with high UF volume (UF > 2.5 L), and red points are from participants with low UF volume, with the 95% CI simple linear regression lines, respectively. The tables below report the MARD for each matched pair regarding glucose range. NA, nonapplicable.

measurements) and with 98.7% and 100%, respectively, in zones A/B (clinically accurate or no risk from error). SEG analysis showed 96.6% of SMBG pairs and 96.3% of vBGM pairs in the green risk zone (no or very low risk for hypo- or hyperglycemia as measurement errors). Measured glucose values with the Dexcom G6-Pro were overestimated in 70% and 74% compared with SMBG and vBGM, respectively, as shown by linear regression curves (Fig. 1); but, this degree of hypoglycemia risk remained slightly lower according to SEG analysis. In exploratory analysis, we showed a correlation significantly different between Dexcom G6-Pro and vBGM values between subjects with high versus low UF volume (ANCOVA $P < 0.001$) (Fig. 1*B*), highlighting a potential impact of fluid overload in the interstitial tissue volume on the CGM's accuracy during hemodialysis sessions.

Glycemic Outcomes From CGM

Throughout 181 cumulative days of glucose monitoring with blinded Dexcom G6-Pro, the median time in range (70–180 mg/dL) was 38.5% (IQR 29.3–57.9), with 28.7% (7.8–40.6) of the time >250 mg/dL and 0.1% (0–1.7) of time <70 mg/dL. The mean coefficient of variation was 34 ± 9.7%. HbA_{1c}, known to be inaccurate in this population, was correlated with the GMI (correlation coefficient 0.701, $P = 0.0006$) but significantly lower: GMI 8.2 ± 1.0% versus HbA_{1c} 7.7 ± 1.3% ($P = 0.02$).

CONCLUSIONS

To our knowledge, this is the first study to assess the performance of a factory-calibrated CGM in outpatients on intermittent hemodialysis. We provide data on the accuracy of the Dexcom G6-Pro CGM compared with SMBG and venous blood samples, including during hemodialysis sessions, a time particularly challenged by rapid perturbations to glucose and its volume of distribution.

A strength of our study is to provide clinicians with practical data comparing CGM to SMBG, currently the standard of care. Our study also confirms HbA_{1c} is inaccurate in this population (1). The distribution of CGM data in our study reveals the poor glycemic control of the hemodialysis population (8). Presently, all CGM devices approved by the U.S. Food and Drug Administration for individuals on hemodialysis require daily calibrations (3). In our study, most participants did not obtain the recommended number of SMBG values per day, underscoring the difficulty clinicians and patients have in using SMBG for glycemic management. Our PEG and SEG analyses found this factory-calibrated CGM device to be reliable, supporting use of a factory-calibrated CGM for clinical assessment of glycemic control compared with HbA_{1c} and to improve patient acceptance compared with multiday SMBG measurements.

We acknowledge that the factory-calibrated CGM tendency to overestimate glucose readings needs further confirmation, as this population is at high hypoglycemia risk (2). Moreover vBGM and SMBG used as reference and by others (9,10) could be impacted by anemia and erroneously underestimate the glucose values compared with plasma samples. Although we did include venous blood samples, we did not use a sufficiently accurate reference measurement system to fulfill standards and regulatory requirements to assess CGM accuracy (8). We also acknowledge the lack of a control group (persons not on hemodialysis) to quantify the impact of hemodialysis on CGM accuracy. In addition, <2% of our data pairs fell <70 mg/dL, limiting our ability to assess accuracy in this glucose range. Finally, although the PEG and SEG methods are commonly used to assess CGM reliability, it is unknown whether these methods translate to this specific population.

In conclusion, we highlight the accuracy and clinical relevance of a factory-calibrated CGM (Dexcom G6-Pro) in outpatients on hemodialysis. Our data open the door to further development and practical use by patients and health care professionals, after regulatory approvals, to achieve better glycemic assessment and control. Further, it is an essential step toward expanded use of diabetes technology for individuals with diabetes and end-stage renal disease on dialysis.

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Author Contributions. O.V. performed the statistical analysis. O.V., M.R.F., H.E.M., R.K.M., and M.M.S. conducted the study. O.V. and Z.S.L. processed the data. O.V. and M.M.S. wrote the first draft of the manuscript. M.D.B., S.R., M.K.V., and A.B. contributed to the study conceptualization and realization. C.A.W. performed project management. M.C.-O. assisted with the development of the protocol and coordinated the regulatory submission. All authors interpreted the data and reviewed and approved the final version of the manuscript. M.M.S. designed, wrote the study protocol, and supervised the study. M.M.S. and O.V. are guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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