Glucose Management Indicator Based on Sensor Data and Laboratory HbA_{1c} in People With Type 1 Diabetes From the DPV Database: Differences by Sensor Type

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The glucose management indicator (GMI) estimates HbA_{1c} from continuous glucose monitoring (CGM) profiles. The formula was developed with real-time CGM (rtCGM) sensors (1). As previous data indicated discrepancies between observed laboratory HbA_{1c} and CGM-derived estimates of HbA_{1c} for some individuals and sensor types (1,2), we aimed to compare observed HbA_{1c} and GMI using both rtCGM and intermittent scanning CGM (iscCGM) profiles collected during routine care in people with type 1 diabetes.

We analyzed 132,361 CGM days from a total of 1,973 individuals with type 1 diabetes for ≥1 year from the German/Austrian/Swiss/Luxembourgian Prospective Diabetes Follow-up Registry (DPV) (3). As measurement ranges of the CGM devices differed, we truncated glucose values to the same range (40–400 mg/dL). We calculated the GMI from up to 90 CGM days per individual (median [interquartile range] 77 [46–89] days per individual) as GMI (%) = 3.31 + 0.02392 · [mean glucose (mg/dL)] (1). We compared GMI and observed HbA_{1c} at the end of the 90-day period overall and by age-group. Absolute differences between GMI and observed HbA_{1c} were illustrated for rtCGM vs. iscCGM and stratified by glucose variability, normal weight vs. overweight, and HbA_{1c} <7.5% vs. ≥7.5% using boxplots. Low/high glucose variability was defined as coefficient of variation (CV = SD divided by the mean) <36/≥36%. Overweight was defined based on German Health Interview and Examination Survey for Children and Adolescents (KiGGs) reference as >90th percentile for individuals aged <18 years and as BMI >25 kg/m^2 for adults.

Median age and duration of type 1 diabetes were 14 [10, 17] and 5 [3, 9] years, respectively; 52% (n = 1,031) were boys/men, and 68% (n = 1,329) were pump users. Mean (± SD) GMI estimated from CGM data were slightly higher than mean observed HbA_{1c} in the overall cohort (7.8 ± 0.9% vs. 7.6 ± 1.2%) and within each age-group (<6 years: 7.5 ± 0.7% vs. 7.2 ± 1.0%, 6 to <12 years: 7.7 ± 0.7% vs. 7.3 ± 0.9%, 12 to <18 years: 8.0 ± 0.9% vs. 7.8 ± 1.3%, ≥18 years: 7.7 ± 1.0% vs. 7.6 ± 1.3%). Overall, 11% (n = 224) had an absolute difference between GMI and observed HbA_{1c} of less than ± 0.1%, and 46% (n = 910) had an absolute difference of at least ± 0.5%.

Stratification by sensor type revealed that mean GMI and HbA_{1c} were similar in rtCGM users (n = 341 CareLink Pro/Personal, n = 64 Dexcom G5; 7.6 ± 0.7% vs. 7.6 ± 1.1%), whereas iscCGM users (n = 1,568 FreeStyle Libre) had higher mean GMI than HbA_{1c} (7.9 ± 0.9% vs. 7.6 ± 1.2%). Similar patterns were observed after stratification by glucose variability or weight (Fig. 1): while absolute differences between GMI and laboratory HbA_{1c} were almost symmetrically distributed around 0 in rtCGM users, GMI was higher than the laboratory HbA_{1c} value in almost three-fourths of iscCGM users. This finding was still observed after additional stratification by age-group (data not shown). Stratification by HbA_{1c} level revealed higher GMI than HbA_{1c} in most individuals with HbA_{1c} <7.5%, with GMI-HbA_{1c} differences being higher in iscCGM users. In contrast, three-fourths of all rtCGM users with HbA_{1c} ≥7.5% had lower GMI than HbA_{1c}, whereas differences in iscCGM users with HbA_{1c} ≥7.5% were almost symmetrically distributed around 0 (Fig. 1).

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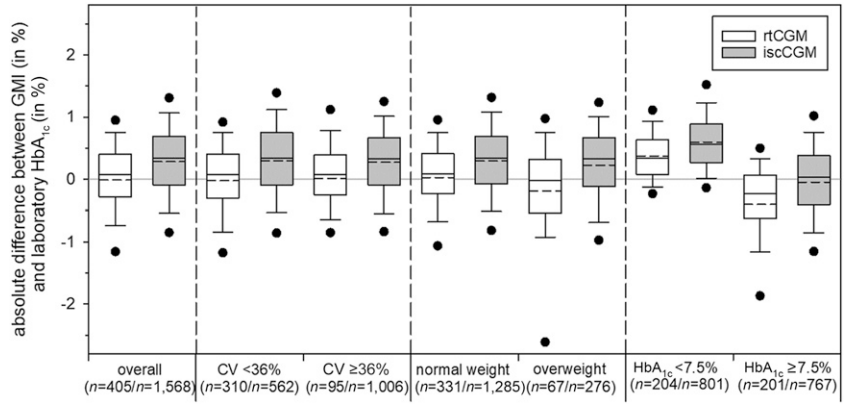

Figure 1—Difference between CGM-derived estimated HbA_{1c} and observed laboratory HbA_{1c}. Difference between laboratory HbA_{1c} and GMI by sensor type, stratified by age-group, glucose variability, and HbA_{1c} (based on truncated sensor values). Boxes represent the interquartile range (IQR = Q3 − Q1), whiskers represent the 1.5-fold IQR, and dots represent 5th and 95th percentiles. Solid and dashed lines within boxes indicate median and mean, respectively.

In conclusion, our analysis of glucose profiles collected during routine care from people with type 1 diabetes revealed discrepancies between CGM-derived GMI and laboratory HbA_{1c} in a considerable subset of individuals. This finding is in line with results from Leelarathna et al., who analyzed data from three different rtCGM sensors. They found an absolute difference between GMI and laboratory HbA_{1c} of $\geq$0.5% in one-third of all participants but found that only 20% of all participants had differences of $<$0.1%. It has been suggested that the difference between laboratory HbA_{1c} and CGM-derived GMI is clinically meaningful and should be considered when therapeutic goals are set (1).

Our analysis, however, found that discrepancies between GMI and HbA_{1c} differed between iscCGM and rtCGM. Measurement ranges as well as distribution of sensor glucose values differed by sensor type. CGM systems typically have a higher accuracy in the euglycemic range, whereas accuracy often decreases in the hypoglycemic and/or hyperglycemic range (4). Moreover, different modes of calibration lead to different sensitivities and specificities in the detection of biochemical hypoglycemia (5). This indicates that it is necessary to adjust the GMI formula for sensor type.

As both measures, CGM-derived GMI and laboratory HbA_{1c}, may affect therapeutic goals and diabetes management, further research is needed to examine potential explanatory factors, for example, duration of CGM usage, indication for usage, sensor type/version, ethnicity, subcutaneous adipose tissue, glucose variability, life span of red blood cells, or hemoglobinopathies that may affect glycosylation. Formulas specific for sensor type that account for the respective measurement range and type of calibration may be needed to accurately estimate GMI.

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