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Validation of Fructosamine-to-HbA1c Conversion Formulas Using Continuous Glucose Monitoring in Surgical Patients

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Abstract

Purpose: To compare the performance of four published fructosamine-to-HbA1c conversion formulas against continuous glucose monitoring (CGM) data in patients undergoing preoperative diabetes optimization.

Methods: This retrospective, cross-sectional study included 30 patients enrolled in a preoperative diabetes optimization program who had both fructosamine values and at least 14 days of overlapping CGM data. Four previously published conversion formulas (Cohen, Wright-Hirsch, Kang, and Young) were evaluated. Pearson correlation analysis examined relationships between fructosamine-derived estimated HbA1c values and CGM-derived glucose management indicator (GMI).

Results: Mean fructosamine was 331.2 ± 70.6 μmol/L, mean CGM glucose was 165.8 ± 34.4 mg/dL, and mean GMI was 7.28% ± 0.82%. Fructosamine demonstrated significant positive correlation with average CGM glucose ($r=0.39$, $p=0.04$). All four conversion formulas showed similar, statistically significant correlations with GMI ($r\approx0.39$, $p\approx0.03$).

Conclusions: All four fructosamine conversion formulas demonstrated comparable performance when validated against CGM data in the preoperative setting. These findings support the clinical utility of fructosamine for short-term glycemic assessment when HbA1c may be unreliable or when recent glycemic changes are clinically relevant, in absence of or when unable to use CGM.

Keywords: fructosamine, continuous glucose monitoring, perioperative glycemic control, HbA1c, diabetes optimization

Introduction:

Hyperglycemia is a prevalent metabolic disturbance in patients undergoing surgery that significantly impacts perioperative outcomes. In patients with and without diabetes, hyperglycemia has been consistently linked to increased morbidity and mortality, with poor glycemic control before, during, and after surgery contributing to higher rates of postoperative complications. Given this, there is a critical need for reliable, standardized measures to assess glycemic control, not only over the long term but also to capture short-term fluctuations that may influence surgical risk [1, 2]. The establishment of such standardized assessments can enhance patient management and improve the quality of care.

Glycosylated hemoglobin, also known as hemoglobin A1c (HbA1c), has conventionally been used to assess glycemic control, and the American Diabetes Association (ADA) recommends aiming for a preoperative HbA1c goal <8% (<64 mmol/mol) within 3 months of surgery, with individualized risk-to-benefit ratio assessment [3]. However, there are instances when HbA1c is unreliable, including hemoglobinopathies, altered erythrocyte turnover, or when evaluating more recent changes in blood glucose levels [4]. Given these limitations, alternative measures such as fructosamine have emerged [5, 6].

Fructosamine is a non-enzymatic, glycated serum protein assay that reflects glycemic control over the past 2–4 weeks due to albumin turnover and has been recognized by the ADA as an alternative to HbA1c [5, 6]. In addition to its ability to better reflect short-term glucose levels, fructosamine is highly correlated with HbA1c values. Similarly, while fructosamine reflects the glycation of multiple circulating serum proteins, glycated albumin is another marker that measures the glycation of albumin specifically and can theoretically provide more specific

information on short-term glucose changes. However, fructosamine is more widely available and is a well-validated assay, making it more practical for large cohort analyses [7].

Specifically in surgical populations, fructosamine has consistently demonstrated comparable to superior predictive value for adverse surgical outcomes compared to HbA1c, which in some studies failed to show any significant correlation at all [8, 9]. With the rise of individualized diabetes management and continuous glucose monitoring (CGM), there has been increasing support for the use of both CGM and fructosamine in perioperative glycemic evaluation and risk stratification [6, 10]. Unfortunately, many barriers to CGM adoption exist. Cost, insurance restrictions, short treatment windows, patient willingness to wear a CGM device, and other device-related challenges may limit patient use of CGM in the preoperative setting, further underscoring the value of fructosamine as an accessible, low-burden alternative to aid perioperative glycemic assessment [11, 12].

There are several formulas available to estimate average glucose from fructosamine values; however, no standardized method exists for converting fructosamine to an estimated average glucose level or to HbA1c. Additionally, existing formulas are derived from different study populations, statistical approaches, and clinical contexts. Thus, these conversion equations can produce meaningfully different glucose and HbA1c estimates from the same fructosamine value, limiting their interchangeability and practical interpretation [13-16].

As previously reported by our team, our institution's preoperative diabetes optimization program (PreDOP) has demonstrated improved perioperative glycemic management using intensified preoperative glucose control strategies, including the use of fructosamine, and more recently, CGM data for assessment of short-term glycemic control and readiness for surgery [4]. The present study was therefore designed to compare the correlation between fructosamine

values and CGM data to determine which of the available conversion formulas may be best suited for use in the preoperative setting.

Methods:

This retrospective, cross-sectional study was conducted as part of a previously approved quality improvement project for which institutional review board waiver had been obtained. Patients enrolled in our institution's Preoperative Diabetes Optimization Program (PreDOP) who were started on continuous glucose monitoring (CGM) and had a fructosamine value obtained prior to surgery were eligible for inclusion. Manual chart review was conducted for eligible patients to ensure fructosamine and CGM data had at least 14 days of overlap. Demographics, fructosamine values, and CGM data from the ambulatory glucose profile (AGP) were extracted from the electronic medical record. Corresponding albumin levels were extracted when available within the appropriate timeline.

Four previously published formulas relating fructosamine to estimated HbA1c or mean glucose were selected for comparison [13-16]:

1. Cohen formula: Based on the glycation gap concept, this formula calculates predicted HbA1c from fructosamine using the population regression equation:

HbA1c (%) = 0.017 X fructosamine level (μmol/L) + 1.61

2. Wright-Hirsch conversion table: This approach provides a reference framework linking fructosamine values to corresponding estimates mean glucose and HbA1c values based on published conversion tables.

3. Kang formula: Derived from a pediatric population with diabetes, this formula relates fructosamine to HbA1c using linear regression:

HbA1c (%) = (45.84 + fructosamine)/ 48.55

4. Young formula: Developed in a veteran population, this formula converts fructosamine to HbA1c using the regression equation:

HbA1c = 0.0154*Fructosamine (mmol/L) + 3.121

Summary statistics were reported using mean and standard deviation for all laboratory values and estimated HbA1c values derived from the four formulas. Dot plot figures were created with best-fit linear regression lines to visualize relationships between fructosamine and average CGM glucose, as well as between each formula's estimated HbA1c and the glucose management indicator (GMI) derived from CGM. Relationships between albumin and fructosamine and between albumin and average CGM glucose were also explored. Pearson's correlation matrix was used to examine correlations between all laboratory variables and HbA1c formulas. A p-value less than 0.05 was considered statistically significant. All data were processed and analyzed using R version 4.0.3.

Results:

A total of 30 patients with both CGM data and fructosamine values were included in the analysis. **Table 1** summarizes the descriptive characteristics of the study population. The mean fructosamine level was 331.2 ± 70.6 μmol/L (reference range: ~200–285 μmol/L), mean CGM glucose was 165.8 ± 34.4 mg/dL (typical target range ~70–180 mg/dL), and mean albumin was 4.16 ± 0.44 g/dL (reference range: ~3.5–5.0 g/dL). **Table 2** shows the CGM-derived glycemic profile of the cohort, reported according to the international consensus on CGM for clinical trials [17]. Mean GMI (7.24 ± 0.81%) and mean time in range (TIR; 66.5 ± 23.7%) both met the ADA Standards of Care in Diabetes 2026 preoperative benchmarks of a 14-day CGM GMI <8% and/or

TIR >50%. Mean estimated HbA1c was similar across the four formulas, averaging approximately 7.87 ± 1.41%.

Figure 1 shows a significant positive correlation between fructosamine and average blood glucose measured by CGM (r= 0.39, p = 0.04). **Figures 2–5** illustrate the relationships between the CGM-derived glucose management indicator (GMI) and estimated HbA1c values calculated using the four previously published fructosamine conversion formulas. Pearson correlation analysis demonstrated moderate, statistically significant correlations between the CGM-derived GMI and estimated HbA1c across all four formulas ($r \approx 0.39$, $p \approx 0.03$). Among the evaluated models, the Wright-Hirsch conversion table demonstrated the strongest correlation with GMI **(Figure 3),** although the differences between the formulas were marginal, and the overall performance was comparable across the models. Scatterplot analysis (**Figures 2–5)** demonstrated consistent positive associations between fructosamine-derived HbA1c estimates and CGM-derived measures of glycemia.

Discussion:

In this retrospective, cross-sectional study of 30 patients enrolled in a preoperative diabetes optimization program with paired CGM and fructosamine data, all four previously described fructosamine conversion formulas demonstrated significant positive correlations with CGM-derived glucose measures, with no meaningful differences in overall performance. The Wright-Hirsch conversion table showed marginally stronger performance, although differences were modest. These findings suggest that multiple validated approaches may be acceptable for translating fructosamine values into clinically useful glycemic estimates in the preoperative setting.

Fructosamine has been validated as a reliable marker of glycemic control with strong correlation to HbA1c in both clinical and epidemiologic studies. In the AMORIS study, fructosamine demonstrated moderate to strong correlation with HbA1c ($r = 0.67–0.75$), excellent discrimination for diabetes with specificities of approximately 97%, and area under the curve (AUC) values ranging from 0.91 to 0.95 [7]. Unlike HbA1c, which reflects average glycemia over 2–3 months, fructosamine reflects glycemic exposure over approximately 2–3 weeks, allowing it to capture more recent changes in glucose control. This shorter assessment window is particularly advantageous in the preoperative setting, where timely assessment of glycemic trends is clinically relevant and may better align with the timelines of preoperative optimization programs [10, 18]. Reassessment using HbA1c often requires waiting months for meaningful changes to be reflected, which can delay surgical scheduling while patients attempt to improve glycemic control [4]. While CGM has emerged as a promising tool for perioperative glycemic evaluation, substantial barriers limit its widespread use. Cost and insurance coverage are the most frequently cited obstacles, with prior authorization requirements and restrictive eligibility criteria disproportionately affecting publicly insured, low-income, and racial and ethnic minority populations [11, 19]. Patient-level factors, including sensor discomfort, skin integrity concerns, low digital literacy, and reluctance to wear the devices, further affects its use [12]. Additionally, CGM devices are not FDA-approved for inpatient or perioperative use due to concerns about sensor accuracy during surgery, where hypothermia, hemodynamic instability, and electrocautery interference can compromise readings [20]. In contrast, fructosamine requires only a single blood draw, reflects glycemic control without dependence on patient adherence to wearable technology, and can be obtained alongside routine preoperative laboratory testing at minimal additional cost [21, 22].

Recent studies further support the clinical utility of fructosamine in perioperative risk stratification. Elevated preoperative fructosamine levels have been associated with increased risk of postoperative complications in patients undergoing foot and ankle surgery [9]. Ngaage et al. demonstrated that fructosamine may better predict surgical outcomes than HbA1c [23]. In orthopedic populations, particularly joint arthroplasty, elevated fructosamine correlates with adverse outcomes including deep infection, readmission, and reoperation. Notably, Shohat et al. showed significant associations between fructosamine and adverse outcomes while HbA1c failed to demonstrate such associations, suggesting that fructosamine may be a more sensitive marker of perioperative glycemic risk in surgical populations [8, 21].

Despite growing interest in fructosamine, no consensus exists regarding which conversion formula should be used in clinical practice. Cohen et al. first described a linear relationship between fructosamine and HbA1c and introduced the concept of a "glycation gap," which refers to discordance between the two glycemic biomarkers [13]. Wright and Hirsch subsequently presented a conversion framework linking fructosamine, estimated mean glucose, and HbA1c values [14]. Kang et al. developed a formula for children and adolescents with diabetes, while Young et al. proposed a conversion approach tailored to a U.S. veteran population [15, 16]. Each formula was derived using different study populations, analytic methods, and clinical contexts, which may limit generalizability. Applying different formulas to the same fructosamine value could yield meaningfully different estimates of average glucose or HbA1c, complicating clinical interpretation. Previous literature has largely focused on validating individual formulas rather than directly comparing their performance within the same patient population, contributing to uncertainty regarding the translation of fructosamine values into clinically actionable glycemic metrics [13-16].

This study has several notable strengths. First, four conversion formulas were directly compared within the same patient population using CGM, rather than HbA1c, as the reference standard. Second, albumin levels were included as a potential confounder in the studied correlations. Third, and to our knowledge, this is the first study to compare multiple fructosamine conversion formulas in the preoperative setting, where the use of fructosamine has been increasing, addressing a significant gap in the literature. However, several limitations should be acknowledged. The relatively small sample size (n=30) and single-institution design may limit generalizability. Fructosamine levels may be falsely low in conditions associated with increased albumin turnover. While albumin measurements were reviewed and included in patient characteristics (Table 1), albumin data were only available within the appropriate timeframe for a subset of patients (n=24), limiting evaluation of the potential impact of altered albumin turnover.

These results support the potential for broader clinical use of fructosamine, particularly in perioperative settings where HbA1c may not reflect recent glycemic control or in populations where HbA1c is less reliable, such as those with anemia or chronic kidney disease, or when CGM data are unavailable due to the access and adherence barriers described above. Identifying a reliable conversion approach may improve the clinical utility of fructosamine and support its broader use in perioperative optimization programs. Future studies should focus on validating these findings in larger, multicenter cohorts and integrating fructosamine-based conversions into clinical workflows to determine whether routine use improves perioperative outcomes and surgical decision-making.

Conclusion:

In conclusion, the positive correlation observed with CGM-derived mean blood glucose confirms the effectiveness of fructosamine as a short-term glycemic marker in the preoperative

setting as a useful tool to help optimize preoperative glycemic control and improve perioperative outcomes. By reflecting glycemic patterns over a 2–3-week span, fructosamine provides timely insights into recent glycemic control changes. At least four formulas are available to estimate average glucose from fructosamine values, none of which is universally preferred. This study showed that all four formulas produced similar and significant outcomes which underscores the potential of fructosamine to fill critical gaps in preoperative glycemic assessment and management by comparing the effectiveness of different fructosamine conversion formulas to HbA1c, thereby advocating for its broader clinical application. Future prospective studies with larger populations may be needed to identify conversion strategies with higher accuracy and performance and to further demonstrate its utility in improving patient outcomes.

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Table 1: Baseline Characteristics of Study Population

	Mean ± SD
Age	61.24 ± 10.33 (n = 25)
Sex	
Male	16 (64.00%)
Female	9 (36.00%)
Race	
Non-Hispanic White	13 (52.00%)
Non-Hispanic Black	10 40.00%)
Other	2 (8.00%)
Fructosamine	331.17 ± 70.60 (n = 30)
Average Glucose CGM	165.80 ± 34.35 (n = 30)
GMI	7.28% ± 0.82% (n = 30)
Albumin	4.16 ± 0.44 (n = 24)
Cohen formula [11]: HbA1c = 0.017 X fructosamine level (μmol/L) + 1.61	7.24% ± 1.20% (n = 30)
Wright/Hirsch conversion table [12]: HbA1c from conversion table, based on fructosamine value	8.26% ± 1.89% (n = 30)
Kang formula [13]: HbA1c = (45.84 + fructosamine)/ 48.55	7.77% ± 1.45% (n = 30)
Young formula [14]: HbA1c = 0.0154*Fructosamine (mmol/L) + 3.121	8.22% + 1.09% (n = 30)

Table 1. Descriptive statistics for patients with concurrent continuous glucose monitoring (CGM) data and fructosamine measurements. Values are presented as mean ± standard deviation. Hemoglobin A1c (HbA1c) estimates were calculated using four previously published conversion formulas: (1) Cohen formula—population regression equation based on the glycation gap concept; (2) Wright-Hirsch conversion table—reference framework linking fructosamine to mean glucose and HbA1c; (3) Kang formula—linear regression derived from a pediatric diabetes population; and (4) Young formula—regression equation developed in a veteran population. Glucose management indicator (GMI) represents the estimated HbA1c based on mean CGM glucose. Reference ranges: fructosamine 200–285 μmol/L, target CGM glucose 70–180 mg/dL, albumin 3.5–5.0 g/dL.

Table 2. CGM-derived Glycemic Profile of Study Population

% Active Sensor Time	92.0 ± 12.9%
Number of Days with Data	13.0 ± 1.53 days
Mean Glucose	164 ± 33.9 mg/dL
Glucose Management Indicator (GMI)	7.24 ± 0.81%
Time Very Below Range (<54 mg/dL)	0.10 ± 0.31%
Time Below Range (TBR) (54-69 mg/dL)	0.77 ± 1.57%
Time in Range (TIR) (70-180 mg/dL)	66.5 ± 23.7%
Time Above Range (TAR) (181-249 mg/dL)	23.6 ± 13.4%
Time Very Above Range (>250 mg/dL)	8.67 ± 14.1%
% Coefficient of Variation	27.3 ± 5.75%

Table 2. CGM-derived glycemic profile of the study population. Values are presented as mean ± standard deviation. CGM metrics, including time very below range (blood glucose <54 mg/dL), time below range (blood glucose 54-69 mg/dL), time in range (blood glucose 70-180 mg/dL), time above range (blood glucose 181-249 mg/dL), time very above range (blood glucose >250 mg/dL), and coefficient of variation are reported above. Percentage of active sensor time and number of days with valid CGM data included to document near-target sampling adequacy of CGM (target ≥14 days with ≥70% wear time).

Figure 1: Correlation Between Fructosamine and Mean Continuous Glucose Monitoring Values

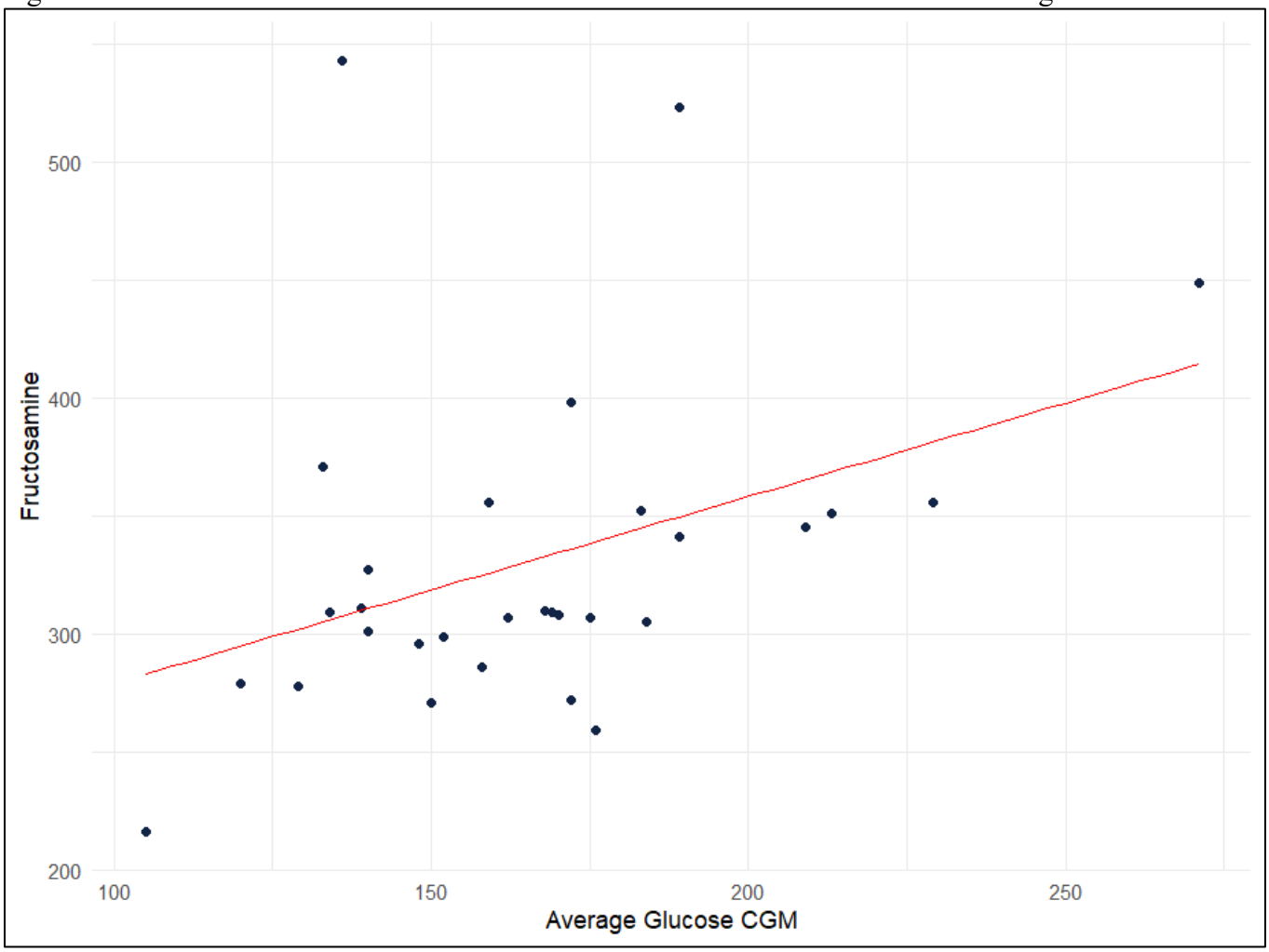


Figure 1. Scatter plot with linear regression line showing the relationship between fructosamine levels (µmol/L) and mean glucose measured by continuous glucose monitoring (CGM, mg/dL). Pearson's correlation coefficient demonstrates a statistically significant positive correlation ($r = 0.39$, $p = 0.04$, $n = 30$).

Figure 2: Correlation Between CGM-Derived and Cohen Formula-Estimated HbA1c

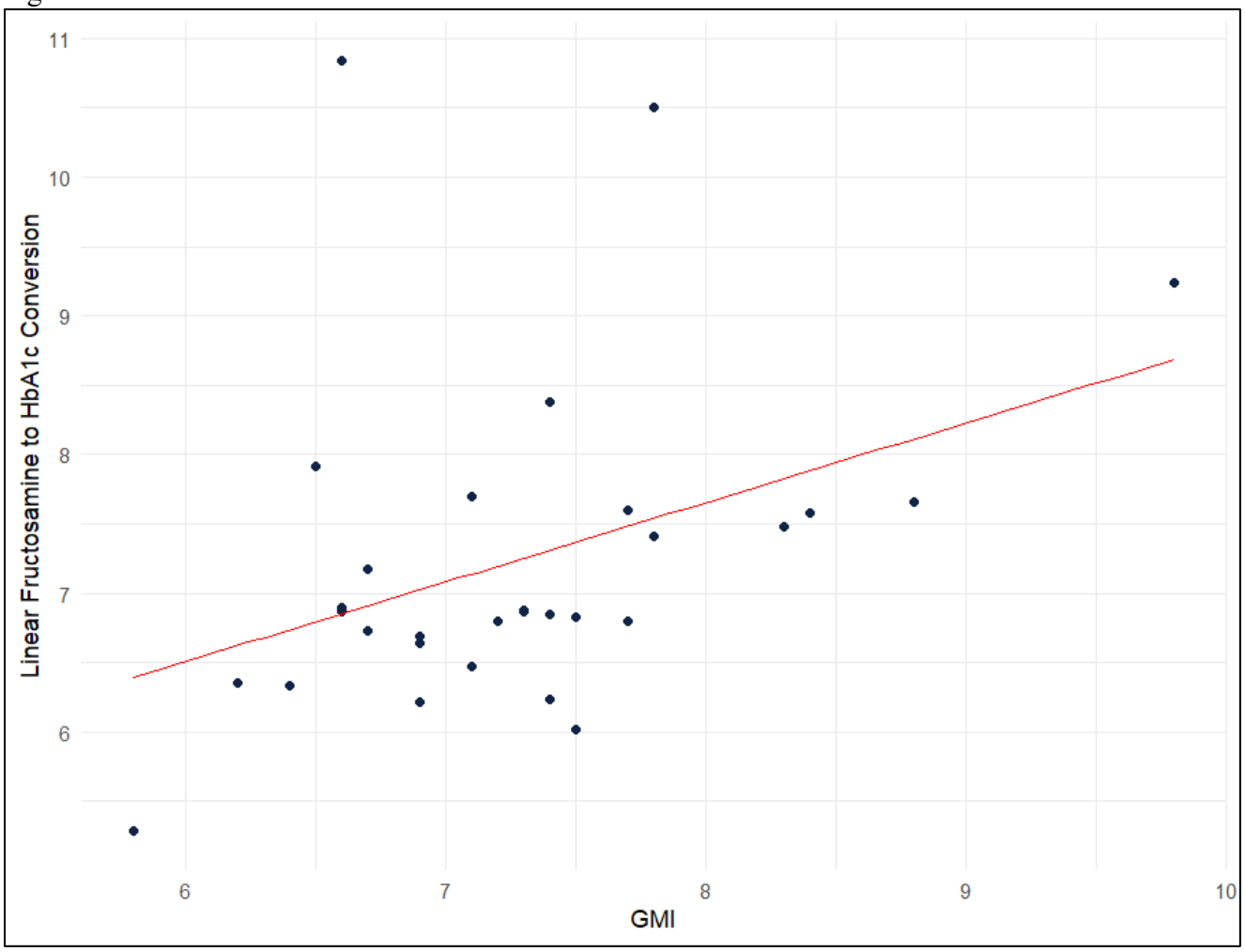


Figure 2. Scatter plot with linear regression line comparing glucose management indicator (GMI, estimated HbA1c derived from continuous glucose monitoring data) to HbA1c estimated using the Cohen formula [HbA1c (%) = 0.017 × fructosamine (µmol/L) + 1.61]. Pearson's correlation coefficient demonstrates a statistically significant positive correlation ($r = 0.39$, $p = 0.03$, $n = 30$).

Figure 3: Correlation Between CGM-Derived and Wright-Hirsch Conversion Table-Estimated HbA1c

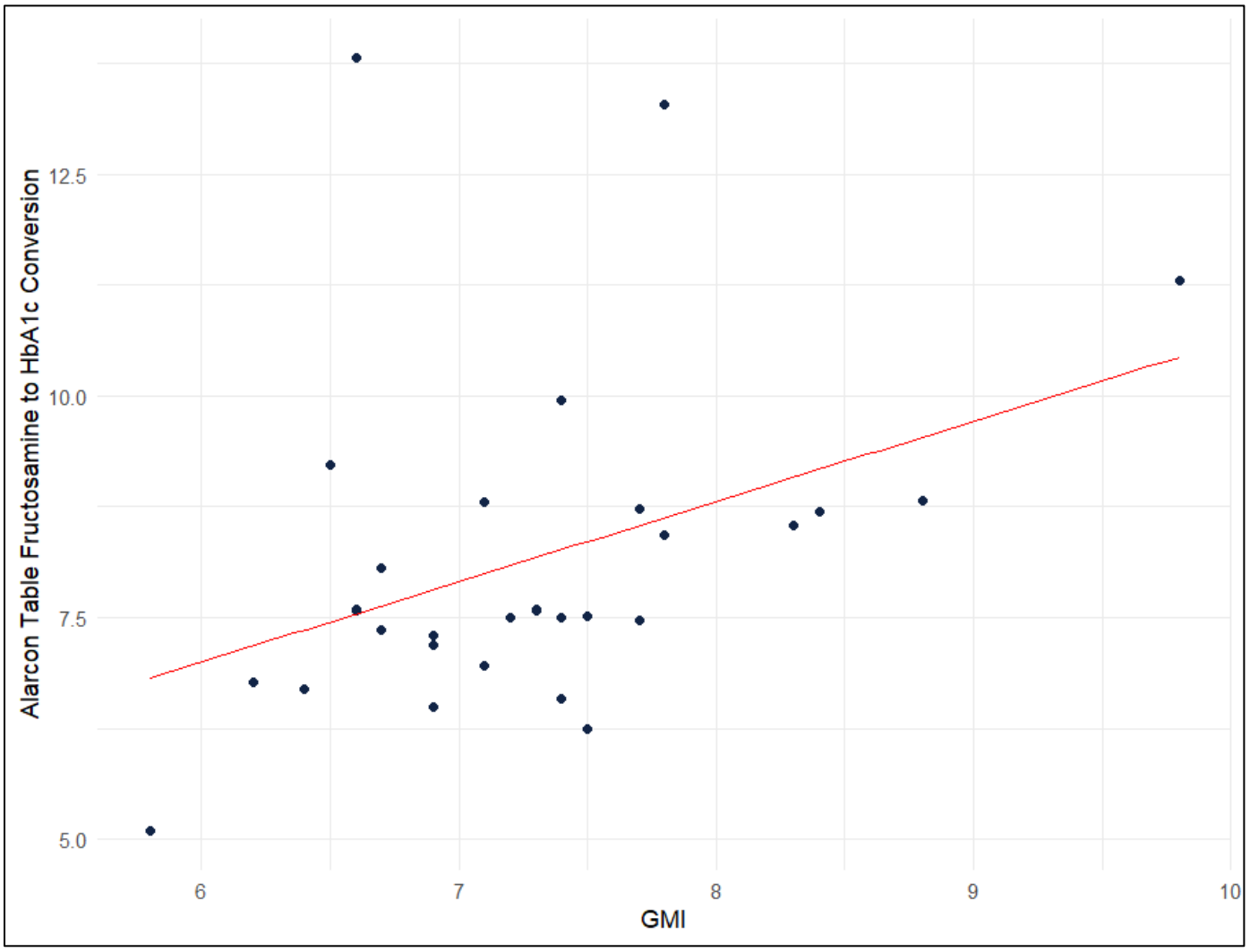


Figure 3. Scatter plot with linear regression line comparing glucose management indicator (GMI, estimated HbA1c derived from continuous glucose monitoring data) to HbA1c estimated using the Wright-Hirsch conversion table. Pearson's correlation coefficient demonstrates a statistically significant positive correlation ($r = 0.39$, $p = 0.03$, $n = 30$).

Figure 4: Correlation Between CGM-Derived and Kang Formula-Estimated HbA1c

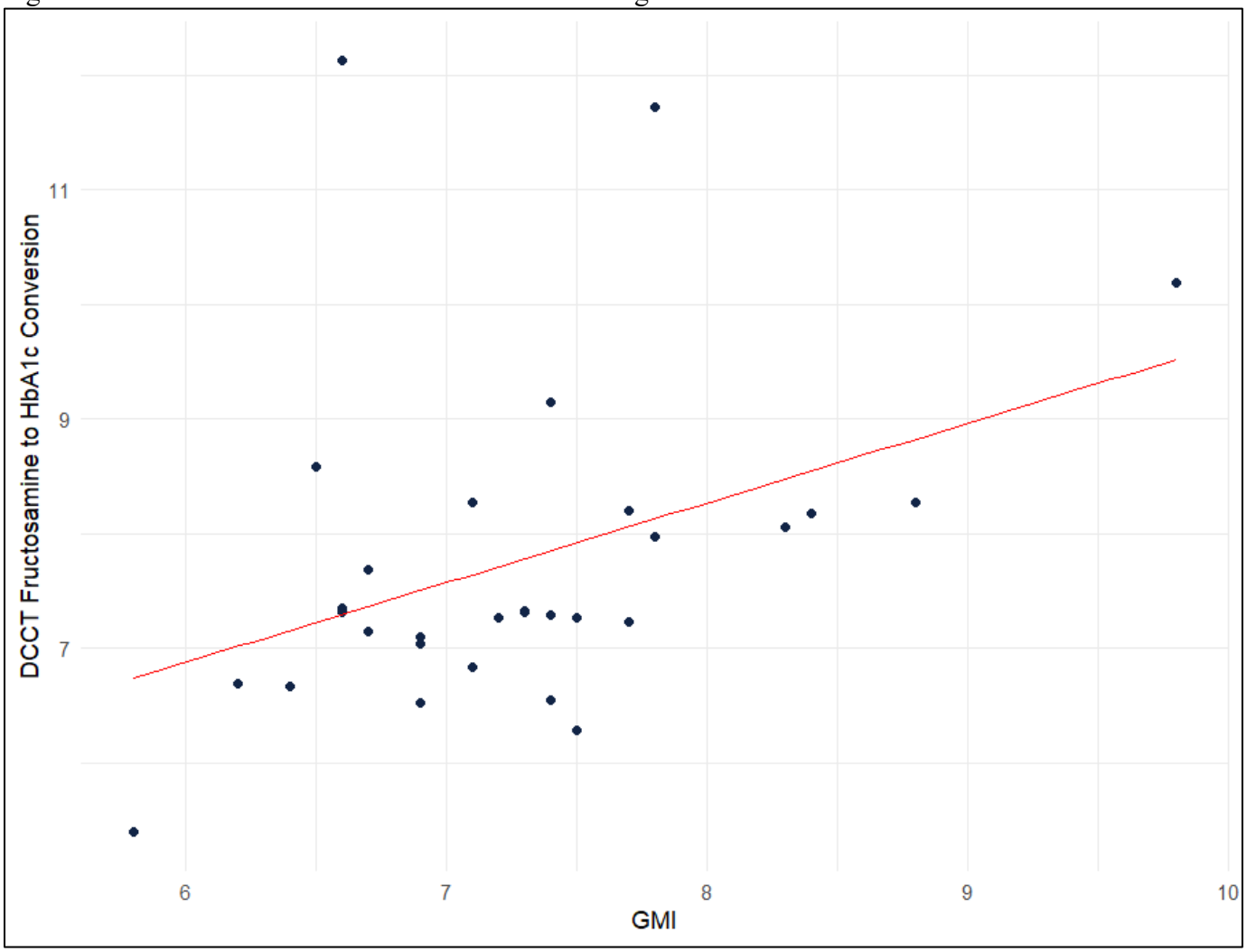


Figure 4. Scatter plot with linear regression line comparing glucose management indicator (GMI, estimated HbA1c derived from continuous glucose monitoring data) to HbA1c estimated using the Kang formula [HbA1c (%) = (45.84 + fructosamine) / 48.55]. Pearson's correlation coefficient demonstrates a statistically significant positive correlation ($r = 0.39$, $p = 0.03$, $n = 30$).

Figure 5: Correlation Between CGM-Derived and Young Formula-Estimated HbA1c

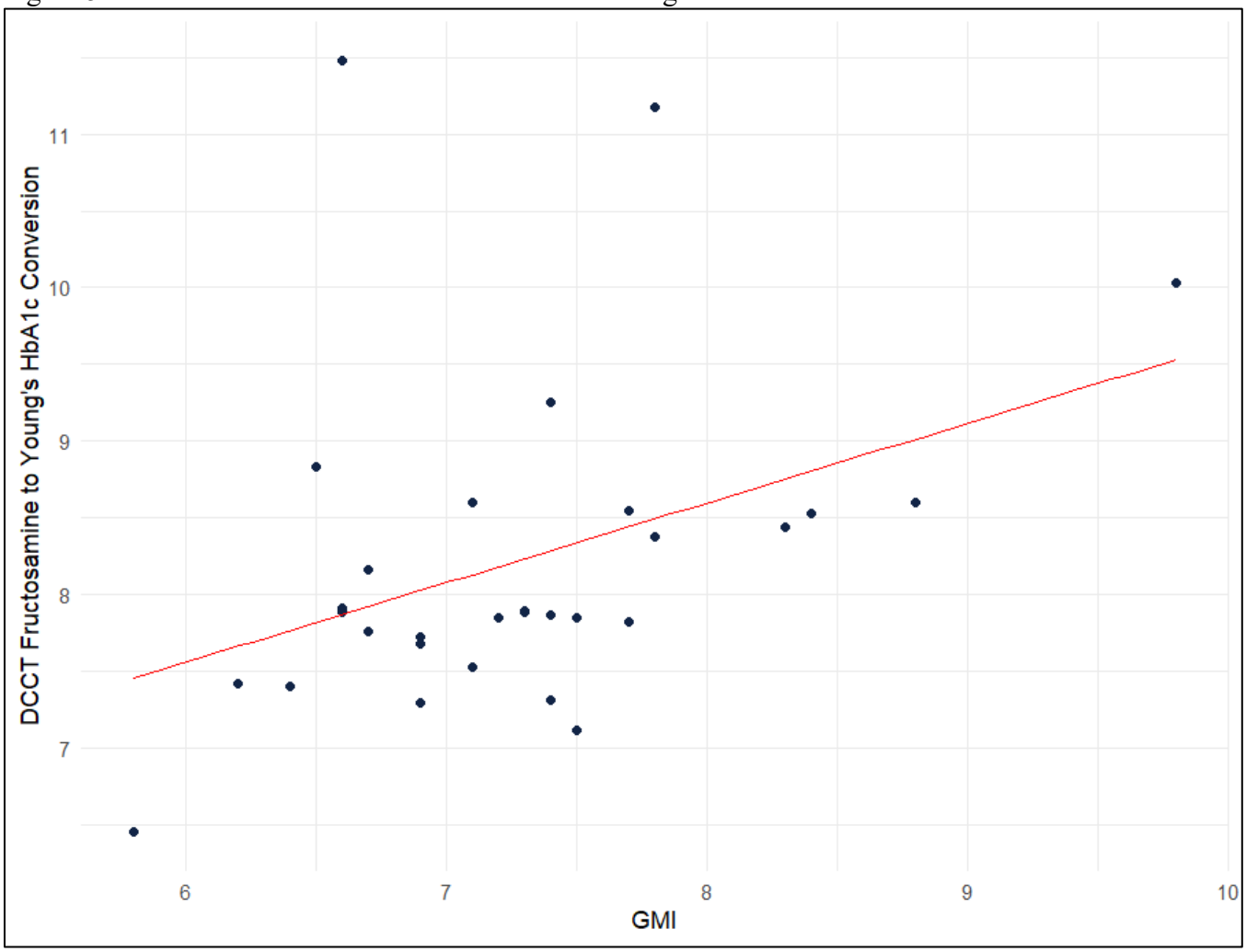


Figure 5. Scatter plot with linear regression line comparing glucose management indicator (GMI, estimated HbA1c derived from continuous glucose monitoring data) to HbA1c estimated using the Young formula [HbA1c (%) = 0.0154 × fructosamine (mmol/L) + 3.121]. Pearson's correlation coefficient demonstrates a statistically significant positive correlation ($r = 0.39$, $p = 0.03$, $n = 30$).