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ORIGINAL RESEARCH

Associations Between HbA1c and Glucose Time in Range Using Continuous Glucose Monitoring in Type 1 Diabetes: Cross-Sectional Population-Based Study

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ABSTRACT

Introduction: Continuous glucose monitoring (CGM) introduces novel indicators of glycemic control.

Methods: This cross-sectional study, based on the Swedish National Diabetes Register, examines 27,980 adults with type 1 diabetes. It explores the relationships between HbA1c (glycated hemoglobin) and various CGM-derived metrics, including TIR (time in range, representing the percentage of time within the range of 4–10 mmol/l for 2 weeks), TAR (time above range), TBR (time below range), mean glucose, standard deviation (SD), and coefficient of variation (CV). Pearson correlation coefficients and linear regression models were utilized for estimation.

Results: The analysis included 46% women, 30% on insulin pump, 7% with previous coronary heart disease and 64% with retinopathy. Mean ± SD values were age 48 ± 18 years, diabetes duration 25 ± 16 years, HbA1c 58.8 ± 12.8 mmol/mol, TIR 58.8 ± 19.0%, TAR 36.3 ± 20.0%, TBR 4.7 ± 5.4%, mean sensor glucose 9.2 ± 2.0 mmol/l, SD 3.3 ± 1.0 mmol/l, and CV 36 ± 7%. The overall association between HbA1c and TIR was − 0.71 (Pearson's r), with R^2 0.51 in crude linear regression and 0.57 in an adjusted model. R^2 values between HbA1c and CGM mean glucose were 0.605 (unadjusted) 0.619 (adjusted) and TAR (unadjusted 0.554 and fully adjusted 0.568, respectively), while fully adjusted R^2 values were 0.458, 0.175 and 0.101 between HbA1c and CGM SD, CGM CV and TBR, respectively.

Prior Presentation: Preliminary results of this study were presented at EASD (European Association for the Study of Diabetes) 2022 (Stockholm, Sweden 19–23 September 2022), and at The International Conference on Advanced Technologies and Treatments of Diabetes 2024 (Florence, Italy 6–9 March 2024).

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Conclusions: This descriptive study demonstrates that the degree of association between HbA1c and new and readily available CGM-derived metrics, i.e., time in range (TIR), time above range (TAR), and CGM mean glucose, is robust in assessing the management of individuals with type 1 diabetes in clinical settings. Metrics from CGM that pertain to variability and hypoglycemia exhibit only weak correlations with HbA1c.

Keywords: Type 1 diabetes; Epidemiology; HbA1c; Continuous glucose measurement

Key Summary Points
This cross-sectional registry-based study explored relationships between HbA1c (glycated hemoglobin) and CGM-derived metrics, including time in range (TIR), mean glucose, standard deviation (SD), and coefficient of variation (CV) in 27,980 adults with type 1 diabetes.
Thirty percent used an insulin pump, the mean age was 48 years, diabetes duration 25 years, with HbA1c 58.8 mmol/mol, TIR (time in range) 58.8, sensor glucose 9.2 ± 2.0 mmol/l, SD (standard deviation) 3.3 ± 1.0 mmol/l, and CV 36%.
The overall associations (R^2) between HbA1c and TIR was 0.57 and CGM mean glucose 0.62, respectively, in adjusted regression models.
The correlation between HbA1c and CGM-derived measures of glycemic exposure is relatively good, but weaker when it comes to measures of variability.
HbA1c appears to be an overall outcome measure in type 1 diabetes, where the CGM-derived measurements have the potential to guide the quality of individual treatment in the short term.

INTRODUCTION

The main objectives of treating diabetes mellitus are to optimize glucose levels to prevent hypo- and hyperglycemia, counteract the development of micro- and macrovascular diseases, and strive for a high quality of life. For over 40 years, glycated hemoglobin (HbA1c) has been the established but indirect measure of glucose levels over 2–3 months. However, despite extensive research on its correlation with patient characteristics and health outcomes, there is both inter- and intra-individual variability, and the practical relationship between HbA1c and a person's actual glucose level may seem abstract [1].

Continuous glucose monitoring (CGM) systems, including real-time CGM (rtCGM) and intermittently scanned CGM (isCGM), allow for the evaluation of new variables in the treatment of diabetes mellitus. In 2019, an international consensus report provided standardized CGM-derived measurements for clinical care, as well as target levels for different patient groups [2]. Key metrics included the percentage of readings and time per day within the target glucose range (TIR, 3.9–10.0 mmol/l, 70–180 mg/dl), time above the target glucose range (TAR), and time below the target glucose range (TBR). TAR can also be divided into TAR level 1 (>180 mg/dl), and TAR level 2 (>250 mg/dl), and similarly TBR in level 1 (<70 mg/dl) and level 2 (<54 mg/dl). Mean glucose, estimated HbA1c (i.e., glucose management indicator, GMI), coefficient of variation (CV), and standard deviation (SD) can also reflect glycemic control. The latest treatment guidelines from the American Diabetes Association also recall that 14-day periods of active CGM use at least 70% of the time should be used to deliver valid data, as well as a target CV equal to or lower than 36% [3]. The same recommendations for nonpregnant adults state that the target levels for HbA1c are <7% (53 mmol/mol), TIR >70% with TBR <4%, but less stringent goals can be applied in individuals with frailty or at high risk of hypoglycemia [3].

Few studies have evaluated the relationships between HbA1c and CGM-derived measures. Beck et al. [4] examined data from randomized clinical trials and found a relatively strong correlation (r=0.67–0.73) between TIR and HbA1c

in type 1 diabetes, while Vigersky and McMahon [5], using similar methods, suggested a higher correlation ($r = -0.84$) between these variables based on paired mean HbA1c and TIR data from 18 published papers. The interpretation of TIR and the other CGM-derived metrics in relation to HbA1c is still subject to debate, as the associations between these and the risks of micro- and macrovascular complications, and excess mortality in people with diabetes still need to be studied on a much larger scale [6].

Against this background, we conducted a cross-sectional study in daily clinical practice to delineate the relationships between HbA1c and CGM-derived measures, including TIR. Our aim was to present an overview of these correlations to support clinical diabetes care. In Sweden, more than 85% of individuals with type 1 diabetes currently use sensor-based glucose monitoring (http://www.ndr.nu). Consequently, we utilized a cohort comprising 27,980 patients from the National Diabetes Register (NDR), a comprehensive national quality register that receives reports from nearly all patients with diabetes in Sweden.

METHODS

The National Diabetes Register (NDR) is a Swedish national quality registry that was initiated in 1996 to collect information on clinical characteristics, risk factors, and complications of diabetes mellitus in patients aged 18 years and above. Since 2016, use of CGM sensors has been reported to the NDR, and since 2020, sensor-based metrics have been reported. These are registered in the medical record at visits in the clinic and subsequently reported to the NDR. In clinical practice, and based on available systems to download CGM-derived measurements during the study period, TIR reported in the medical records could be 4.0–10.0 mmol/l (72–180 mg/dl) or 3.9–10.0 mmol/l (70–180 mg/dl), both reported to the NDR as TIR 4–10 mmol/l. This is a cross-sectional nationwide study that included people aged 18 years and above with type 1 diabetes who used real-time continuous glucose monitoring (rtCGM) or intermittently scanned continuous glucose monitoring (isCGM) and had at least one registration of time in range (TIR) in the NDR between January 1, 2020, and December 22, 2021 (Fig. 1). We only included patients with type 1 diabetes, as diagnosed by their clinicians.

In this study, we defined TIR as the proportion of glucose measurements between 4–10 mmol/l (as reported to the NDR), with time above range (TAR) defined as glucose measurements >10 mol/l and time below range (TBR) defined as glucose measurements ≤3.9 mmol/l. All CGM-derived metrics reported to the NDR are recommended to be based on the most recent 2-week

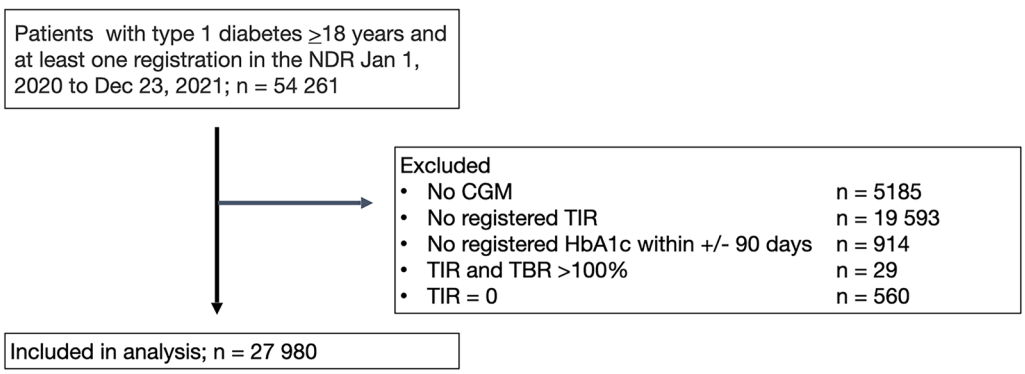

Fig. 1 Flowchart that includes people aged 18 years and above with type 1 diabetes who used real-time continuous glucose monitoring (rtCGM) or intermittently scanned continuous glucose monitoring (isCGM) and had at least one registration of time in range (TIR) in the NDR between January 1, 2020, and December 22, 2021. *NDR* National Diabetes Register, *CGM* continuous glucose monitoring, *TIR* time in range, *TBR* time below range

period before a planned appointment with sensor use for at least 70% of the time. Each TIR value was matched to the HbA1c value closest in time (up to 90 days). Patients with more than one TIR and HbA1c pairing had one observation selected at random. Other sensor data variables were collected from the same registration as the selected TIR value, and for the other variables in the NDR, the latest registered value within 365 days before the TIR registration was used.

We assessed the linear association between HbA1c and TIR using the Pearson correlation coefficient in the entire cohort and in subgroups. We estimated linear regression models between HbA1c and TIR with and without adjustment for TBR, diabetes duration, sex, insulin delivery method, and kidney function. Severe hypoglycemia was defined as requiring the help of another person to remedy, and the estimated glomerular filtration rate (eGFR) was calculated using the Modification of Diet in Renal Disease (MDRD) study prediction equation [7]. We used R statistical software for all calculations.

Approval for this study was granted by the Swedish Ethical Review Authority (diary numbers 2021-03236 and 2021-05785-02). In adherence to Swedish law (Patient Data Act 2008:355, chapter 7), individual consent is not necessary to report patients to national healthcare quality registries or to enroll them in this study. Permission is required to access and use the data from the registry, although summarized results are available online (https://ndr.registercentrum.se/). All exported study data is anonymized. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

RESULTS

The present analysis comprises a cohort of 27,980 individuals with type 1 diabetes, with their clinical characteristics presented in Table 1. The mean age of the cohort was 47.6 (±17.8) years, with 46% being women. The mean duration of diabetes was 24.7 (±15.8) years, and the mean HbA1c was 58 (±13) mmol/mol. Among the cohort, 30% used an insulin pump, 7% had a history of coronary heart disease, and 64% exhibited some degree of diabetic retinopathy. The mean values of the CGM-derived metrics were as follows: TIR 58.8% (±19.0), TAR 36.3% (±20.0), TBR 4.7% (±5.4), sensor mean glucose 9.2 mmol/l (±2.0), sensor glucose SD 3.3 mmol/l (±1.0), and mean coefficient of variation (CV) 36% (±7).

Participants' clinical characteristics are given in Table 1 and Supplementary Tables 1 and 2, while Supplementary Fig. 1A–D shows the distribution of TIR in subgroups. Insulin pump users, who were younger but had a similar duration of diabetes, exhibited numerically higher TIR and other CGM-derived metrics, as well as lower HbA1c (Table 1). The grouping according to kidney function revealed that older age and longer diabetes duration were associated with lower eGFR and a higher incidence of retinopathy and ischemic heart disease, but no apparent differences in CGM-derived measures (Supplementary Table 1). The youngest patients with the highest eGFR had the highest HbA1c, CGM mean glucose, and lowest TIR.

Figure 2A–F depicts scatter plots illustrating the association between HbA1c and the CGM-derived metrics in the entire cohort. The Pearson coefficient for the correlation between HbA1c and TIR was – 0.71 in the entire cohort, with similar results for subgroups divided by sex, insulin delivery method, age groups, and eGFR strata. An increase of 5 percentage points in TIR corresponded to a reduction in HbA1c of 2.4 mmol/mol in the overall cohort. The Pearson correlation coefficient was 0.74 between HbA1c and TAR, 0.78 between HbA1c and CGM mean glucose, 0.58 between CGM SD glucose, and 0.05 between HbA1c CV glucose.

Table 2 presents the results of the linear regression models for the entire cohort, both unadjusted and adjusted for TBR, diabetes duration, sex, insulin delivery method, and kidney function. When all covariates were considered, R^2 increased from 0.508 to 0.566 for the relationship between HbA1c and TIR. A stronger relationship (R^2) was observed between HbA1c and CGM mean glucose (unadjusted 0.605 and fully adjusted 0.619, respectively) and TAR (unadjusted 0.554 and fully adjusted 0.568,

Table 1 Clinical characteristics

	Entire cohort	Missing	Men	Women	MDI	Insulin pump
Numbers	27,980		15,199	12,781	19,206	8335
Age, years	47.6 (17.8)	0	47.5 (17.6)	47.8 (18.1)	50.3 (17.8)	41.5 (16.2)
Diabetes duration, years	24.7 (15. 8)	0.1	24.3 (15.6)	25.1 (16.0)	24.5 (16.5)	25.2 (14.0)
CGM TIR, %	58.8 (19.0)	0	58.3 (18.9)	59.3 (19.0)	57.6 (19.3)	61.6 (17.8)
CGM TAR, %	36.3 (20.0)	5.6	36.6 (19.9)	36.0 (20.2)	37.0 (20.7)	34.6 (18.3)
CGM TBR, %	4.7 (5.4)	5.7	4.8 (5.3)	4.5 (5.4)	5.2 (5.7)	3.6 (4.4)
CGM mean glucose, mmol/l	9.2 (2.0)	4.6	9.3 (2.0)	9.2 (2.0)	9.3 (2.1)	9.1 (1.8)
CGM SD, mmol/l	3.3 (1.0)	27.8	3.3 (1.0)	3.2 (0.9)	3.4 (1.0)	3.2 (0.9)
CGM CV, %	36 (7)	28.2	36 (7)	35 (7)	36 (7)	35 (7)
HbA1c, mmol/mol	58.8 (12.8)	0	58.5 (12.7)	59.1 (12.9)	59.4 (13.3)	57.1 (11.2)
Systolic blood pressure, mmHg	127 (15)	10.8	129 (14)	125 (15)	128 (15)	125 (14)
Diastolic blood pressure, mmHg	75 (9)	11.0	75 (9)	73 (9)	75 (9)	75 (9)
BMI, kg/m^2	26.6 (4.7)	22.8	26.6 (4.4)	26.6 (5.2)	26.5 (4.7)	26.8 (4.8)
Total cholesterol, mmol/l	4.4 (0.9)	15.6	4.3 (0.9)	4.6 (0.9)	4.4 (1.0)	4.4 (0.9)
HDL cholesterol, mmol/l	1.6 (0.5)	18.2	1.5 (0.4)	1.8 (0.5)	1.6 (0.5)	1.6 (0.5)
LDL cholesterol, mmol/l	2.4 (0.8)	13.2	2.4 (0.9)	2.5 (0.8)	2.4 (0.8)	2.4 (0.8)
S-Creatinine, µmol/l	76.6 (46.0)	11.4	84.1 (52.4)	67.7 (35.2)	77.7 (49.1)	74.0 (37.3)
eGFR, ml/min/1.73 m^2	93.9 (26.2)	11.4	96.5 (26.4)	90.7 (25.7)	93.2 (26.9)	95.1 (24.4)
U-Alb/creatinine, mg/mmol	6.0 (35.5)	45.9	6.7 (37.5)	5.0 (32.7)	6.7 (38.2)	4.2 (28.0)
Age category, %		0				
18–29 years	5691 (20.3)		3066 (20.2)	2625 (20.5)	3121 (16.3)	2501 (30.0)
30–44 years	6903 (24.7)		3802 (25.0)	3101 (24.3)	4461 (23.2)	2322 (27.9)
45–59 years	7337 (26.2)		4078 (26.8)	3259 (25.5)	5037 (26.2)	2178 (26.1)
60–74 years	5934 (21.2)		3170 (20.9)	2764 (21.6)	4708 (24.5)	1138 (13.7)
≥ 75 years	2115 (7.6)		1083 (7.1)	1032 (8.1)	1879 (9.8)	196 (2.4)
Sex, women, %	12,781 (45.7)	0			8108 (42.2)	4490 (53.9)
Insulin pump, %	8335 (30.3)	1.6	3845 (25.7)	4490 (35.6)		
Severe hypoglycemia, *n* during the last year		4.8				
0	26,089 (98.0)		14,246 (98.1)	11,843 (97.7)	17,916 (97.9)	7786 (98.2)
1–2	494 (1.9)		247 (1.7)	247 (2.0)	356 (1.9)	130 (1.6)
3–5	30 (0.1)		14 (0.1)	16 (0.1)	23 (0.1)	5 (0.1)

Table 1 continued

	Entire cohort	Missing	Men	Women	MDI	Insulin pump
≥ 6	21 (0.1)		10 (0.1)	11 (0.1)	14 (0.1)	7 (0.1)
Ischemic heart disease, %	1844 (6.7)	2.3	1093 (7.4)	751 (6.0)	1423 (7.6)	390 (4.8)
Retinopathy, %	17,957 (67.7)	5.1	9861 (68.4)	8096 (66.8)	12,084 (66.6)	5626 (70.6)

respectively). The fully adjusted R^2 values were 0.458, 0.175, and 0.101 for the relationships between HbA1c and CGM SD, CGM CV, and TBR, respectively.

DISCUSSION

This research, conducted on a cohort of 27,980 individuals diagnosed with type 1 diabetes in clinical settings and with data available at regular diabetes clinic visits, reveals distinct associations between HbA1c and certain metrics provided by continuous glucose monitoring (CGM). However, the correlation with time in range (TIR) does not surpass 0.71. When accounting for other known patient characteristics available in this study, the explanatory power reaches approximately 57%. The relationship with HbA1c exhibited relatively stronger associations with CGM-derived mean glucose and time above range (TAR) over a 2-week period but notably weaker associations with time below range (TBR) and particularly with measures of variability (standard deviation and coefficient of variation).

HbA1c is a specific glycated hemoglobin caused by the binding of glucose to the β-chain of the hemoglobin molecule [1]. A measured HbA1c value is a function of blood glucose concentration and of the lifespan of the erythrocyte, which usually is around 120 days. Therefore, HbA1c is usually considered to depict the integrated glucose concentration over the past 8–12 weeks, but it is consequently not a validated measure of variations in the blood glucose level. HbA1c measurements began to be used extensively in the 1980s, initially with different analysis methods, but later standardized (International Federation of Clinical Chemistry) [8].

In other words, HbA1c, which is certainly an indirect measure of recent glucose levels, can be influenced by both biological and analytical factors. There is also a clear interindividual variation, especially in diabetes, which have been suggested to be explained by the degree of hyperglycemia or the degree of glycation [9]. Consequently, the relationships between HbA1c and other measures of glucose level and variability measured by CGM are logical but variable for several reasons. However, the historical as well as current and future importance of HbA1c for the evaluation of diabetes treatment at patient as well as care unit level cannot be overestimated, nor regarding the development of new treatments, methods, or drugs.

Glucose level variability has been reviewed and discussed extensively recently, not only in terms of its possible long-term consequences, but its importance to the individual, especially with insulin-treated type 1 diabetes [10]. However, the results of our study remind us that the correlations between HbA1c and different measures of variability, and even TBR, are weak. The ability to follow the subcutaneous glucose level in real time, and thereby reduce variations in glucose, can mean great benefits for patients. It seems reasonable today that calculations of the coefficient of variation or standard deviation can become performance measures that both the healthcare system and patients learn to become familiar with, in combination with plasma glucose measurements and HbA1c [3].

Continuous glucose measurement is now recommended in modern treatment guidelines, especially for patients with type 1 diabetes in children and adults, but also for patients with type 2 diabetes treated with insulin who are not well controlled [11–13]. The National Institute for Health and Care Excellence has evaluated the data for CGM and notes that both HbA1c

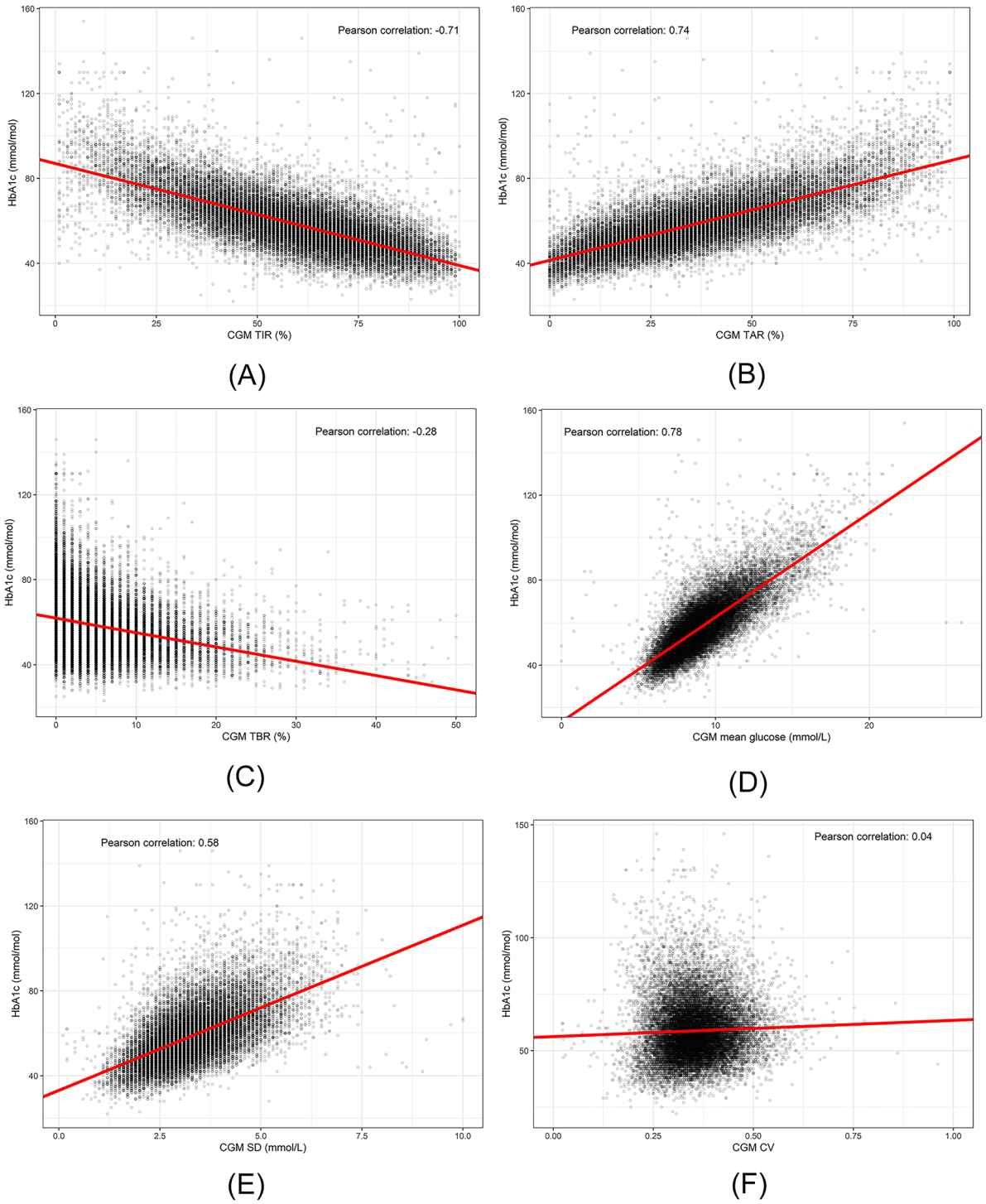

Fig. 2 **A–F** Associations between HbA1c and the CGM-derived metrics. *TIR* time in range, *CGM* continuous glucose monitoring, *CGM CV* continuous glucose monitoring coefficient of variation

Table 2 Pearson's correlation coefficients and regression models

	Pearson's *r*		Regression				
			Estimate	R^2	R^2 adjusted	Adjustment	*p* value
HbA1c and TIR	Unadjusted	− 0.71	− 0.48 (− 0.48, − 0.47)	0.508			< 0.001
			− 0.47 (− 0.47, − 0.46)		0.554	TBR	< 0.001
			− 0.48 (− 0.49, − 0.48)		0.518	Duration, sex, MDI/pump	< 0.001
			− 0.47 (− 0.47, − 0.46)		0.569	TBR, duration, sex, MDI/pump	< 0.001
			− 0.47 (− 0.47, − 0.46)		0.566	TBR, duration, sex, MDI/pump, eGFR	< 0.001
HbA1c and TAR	Unadjusted	0.74	41.5 (41.2, 41.7)	0.554			< 0.001
			41.8 (41.5, 42.0)		0.554	TBR	< 0.001
			40.1 (39.8, 40.4)		0.570	Duration, sex, MDI/pump	< 0.001
			40.6 (40.3, 40.9)		0.570	TBR, duration, sex, MDI/pump	< 0.001
			0.47 (0.46, 0.47)		0.568	TBR, duration, sex, MDI/pump, eGFR	< 0.001
HbA1c and TBR	Unadjusted	− 0.28	− 0.67 (− 0.69, − 0.64)	0.079			< 0.001
			− 0.67 (− 0.69, − 0.64)		0.079	TBR	< 0.001
			− 0.71 (− 0.74, − 0.68)		0.098	Duration, sex, MDI/pump	< 0.001
			− 0.71 (− 0.74, − 0.68)		0.098	TBR, duration, sex, MDI/pump	< 0.001
			− 0.72 (− 0.75, − 0.69)		0.101	TBR, duration, sex, MDI/pump, eGFR	< 0.001

Table 2 continued

	Pearson's *r*		Regression				
			Estimate	R^2	R^2 adjusted	Adjustment	*p* value
HbA1c and CGM mean glucose	Unadjusted	0.78	4.88 (4.83, 4.92)	0.605			< 0.001
			5.01 (4.96, 5.06)		0.604	TBR	< 0.001
			4.90 (4.86, 4.95)		0.623	Duration, sex, MDI/pump	< 0.001
			5.01 (4.96, 5.06)		0.621	TBR, duration, sex, MDI/pump	< 0.001
			5.03 (4.97, 5.08)		0.619	TBR, duration, sex, MDI/pump, eGFR	< 0.001
HbA1c and CGM CV glucose	Unadjusted	0.05	8.33 (5.85, 10.82)	0.002			< 0.001
			54.82 (52.01, 57.63)		0.146	TBR	< 0.001
			7.33 (4.84, 9.83)		0.013	Duration, sex, MDI/pump	< 0.001
			56.01 (53.23, 58.8)		0.173	TBR, duration, sex, MDI/pump	< 0.001
			55.76 (52.77, 58.75)		0.175	TBR, duration, sex, MDI/pump, eGFR	< 0.001
HbA1c and CGM SD glucose	Unadjusted	0.58	7.83 (7.68, 7.98)	0.342			< 0.001
			7.96 (7.82, 8.10)		0.437	TBR	< 0.001
			7.85 (7.70, 8.00)		0.355	Duration, sex, MDI/pump	< 0.001
			7.95 (7.81, 8.09)		0.460	TBR, duration, sex, MDI/pump	< 0.001
			7.95 (7.80, 8.10)		0.458	TBR, duration, sex, MDI/pump, eGFR	< 0.001

and other performance measures show clear advantages compared to capillary glucose measurement, with no obvious differences between isCGM and rtCGM [12]. The performance and safety of the various CGM systems have been investigated and found to be adequate for clinical use, although there may be pros and cons regarding practical use as well as costs [14]. In practice, each patient's individual needs should be considered when choosing a CGM system. The overall goal is to use these tools to optimize glucose control by reducing variations, thereby increasing well-being, and reducing the risk of diabetes complications.

However, there are still few studies that have addressed the associations between CGM-based metrics and micro- or macrovascular diabetes complications. To exemplify, two studies conducted in China have suggested an association between TiR and both diabetic retinopathy and mortality [15, 16]. However, these studies have a different methodology than the standards that are currently recommended, such as basing TIR on CGM and not on self-monitoring of blood glucose (SMBG), or

3–6 days of recorded values instead of 14 days. Similarly, Beck et al. [17] used SMBG data from the DCCT and showed that a 10% reduction in TIR increased the risks of retinopathy and albuminuria by 64% and 40%, respectively. In a subgroup of a study investigating the relationship between treatment-induced change in TIR and albuminuria in subjects with type 1 diabetes treated with sensor-augmented insulin pumps (SAPs), a beneficial effect was noted [18]. In another cross-sectional study of sensor-enhanced pump therapy users, lower TIR was associated with the presence of microvascular complications, severe hypoglycemia, or ketoacidosis [19]. It is certainly likely that CGM-based metrics including TIR will soon be widely used in prospective scientific studies as well as in clinical everyday life, which is why knowledge of their value as a long-term risk marker alongside HbA1c need to be established. However, it seems unlikely that these measures will be studied in dedicated studies to assess their utility per se, due to methodological challenges and considerable costs.

The strengths of this study are the large number of people whose CGM-metrics and HbA1c-values have been reported, not least because to the rapid increase in continuous glucose monitoring after isCGM appeared on the market in 2017. The opportunity to report CGM data to NDR was made available in 2020. In addition, we have available data regarding a range of patient characteristics that could be used for adjustments in regression analyses. HbA1c analyses are also always standardized according to IFCC [8].

There are some obvious limitations in this study that are important in interpreting the results. One is that we used single and not repeated measurements in the analyses. However, this will be possible in the future with continued and increased use of CGM and reporting to the NDR. To maximize the number of measurement values in the analyses we have not required that the HbA1c value be checked during the recommended 2-week period with CGM data but allowed a value from within the last 90 days. This is justified since blood sampling are not taken at every visit in the clinic in practice, and the intention of our study was to reflect the relationships between the outcome variables in regular routine work at specialist clinics. It is also possible that a longer time interval for the acquisition of CGM data should be standard, as discussed recently [20, 21]. Pregnant women are usually checked at specialized maternity care centers that do not report to the NDR. However, it is conceivable that a small number of pregnant women are included in this analysis. Other factors that could influence the HbA1c level [22], such as information on conditions affecting the hemoglobin value or erythrocyte survival, ethnicity, or analysis methods, have not been available in this project apart from renal function measured by eGFR. We also have not analyzed the results in users of different CGM systems or versions of these, and it is not possible to report the CGM derived glucose monitoring indicator (GMI) to the NDR.

In Sweden, the SI system is used for indicating glucose concentration (mmol/l). This is why the target level of 4–10 mmol/l is used in practice and when reporting to NDR. In international guidelines the target level is 70–180 mg/dl, which converted corresponds to 3.88–10.0 mmol/l. When the reporting of CGM data to the NDR started, there was not yet a clear international consensus on the target levels, and systems to download CGM data in Sweden had both TIR 4.0–10.0 mmol/l (72–180 mg/dl) or 3.9–10.0 mmol/l (70–180 mg/dl), which is why both are reported to the NDR as TIR 4–10 mmol/l. In this study we have the information from the NDR and we thus have no information on the relationships between HbA1c and other glucose ranges but judge that the differences must be minimal and clinically insignificant.

We find compelling correlations between HbA1c and TIR, TAR, and CGM mean glucose in adults diagnosed with type 1 diabetes. These associations imply reliable indications of glucose exposure, presenting a viable substitute for HbA1c in routine clinical settings, potentially requiring less frequent monitoring. Measures of variability and hypoglycemia serve other roles and in the management of people with type 1 diabetes. The role and validity of TIR and other CGM-derived measures compared

with glycated hemoglobin for the long-term development of micro- and macrovascular as well as other complications and mortality remain to be determined. Today, however, it appears that HbA1c is becoming an overall outcome measure in type 1 diabetes, with the CGM-derived measurements having the potential to provide guidance on the quality of the individual treatment.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Björn Eliasson reports personal fees from Amgen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck Sharp and Dohme, Mundipharma, Novo Nordisk and Sanofi, all outside the submitted work. Elin Allansson Kjölhede declare no conflict of interest relevant to this article. Sofia Salö and Nick Fabrin Nielsen are employed by NovoNordisk. However, the views expressed in this study are their own and not those of NovoNordisk. Katarina Eeg-Olofsson has received personal lecture fees and/or honoraria for consulting from Sanofi, Eli Lilly, Novo Nordisk and Abbott, all outside the submitted work.

Ethical Approval. Approval for this study was granted by the Swedish Ethical Review Authority (diary numbers 2021-03236 and 2021-05785-02). In adherence to Swedish law (Patient Data Act 2008:355, chapter 7), individual consent is not necessary to report patients to national healthcare quality registries or to enroll them in this study. This study was performed in accordance with the Helsinki Declaration of 1964 and its later amendments.

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