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The Importance of Time in Range (TIR) for Continuous Glucose Monitoring (CGM) in the Clinical Practice for Diabetes

Hiroshi Bando*

Affiliation: Tokushima University/Medical Research, Tokushima, Japan

***Corresponding author:** Hiroshi Bando, Tokushima University/Medical Research, Nakashowa 1-61, Tokushima 770-0943, Japan
Tel: +81-90-3187-2485, E-mail: pianomed@bronze.ocn.ne.jp

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Abstract

As to the development of treatment for diabetes, Continuous Glucose Monitoring (CGM) has been recently prevalent rapidly. By the analysis of real-time CGM, Ambulatory Glucose Profile (AGP) has been used. It includes time in range (TIR, 70-180 mg/dL), time above range (TAR, >181mg/dL), time below range (TBR, <69 mg/dL), Glycemic Variability (GV), Glucose Management Indicator (GMI), Glycemic variability, Coefficient Of Variation (CV%) and so on. TIR value indicating approximately 70% seems to correlate closely with the HbA1c level of 6.7-7.0%. Marked discordance of HbA1c values has been found between laboratory HbA1c and estimated HbA1c (eA1c) using GMI from CGM.

Keywords: Diabetes, Glucose, Carbohydrate.

Abbreviations: TIR-Time in Range, CGM-Continuous Glucose Monitoring, AGP-Ambulatory Glucose Profile, GMI-Glucose Management Indicator, eA1c-Estimated HbA1c.

As to the development of treatment for diabetes, Continuous Glucose Monitoring (CGM) has been prevalent rapidly, including both of real-time CGM (rtCGM) and intermittently scanned CGM (isCGM). Lots of studies demonstrated remarkable benefits of CGM for diabetes patients [1]. However, absence of clarified glycemic targets was observed from both patients and diabetes team cooperating together. Consequently, the Advanced Technologies and Treatments for Diabetes (ATTD) congress were convened for better management of practice and research. The objective included the development of clinical CGM-derived times in glucose ranges, such as above target range, within target range and below target range.

CGM continuously provides diabetic patients and medical staffs current glucose values and related data in order to make adequate treatment management [2]. Furthermore, real-time CGM systems can give attention for higher and lower glucose levels which allow necessary intervention for additional insulin or carbohydrate per os [3].

In recent report, T1DM patients with rtCGM (n=70) were compared with control for impaired hypoglycemia awareness related to the HypoDE (Hypoglycemia in Deutschland) study. As a result, glucose threshold at taking rescue carbohydrate was increased from 71mg/dL to 79mg/dL in the rtCGM group. It suggested earlier awareness for hypoglycemia with preventing hypoglycemia episodes [3].

For T2DM cases with basal insulin without prandial insulin (n=175), glucose variability was compared for CGM group vs traditional blood glucose meter (BGM) group [1]. The comparative results for 8 months in both groups were as follows: HbA1c changes 9.1 to 8.0% vs 9.0 to 8.4%, TIR (70-180mg/dL) 59% vs 43%, TAR (>250mg/dL) 11% vs 27% and mean glucose levels 179mg/dL vs 206mg/dL. Consequently, CGM group showed more effective response.

According to American Diabetes Association (ADA), diabetic patients with intensive insulin treatment are encouraged to check glucose changes by CGM [4]. Glucose profile was captured by CGM which was optimal method to clarify current glucose variability [5]. From the data of CGM, Time in Range (TIR) refers the time period of 70-180 mg/dL during 24 hours. Furthermore, TIR is useful for estimating insulin response during short-term Continuous Subcutaneous Insulin Infusion (CSII) treatment. Recently, TIR value was reported to show both of micro vascular and macro vascular complications [6], neuropathy [7] and micro albuminuria [8].

For CGM report, Ambulatory Glucose Profile (AGP) is used [9]. In some studies, lower Coefficient of Variation (CV%) targets would be adequate for 33% in the case who are treated by insulin or sulfonylureas [10]. Standardized CGM metrics for clinical care are as follows [5]: i) Number of days CGM worn (14-days recommended), ii) Percentage of time CGM (70% recommended), iii) Mean glucose, iv) Glucose Management Indicator (GMI), v) Glycemic variability (%CV <36%), vi) Time Above Range (TAR): >250mg/dL level 2, vii) TAR: 181-250mg/dL, level 1, viii) TIR: 70-180 mg/dL, ix) Time Below Range (TBR): 54-69mg/dL level 1, x) TBR: <54mg/dL level 2.

CGM-based targets for some patients are recommended. Target percentages of each factor are shown in the following: TIR >70%, TAR-L2 <5%, TAR-L1 <25%, TBR-L1 <4%, TBR-L2 <1% in type 1 and type 2 diabetes, and TIR >50%, TAR-L2 <10%, TAR-L1 <50%, TBR-L1 <1%, in older/high-risk of type 1 and type 2 diabetes [5].

TIR and other metrics from CGM have become standardized factors from international consensus. TIR value of about 70% correlates closely with HbA1c level of 6.7-7.0% [11]. Several evidences are found on the relationship of TIR and diabetic complications, in which each 10% TIR elevation brings risk decrease for long-term complications.

CGM data were collected for 5901 T2DM cases for 5 years, and analyzed for 3 profiles of Glycemic Variability (GV) [12]. They are i) TIR profile, ii) hypo profile, iii) hyper profile (N=2271, 1471, 2159, respectively). Comparative data between group i) vs iii) showed that fasting glucose 167 vs 203 mg/dL, 2-hr post prandial glucose 256 vs 302 mg/dL, and HbA1c 8.6 vs 9.7%. Odds Ratio (OR) of ii) and iii) for i) showed that non-proliferative Diabetic Retinopathy (PDR) 1.44 and 1.33, macro albuminuria 1.58 and 1.37, and diabetic kidney disease (DKD) 1.65 and 1.88 compared with i)TIR profile. Especially, ii) showed OR 2.84 for PDR.

Recent report showed the relationship between TIR by CGM and body fat percentage in T2DM [13]. Subjects were 85 T2DM cases and they received CGM during short-term CSII therapy. As a result, T2DM cases with higher body fat exhibited lower TIR ($p=0.004$) and higher mean blood glucose levels ($p=0.001$). Thus, weight reduction can be therapeutic target to obtain better glucose variability for obese cases, which may get less beneficial effect from intensive insulin therapy.

For CGM study for T1DM, TIR and CV% were analyzed for 95 cases [14]. Subjects number for HbA1c was 20 for ≤7%, 44 for 7-8%, 31 for >8%. TIR was negatively associated with HbA1C, mean blood glucose (MBG) and time spent in hyperglycemia ($p<0.001$), but not with time in hypoglycemia. The results suggested that TIR would be strongly related with hyperglycemia and CV% would be reflective of hypoglycemic risk.

Lots of diabetic patients and related medical staffs have felt marked discordance of HbA1c values, between laboratory HbA1c and estimated HbA1c (eA1c) using GMI from CGM [15]. According to latest report, much data from 641 separate offices were analyzed. Subjects showed T1DM in 91% with mostly history of >20 years and 24.5 days duration of CGM. As a result, 11% cases discordance <0.1%, 50% vs 22% cases showed differences ≥0.5% vs ≥1%. Elevated discordance was found with advanced Chronic Kidney Disease (CKD), in which Estimated Glomerular Filtration Rate (eGFR) <60 mL/min/1.73m2). Consequently, substantial discordance is present between laboratory HbA1c and eA1C in the actual clinical practice.

References

1. Martens T, Beck RW, Bailey R, Ruedy KJ, Calhoun P, et al. A randomized clinical trial (2017) JAMA 317: 371-378. https://doi.org/10.1001/jama.2016.19975
2. American Diabetes Association. 6. Glycemic targets: Standards of Medical Care in Diabetes 2021 (2021) Diabetes Care 44: S73-S84. https://doi.org/10.2337/dc21-S006
3. Waldenmaier D, Freckmann G and Pleus S. Therapy adjustments in people with type 1 diabetes with impaired hypoglycemia awareness on multiple daily injections using realtime continuous glucose monitoring: a mechanistic analysis of the HypoDE study (2021) BMJ Open Diab Res Care 9. https://doi.org/10.1136/bmjdrc-2020-001848
4. American Diabetes Association. 7. Diabetes Technology: Standards of Medical Care in Diabetes-2020 (2020) Diabetes Care 43: S77-S88.
5. Battelino T, Danne T and Bergenstal RM. Clinical targets for continuous glucose monitoring data interpretation: recommendations from the international consensus on time in range (2019) Diabetes Care 42: 1593-1603. https://doi.org/10.1136/bmjdrc-2020-001848
6. Lu J, Ma X and Shen Y. Time in range is associated with carotid intima-media thickness in type 2 diabetes (2020) Diabetes Tech and Therapeutics 22: 72-78. https://doi.org/10.1089/dia.2019.0251
7. Beck RW, Bergenstal RM and Riddlesworth TD. Validation of time in range as an outcome measure for diabetes clinical trials. Diabetes Care 2019 42: 400-405. https://doi.org/10.2337/dc18-1444
8. Li F, Zhang Y and Li H. TIR generated by continuous glucose monitoring is associated with peripheral nerve function in type 2 diabetes (2020) Diabetes Research and Clinical Practice 166. https://doi.org/10.1016/j.diabres.2020.108289
9. Danne T, Nimri R, Battelino T, Bergenstal RM, Close KL, et al. International consensus on use of continuous glucose monitoring (2017) Diabetes Care 40: 1631-1640. https://doi.org/10.2337/dc17-1600
10. Rama Chandran S, Tay WL, Lye WK, Lim LL, Ratnasingam J, et al. Beyond HbA1c: comparing glycemic variability and glycemic indices in predicting hypoglycemia in type 1 and type 2 diabetes (2018) Diabetes Technol Ther 20: 353-362. https://doi.org/10.1089/dia.2017.0388
11. Aleppo G. Clinical application of time in range and other metrics (2021) Diabetes Spectrum 34: 109-118. https://doi.org/10.2337/ds20-0093
12. Varghese JS, Ho JC, Anjana RM, Pradeepa R, Patel SA, et al. Profiles of intraday glucose in type 2 diabetes and their association with complications: an analysis of continuous glucose monitoring data (2021) Diabetes Technol Ther https://doi.org/10.1089/dia.2020.0672
13. Ruan Y, Zhong J, chen R, Zhang Z, Liu D, et al. Association of body fat percentage with time in range generated by continuous glucose monitoring during continuous subcutaneous insulin infusion therapy in type 2 diabetes (2021) J Diabetes Res 1-9. https://doi.org/10.1155/2021/5551216
14. Helleputte S, De Backer T, Calders P, Pauwels B, Shadid S, et al. The added and interpretative value of cgm-derived parameters in type 1 diabetes depends on the level of glycemic control (2021) Endocr Pract 27: 44-50. https://doi.org/10.4158/EP-2020-0293
15. Perlman JE, Gooley TA, McNulty B, Meyers J and Hirsch IB. Hba1c and glucose management indicator discordance: a real-world analysis (2021) Diabetes Technol Ther 23: 253-258. https://doi.org/10.1089/dia.2020.0501