Old and new approaches to glycemic management in diabetes

Ceriello A, et al. Lancet Diabetes Endocrinol. 2022;10(1):75–84.

sanofi

KEY TAKEAWAY

This review on old and new approaches to glycemic management in diabetes suggested that:

Concept of **hyperglycemia management** has **changed profoundly**

HbA1c alone is **not enough** to comprehensively evaluate glycemic control in diabetes

Besides HbA1c and FPG, new findings support need to **control PP hyperglycemia, GV, and extend TIR:**

All **goals** must be **achieved simultaneously** without inducing hypoglycemia

If there is **hypoglycemia**, **recovery** should focus on **inducing normoglycemia**

Each emerging aspect of **glycemic control** directly affects development of **diabetes complications**

New technologies — **isCGM** and **CGM** can help to develop feasible strategies to control multifaceted aspects of glycemic control:

- **AI** can help with advising on **therapy decision-making**

New drug therapies in addition to **new technologies** may help to holistically manage glycemic control within a connected care environment

Studies are needed to validate **contribution** and **weight** of **each variable** on:

- Late complications
- Metabolic memory

WHY THIS MATTERS

HbA1c is a **useful marker** for glycemic control and diabetes complications in T1D and T2D

However, a milestone study by *Lind et al. 2014* suggested **inadequacy of HbA1c use** as sole marker of glucose control in T1D patients

This **review** described **emerging aspects** of **hyperglycemia** to consider for optimal diabetes management

KEY HIGHLIGHTS

POSTPRANDIAL HYPERGLYCEMIA (NON-PREGNANCY)

First additional aspect of glycemic control considered with HbA1c

Essential to prevent adverse outcomes

Intrinsic value as CVD risk factor still debated

Considered as integral part of diabetes management

- Many guidelines recommend controlling PP hyperglycemia in diabetes (*Table*)
- Although timing to check PP hyperglycemia is 2 h after meals, measuring at 1 h may be a better predictor of risk factor for CVD

Please click on the hyperlink for additional information on *PP hyperglycemia*

CVD, cardiovascular disease; h, hour; HbA1c, glycated hemoglobin; PP, postprandial.

GLUCOSE VARIABILITY

May have possible role in development of DM complications, especially CV complications

Many observational studies and post-hoc analyses of trials in T2D suggest GV correlation with increased risk of:

- Microvascular and macrovascular complications
- All-cause mortality

Defined by measurement of glucose fluctuations or other related parameters of glucose homeostasis over given time interval

- Short-term variability → Both within-day and between-day GV
- Long-term variability → Serial determinations over long period using HbA1c or FPG (or both)

Please click on the hyperlink for additional information on *glucose variability*

CV, cardiovascular; DM, diabetes mellitus; FPG, fasting plasma glucose; GV, glucose variability; HbA1c, glycated hemoglobin; T2D, type 2 diabetes.

TIME IN RANGE

Denotes proportion of **time** glucose concentration falls **within desired target range (3.9–10.0 mmol/L)**

Most with **T1D** are **unable to spend** largest part of day with glucose concentrations in **3.9–7.8 mmol/L range**

Representative of **day-to-day experience** of DM patients

Can **predict future risk** of complications

Please click on the hyperlink for additional information on *time in range*

DM, diabetes mellitus; T1D, type 1 diabetes.

HYPOGLYCEMIA

Trying to avoid hypoglycemia while maintaining normoglycemia over lifetime is challenging

Linked to increased risk of CV events, brain damage, retinopathy worsening

Pro-atherosclerotic risk factor

GV is accompanied by high hypoglycemia risk

Please click on the hyperlink for additional information on *hypoglycemia*

CV, cardiovascular; GV, glucose variability.

POTENTIAL LEGACY EFFECT OF GLYCEMIC VARIABLES

Refers to long-term

- Benefit of previous periods of normoglycemia
- Harms with previous periods of hyperglycemia

Long-term follow-up of DCCT (T1D)

- Suggests lower macrovascular and microvascular complications with intensive glucose lowering regimen vs less intensive regimen and effect persisted after 17 years

Similar results seen in *UKPDS (T2D)*

Evidence becomes *less clear* in long-duration diabetes and pre-existing macrovascular disease

Patients with early diabetes more likely to benefit from legacy effect of intensive glycemic control (*Prattichizzo et al. 2020*)

Acute hyperglycemia post meal or during GV and hypoglycemia leads to → Legacy effect on some pathways related to → Development of diabetic complications

Possible legacy effect of glycemic control usually **not considered** in large studies assessing long-term consequences of glucose control

Please click on the hyperlink for information on *correlation and non-redundancy between glycemic variables*

DCCT, Diabetes Complications and Control Trial; GV, glucose variability; T1D, type 1 diabetes; T2D, type 2 diabetes; UKPDS, UK Prospective Diabetes Study.

ADVANCES IN DIABETES TECHNOLOGY

GLYCEMIC PARAMETERS AND EFFECTS ON VASCULATURE

AGENTS TARGETING GLUCOSE INSTABILITY

Please click on the respective hyperlinks for additional information

For additional details, refer the source publication *Ceriello A, et al.*

ABBREVIATIONS:
AI, artificial intelligence; CGM, continuous glucose monitoring; CVD, cardiovascular disease; FPG, fasting plasma glucose; GLP-1, glucagon-like peptide-1; GV, glucose variability; HbA1c, glycated hemoglobin; isCGM, intermittently scanned glucose monitoring; PP, post-prandial; SGLT2, sodium-glucose co-transporter 2; T1D, type 1 diabetes; T2D, type 2 diabetes; TIR, time-in-range.

REFERENCE:
Ceriello A, Prattichizzo F, Phillip M, Hirsch IB, Mathieu C, Battelino T. Glycaemic management in diabetes: old and new approaches. *Lancet Diabetes Endocrinol*. 2022;10(1):75–84. doi: 10.1016/S2213-8587(21)00245-X. PMID: 34793722.