Blood Glucose Trends in Relationship to Metabolic Health, Stress, and Sleep

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Specific Aims

1. To measure **postprandial glucose fluctuations** in patients at risk for diabetes and correlate with food intake and metabolic parameters
   a. Evaluate glucose excursions in relationship **to waist circumference, hypertension, triglycerides, and coronary score.**
2. To record **daily stress** with validated instruments such as PSS and correlate with glucose excursions
3. To **use CGM technology** to define personalized approaches for glycemic control

Background

- As the global prevalence of **Type 2 Diabetes (T2D)** and **cardiovascular disease (CVD)** continues to rise, the relevance of lifestyle factors including **diet, sleep, and stress**, and their metabolic consequences are marked.
- Postprandial hyperglycemia has been found to raise the risk of CVD, coronary heart disease (CHD) and cardiovascular mortality, **even in individuals with normal fasting glucose.** [1,2]
- Growing evidence suggests that **glycemic responses to the same foods differ significantly among individuals a**nd postprandial triglyceride level is more predictive of CVD than are fasting glucose concentrations. [3, 4]
- An individual's unique postprandial glycemic responses are likely attributable to their **biological and lifestyle characteristics.**
- **Metabolic responses to food** influence risk of hyperglycemia leading to greater cardiometabolic disease burden, but large-scale high-resolution studies are lacking.

What is CGM Technology?

- CGM technology provides the potential to assess blood glucose trends including **rates of rises and drops** in response to meals, exercise, sleep, etc.
- **Time-in-range, or TIR**, has become a standard part of conversation between patient and healthcare professional amongst CGM users,
  – Consensus recommendations have recently been produced to facilitate the adoption of standardized TIR targets in diabetes management and care
- Using CGM technology to understand post-prandial blood glucose patterns amongst **non-diabetic patients** provides potential for a greater depth of understanding of **endogenous glucose patterns**

Figure 1. Freestyle Libre sensor (left) and monitor (right) [13]

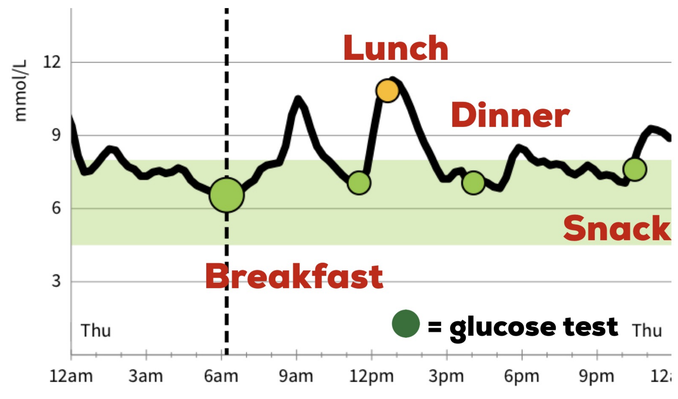

Figure 2. Sample CGM Trend [13]

Literature Review

- Relationships between metabolic health and glycemic control have long been investigated, with **waist circumference posed to be a stronger predictor of metabolic syndrome** and thus a diabetes risk. [5]
  – Relative risk of developing T2D among persons of **low or normal weight with large waist circumference** was at least as high as that among overweight persons with a small waist circumference. [6, 7]
- A clear role for sleep has also been shown in the maintenance of normal glucose homeostasis. [8]
  – Sleep loss and partial sleep deprivation, both which have been increasing over the last 30 years, can lead to impairments in glucose metabolism and increases in insulin levels, which could increase the risk of the development of diabetes.
  – **Reduced sleep quality with low levels of slow-wave sleep**, as occurs in aging and in many obese individuals, contributes to increase the **risk of poor glycemic control and T2D.** [9]
- **Stress** is known to have significant impacts on blood glucose but has not been studied extensively in glucose trends amongst non-diabetic patients.
  – Stress-induced **rises in plasma GH, catecholamines, and cortisol as well as plasma glucagon concentration** precede rises in plasma glucose concentration [11]
  – A primary role for stress hormones is noted in initiating **metabolic decompensation** amongst patients experiencing stress. [12]

Methods

1. CGM

To assess glucose trends, we will use continuous glucose monitoring for two weeks that will be performed with the Freestyle Libre 14 Day System™ (FreeStyle CGM, Abbott Diabetes Care, Alameda, CA), according to the manufacturer's labeling. The monitor will be placed on the baseline visit and monitored for 7 days. Data from each subjects' FreeStyle Libre Glucose Sensor will be downloaded from their linked Reader using the manufacturer (Abbott) software into an EXCEL spreadsheet format.

2. Metabolic Parameters

The continuous glucose monitoring will start at baseline testing. At initial visit, patient's waist circumference, total cholesterol, HDL-cholesterol, triglycerides, and resting blood pressure will be measured. Waist circumference, body composition, systolic and diastolic blood pressure will be measured after participants arrive at the Center for Human Nutrition at the first visit after resting for 15 min. Blood samples (10 ml) will be drawn for serum total cholesterol, HDL-cholesterol and triglyceride determination.

3. Perceived Stress Scale

The Perceived Stress Scale questionnaire will be used to assess participants' stress levels and evaluate any correlation between stress and blood glucose trends.

4 Daily Food Log

A Daily Food Log template will be provided and the patient will be asked to keep a record of their diet over the course of the week as per the directions provided on the log.

5. Statistical analyses

Outcomes including post-prandial blood glucose, time in range, and time above or below range will be measured at baseline and continuously for 7 days. The longitudinal trends will be analyzed via Microsoft Excel. Descriptive statistics will be reported as mean ± standard deviation for continuous variables, and frequency count (%) for categorical variables. The mixed effects model will be used to examine the effect of metabolic variables, diet, and stress, on blood glucose.

References

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6. Rothman, "BMI-Related Errors in the Measurement of Obesity."
7. Orgel et al., "Limitations of Body Mass Index to Assess Body Composition Due to Sarcopenic Obesity during Leukemia Therapy."
8. "Impact of Sleep and Sleep Loss on Glucose Homeostasis and Appetite Regulation."
9. Tasali et al., "Slow-Wave Sleep and the Risk of Type 2 Diabetes in Humans."
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11. Evans, "Emotional Stress and Diabetic Control."
12. Advani, "Positioning Time in Range in Diabetes Management."