Continuous Glucose Monitoring: The Future of Diabetes Care

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Diabetes TeleHealth Series
Objectives

• Understand the principles of continuous glucose monitoring including indications, benefits and limitations thereof.

• Recognize the differences between currently available CGM systems.

• Review key uses of CGM data including real-time trending, retrospective trending, high and low alerts.

• Briefly discuss the future of continuous glucose monitoring.
Introduction

- Diabetes mellitus is associated with long-term complications.
- Most glycemic control in patients with type 1 diabetes is suboptimal.
- Glycemic control is limited by poor adherence to prescribed regimens.
- Adherence is limited, in part, by fear of hypoglycemia.
- Recent evidence links severe hypoglycemia to morbidity and mortality.
Current Metrics for Diabetes Control

- DCCT established HbA1c as gold standard evaluating for glycemic control.
- Self monitored blood glucose (SMBG) protocols vary.
- Blood glucose measured during in-house study-day typically involves 10-24 measurements.
- Frequency of hypoglycemic events is analyzed using study criteria with pre-defined thresholds and patient reports.
Limitations of Current Metrics

- HbA1c reflects mean blood glucose for preceding 120 days.
- SMBG often misses peak post-prandial glucose.
- Self-report and SMBG data unreliable for hypoglycemia.
Absolute risk of sustained retinopathy progression as a function of updated mean A1c during DCCT and time of follow-up during study years.

Glycemic Variability

- DCCT illustrated importance of relative glycemic control to prevent microvascular complications
- Some data at that time suggested deleterious effects of glycemic variability
- Pathophysiologic data indicates increased oxidative stress with fluctuating glucose levels
- Epidemiologic studies suggest correlation between elevated PPG and micro/macrovascular outcomes
- Clinical trial data is limited
OVERVIEW: CGM

- Continuous Glucose Monitor = device that provides “real-time” glucose readings & data about trends in glucose levels
- Measures interstitial glucose every 5 minutes
- Alerts user to high and low glucose values
  - Also predicted “highs” and “lows”
  - Rate changes
- 4th era in diabetes management
CGM Components

- Sensor/transmitter
- Wireless monitor

CGM: Subcutaneous Sensor
Fingerstick “Snapshot” of BG

[Graph showing blood glucose levels at different times of the day, with points marked for Pre-Lunch at 80 mg/dL and Pre-Dinner at 121 mg/dL.]
CGM “Full Disclosure” of BG Trends
Types of Data: Real Time Trending

*(Understanding Pumps and CGMs, p.103)*
Types of Data:
Retrospective Trending
CGM: Short-Term Benefits

- Minimize extreme BG
- Immediate feedback impact of food/exercise/stress on BG
- Know direction BG is trending (whether pt needs more or less insulin)
- Adds meaning to fingersticks
Blinded vs Nonblinded CGM Tracings

- 21% less time <55 mg/dl, p-value <0.001
- 23% less time >240 mg/dl, p-value <0.001
- 26% more time in target (81 – 140 mg/dl), p-value <0.001

(Garg et al, Diabetes Care 27:1922, 2004)
CGM: Long-Term Benefits

- Reduce HbA1c
- Identify patterns
- Test and fine-tune basal, ISF, and I:C
- Improve hypoglycemia unawareness
HbA1c: Comparing CGM with SMBG and SAP

### Table 2. Summary of the Subgroup Analyses in the Between-Group Change From Baseline HbA$_{1c}$ Among Patients With T1DM Comparing rt-CGM with SMBG

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Studies Included (Participants Included), n (n)</th>
<th>Mean Difference in HbA$_{1c}$ (95% CI), %</th>
<th>$p$, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All studies*</td>
<td>8 (1066)$^\dagger$</td>
<td>$-0.26$ ($-0.33$ to $-0.19$)</td>
<td>66.6</td>
</tr>
<tr>
<td>Adults $\geq 18$ y$^\ddagger$</td>
<td>3 (312)$^\S$</td>
<td>$-0.38$ ($-0.53$ to $-0.23$)</td>
<td>77.3</td>
</tr>
<tr>
<td>Children $&lt;18$ y$</td>
<td></td>
<td>$</td>
<td>5 (434)$^\P$</td>
</tr>
<tr>
<td>Adherence $&gt;60%$</td>
<td>7 (705)$^{**}$</td>
<td>$-0.36$ ($-0.44$ to $-0.27$)</td>
<td>40.8</td>
</tr>
</tbody>
</table>

HbA$_{1c}$ = hemoglobin A$_{1c}$; rt-CGM = real-time continuous glucose monitoring; SMBG = self-monitoring of blood glucose; T1DM = type 1 diabetes mellitus.

* Three studies (53–55) reported results combining all age groups.
+ References 53 to 60.
$^\ddagger$ Only patients aged $\geq 25$ y in reference 56 were included in this subgroup analysis.
$^\S$ References 56, 57, and 59.
$||$ Only patients aged $<15$ y in reference 56 were included in this subgroup analysis.
$^\P$ References 56 to 60.
$^{**}$ References 53 to 59.
Sensor Adherence and Difference in HbA1c Between rt-CGM and SMBG

CGM in Pediatrics: Consensus Statement

- RT-CGM: effective for lowering HbA1c, reaching target HbA1c and reducing MAGE without increased frequency of severe hypoglycemia.
- RT-CGM: Effective for reducing severe hypoglycemia & reducing time spent in hypoglycemic range.
- Effectiveness of RT-CGM in pediatric population with T1D significantly related to amount of sensor use.
- SAP effective means to treat youth of all ages at onset of disease.
- SAP effective in lowering HbA1c among those with elevated HbA1c on MDI with SMBG.
- Intermittent, retrospective or real-time CGM can be used to detect dawn phenomenon, post-prandial hyperglycemia, asymptomatic & nocturnal hypoglycemia & evaluating effects of changes in treatment.
CGM in Pregnancy

Comparison of risk transform functions

Mean HbA1c levels every four weeks in women receiving standard antenatal care (n=33) or antenatal care plus continuous glucose monitoring (n=38).

Murphy H R et al. BMJ 2008;337:bmj.a1680
Distribution of birthweight standard deviation scores for 62 healthy living singletons of mothers in continuous glucose monitoring arm (n=32) or standard antenatal care arm (n=30). *Infants of mothers who withdrew from intervention arm (included in intention to treat analysis).

Murphy H R et al. BMJ 2008;337:bmj.a1680
RT-CGM in Pregnancy

CGM in Type 2 Diabetes

• Adults with type 2 diabetes NOT on prandial insulin had A1c decrease (mean – 1.16% over a year) with RT-CGM used intermittently for 12 weeks.

• CGM tracings can prompt changes in lifestyle or adherence to medications more so than SMBG

Vigersky R A et al. Dia Care 2012;35:32-38
CGM: Indications
CGM: Indications

- Those with type 1 diabetes and ...
  - Hypoglycemic unawareness/frequent hypoglycemia “judged to be excessive, potentially disabling or life-threatening”
  - Excess glycemic variability
  - Requiring HbA1c reduction without increased hypoglycemia
  - Preconception and pregnancy

- Children and adolescents with HbA1c <7% (highly motivated patient and family)

- Youth with HbA1c >7% who will use it on a near-daily basis
CGM: Indications (cont)

- Good candidates but trial for 2-4 weeks recommended
  - Youth with frequent SMBG
  - Committed families of young children (<8 years), especially if problems with hypoglycemia.
CGM: Available Options
Medtronic Guardian® Real-time

- Integrated with MiniMed Paradigm® Revel insulin pump
- Predictive alerts
- FDA approved for children
- FDA approved for 3 day use
- Data downloadable to online program with detailed analysis & excellent graphics
- Accuracy: MARD = 20%
- Introducer needle: 22 gauge
- Lag time 10-20 minutes
- Data withheld if miss calibration
- Must calibrate when blood glucose is stable
Dexcom G4™ Platinum

- Can be worn with any therapy
- Can input insulin, activity, illness
- Customizable alerts (including high-volume)
- FDA approved for 7 days
- Data downloadable to software with detailed analysis and graphics
- Accuracy: MARD = 13%
- Introducer needle 26 gauge
- Lag time 5-10 minutes
- Can calibrate regardless of rate of change
- Acetaminophen falsely elevates readings
- Plans for integration with: Animas (Vibe), Tandem etc.
Differences Between Systems

<table>
<thead>
<tr>
<th></th>
<th>MARD</th>
<th>% in Clark A</th>
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<tbody>
<tr>
<td>SMBG</td>
<td>10-15%</td>
<td></td>
</tr>
<tr>
<td>Dexcom Seven Plus™</td>
<td>15.9%</td>
<td>69%</td>
</tr>
<tr>
<td>Dexcom G4™</td>
<td>14%</td>
<td>78%</td>
</tr>
<tr>
<td>Medtronic Paradigm®</td>
<td>19.7%</td>
<td>61.7%</td>
</tr>
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Using CGM Data in Patient Care
Using CGM Info

• Download review:
  o Basal check
  o Insulin:carb check
  o Correction factor check
  o Trending

• Real-time data:
  o Adjust correction factor and I:C for hyper- and hypoglycemia
  o Glucose if dropping
  o “Stay between the lines”
Downtrending Blood Glucose

- Predictive hypo or 1 arrow down and stabilizing:
  - Less treatment
    - Less than usual carbs for correction
    - Medium GI food
    - Decrease bolus 10%
- Hypo alert or rapid drop (2 arrows down):
  - Aggressive treatment:
    - High GI food
    - Full or increased carbs
    - Decrease bolus 20%
Uptrending Blood Glucose

- BG stable - flat
  - Usual I:C + ISF
- BG rising gradually (1 arrow up)
  - Increase bolus 10%
- BG rising sharply (2 arrows up)
  - Increase bolus 20%
Future of CGM
Combined Technologies ➔ Artificial Pancreas

Artificial Pancreas

- Desired glucose level
- Glucose error signal = desired glucose level – actual glucose level
- Blood glucose feedback
- Sensed glucose level
- Continuous blood glucose monitoring
- Insulin Pump
  - Gain (insulin dose), bolus shaping (timing), adaptive filtering (learn from past experiences)
- Predicted Insulin Delivery
- Actual Insulin Need

Actual Endocrine Physiology

- Dynamic physiology (eating, exercise, stress and illness)
- Prevention of Long-term complications
- Happy User!

Actual glucose metabolism
Multiple Studies

• Multiple Groups
  • JDRF
  • Helmsley Trust
  • Government funding bodies
  • Medical device companies
  • Independent research groups

• Variations: CGM +
  • Insulin + glucagon
  • Insulin + pramlintide
  • Insulin + Heat patch
“Smart” Tattoos


Eye Sensor

Functional Contact Lens

Conclusions

• Diabetes is associated with long-term complications caused by “dysglycemia.”
• Adequately controlling blood glucose values without increasing the risk of hypoglycemia is difficult.
• Continuous glucose monitoring can help patients and their healthcare providers to optimize their diabetes regimen while limiting hypoglycemia.
• Current CGM systems use subcutaneous sensors that measure interstitial glucose electrochemically.
• Alternative approaches to continuous glucose monitoring are in development.
• Prediction: continuous glucose monitoring will be the standard of care.
References


Cryer PE. Hypoglycemia: the limiting factor in the glycaemic management of Type I and Type II diabetes. Diabetologia 2002; 45: 937-948.


Questions?