

Differentiation of Post-Prandial Glucose Profiles Using the FreeStyle Navigator® Continuous Glucose Monitoring System

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Abstract

Continuous glucose monitoring (CGM) provides an unprecedented opportunity to assess glucose fluctuations in a home use setting. Glycemic changes around meals have the potential to provide direct and accurate assessment of diabetes therapy. Meal profiles collected from a 40-day home use study with the FreeStyle Navigator system (investigational device) have been analyzed. Subjects (T1DM or T2DM, n=122) were masked to sensor data and alarms for the first 20 days and unmasked thereafter.

The system stored glucose values every 10 min and meal data entered by participants. Retrospectively, 4734 post-meal glucose profiles could be identified with ≥3 hrs between meals, at least 6 measurements spanning ≥120 min, and reported carbohydrate >20 grams. Profiles were categorized by the time of maximum glucose after the meal as “Early” (0-30 min), “Middle” (30-150 min) or “Late” (150-180 min) and by meal time. Glucose data were combined for all participants and mean and median glucose profiles were compared.

Frequencies were 17%, 62% and 21% for the Early, Middle, and Late categories, respectively. No differences were found between pump versus MDI, type of diabetes, or between the masked and unmasked study phases (likely due to study design). The distribution at lunch (18%, 59%, 23%) was similar to overall, but different at breakfast (10%, 74%, 16%) and dinner (22%, 55%, 23%). Figure 5 shows Early profiles had high premeal glucose (198±66 mg/dL, mean±SD) and steadily fell thereafter. Late profiles had a premeal glucose of 130±52 mg/dL and steadily increased to 231±70 mg/dL. Middle profiles starting at 150±51 mg/dL had an increase and decrease peaking ~75 min, but did not return to baseline within 3 hrs.

Use of CGM identified a variety of glucose profiles around meals. Premeal glucose values are likely to affect insulin dosing decisions, which appear more aggressive for Early and insufficient for Late profiles. Middle profiles may need improved balance of meal and insulin. While this protocol did not support therapy adjustment based on CGM, using CGM will enrich therapeutic knowledge and potentially aid tailoring of individual therapy in the future.

Study Protocol

This multi-center clinical study, sponsored by Abbott Diabetes Care, enrolled a total of 137 patients at six clinical centers. Subjects used the FreeStyle Navigator system for 40 consecutive days. For the first 20 days subjects were masked to glucose data. Glucose data was displayed (unmasked) for the following 20 days. Subjects were asked to maintain the same insulin therapy regimen over the entire study.

Sensor insertions were performed by subjects either in the arm or the abdomen. Subjects performed sensor or calibrations with finger capillary BG values obtained at approximately 10, 12, 24 and 72 hours after insertion using the built-in FreeStyle blood glucose meter.

The system recorded glucose measurements every ten minutes and meal times and carbohydrate intake estimates as entered by the subjects. 122 of 137 enrolled subjects at the six clinical centers entered meal times during CGM.

The glucose profiles that met the acceptance criteria were analyzed to determine the premeal glucose (closest within 30 minutes before meal), maximum glucose, time of maximum, minimum, 2-hour and 3-hour post-prandial values.

FreeStyle Navigator System

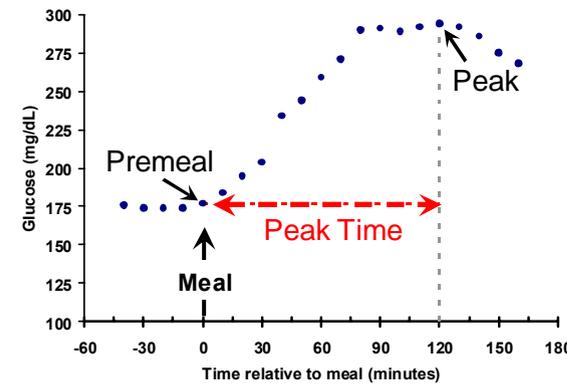
FreeStyle Navigator Continuous Glucose Monitoring System measures interstitial fluid glucose in subcutaneous tissue every minute. The system consists of a disposable five-day sensor, a reusable transmitter and a handheld receiver with a built-in FreeStyle® blood glucose meter.

The sensor uses Wired Enzyme™ amperometric technology to convert interstitial fluid glucose into an electrical signal which is calibrated to give real-time glucose values. The system was developed by Abbott Diabetes Care and is currently available for Investigational Use Only.



Methods

Figure 1. Example Post-Prandial Glucose Profile.



Post-prandial glucose profiles meeting the following criteria were included in this analysis:

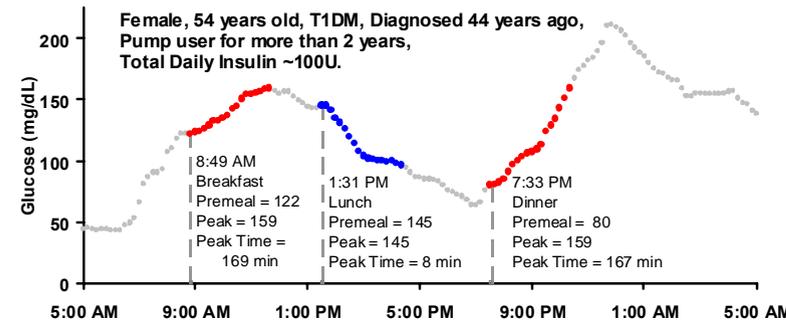
- No other meal recorded within 3 hrs.
- Carbohydrate intake of at least 20 grams.
- At least 1 CGM value in the 30 min prior to the meal.
- At least 6 CGM values spanning at least 2 hours of the post-prandial period.

The meals were assigned according to time of day:

- Breakfast: 12AM to 10AM
- Lunch: 10AM to 4PM
- Dinner: 4PM to 12AM

Results

Figure 2. 24-Hour Example of Meals and FreeStyle Navigator Measurements



The three distinct times of post-prandial glucose peaks and their observed properties were:

- Early** – Peak within 30 minutes of the meal, associated with above target premeal glucose values that return to target within 3 hours of the meal.
- Middle** – Peak between 30 and 150 minutes after the meal, associated with premeal glucose values within or just above target and glucose returning to near target within 3 hours of the meal.
- Late** – Peak later than 2.5 hours after the meal, associated with premeal glucose values within or just below target, rising well above target 3 hours after the meal.

Figure 3. Distribution of Post-Prandial Glucose Peak Times.

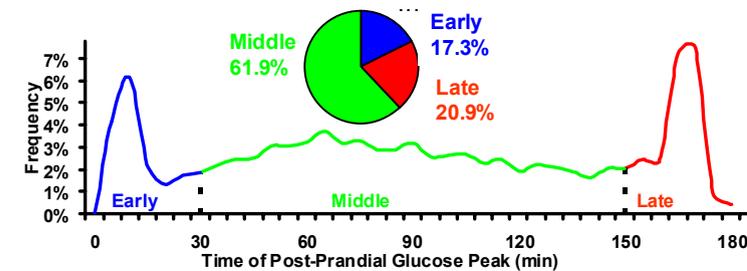


Figure 4. Frequency of Post-Prandial Peak Categories per Subject.

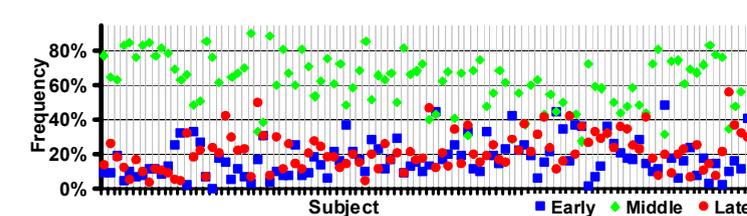


Figure 5. Glucose Profiles for Peak Categories.

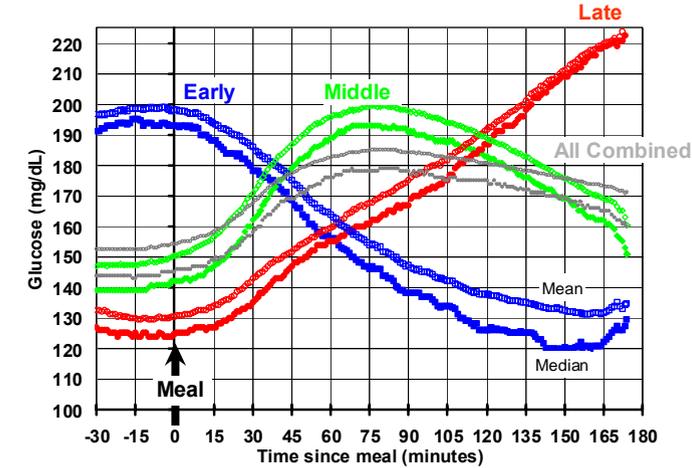


Table 1. Frequencies of Post-Prandial Peak Categories by Meal, Study Phase, Diabetes Type and Pump Use.

	n	Early	Middle	Late	p*
All meals	4734	17.3%	61.9%	20.9%	-
Breakfast	1407	10.2%	74.1%	15.7%	-
Lunch	1559	18.3%	58.9%	22.8%	<0.0001
Dinner	1768	21.9%	54.7%	23.4%	-
Masked Phase	2493	17.6%	61.5%	20.9%	0.569
Unmasked Phase	2241	16.8%	62.3%	20.9%	-
T1DM	3567	17.3%	62.3%	20.5%	0.314
T2DM	1167	17.2%	60.6%	22.2%	-
Pump Users	2391	17.7%	60.9%	21.4%	-
Non-Pump Users	2343	16.8%	62.8%	20.4%	0.198

* p-value comparing Middle category frequencies by χ^2 statistic.

Table 2. Glucose Profile Metrics by Peak Categories.

Median [25th, 75th percentile]	Early	Middle	Late	All Combined
Premeal Glucose	193 [153, 239]	142 [103, 186]	125 [93, 160]	145 [106, 192]
Post-Prandial Peak	194 [155, 240]	211 [169, 260]	218 [169, 262]	208 [166, 257]
Peak Time (min)	8 [5, 17]	82 [58, 111]	163 [160, 167]	85 [45, 139]
Post-Prandial Minimum	109 [77, 154]	125 [91, 168]	118 [85, 153]	120 [86, 162]
Post-Prandial Excursion ^a	70 [44, 105]	76 [52, 106]	85 [57, 126]	77 [52, 110]
Post-Prandial Delta ^b	-1 [-6, 8]	59 [32, 95]	78 [45, 122]	51 [18, 92]
2hr Post-Prandial Glucose	127 [93, 175]	183 [137, 236]	185 [143, 235]	175 [128, 228]
3hr Post-Prandial Glucose	123 [91, 167]	162 [118, 213]	216 [169, 261]	166 [120, 220]

^aExcursion defined as post-prandial peak minus post-prandial minimum.

^bDelta defined as post-prandial peak minus premeal glucose.

Note: All values in mg/dL except post-prandial peak time.

Discussion and Conclusions

Combining automatic CGM and accurate meal times allows a feasible means to examine post-prandial glucose profiles in a realistic, home use setting. CGM enables detection of both the time and amplitude of post-prandial glucose peaks.

The present study identified three major categories of post-prandial glucose profiles, revealing the variety of challenges patients face related to glucose levels when making mealtime therapy decisions. The post-prandial glucose profiles were not simply amplified versions of the “bolus-shaped” profile observed in people without diabetes. Three distinct profiles over time, or “peak categories” were observed (Figure 3).

Individual subjects were observed to have all three peak categories in almost all cases, with middle peak category frequency ranging from 30% to 90% (Figure 4). The variability of peak frequency was not easily explained by pump usage or diabetes type (Table 1) and warrants further investigation.

Middle peak category frequency was found to be significantly greater at Breakfast compared to Lunch and Dinner (Table 1). Middle and Late profiles had similar 2 hour post-prandial glucose values, but continued in opposite trends (Figure 5, Table 2). Early and Late profiles had extremely different premeal glucose values (Table 2). Combining all peak categories showed a potentially misleading post-prandial glucose profile that dampened the excursion and removed detail of peak time. (Figure 5, Table 2).

Dividing peak categories may identify treatment behaviors:

- Early profiles may have been corrections required from prior imbalances of therapy that caused high glucose. Therapy challenges such as dose timing and amount, rapidly changing glucose levels, gastroparesis, food content, or illness may have contributed to these situations.
- Middle profiles showed expected post-prandial glucose behavior, but still show a need to improve glucose levels before meals and the amplitude of excursions after meals, perhaps by tuning dose timing and amount.
- Late profiles may have resulted from incorrect dose timing or inadequate dose amount at mealtimes, perhaps due to over-caution when below ~125 mg/dL.

This observational study highlights the challenges of improving therapy around meals, and identifies the benefits of CGM to address these challenges by providing the opportunity to inform on-going, individualized diabetes therapy.

Acknowledgements

We gratefully acknowledge the efforts of the site study teams headed by doctors Bruce Bode, Richard L. Weinstein, Sherwyn L. Schwartz, David Kendall, Richard Bergenstal, Richard Bernstein, and Samer S. El Deiry.