Glycemic Index Predicts Individual Glucose Responses after Self-Selected Breakfasts in Free-Living, Abdominally Obese Adults¹–³

Angela M. Kochan,⁴,⁵,⁹ Thomas M. S. Wolever,⁴*,⁶ V. Tony Chetty,⁶ Sonia S. Anand,⁴–⁷ Hertzel C. Gerstein,⁵–⁸ and Arya M. Sharma⁵,¹⁰

¹Department of Nutritional Sciences, University of Toronto, Toronto, Ontario, Canada; and ²Department of Medicine, ³Department of Clinical Epidemiology and Biostatistics, and ⁴Population Health Research Institute, McMaster University, Hamilton, Ontario, Canada

Abstract

The degree to which an individual’s glycemic response to a meal is determined by the glycemic index (GI) and other components of the meal remains unclear, especially when meals are not consumed in a highly controlled research setting. To address this question, we analyzed data collected during the run-in period of a clinical trial. Free-living, non-diabetic adults (n = 57) aged 53.9 ± 9.8 y (mean ± SD) with a BMI of 33.9 ± 5.3 kg/m² and waist circumference of 109 ± 11 cm underwent a 75-g oral glucose tolerance test (OGTT) and, on a separate day, wore a continuous glucose-monitoring system (CGMS) for 24 h during which time they recorded all foods consumed. The protein, fat, and available carbohydrate (avCHO) content and GI of the breakfast meals were calculated from the food records and the incremental areas under the glycemic response curves (iAUC) for 2 h after breakfast (iAUCbreakfast) were calculated from CGMS data. Values for iAUCbreakfast, avCHO, fat, fiber, and BMI were normalized by log-transformation. The ability of participant characteristics and breakfast composition to predict individual iAUCbreakfast responses was determined using step-wise multiple linear regression. A total of 56% of the variation in iAUCbreakfast was explained by GI (30%; P < 0.001), iAUC after the OGTT (11%; P < 0.001), avCHO (11%; P < 0.001), and waist circumference (3%; P = 0.049); the effects of fat, protein, dietary fiber, age, sex, and BMI were not significant. We concluded that, in free-living, abdominally obese adults, GI is a significant determinant of individual glycemic responses elicited by self-selected breakfast meals. In this study, GI was a more important determinant of glycemic response than carbohydrate intake.


Introduction

The GI¹¹ was developed in 1981 as a classification of the blood glucose-raising potential of carbohydrate-containing foods (1).

¹ Supported by the Institute of Nutrition, Diabetes and Metabolism, Canadian Institutes of Health Research, the Heart and Stroke Foundation of Ontario, and Boehringer Ingelheim Canada, Ltd. Medtronic, Inc. kindly donated the continuous glucose monitoring devices and probes.

² Author disclosures: T.M.S. Wolever is president of Glycemic Index Laboratories, Inc., a contract research organization; president of Glycaemic Index Testing, Inc., which provides laboratory services; and is coauthor of a range of popular diet books about the glycemic index. A. M. Kochan, V. T. Chetty, S. S. Anand, H. C. Gerstein, and A. M. Sharma, no conflicts of interest.

This trial was registered at clinicaltrials.gov as NCT00147264.

² This trial was registered at clinicaltrials.gov as NCT00147264.

³ Present address: School of Community and Liberal Studies, Sheridan Institute of Technology and Advanced Learning, Brampton, Ontario, Canada.

¹⁰ Present address: Department of Medicine, University of Alberta, Edmonton, Alberta, Canada.

¹¹ Abbreviations used: avCHO, available carbohydrate (total carbohydrate minus dietary fiber); CGMS, continuous glucose-monitoring system; GI, glycemic index; 2hPGC; plasma glucose 2 h after 75 g oral glucose; iAUC, incremental area under the glycemic response curve; iAUCbreakfast, iAUC for 2 h after breakfast; iAUCOGTT, iAUC for 2 h after 75 g oral glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test.

* To whom correspondence should be addressed. E-mail: thomas.wolever@utoronto.ca.

Low-GI diets improve glycemic control in diabetes (2,3) and may decrease the risk of developing type 2 diabetes (4). However, there is controversy about the relevance of GI for free-living individuals because of concerns that it is difficult to choose low-GI foods, that GI values are imprecise, and that the GI does not predict the glycemic responses of individuals consuming normal mixed meals due to the high day-to-day variation of glycemic responses and the confounding effects of fat and protein (5–9). Previous studies showed that GI predicts the postprandial glucose responses elicited by mixed meals in groups of normal individuals (10,11), adults with type 2 diabetes (12), and youths with type 1 diabetes (13). However, because these studies examined the mean glycemic responses of groups of participants under controlled conditions, the degree to which an individual’s glycemic response to self-selected meals is determined by the GI remains unclear. Variation in glycemic responses arises from at least four major sources: diurnal variation (time of day), meal-related factors, participant-related factors (between-individual variation), and unexplained day-to-day variation (within individuals) (14). We hypothesized that, after controlling for the effects of other variables, GI would be a significant determinant of individual glycemic responses. To
test this, we studied free-living, abdominally obese adults after they consumed self-selected breakfast meals. Only breakfast meals were included to remove the confounding effects of diurnal variation. Abdominally obese adults were studied, because they represent a population at high risk for developing type 2 diabetes and may benefit from dietary approaches to reducing risk for diabetes.

Research Design and Methods

We report the results of an analysis of data collected during the run-in period of a randomized clinical trial to determine the effects of a low-GI diet and telmisartan on intra-myocellular fat (TRIM study). Participants were males and nonpregnant, nonlactating females aged 30–70 y with a waist circumference >102 cm for males and >88 cm for females and fasting plasma glucose <7.0 mmol/L on screening. Exclusion criteria included a history of diabetes mellitus or use of any antidiabetic drug, uncontrolled hypertension, serum TG >10 mmol/L, active malignancy, chronic inflammatory disorders, endocrine dysfunction, renal dysfunction, hepatic dysfunction, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers in the last 3 mo, and use of a lipid-lowering medication, the dose of which had not been stable for at least 3 mo. The protocol was approved by the research ethics board of Hamilton Health Sciences, McMaster University, and all participants gave informed consent prior to entering the study.

After recruitment, the study participants underwent a 6-wk run-in period during which time there were three dietary counseling visits at which participants were given advice on a low-fat diet (<30% of energy from total fat and <10% saturated fat). One to 2 wk before the end of the run-in period, participants underwent 24-h continuous glucose monitoring for 3 d using a Medtronic MiniMed CGMS monitor. The CGMS monitor included a sensor that was inserted using a sensor inserter applicator into the s.c. adipose tissue of the abdominal area, a monitor that recorded a mean of 30 signals from the sensor every 5 min for a total of 288 readings for a 24-h period, and a docking station that downloaded the data into a computer. The participants were instructed on the use of a blood glucose meter to enter four blood glucose values per day to calibrate the CGMS monitor. Starting on the second day of CGMS monitoring, participants were asked to record their food intake for 3 d in a food diary. The 3-d food diary was returned by the participant and analyzed using the Food Processor SQL Nutrition Analysis and Fitness software package version 9.5 (ESHA Research) for macronutrient composition as a measure of the participant’s habitual dietary intake at baseline for use in the long-term trial. For the purposes of this report, we used the composition of the breakfast meal during 1 of the 2 d that included the CGMS monitoring. The GI of the meal was calculated separately as described below. If valid data, as defined below, existed for more than one breakfast meal, one meal per participant was chosen at random for analysis. At the end of the run-in period, participants underwent a 75-g OGTT after an overnight fast; blood glucose was measured 15, 30, and 60 min after ingestion of the glucose load and at 120 min after starting the glucose drink. Fasting blood glucose was taken to be the mean of the three readings following the fast.

All individuals recruited for the TRIM study were eligible to be included in the present analysis, but, in addition, all of the following criteria had to be met: food intake, including a breakfast meal (defined as first food intake before noon of >99 kcal), recorded for at least 1 d of CGMS monitoring; valid and complete CGMS data on the day food intake was recorded (defined as the existence of 288 sensor readings, at least three meter readings entered by the participant, and no sensor errors detected); the time between breakfast and the next food intake being at least 2 h (because GI is a measure of glycemic response over 2 h); and the existence of a complete and valid OGTT. The start of breakfast for the CGMS data analysis was determined by examining the CGMS glucose values near the time the participant indicated that breakfast was consumed to find when blood glucose started to increase, defined as when the second of two successive glucose readings differed by ≥0.2 mmol/L from the first. Fasting blood glucose was taken to be the mean of the four values (0, 5, 10, and 15 min) before the first increase in blood glucose. The glycemic response was measured for 120 min (24 readings) after the start of breakfast.

All data are presented as means ± SD unless otherwise indicated. Calculations for iAUCbreakfast and iAUCOGTT, ignoring area beneath the baseline, were determined as previously described (13). The GI of the breakfast meal, calculated as the sum for all foods in the breakfast meal, of GI × g f/g f, where g f is the amount of avCHO in the portion of food consumed, GI f is the GI of that food (glucose = 100), and g b is the amount of avCHO in the breakfast meal (11). The GI values for the foods were derived from published tables by using locally tested values where possible as previously described (11). The values for iAUCbreakfast were divided into tertiles, and the mean values for iAUCOGTT, protein, fat, avCHO, fiber, and GI for participants within the iAUCbreakfast tertiles were compared by ANOVA. The independent contributions of iAUCOGTT, BMI, waist circumference, protein, fat, avCHO, fiber, and GI to predicting iAUCbreakfast was determined by step-wise multiple linear regression (Lotus 123, Lotus Development) using the step-up procedure (16), with age and sex included in all models (because some anthropometric and breakfast intake variables were significantly related to age and sex). The variable with the most significant correlation with iAUCbreakfast was added to the model first, all remaining variables were then tested, and the most significant added sequentially to the model until no further significant reduction in the residual variation was obtained. Prior to regression analysis, non-normally distributed variables based on D’Agostino’s test (iAUCbreakfast, avCHO, BMI, fat, and fiber) were normalized by log-transformation. The criterion for significance was taken to be 2-tailed P < 0.05, with comparisons between individual means adjusted for multiple comparisons using Tukey’s method.

Results

Of the 121 participants recruited for the main study, 93 agreed to CGMS monitoring and of these 57 met the inclusion criteria (Table 1). Reasons for exclusion were: CGMS criteria not met (n = 11), no food diary recorded (n = 9), incomplete OGTT results (n = 7), did not eat breakfast (n = 1), or dropped out after CGMS inserted (n = 8). The OGTT showed 36 participants with normal fasting glucose (<5.6 mmol/L) of whom 19 had normal 2hPCG (<7.8 mmol/L), 16 had IGT (7.8 ≤ 2hPCG < 11.1 mmol/L), and 1 had diabetes (2hPCG ≥ 11.1 mmol/L); 20 participants had impaired fasting glucose (5.6 ≤ fasting glucose < 7.0 mmol/L) of whom 8 had normal 2hPCG, 6 had IGT, and 6 had a diabetic 2hPCG; 1 individual had diabetic values for both
fasting and 2hPCG. Participants with diabetes based on the OGTT had higher iAUCOGTT (mean ± SD, 405 ± 41 vs. 232 ± 74 mmol × min/L) and iAUCbreakfast (204 ± 92 vs. 114 ± 83 mmol × min/L) than those without diabetes, but avCHO intake (60 ± 21 vs. 68 ± 40 g, respectively) and GI (64 ± 10 vs. 60 ± 9) at breakfast did not significantly differ.

Mean fasting glucose before breakfast was similar across the tertiles of iAUCbreakfast (Table 1), but participants in the highest tertile had significantly higher glycemic responses after breakfast (Fig. 1), higher fasting glucose before the OGTT, and a higher glycemic index (Table 1). Despite large ranges of intakes of avCHO, fat, protein, and fiber, only GI significantly differed between the highest and lowest tertiles of iAUCbreakfast (Table 1).

Neither iAUCOGTT nor iAUCbreakfast were significantly related to age, sex, BMI, waist circumference, protein, or fiber; however, iAUCOGTT was related to iAUCbreakfast (Table 2). There was no significant relationship between avCHO intake and GI. When considered individually, the variable that explained most of the variation in iAUCbreakfast was GI (r² = 0.30) followed by 2hPCG (r² = 0.16), iAUCOGTT (r² = 0.14), and avCHO (r² = 0.12). Multiple regression analysis showed that, whereas age and sex were not significantly related to iAUCbreakfast, GI, iAUCOGTT, and avCHO had significant independent effects that together explained 56% of the variation in iAUCbreakfast (Table 3); waist circumference, BMI, protein, fat, and fiber had no significant effects when added to the model.

When the 8 participants with diabetes by OGTT or fasting glucose were excluded, the results of multiple regression analysis were similar to those for the total population, with age (standardized β = –0.15 ± 0.11; P = 0.17), sex (standardized β = 0.16 ± 0.14; P = 0.24), GI (standardized β = 0.51 ± 0.11; P < 0.001), avCHO (standardized β = 0.45 ± 0.13; P = 0.001), and iAUCOGTT (standardized β = 0.28 ± 0.12; P = 0.018) explaining 51% of the variation in iAUCbreakfast.

**Discussion**

The results showed that in free-living participants with nondiabetic fasting glucose on recruitment, a high waist circumference, and a wide range of nutrient intakes, the GI of self-selected breakfast meals varied over a considerable range and was a highly significant determinant of individual glycemic responses. The 2.3-fold variation in meal GI (37–85) was a more important determinant of iAUCbreakfast than the 13.8-fold variation in recorded avCHO intake (16–222 g). The variation in recorded protein (3–43 g), fat (1–28 g), and fiber (0–56 g) intakes had a negligible effect.

The present results are consistent with those of previous studies (11,17) showing that GI was a significant determinant of the glycemic response elicited by mixed breakfast meals containing variable amounts of energy, avCHO, protein, fat, and fiber. In the present study, however, avCHO and GI together explained ~40% of the variation in iAUC compared to ~90% in previous studies. There are two main reasons for this; one is...
because each value of iAUC used in the regression analysis was the response of a single individual on one occasion as opposed to the mean for 8–12 individuals in previous studies. Because the within-individual CV (100 × SD/mean) of glycemic responses is ~2.5% (15), the 95% CI of an individual response (mean ± 2 SD) covers a 3-fold range (mean ± 50%). However, because 95% CI of the mean of n values is reduced by a factor of 1/√n, the 95% CI for 8–12 participants spans only a 1.4-fold range (mean ± 16%). The other reason is that in earlier studies, between-individual variation was reduced to zero by having every participant eat all the test meals. Here, because every participant ate different test meals, the variation in iAUCOGTT includes between-individual variation. We used iAUCOGTT to control for between-individual variation, but iAUCOGTT is an imprecise estimate of each person’s true response because of within-individual variation.

Upon enrollment, all participants met the eligibility criterion of fasting glucose (<7.0 mmol/L; i.e., nondiabetic). However, during the OGTT, 8 participants had 2hPG values in the diabetic range and one of these also had fasting glucose of 7.6 mmol/L, which is in the diabetic range. The differences in classification based on 2hPG compared to fasting glucose were not unexpected, because raised 2hPG tends to occur earlier in the natural history of type 2 diabetes than raised fasting glucose (18) and studies show that when people not known to have diabetes are screened with an OGTT, 30–40% of those with a 2hPGC in the diabetic range have nondiabetic fasting glucose (19–21). Day-to-day variations in fasting glucose, occurring presumably due to variations in recent diet, activity, sleep, stress, and illness, may account for differences in classification of diabetes on repeated testing; even analytic variation (CV = 3%) is large enough to account for fasting glucose varying from 6.8 to 7.6 (± 6% of a true value of 7.2 mmol/L). We chose not to exclude participants who had diabetic 2hPCG from the primary analysis, because they met the inclusion criteria of a normal glycemic index; 2hPCG; plasma glucose 2 h after 75 g oral glucose; iAUCbreakfast, incremental area under the glycemic response curve for 2 h after breakfast; iAUCOGTT, incremental area under the glycemic response curve for 2 h after 75 g oral glucose; OGTT, oral glucose tolerance test.

Our results showed that variation in the protein and fat content of self-selected breakfast meals had a negligible effect on the glycemic responses they elicited. It is generally considered that protein and fat reduce glycemic responses by delaying gastric emptying and increasing insulin secretion (6,22). The interquartile ranges (25th–75th percentiles) for our participants’ protein and fat intakes were 10–20 and 3–10 g, respectively, and the 10th and 90th percentiles were 8–27 and 2–13 g. Thus, the variation in protein and fat intakes in our population was within the range used in previous studies examining whether adding 10–20 g protein or 5–15 g fat to avCHO reduces glycemic responses. However, the results of these studies are inconsistent; the effect of 10–20 g protein

### TABLE 2

| Correlation grid among study variables
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic/anthropometric</strong></td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>iAUCbreakfast</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
</tr>
<tr>
<td>Waist, cm</td>
</tr>
<tr>
<td>avCHO, g</td>
</tr>
<tr>
<td>GI</td>
</tr>
<tr>
<td>Fiber, g</td>
</tr>
<tr>
<td>Protein, g</td>
</tr>
<tr>
<td>Fat, g</td>
</tr>
<tr>
<td>2hPOG, mmol/L</td>
</tr>
</tbody>
</table>

1 Values are Pearson correlation coefficients, n = 57 participants: *P < 0.05; +P < 0.01; +P < 0.001. avCHO, available carbohydrate (total carbohydrate minus dietary fiber); GI, glycemic index; 2hPCG; plasma glucose 2 h after 75 g oral glucose; iAUCbreakfast, incremental area under the glycemic response curve for 2 h after breakfast; iAUCOGTT, incremental area under the glycemic response curve for 2 h after 75 g oral glucose; OGTT, oral glucose tolerance test.

2 Sex, 0 = male, 1 = female

3 Values normalized by log-transformation.

### TABLE 3

| Results of step-wise multiple linear regression analysis with log(AUCbreakfast) (mmol × min/L) as the dependent variable
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Independent variables</strong></td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Step 1</td>
</tr>
<tr>
<td>Step 2</td>
</tr>
<tr>
<td>Step 3</td>
</tr>
<tr>
<td>Step 4</td>
</tr>
</tbody>
</table>

1 Values are standardized β coefficients ± SEM, n = 57: *P < 0.01; +P < 0.001. avCHO, available carbohydrate (total carbohydrate minus dietary fiber); AUCOGTT, area under the glycemic response curve for 2 h after 75 g oral glucose; GI, glycemic index.
varies from none (23,24), to modest (15–40%) (25,26), to large (40–50%) (27), and the effect of 5–15 g fat varies across a similar range (25,26,28–31). The present results do not challenge the concept that adding fat and protein to avCHO reduces glycemic responses; rather, they challenge the ability to extrapolate the results of this experimental design to normal mixed meals. The experimental model of adding protein or fat to a fixed amount of avCHO does not reflect normal eating patterns in which meals vary in the amounts of all the nutrients they contain. To maintain energy balance, meals high in protein or fat would be low in avCHO; the latter would have more influence on the glycemic response than the former. For example, adding 15 g fat to 50 g avCHO from bread would reduce the glycemic response by ~20% (30); however, to make the meal isocaloric, the amount of avCHO would have to be reduced to 16 g, which would reduce the glycemic response by ~55% (32).

A perceived barrier to the clinical use of GI is a concern that it limits food choice (33). However, many commonly eaten foods have a low GI; in this study, 28% of self-selected breakfast meals had a low GI (i.e., ≤55). Thus, the barrier may not be that it is limiting to choose low GI foods because they are uncommon, but rather because it is difficult to know which specific foods have a low GI. This difficulty arises because most foods are not labeled with their GI value, and the GI values of foods reported in the International GI Tables vary considerably; e.g., there are 100 GI values for various types of rice (34); 34% are <6 (low GI) and 33% are >69 (high GI). The present results do not address this issue directly, although they show it is possible to select GI values for the foods recorded on a food record that predict the glycemic response elicited by a mixed meal. It has been suggested that the variation in GI values for similar foods is due to imprecise method of measuring GI (8); however, when performed correctly, the GI method is precise enough to distinguish between high- and low-GI foods with 95% certainty (35). This suggests that the variation of GI values for similar foods arises either from use of incorrect methods or from real differences among foods due to differences in starch structure (36–38) related to genetic variety (39,40), food processing, cooking, storage, and serving methods (41–43).

Because we considered only the glycemic response elicited by breakfast, the present results cannot necessarily be extrapolated to other meals of the day. The glycemic response after lunch (and possibly dinner) depends on many factors other than the composition of the meal; these include the composition of the previous meal (44–48), the time interval between meals (49,50), and the time of day (51,52). Other weaknesses of the present study include that facts that less than one-half of the eligible participants (57 of 121 or 47%) were included in the study and that the number included was small in relation to the number of variables available for inclusion into the multiple regression model. Thus, the results need to be interpreted with caution. In addition, the results are only applicable to the population studied and are limited to the range of nutrient intakes selected by the participants. The relative importance of the variables studied here in determining glycemic responses may vary in different populations; e.g., BMI is a significant determinant of glycemic response in the general population (35) but had no significant effect here, presumably because all participants were abdominally obese.

We conclude that, in free-living, abdominally obese adults, GI is a significant determinant of individual glycemic responses elicited by self-selected breakfast meals. In this study, GI was a more important determinant of glycemic response than avCHO intake.

Acknowledgments
A.M.S. and V.T.C. conceived of the overall project, obtained funding, and provided study oversight; A.M.K., T.M.S.W., V.T.C., S.S.A., H.C.G., and A.M.S contributed to the planning and design of the study; A.M.K. conducted the research; T.M.S.W. and A.M.K. performed statistical analysis of the results reported here; A.M.K. drafted the manuscript; and T.M.S.W. had primary responsibility for final content. All authors have read and approved the final manuscript.

Literature Cited