

Journal of Health, Sports, and Kinesiology, 2021, 2(3), 39-40. <https://doi.org/10.47544/johsk.2021.2.3>
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15 ■ ORIGINAL RESEARCH

The combination of novel biomarkers identifies individuals of heighten risk for type 2 diabetes

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Keywords: oral glucose tolerance test, one-hour glucose concentration, glucose response curve

ABSTRACT

Introduction: In adults, both the glucose response curve (GRC) and one-hour glucose concentration (1HGC) during an oral glucose tolerance test (OGTT) have emerged as sensitive risk biomarkers for type 2 diabetes (T2D). Adults with monophasic response curve (MRC) compared with biphasic response curve (BRC) and 1HGC $\geq 155\text{mg/dL}$ (above155) compared with 1HGC $< 155\text{mg/dL}$ (below155) exhibited worse insulin sensitivity and β -cell dysfunction, indicating a high risk for T2D. Although those two biomarkers are derived from the same test, a recent study in youth found that only 50% of individuals with above155 had MRC (Cree-Green, JES, 2018), signifying a unique pathophysiology involved in those two. Currently, it is unknown if simultaneous use of GRC and 1HGC as a risk identification tool can provide a clinical relevance. Therefore, the purpose of this study is to investigate whether the combination of GRC and 1HGC can differentiate pathophysiological risk factors for T2D in Latino adults.

Methods: A total of 434 Latino adults (age 37.0 ± 9.5 [SD] years; 269F/165M; body mass index: 29.8 ± 5.6 kg/m^2) underwent a 2-hour OGTT (75g dextrose) and venous blood samples were obtained at -15, 0, 30, 60, 90, and 120 minutes for the measurement of glucose and insulin concentrations. All participants were divided into 4 groups based on their GRC and 1HG phenotypes: below155/biphasic (BB), above155/biphasic (AB), below155/monophasic (BM), and above155/monophasic (AM). Matsuda index (i.e., whole-body insulin sensitivity index) was calculated as $10,000/\sqrt{(\text{fasting glucose} \times \text{fasting insulin}) \times (\text{mean OGTT glucose} \times \text{mean OGTT insulin})}$, insulinogenic index (IGI) as $(\Delta\text{Ins}_{0-30})/(\Delta\text{Glu}_{0-30})$, and oral disposition index (oDI) as (Matsuda index \times IGI). One-way ANOVA with Bonferroni's post-hoc tests was used to examine differences in insulin sensitivity and β -cell function among 4 groups, significance was set at $p < 0.05$.

Results: There is a significant difference in Matsuda index among the four groups, with the two highest values observed in the group of BB and BM (6.3 ± 3.6 and 6.2 ± 3.7 , respectively) compared with the

other two including AB and AM (3.4 ± 2.0 and 4.1 ± 3.4 , respectively) (ANOVA $p<0.001$). Additionally, the similar pattern of the highest oDI being observed in the BB and BM groups (8.5 ± 5.6 and 8.1 ± 5.0 , respectively) compared with the other two of AB and AM (3.2 ± 2.1 and 3.1 ± 2.0 , respectively) was found (ANOVA $p<0.001$). However, there was no difference in IGI between the groups ($p=0.8$).

Conclusion: The combination of the GRC and 1HGC was able to identify adults who were pathophysiological progressed toward the development of T2D, evidenced by consistent observations of the above155 (regardless of their GRC phenotypes) having severe insulin resistance (lower whole-body insulin sensitivity) and worse β -cell function (lower oDI). It is notable that decrement of oDI is the best metabolic predictor of future T2D in adults. Prospective studies should be warranted to examine whether the combination of the novel biomarkers, GRC and 1HGC of 155 mg/dL, can predict future development of T2D.

Funding: National Institutes of Health/National Institute on Minority Health and Health Disparities (P20MD002316).

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