Estimation of Insulin Sensitivity from Continuous Glucose Monitoring Data During an Intravenous Glucose Tolerance Test

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Insulin sensitivity is an important physiological indicator describing the ability of insulin to facilitate the uptake of plasma glucose by muscle and adipose tissue cells, which often becomes impaired years prior to a type 2 diabetes (T2D) diagnosis. However, despite its importance in disease progression, current methods for estimating insulin sensitivity are costly, invasive, and time consuming as they require clinical testing in an in-patient setting. Continuous glucose monitors (CGMs) capture blood glucose profiles with greater granularity and frequency than before, opening the doorway for rapid, dynamic estimates of insulin sensitivity using a non-invasive method. Here, we recast an existing mathematical model describing the glucose-insulin dynamics during an intravenous glucose tolerance test (IVGTT) into a second-order single delay differential equation (DDE) model that no longer requires information about insulin to estimate the key physiological parameters governing human glucose metabolisms. Parameter estimation was performed by fitting the DDE model to CGM-obtained IVGTT glucose data from 42 healthy individuals using a modified-form of non-linear least squares. The estimated insulin sensitivity parameters for all the subjects were shown to be identifiable (CV < 0.52). Furthermore, the model-derived insulin sensitivity parameters showed a strong, linear correlation ($r = 0.89$) to the insulin sensitivity indices obtained from hyperinsulinemic-euglycemic clamp tests, the gold standard test for measuring insulin sensitivity. Thus, this novel methodology may aid attempts at early identification of prediabetics and T2D diagnosis by providing easier access to the state of an individual's glucose metabolism.