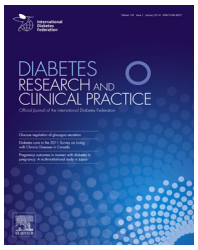
Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation



Do static and dynamic insulin resistance indices perform similarly in predicting pre-diabetes and type 2 diabetes?

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ARTICLE INFO

Article history:
Received 13 November 2013
Received in revised form
11 April 2014
Accepted 21 April 2014
Available online 30 April 2014

ABSTRACT

Aims: We designed a study to compare the predictive power of static and dynamic insulin resistance indices for categorized pre-diabetes (PDM)/type 2 diabetes (DM).

Methods: Participants included 1134 adults aged 18–60 years old with normal glucose at baseline who completed both baseline and 6-years later follow-up surveys. Insulin resistance indices from baseline data were used to predict risk of PDM or DM at follow-up. Two static indices and two dynamic indices were calculated from oral glucose tolerance test results (OGTT) at baseline. Area under the receiver operating characteristic curve (AROC) analysis was used to estimate the predictive ability of candidate indices to predict PDM/DM.

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Abbreviations: PDM, pre-diabetes; DM, diabetes; OGTT, oral glucose tolerance test; IFG, isolated impaired fasting glucose; IGT, isolated impaired glucose tolerance; IFG&IGT, combined IFG and IGT; AROC, area under the receiver operating characteristic curve; QUICKI, quantitative insulin sensitivity index; ISIgly_b, Belfiore (basal) index; ISI_0, 120Gutt insulin sensitivity index; SiM, Avignon's SiM; GEE, general estimation equation.

http://dx.doi.org/10.1016/j.diabres.2014.04.014

Keywords:
Insulin resistance indices
Predict
Pre-diabetes
Type 2 diabetes
Chinese
Adult

A general estimation equation (GEE) model was applied to assess the magnitude of association of each index at baseline with the risk of PDM/DM at follow-up.
Results: The dynamic indices displayed the largest and statistically predictive AROC for PDM/DM diagnosed either by fasting glucose or by postprandial glucose. The bottom quartiles of the dynamic indices were associated with an elevated risk of PDM/DM vs. the top three quartiles. However, the static indices only performed significantly to PDM/DM diagnosed by fasting glucose.
Conclusions: Dynamic insulin resistance indices are stronger predictors of future PDM/DM than static indices. This may be because dynamic indices better reflect the full range of physiologic disturbances in PDM/DM.

1. Introduction

Insulin resistance (IR) is typically defined as decreased sensitivity or responsiveness to the metabolic action of insulin, such as insulin-mediated glucose disposal and inhibition of hepatic glucose production. Insulin resistance plays a major pathophysiological role in the development of type 2 diabetes (DM) [1]. Both β-cell dysfunction and insulin resistance can be detected long before type 2 diabetes and pre-diabetes (PDM) within individuals with a family history of diabetes [2]. Therefore, the ability to accurately measure IR may enable the prediction of those at risk for PDM and DM and assist with targeted interventions.

IR can be quantified using detailed physiological protocols, such as the hyperinsulinemic–euglycemic clamp technique [3]. This method, however, is complicated, invasive and costly for use in large epidemiological studies. Accordingly, a number of surrogate indices have been proposed to estimate IR in large numbers of subjects [4]. These indices are formulated using static and dynamic insulin and glucose measurements during a glucose tolerance test (OGTT), and the criterion validity of these measurements has been demonstrated in various populations [4]. Although several studies have reported the degree to which these indices are able to predict DM in prospective analyses and have discovered a disparity in their predictive ability for DM [5–7], little research has been conducted to explore the reasons for such disparity. Given that the diagnostic criteria of DM embraces two glucose cutoffs, fasting and stimulated glucose concentrations, the predictive ability of IR indices may be dependent on the strength of their correlation with elevated fasting or stimulated glucose concentration at diagnosis. Thus, in predicting PDM/DM, those indices that correlate well with both glucose concentrations would perform better than other indices that correlate well with just one glucose concentration. However, this hypothesis has never been tested. The large dataset of the Anqing Twin Cohort, which includes data for OGTT at both baseline and follow-up and allows for the formulation of insulin sensitivity indices at baseline and categorization of PDM/DM at follow-up, provides a unique opportunity to investigate this hypothesis. We selected two static and two dynamic IR indices from a previous study [6] that exhibited the best predictive ability for DM, and compared their powers to predict categorized PDM/DM using longitudinal data from the Anqing Twin Cohort Study.

2. Methods and procedures

2.1. Study sample

We used data from the longitudinal Anqing Twin Cohort Study, which has been previously described [8]. Briefly, a baseline survey was carried out in eight rural counties of Anqing from 1998 to 2000; and follow-up data were collected from 2005 to 2006. OGTT was administrated at both the baseline and follow-up examination for diagnosis of PDM/DM. In addition, participants were invited to a central office to complete an interview-based questionnaire and physical exam at both times. Subjects were included in the present study if they met the following criteria: (1) age ≥ 18 at baseline; (2) without reported or diagnosed DM/PDM by OGTT at baseline; and (3) complete OGTT at both time points. After the exclusion of 10 subjects with outlier values (outside ± 3 standard deviation) for insulin resistance indices, 1134 subjects were eligible for this proposed study. The study protocol was approved by the Institutional Review Boards of Ann & Robert H. Lurie Children's Hospital of Chicago (formerly Children's Memorial Hospital), Chicago, USA and the Institute of Biomedicine, Anhui Medical University, Hefei, China. All participants gave written consent.

2.2. Anthropometric measures

Height was measured without shoes to the nearest 0.1 cm on a portable stadiometer. Weight was measured without shoes to the nearest 0.1 kg with the subject standing motionless in the center of a calibrated scale. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

2.3. Definition of insulin resistance/sensitivity indices and PDM/DM

OGTT was conducted using standard procedures in all subjects. A 75 g oral glucose equivalent load was administered after a 12–14 h fast. Blood specimens were obtained at 0 h and 2 h for the determination of plasma glucose and serum insulin concentration. Laboratory assay methods have been described previously [9]. We selected four IR indices with the best predictive ability for DM from a previous study [6] that assessed 19 IR indices in a multiethnic population. Definitions of the IR indices for QUICKI [10], ISIgly_b [11], SiM [12] and