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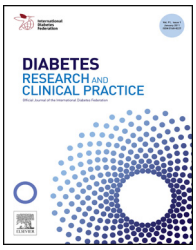

Evaluation of EZSCAN as a screening tool for impaired glucose metabolism☆

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ABSTRACT

Aims: To evaluate the performance of EZSCAN as a screening tool for impaired glucose metabolism (IGM), including impaired glucose tolerance, impaired fasting glucose and undiagnosed diabetes in a Chinese population.

Methods: 876 subjects participated in the study. All subjects underwent tests of EZSCAN, glycated hemoglobin, fasting plasma glucose (FPG), and oral glucose tolerance test (OGTT). Correlation of electrical skin conductance (ESC) with glucose level was evaluated by Pearson correlation coefficient. EZSCAN performance was assessed by receiver operating characteristic curve.

Results: Among the 876 subjects, 53% had normal glucose tolerance (NGT), and 47% had IGM. The ESC for the hands and feet was 72 ± 10 μS and 75 ± 7 μS, respectively, in NGT group; and 64 ± 13 μS and 67 ± 11 μS, respectively, in IGM group. The ESC at hands and feet was significantly correlated with both 2h-OGTT and FPG ($p < 0.001$). NGT group demonstrated a EZSCAN score of $33 \pm 11\%$, which is significantly lower than that of IGM group ($44 \pm 12\%$, $p < 0.001$). The cut-off point of EZSCAN for IGM detection was 40% with a sensitivity of 80% and a specificity of 72%.

Conclusions: EZSCAN is a useful screening tool for identifying subjects at increased risk for impaired glucose metabolism in prediabetes and diabetes. Diagnostic laboratory test should be performed in subjects with EZSCAN scores greater than 40%.

1. Introduction

The prevalence of diabetes is increasing rapidly in mainland China [1]. Strong evidence has shown that diabetes can be prevented by diet and lifestyle modification in high risk individuals [2–4]. Therefore it is important to have a screening tool for early identification of individuals at high risk of diabetes. Prediabetes, including impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), is a state with intermediate hyperglycemia and is a risk factor for diabetes. An

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Abbreviations: IGM, impaired glucose metabolism; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; FPG, fasting plasma glucose; HbA1c, glycated hemoglobin; OGTT, oral glucose tolerance test; ESC, electrical skin conductance; ROC, receiver operating characteristic; NGT, normal glucose tolerance; OR, odds ratio; CI, confidence interval; AUC, area under the ROC curve.

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estimated 5–10% of individuals with prediabetes will progress to diabetes [5]. Life style modification can lower the relative risk for diabetes by 40–70% [5]. Therefore, any screening tool that can detect prediabetes will be significant in the context of diabetes prevention.

Currently recommended screening tools include measurement of fasting plasma glucose (FPG), and oral glucose tolerance test (OGTT). However, they are invasive and/or time consuming (especially OGTT). Risk assessment questionnaire is another approach to evaluate risk of diabetes. A recently developed EZSCAN system (Impeto Medical, Paris, France) provides a new approach for the detection of diabetes by evaluating sweat gland function [6]. The basic pathophysiological mechanism behind this technology is that small autonomic nerve fibers innervating the eccrine glands are injured with poor glycemic control and respond differently to electric current stimulus [7–10]. As a rapid, noninvasive and reproducible measurement, EZSCAN has gained increasing attention and has been tested in several countries for its validity as a screening tool for the detection of diabetes [11–13]. However, no previous studies have clearly demonstrated a specific cut-off point for further diagnostic tests after EZSCAN. Moreover, most studies have focused on the detection of diabetes with limited consideration of prediabetes [11–13]. Individuals with IGT and IFG have a high risk for the future development of diabetes [14]. Therefore, the aim of present study was to evaluate the performance of EZSCAN as a screening tool for detecting individuals with impaired glucose metabolism (IGM), including prediabetes and undiagnosed diabetes, in an urban Chinese population, and to determine the cut-off point of EZSCAN score for further diagnostic testing.

2. Subjects, materials and methods

2.1. Subjects

The study was performed between August 2012 and October 2012. The subjects were recruited from individuals visiting Peking University People's Hospital (Beijing, China) for routine health checks. Subjects were included if they were over 18 years old. Exclusion criteria included previously diagnosed prediabetes or diabetes, cancer, severe psychiatric disturbance, epilepsy, pregnancy, use of medications known to influence blood glucose levels (corticosteroids, diuretics, epinephrine, lithium, phenytoin), use of medications known to influence the sympathetic nervous system (beta-blockers), amputation of arm or leg, implantable electrical devices (e.g. pacemaker and defibrillator), known sensitivity to nickel or any other standard electrodes.

A total of 1100 qualifying subjects were invited to participate in the study and 876 (79.6%) agreed to undergo an OGTT. Informed consent was obtained from all participants and the study protocol was approved by the Medical Ethics Committee of the Peking University People's Hospital.

2.2. Anthropometric and laboratory measurements

All participants' weight, height, waist circumference and blood pressure were measured by trained nurses and their medical histories recorded. Body mass index (BMI) was calculated as weight in kg/height in m^2. Blood pressure was measured 3 times following standardized procedures. Blood samples were collected after an overnight fasting for FPG, glycated hemoglobin (HbA1c) and lipid profile analyses, then a standard OGTT was performed according to the WHO recommendations in subjects without known diabetes mellitus [15]. Plasma glucose was measured by glucose oxidase method. HbA1c was measured by high performance liquid chromatography. Serum lipid profiles, including total cholesterol, triglycerides, high-density lipoprotein cholesterol and low-density lipoprotein, were measured by standard enzymatic procedures.

Based on the OGTT results, participants were categorized as having normal glucose tolerance (NGT, fasting plasma glucose < 6.1 mmol/L and 2h-OGTT plasma glucose < 7.8 mmol/L); IGT (2h-OGTT plasma glucose 7.8–11.0 mmol/L); IFG (fasting plasma glucose 6.1–6.9 mmol/L), and diabetes (fasting plasma glucose ≥ 7.0 mmol/L and/or 2h-OGTT plasma glucose ≥ 11.0 mmol/L) according to the 1999 World Health Organization criteria [16].

Individuals with IFG, IGT and diabetes were categorized collectively as the group with IGM.

2.3. Measurement of EZSCAN scores

The EZSCAN device is designed to accurately evaluate the sweat gland function through reverse iontophoresis and chronoamperometry. Essentially, EZSCAN measures electrochemical skin conductance (ESC) based on an electrochemical reaction between sweat chlorides and nickel electrodes.

The apparatus consists of two sets of large-area nickel electrodes, as well as a headband. Six electrodes in total are connected to a computer for data recording and management. During the test, each electrode was placed on areas of skin enriched in sweat glands, namely the forehead, the palmar side of the hands, and the plantar side of the feet. A direct-current at an incremental voltage of ≤ 4 V is applied to the electrode and the ESC (measured in μS; the ratio between current generated and the constant DC stimulus) was calculated for the face, hands, and feet. EZSCAN score is then derived from these ESC measurements with an algorithm that accounts for sex, age, BMI, and systolic blood pressure. The EZSCAN score ranges from 0 to 100%. The test requires no preparation and takes 2–3 min to complete.

2.4. Statistical analysis

Statistical analyses were performed using the SPSS software package version 16.0 (SPSS, Chicago, USA). The data are presented as mean $\pm$ SD, median (25–75th percentile), or percentage. Student's t test and Mann–Whitney test were used for comparisons between continuous variables and chi-squared test was used for categorical variables. The receiver operating characteristic (ROC) was used to evaluate the performance of EZSCAN for the detection of IGM. The area under the ROC curve (AUC) with 95% confidence interval (CI) was calculated and the optimal cut-off point was the peak of the curve where the sum of sensitivity and specificity is maximal. Pearson correlation coefficient was used to evaluate