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The cutoffs and performance of glycated hemoglobin for diagnosing diabetes and prediabetes in a young and middle-aged population and in an elderly population

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ABSTRACT

The aims were to compare the appropriate cutoffs of glycated hemoglobin (HbA1c) in a population of varying ages and to evaluate the performance of HbA1c for diagnosing diabetes and prediabetes. A total of 1064 participants in the young and middle-aged group and 1671 in the elderly group were included and underwent HbA1c testing and an oral glucose tolerance test (OGTT). Sensitivity, specificity, and area under the receiver operating characteristic curve (AUC) were calculated to evaluate the optimal HbA1c cutoffs. Kappa coefficients were used to test for agreement between HbA1c categorization and OGTT-based diagnoses. The optimal HbA1c cutoffs for diagnosing diabetes were 5.7% (39 mmol/mol) in the young and middle-aged group with a sensitivity of 66.7%, specificity of 86.7%, and AUC of 0.821 (95% CI: 0.686, 0.955) and 5.9% (41 mmol/mol) in the elderly group with a sensitivity of 80.4%, specificity of 73.3%, and AUC of 0.831 (0.801, 0.861). The optimal cutoffs for diagnosing prediabetes were 5.6% (38 mmol/mol) and 5.7% (39 mmol/mol) in the young and middle-aged group and in the elderly group, respectively. Agreement between the OGTT-based diagnosis of diabetes or prediabetes and the optimal HbA1c cutoff was low (all kappa coefficients <0.4). The combination of HbA1c and fasting plasma glucose increased diagnostic sensitivities or specificities. In conclusion, age-specific HbA1c cutoffs for diagnosing diabetes or prediabetes were appropriate. Furthermore, the performance of HbA1c for diagnosing diabetes and prediabetes was poor. HbA1c should be used in combination with traditional glucose criteria when detecting and diagnosing diabetes or prediabetes.

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1. Introduction

Diabetes is a major risk factor for cardiovascular disease, which caused an estimated 12.9 million deaths globally in 2010 [1,2]. The prevalence of diabetes has significantly increased in recent decades. In China, the prevalence of diabetes increased from less than 1% in 1980 [3] to 2.5% in 1994 [4] and to 11.6% in 2010 [5]. The prevalence of impaired glucose tolerance in Chinese adults also increased from 3.2% in 1994 to 12.5% in 2007 [4,6]. Considering the effects of diabetes and its complications and the benefits of aggressive treatment [7], early identification and management of individuals with diabetes or prediabetes is very important.

However, the diagnosis of diabetes can be very complicated, due to variations in the symptoms of diabetes [8]. Over the past four decades, although there have been significant changes in the diagnostic and classification criteria for diabetes and prediabetes, the most widely accepted diagnostic test remains the fasting plasma glucose and the 2-h plasma glucose by an oral glucose tolerance test (OGTT) [9]. However, the use of the OGTT for the diagnosis of diabetes was discouraged for use in clinical settings due to its inconvenience, high cost, and poor reproducibility [8,10].

Recently, the American Diabetes Association (ADA) integrated glycated hemoglobin (HbA1c) into the diagnostic criteria for diabetes because HbA1c has several favorable properties [11]. Compared with plasma glucose, HbA1c is more reproducible, provides a better reflection of chronic glucose exposure and correlates well with diabetes-related complications [12–15]. Although the role of HbA1c as a diagnostic indicator was recognized, more longitudinal epidemiological studies have reported that demographic and ethnic factors may contribute to complications in using HbA1c for the diagnosis of diabetes, and the optimal diagnostic HbA1c cutoff of is debated and varies due to genetic and biological variations [16–18]. Moreover, previous studies demonstrated that there are normal age-related increases in HbA1c [19,20], suggesting possible differences in HbA1c cutoffs in populations of different ages. Recently, Yang et al. [21] also reported the effect of age on HbA1c for diagnosing diabetes, but most of the subjects in his study were patients with diabetes and the performance of age-specific HbA1c criteria was not evaluated. However, few studies have focused on age-specific cutoffs of HbA1c and the performance of HbA1c as a diagnostic tool in a general population, especially in a population of different ethnicity than the published study population.

Our aims were to compare the appropriate diagnostic cutoffs of HbA1c in populations of different ages and to evaluate the performance of HbA1c as a diagnostic tool for diagnosing diabetes and prediabetes using two diverse population-based cohorts: a college-based young and middle-aged population and a community-based elderly population.

2. Methods

2.1. Study population

Data were collected from participants in both a college-based survey and a community-based survey in Beijing, China. In the college-based survey, all 1184 employees from the College of Engineering were recruited, and they were all less than 60 years old. In the community-based survey, all 2132 seniors who lived in a community related to the college were recruited. All surveys were conducted from September 2012 to June 2013 and investigated epidemiological information. All participants underwent a routine physical examination and OGTT test. Individuals with known diabetes or the use of hypoglycemic oral medication or insulin, chronic kidney disease with an estimated glomerular filtration rate (GFR) $<$60 ml/min/1.73 m^2, glucocorticoid treatment, anemia, or incomplete demographic information were excluded. Finally, 1064 participants from the college-based survey (age range, 20 to 59 years) and 1671 participants from the community-based survey (age range, 60 to 94 years) were included for the analysis. In the present study, the college-based population was classified as the young and middle-aged group, and the community-based population was classified as the elderly group. The study was approved by the Medical Ethics Committee of Chinese PLA General Hospital. Informed written consent was obtained from all participants.

2.2. Data collection

Demographic characteristics, history of diseases, and medication use were obtained by a standard questionnaire. All participants wore light clothing and stood in the upright position without shoes during measurements. Weight was measured to the nearest 0.1 kg and height to the nearest 0.1 cm. Body mass index was calculated as weight in kilograms divided by the square of height in meters. Waist circumference was measured at the midpoint between the lower ribs and the pelvic bone and to the nearest 0.1 cm.

2.3. Laboratory measurements

Blood samples were collected in the morning after at least 10-h of overnight fasting. After a 75-g OGTT, 2-h postload blood samples were collected. Fasting and 2-h postload plasma glucose levels, total, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterols, triglycerides, and creatinine were measured by routine laboratory methods using a Hitachi Automatic Analyzer 7600 (Hitachi, Tokyo, Japan). The estimated GFR was calculated using the Modification of Diet in Renal Disease equation [22]. HbA1c was measured using high performance liquid chromatography (Variant II, Bio-Rad, Hercules, CA, USA), which was certified by the National Glycohemoglobin Standardization Program. The inter- and intra-assay coefficients of variation for HbA1c were 0.9% (10 mmol/mol) and $<$3%, respectively. All measurements were performed by trained personnel blinded to the data.

2.4. Definitions and diagnostic criteria

In accordance with the 1999 World Health Organization diagnostic criteria [23], newly diagnosed diabetes was defined as a fasting plasma glucose $\geq$7.0 mmol/L and/or 2-h postload plasma glucose $\geq$11.1 mmol/L, and prediabetes was defined as either an impaired fasting glucose (fasting plasma glucose $\geq$6.1 mmol/L and $<$7 mmol/L) and/or an impaired glucose tolerance (2-h postload plasma glucose $\geq$7.8 mmol/L and