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Comparison of β-cell dysfunction and insulin resistance correlating obesity with type 2 diabetes: A cross-sectional study

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ABSTRACT

Aim: To assess the contribution of β-cell dysfunction and insulin resistance to type 2 diabetes (T2D) in obese and non-obese Chinese people.
Methods: In this cross-sectional study, we recruited 1384 newly diagnosed T2D patients and 1712 healthy controls. Insulin resistance was estimated by homeostasis model assessment of insulin resistance (HOMA-IR). β-cell function was estimated by homeostasis model assessment of β-cell function (HOMA-β) and 60 min insulinogenic index (IGI_{60}). We compared the insulin resistance and β-cell function of obese and non-obese Chinese patients with and without T2D.
Results: 50.18% of control participants and 62.28% of T2D patients were obese (BMI ≥ 25 kg/m^2). HOMA-IR, HOMA-β and IGI_{60} were significantly higher in obese than non-obese, irrespective of T2D. Non-obese T2D patients had significantly greater HOMA-IR, and lower HOMA-β and IGI_{60} than non-obese control participants. The obese T2D group had lower HOMA-β and IGI_{60} than the obese control group. There was no significant difference in HOMA-IR between the obese T2D and obese control groups. Multivariate logistic regression analysis revealed that HOMA-IR was associated with T2D only in non-obese group, and HOMA-β and IGI_{60} were associated with T2D in both non-obese and obese groups.
Conclusions: HOMA-β and IGI_{60} were associated with T2D in obese and non-obese patients, but HOMA-IR was associated with T2D in non-obese Chinese.

1. Introduction

Type 2 diabetes (T2D) is a growing public health concern worldwide (Guariguata et al., 2014; Lee, Brancati, & Yeh, 2011). The etiology for T2D has been well studied (Abdul-Ghani, Tripathy, & DeFronzo, 2006; Kahn, 2003; Kim, Kim, Kim, Bae, & Park, 2013). β-Cell dysfunction and insulin resistance are the two important contributors in the pathogenesis of T2D (Abdul-Ghani et al., 2006; Kahn, 2003; Kim et al., 2013). East Asian patients with diabetes accounted for over a fourth of the global diabetes population (Guariguata, 2013). Epidemiologic studies showed that there are some profound differences in T2D pathophysiology of East Asians (Chan et al., 2009; Cho, 2015; Morimoto et al., 2013; Ohn et al., 2016; Yabe, Seino, Fukushima, & Seino, 2015). East Asians have relatively lower body weight index (BMI) at onset of diabetes and significant β-cell dysfunction compared with Caucasian (Chan et al., 2009; Cho, 2015; Morimoto et al., 2013; Ohn et al., 2016; Yabe et al., 2015). Most of the above-mentioned data are from Korea and Japanese. As a big country in population, the prevalence of T2D in China has recently reached about 9.7% (Yang, Dou, & Song, 2010). However, the data from China regarding the contributions of β-cell dysfunction, insulin resistance and their interaction to T2D are still less.

Obesity is a major risk factor for T2D (Sanada et al., 2012). Epidemiological studies indicate that in Chinese people, marked insulin resistance is often detected in patients with a relatively low BMI (Chiu, Austin, Manuel, Shah, & Tu, 2011; Lee et al., 2011; Ma & Chan, 2013). Obesity in Asians is defined as BMI ≥ 25 kg/m^2 according to the diagnostic criteria of WHO (WHO Expert Consultation, 2004). In this study, we assessed the relative contribution of β-cell dysfunction and insulin resistance in obese and non-obese Chinese people who were recently diagnosed with T2D, and determined the associated risk factors for T2D in obese or non-obese patients.

2. Subjects

A total of 3096 participants aged ≥ 25 years, including 1712 healthy controls and 1384 newly diagnosed T2D patients were

Conflict of interest: None.

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recruited from the Physical Examination Center and Endocrinology Department of Beijing Chao-yang Hospital, Affiliated to Capital Medical University, between March and October 2013. Newly diagnosed T2D was defined by oral glucose tolerance test (OGTT) within the preceding 6 months, according to the WHO criteria (1999). Exclusion criteria were: pregnancy; receipt of agents known to influence glucose or lipid metabolism; history of pre-diabetes (impaired fasting glucose and/or impaired glucose tolerance), family history of diabetes, the presence of diabetes antibodies, coronary artery disease, impaired liver function, impaired renal function, systemic inflammatory disease, infectious disease or cancer. Because all the patients aged ≥ 25 years had no diabetes antibodies and no family history of diabetes, it might properly exclude the possibility of type 1 diabetes or maturity onset diabetes in young (MODY). All enrolled participants provided written informed consent, and this study was approved by the Ethics Committee of the Beijing Chao-yang Hospital, Capital Medical University.

3. Materials and methods

3.1. Clinical and biochemical measurements

A standard questionnaire was used to collect information about participant health status, medications and lifestyle. During physical examination height and weight were recorded and BMI was calculated. Blood pressure was measured in the non-dominant arm after patient was seated for 10 min, using a sphygmomanometer. Venous blood samples were obtained after overnight fasting. Plasma samples were stored at −80 °C. High-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG) and total cholesterol (TC) levels were measured by colorimetric enzymatic assays using an autoanalyzer (Hitachi 7170). Fasting blood glucose (FBG), fasting insulin (FINS), alanine amino transferase (ALT), and aspartate amino transferase (AST) levels were measured at the central chemistry laboratory of Beijing Chao-yang Hospital, Capital Medical University. Insulin resistance was estimated by homeostasis model assessment of insulin resistance (HOMA-IR) [FINS (μIU/mL) × FBG (mmol/L)/22.5] (Bermudez et al., 2008; Katsuki et al., 2001). β-Cell function was estimated by homeostasis model assessment of β-cell function (HOMA-β) [20 × FINS (μIU/mL)/FBG (mmol/L) − 3.5] and 60 min insulinogenic index (IGI_{60}) [($insulin_{60min}$ − $insulin_{0min}$ (μIU/mL))/($glucose_{60min}$ − $glucose_{0min}$ (mmol/L))] (Bermudez et al., 2008; Ohn et al., 2016).

3.2. Statistical analysis

Normally distributed variables were expressed as mean ± standard deviation (SD), while variables with a skewed distribution including ALT, AST, TG, FINS, HOMA-IR, HOMA-β and IGI_{60} were expressed as medians, and the upper and lower quartiles. Variables that were not normally distributed were log-transformed before analysis. Groups were compared using independent t-test or the Mann–Whitney U test. Differences between proportions were analyzed using chi-square test. Logistic regression analyses were performed to calculate the relative risk of T2D, after adjusting for confounding variables. All statistical analyses were performed with SPSS 17.0 (SPSS, Inc, Chicago, IL) and the results were considered statistically significant when two-tailed $P < 0.05$.

4. Results

4.1. Clinical characteristics of the control and T2D groups

A total of 3096 participants, including 1712 healthy controls and 1384 newly diagnosed T2D patients were analyzed in this study, and 50.18% of control participants and 62.28% of T2D patients were obese (BMI ≥ 25 kg/m^2) (Fig. 1 and Table 1). The mean age of patients in the T2D group was 50.3 ± 10.80 years, and mean age of the control group was 43.20 ± 11.50 years. The control group was 81.30% male, and T2D group was 63.70% male.

The mean BMI and DBP of patients in the T2D group (25.96 ± 3.17 kg/m^2 and 79.70 ± 9.27 mm Hg, respectively) were significantly higher than those in the control group (25.07 ± 3.51 kg/m^2 and 76.97 ± 11.07 mm Hg, respectively; all $P < 0.01$). The mean SBP of patients in the T2D group (124.96 ± 14.50 mm Hg) was significantly lower than in the control group (126.18 ± 15.50 mm Hg, $P < 0.05$). The median ALT and AST levels of patients in the T2D group (26.00 and 22.00 U/L, respectively) were also significantly higher than those in the control group (23.00 and 20.00 U/L, respectively; all $P < 0.01$) (Table 1).

T2D patients had significantly higher TC, TG and LDL-C than the control participants (all $P < 0.01$). T2D patients had significantly higher mean FBG levels and median HOMA-IR (8.27 ± 2.10 mmol/L and 3.37, respectively) than the control participants (5.50 ± 0.48 mmol/L and 2.95, respectively, all $P < 0.01$), while the median FINS, HOMA-β and IGI_{60} were significantly lower in the T2D group (9.70 μIU/mL, 44.87 and 1.63, respectively) than control participants (11.95 μIU/mL, 120.35 and 23.30; all $P < 0.01$) (Table 1).

4.2. Subgroup analysis of the control and T2D groups

Based on whether their BMI ≥ 25 kg/m^2 (WHO Expert Consultation, 2004), we categorized all participants into four subgroups: non-obese control group, obese control group, non-obese T2D group and obese T2D group. Of the 1712 control participants, 859 (50.18%) were categorized as the obese control group, and of the 1384 T2D patients enrolled, 862 (62.28%) were obese (Table 2). In the control group, obese patients were significantly older, had significantly higher SBP, DBP, ALT, AST, TC, TG, LDL-C, FINS, HOMA-IR, HOMA-β and IGI_{60}, and significantly lower HDL-C levels than non-obese participants. In T2D group, obese patients were significantly younger, had significantly higher SBP, DBP, ALT, AST, TC, TG, LDL-C, FINS, HOMA-IR, HOMA-β and IGI_{60}, and significantly lower HDL-C levels than non-obese participants. In addition, the mean FBG of obese control patients was significantly higher than non-obese control participants, but mean FBG of obese T2D patients was significantly lower than non-obese T2D participants (all $P < 0.01$; Table 2). Furthermore, the incidence of T2D in obese participants is 50.09% (862/1721), which was significantly higher than in non-obese participants (37.96%, 522/1375) (OR = 1.64, $P < 0.001$; Table 3)

HOMA-IR, HOMA-β and IGI_{60} were significantly higher in obese than in non-obese participants diagnosed with or without T2D (HOMA-IR and HOMA-β: $P < 0.01$; IGI_{60}: $P < 0.05$; Fig. 2A and B). HOMA-IR was significantly higher in T2D participants without obesity compared with control without obesity ($P < 0.01$, Fig. 2A), but there were no differences between control with obesity and T2D participants with obesity ($P > 0.05$, Fig. 2A). However, HOMA-β and IGI_{60} were significantly lower in T2D participants either with or without obesity compared with control either with or without obesity, respectively (all $P < 0.01$; Fig. 2B).

4.3. Multivariate logistic regression analysis in non-obese and obese patients

Multivariate logistic regression analysis using the forward method was carried out on the significant variables found by univariate logistic regression analysis. The results indicated that there were eight factors significantly associated with T2D in non-obese group, which were sex (OR = 0.163, 95% CI 0.076 to 0.353), BMI (OR = 1.286, 95% CI 1.066 to 1.551), TC (OR = 0.178, 95% CI 0.075 to 0.42), TG (OR = 2.614, 95% CI 1.515 to 4.508), LDL (OR = 5.41, 95% CI 2.21 to 13.245), HOMR-IR (OR = 7.146, 95% CI 4.918 to 10.381), HOMR-β (OR =