

(様式4) (Form4)

学位論文の内容の要旨

Dissertation Abstract

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(学位論文のタイトル) Title

Association between insulin resistance and cardinal rheological parameters in young healthy Japanese individuals during 75 g oral glucose tolerance test

([健康若年日本人の75g経口糖負荷試験におけるインスリン抵抗性と血液流動性の指標との関連])

(学位論文の要旨) 2,000字程度、A4判 (approx. 800 Words in English /A4 size)

Background: The prevalence of childhood obesity and consequently type 2 diabetes mellitus (T2DM) is rising, hence, there is an increasing interest in insulin resistance as a generally recognized predictor and risk factor for T2DM. T2DM raises health care costs and is an encumbrance; therefore, the monitoring of insulin resistance in children and adolescents at risk for T2DM is important to prevent T2DM. Our recent data from a 75 g oral glucose tolerance test (75-g OGTT) revealed that there is a sequential decrease in insulin sensitivity and secretion even in young and healthy Japanese individuals within the physiological range of glycemic control. Insulin resistance affected blood rheology in subjects with obesity, hypertension, and metabolic disorders. We previously showed that fasting circulating insulin levels and insulin resistance evaluated by homeostasis model assessment-estimated insulin resistance (HOMA-IR) were associated with blood rheology through modulating hematological and lipid parameters in young adults within the physiological range of glycemic control. Most previous studies, including our report, adopted HOMA-IR to evaluate insulin resistance. The HOMA-IR index represents the relationship between pancreatic insulin secretion and the capacity to maintain adequate glycemic levels. In contrast, the Matsuda index represents both hepatic and peripheral tissue sensitivity to insulin, requiring 75-g OGTT for estimation. Therefore, further studies that investigate the association between hemorheological parameters and indices of insulin resistance evaluated by 75-g OGTT, such as Matsuda index, are required.

Objective: To reveal the association between hemorheological parameters and indices of insulin resistance evaluated by 75-g OGTT, such as Matsuda index and disposition index.

Subjects and Methods: This study is an addition to our previous report which demonstrated that even in young and healthy Japanese individuals within the physiological range of glycemic control; there was a sequential decrease in insulin sensitivity and secretion. A total of 575 healthy young Japanese participants in around 22- 29 years of age took 75-g OGTT. The 75-g OGTT was performed after 10-hour fasts with 0-, 30-, 60-, and 120-minutes samplings to establish plasma glucose and

insulin levels, and at the pre-load time, serum total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and hemoglobin A1c (HbA1c) were measured. Hematological parameters were measured at 0-minutes. We measured hematocrit (Ht), hemoglobin (Hb) levels, red blood cell (RBC) count, white blood cell (WBC) count, platelet count, serum TC, HDL-C, LDL-C, TG, insulin, plasma glucose concentrations and HbA1c levels. We calculated the insulinogenic index, HOMA-IR, homeostasis model assessment of β cell function (HOMA- β), Matsuda index and disposition index during OGTT. Spearman's correlation analyses were conducted to determine the relationships between indices of insulin resistance or release and the clinical parameters.

Results: Our results showed that the HOMA-IR was significantly correlated with Ht, Hb, RBC, WBC, platelet count, lipid parameters and BMI. The Matsuda index was negatively correlated with RBC count, WBC count, platelet count, serum TC, LDL-C, TG and positively correlated with HDL-C. The disposition index was negatively correlated with Hb, RBC count, LDL-C and BMI, and positively correlated with HDL-C. HOMA- β was positively correlated with WBC count, platelet count, TC, LDL-C and TG. The insulinogenic index was positively correlated with WBC count, platelet count and TC. Multiple regression analysis revealed that HOMA-IR was independently associated with TG, and the Matsuda index was independently associated with TG, WBC count, and platelet count. The insulinogenic index was independently associated with WBC count.

Conclusion: This cross-sectional study found that among healthy young Japanese individuals within physiological range of glycemic control, TG, WBC count, and platelet count might be independent predictors of IGT and T2DM. The Matsuda index was independently associated with TG, WBC count, and platelet count, while HOMA-IR was independently associated with TG. Additionally, WBC count was independently associated with the insulinogenic index. This study suggests that even in young and healthy Japanese individuals with physiologically normal glycemic indices, higher indices of insulin resistance and impairment of insulin release are associated with higher hematological parameters. This can possibly promote diabetes mellitus through influencing erythropoiesis and lipid metabolism.