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ORIGINAL ARTICLE

Role of adiponectin gene variants, adipokines and hydrometry-based percent body fat in metabolically healthy and abnormal obesity

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KEYWORDS
Adiponectin T45G polymorphism;

Summary
Objective: Metabolically healthy obesity (MHO) subjects have better metabolic parameters than metabolically abnormal obesity (MAO) subjects, but the possible

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Metabolically healthy obesity;
Metabolically abnormal obesity;
Adipokine;
Percent body fat

mechanisms underlying this remain unknown. Our study was designed to investigate the interrelationships among genes, adipokines, body fat and its distribution in MHO and MAO.

Methods: From 2007 to 2009, 103 males and 131 females aged 18—50 years were enrolled by an intention-to-treat design in a weight management clinic. Participants were divided into MHO and MAO groups. Percent body fat (PBF) was measured by a deuterium oxide dilution method. Four polymorphic variants, including PPARγ2 (Pro12Ala and C1431T) and adiponectin (T45G and G276T) genes, and three adipokines (adiponectin, leptin and resistin) were obtained.

Results: Of the 234 obese subjects, 130 (55.6%) were MHO. In the univariate analysis, the MAO group has significantly higher anthropometric, metabolic indices and leptin levels than the MHO group. Logistic regression analysis revealed that age, male gender, the T allele of adiponectin T45G polymorphism, leptin and PBF were positively associated with MAO. ANCOVA analysis revealed that the T allele of adiponectin T45G polymorphism was associated with higher fasting and postprandial glucose levels. We further found that TT genotype has a lower high molecular weight (HMW)/low molecular weight (LMW) adiponectin ratio than GG genotype.

Conclusions: The factors associated with MAO are age, male gender, the T allele of adiponectin T45G polymorphism, leptin, and PBF. The net effects of T45G polymorphism on the MAO phenotype may be achieved by changes in the adiponectin oligomer ratio and glucose levels.

Introduction

The prevalence of obesity is increasing at an alarming rate in both the West and Asia, including Taiwan [1]. The impact of obesity on health is multi-dimensional, and may increase the risk of developing type 2 diabetes mellitus (T2DM), hypertension, hypercholesterolemia, and cancer [2]. Although obesity individuals are thought to be metabolically abnormal (metabolically abnormal obesity, MAO), literature reports one subset of obesity individuals have a relatively normal metabolic profile and insulin sensitivity, termed the metabolically healthy obesity (MHO) [3]. The prevalence of MHO in obesity is different, ranging from 18% to 44% by the criteria [3]. Evidence suggests that MHO may be partly due to a lower amount of visceral fat or earlier onset of obesity [3]. Therefore, a critical question is raised why certain obesity people develop MAO but others do not.

Adipose tissue is now been considered as an endocrine organ, which secretes multiple hormones, including leptin, adiponectin and resistin [4,5]. Dysregulation of adipokine production may result in metabolic disorders and cardiovascular diseases (CVDs), such as T2DM, stroke, myocardial infarction and atherosclerosis in obesity individuals [6,7]. In contrast, some adipokines with anti-inflammatory or insulin-sensitising properties, such as adiponectin, may decrease these risks [8—10]. Adiponectin levels of MHO subjects have been found to be the same as those of lean subjects [11], suggesting that adiponectin may have a protective role in such individuals. Therefore, whether dysregulation of adipokines underlies susceptibility to MAO remains unclear.

Human peroxisome proliferator-activated receptor γ (PPARγ) and adiponectin gene variants may predispose subjects to T2DM and CVDs [12]. PPARγ, a nuclear receptor, is a key regulator of lipid metabolism, adipogenesis and insulin sensitivity [13]. Two variants in the coding region of PPARγ2 gene have been intensively studied: Pro12Ala missense and C1431T silent mutations [14]. In addition, adiponectin plays a role in the pathogenesis of metabolic dysregulation [15]. Serum adiponectin levels are reduced in insulin-resistant mice and humans with obesity and T2DM, but can be normalised by PPARγ agonist [16,17]. The improvement in the glucose metabolism due to PPARγ activation may be through up-regulation of circulating adiponectin levels [18]. Two variants in adiponectin gene, T45G and G276T, are associated with metabolic syndrome [19], insulin resistance, and T2DM in some populations [20], but not others [21].

While very few studies focus on the association between MHO, MAO and gene variants for PPARγ2 and adiponectin [22], their results remain inconclusive. Our study was thus designed to investigate the relationships among gene variants for PPARγ2 and adiponectin, adipokines, anthropometric indices and two obesity phenotypes (MHO and MAO), which may lead to a better understanding of

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