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ORIGINAL ARTICLE

Metabolic Abnormalities, but not Metabolically Healthy Obesity, are Associated with Left Ventricular Hypertrophy

Naijin Zhang, MD, Yintao Chen, MD, Xiaofan Guo, MD, Guozhe Sun, MD, Dongxue Dai, MD, Yingxian Sun, MD, PhD *

Department of Cardiology, the First Hospital of China Medical University, Shenyang, Liaoning, P.R. China

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Background Obesity has been found to be a predictor of left ventricular hypertrophy (LVH). However, studies which divide obesity into metabolically healthy obesity (MHO) and metabolically unhealthy obesity (MUO) to study the effect of obesity on LVH have been rare. The present study aims to make clear the effects of various obese phenotypes and metabolic abnormalities on LVH.

Methods A total of 10,804 participants were involved in this cross-sectional study. ''Obesity'' and ''metabolically healthy'' were defined as BMI $\geq$ 25 kg/m^2 and having none of the metabolic factors respectively.

Results It was found that metabolically unhealthy non-obesity (MUNO) (OR, 2.675; 95%CI, 1.603-4.462, P < 0.001) and MUO (OR, 9.067; 95%CI, 5.474-15.020, P < 0.001) were significantly associated with LVH, while it went in reverse for MHO (OR, 1.968; 95%CI, 0.560-6.920, P = 0.291), after adjustment for age, race, gender, educational status, physical activity, annual income, current smoking status, current drinking status, sleep duration and BMI. And after further adjustment for metabolic abnormalities, MUNO (OR, 0.567; 95%CI, 0.316-1.018, P = 0.794) and MUO (OR, 0.632; 95%CI, 0.342-1.166, P = 0.142) tended not to be associated with LVH any longer. However, among the five metabolic components of metabolic abnormalities, high blood pressure (OR, 4.358; 95%CI, 3.266-5.815, *P* < 0.001) and high waist circumference (OR, 1.530; 95%CI, 1.139-2.054, *P* = 0.005) were significantly associated with LVH.

Conclusions Metabolic abnormalities, but not MHO, were significantly associated with LVH. In addition, metabolic abnormalities were probable to mediate the connection between MUNO/MUO and LVH.

Keywords Metabolically healthy obesity • Metabolic abnormalities • Left ventricular hypertrophy • Cardiovascular risk

Introduction

With the constant rise worldwide, so far obesity has been regarded as an important public health problem [1]. What is more, obesity also serves as an important predictor for many diseases such as diabetes mellitus type II and cardiovascular disease (CVD) [2,3]. Often associated with obesity are metabolic abnormalities which also rank among the major risk factors for CVD [4]. Therefore, it has been increasingly recognised that the correlation between obesity and cardiovascular problems is caused by obesity-related metabolic abnormalities. Such metabolic abnormalities include

*Corresponding author at: 155 Nanjing North Street, Heping District, Shenyang, 110001, People's Republic of China. Telephone Number: +86 13804068889, Email: yxsun@mail.cmu.edu.cn

abdominal obesity, dislipidaemia, hyperglycaemia and hypertension [5]. Currently, many studies focus on a certain subgroup of obesity not accompanied by metabolic abnormalities, which is also known as metabolically healthy obesity (MHO) [6]. As far as we know, a unified criterion to classify obese phenotypes hasn't been available [7]. Based on whether or not there are obesity and various metabolic abnormalities, obese phenotypes usually fall into four types: metabolically healthy non-obesity (MHNO), metabolically healthy obesity (MHO), metabolically unhealthy non-obesity (MUNO) and metabolically unhealthy obesity (MUO) [6]. Numerous studies have shown that MHO appears to be of lower risk to cardiovascular disease mortality, heart failure and cardiovascular events [8,9]. However, there is also conflicting evidence that MHO is significantly associated with heart failure, subclinical markers of atherosclerosis and risk of CVD [10–12]. At present, the benefits of the novel concept of MHO have no clear conclusion.

As a very important predictor for cardiovascular diseases, left ventricular hypertrophy (LVH) is significantly associated with myocardial infarction, stoke and arrhythmia [13–15]. Some recent studies have shown that both metabolic abnormalities and obesity are significant risk factors of LVH [16–19]. However, reports on researches which divide obesity into MHO and MUO to study the effect of obesity on LVH have been rare. Therefore, the correlations between MHO and LVH still remain to be verified. In addition, the effect of various obesity phenotypes and metabolic abnormalities on LVH is still uncertain.

In view of this, this large-scale and cross-sectional study is designed to probe whether MHO is significantly associated with LVH. As well, it aims to make clear the effects of various obesity phenotypes and metabolic abnormalities on LVH.

Materials and Methods

Study Population

This study was conducted from January 2012 to August 2013. A representative sample from the participants, who were aged over 35 years, was selected to assess the prevalence, incidence and natural history of cardiovascular risk factors in rural areas of Liaoning Province in China. The study adopted a multi-stage, stratified and random cluster-sampling scheme. In the first stage, three counties including Dawa, Zhangwu and Liaoyang County were randomly selected from Liaoning province. In the second stage, one town was randomly selected from each county (for a total of three towns). In the third stage, six to eight rural villages from each town were randomly selected (for a total of 26 rural villages). A total of 14,016 eligible participants were enrolled in this survey. Among those, 11,956 participants completed this study with a response rate of 85.3%. The participants who were pregnant or had malignant tumours or mental disorders or other missing variables for our multivariable logistic regression models were excluded. Finally, a sample size of 10,804 was accepted. The study was approved by the Ethics Committee of China Medical University, Shenyang, Liaoning province, China and all procedures were performed under ethical standards. Written consent was obtained from all the participants after they had been informed of objectives, benefits, medical items and confidentiality agreement of their personal information. Written informed consent was obtained from the proxies of the participants who were illiterate.

Echocardiography Measurements

Echocardiograms were performed on each participant by professional sonographers with a commercially available Doppler echocardiograph (Vivid, GE Healthcare, United States), using a 3.0-MHz transducer. Subjects were maintained in the supine position, and transthoracic echocardiogram included M-mode, two-dimensional, spectral and colour Doppler. Echocardiogram analyses were performed by three doctors who specialised in echocardiography and consultations were made with two other doctors if questions or uncertainty arose. M-mode and two-dimensional images of the left ventricular (LV) wall thickness, internal diameter, aortic root and left atrium was recorded by each participants' parasternal acoustic window. Correct orientation of planes for Doppler recordings and imagings were verified according to previously described procedures [20,21]. Left ventricular internal dimensions (LVID), posterior wall thickness (PWT) and interventricular septal thickness (IVST) were obtained according to American Society of Echocardiography recommendations [21,22]. Left ventricular mass was calculated according to the formula LVM=0.81 (1.04 [LVID + IVST + PWT]) 3 - (LVID) 3+0.06 [23]. Left ventricular mass index (LVMI) was normalised for body height in $m^{2.7}$ and LVH was defined as the LVMI $\geq$51 $g/m^{2.7}$ for both men and women [24].

Data Collection and Measurements

Information on covariates, such as demographic characteristics, lifestyle risk factors, family income and family history of chronic diseases, was collected during a single clinic visit by cardiologists and trained nurses by face-to-face interview using a standard questionnaire. Before the survey was performed, all eligible investigators attended an organised training session which included the purpose of this study, how to administer the questionnaire, the importance of standardisation, the standard method of measurement, and the study procedures. After this training, a strict test was used for evaluation, and only those who scored perfectly on the test could become investigators. During data collection, there was a central steering committee which also had a subcommittee for quality control to ensure that all data were collected by well-known standards.

Race was categorised as Han or others, which included some ethnic minorities in China, such as Mongol and Manchu. Educational levels were three categories including primary school or below, middle school and high school or above. Self-reported sleep duration which included nocturnal and nap duration, was obtained from the questionnaire