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Cardiovascular risk in different obesity phenotypes over a decade follow-up: Tehran Lipid and Glucose Study

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ABSTRACT

Background and aims: Considering the inconsistent data available on cardiovascular (CV) risk of different obesity phenotypes, the aim of this study was to investigate the development of cardiovascular disease (CVD) in different obesity phenotypes over a median follow-up of 12 years.
Methods: In this large population-based cohort, 7842 participants (44.8% men), aged ≥ 30 years, were enrolled. Participants were divided into six phenotypes based on body mass index and metabolic status. Metabolic health was defined based on two definitions: 1) having ≤1 component of metabolic syndrome using the Joint Interim Statement (JIS) criteria and 2) homeostasis model assessment-insulin resistance (HOMA-IR) < 2.6 mole × μU/L^2. Multivariate adjusted hazard ratios (HRs) were calculated for cardiovascular events.
Results: A total of 712 new CVD events occurred. CV risk increased in all metabolically unhealthy phenotypes. Multivariable adjusted HRs for CVD events in metabolically healthy overweight (MHOW) and metabolically healthy obese (MHO) participants were 1.22 (0.73–2.04) and 1.74 (0.68–4.44), respectively. CV risk increased in all obesity phenotypes based on insulin resistance except the insulin resistance-normal weight group. However, this increased risk disappeared after further adjustment for metabolic risk factors.
Conclusions: Our findings showed that CV risk did not increase in MHOW and MHO phenotypes over a 12-year follow-up. However, all metabolically unhealthy phenotypes were associated with increased incident CVD. Further studies with longer follow-up are needed to confirm the benign nature of MHOW/MHO phenotypes.

1. Introduction

Obesity is considered to be one of the most important risk factors for morbidity and mortality, particularly with respect to cardiovascular disease (CVD) [1–3]. However, there is significant variability in the risk of development of cardiovascular (CV) events in obese persons [4,5]. Variable distribution of CVD risk factors across the spectrum of body mass index (BMI) has resulted in description of several phenotypes combining BMI and metabolic profile in the medical literature. There are two common phenotypes of obesity: 1) metabolically healthy obese (MHO) with a postulated resistance to CV morbidity and 2) metabolically unhealthy normal weight (MUNW) [3,6]. Based on the results of a recent meta-analysis, it is estimated that the overall prevalence of MHO and MUNW is 7.27% (95% CI 5.92–8.90%) and 19.98% (95% CI 16.54–23.94%), respectively [7].

Data regarding the effect of different obesity phenotypes on CV morbidity and mortality is conflicting. In short term follow-ups, MHO was considered to be a benign condition [8,9], whereas findings of a few studies with long term follow-ups documented contradictory results [10,11]. Two systematic reviews evaluating CV risk in MHO phenotype showed that MHO is not a benign condition

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in the long term [4,5]; although it should be noted that included studies used different definitions for the phenotypes and CV outcomes [12].

In our previous study on 6215 subjects from the Tehran Glucose and Lipid Study (TLGS), during 8.1 years of follow-up, CV risk did not increase in the MHO group compared to the normal-weight subjects without dysmetabolic aspects [9]. The aim of the present study was to examine CV risk of different obesity phenotypes (according to new definitions) during a 12-year follow-up.

2. Materials and methods

2.1. Study subjects

The Tehran Lipid and Glucose Study (TLGS) is a prospective, population-based study designed to determine the risk factors for non-communicable diseases among a representative Tehran urban population. Details of the study protocol are available elsewhere [13]. For the present study, 9752 participants aged ≥30 years, enrolled in the first (1999–2001) or second phases (2002–2005) of TLGS, were selected. After exclusion of pregnant women (n = 39), subjects with history of cardiovascular disease (CVD) at baseline (n = 562), known cases of diabetes mellitus or anti-hyperglycemic agent users (n = 424), subjects with BMI < 18.5 kg/m^2 (n = 127), chronic use of corticosteroids (n = 207), history of cancer (n = 52) and those with missing data for anthropometric or metabolic parameters (n = 499), 7842 participants were entered in baseline categorization of obesity phenotypes. Of these, 675 participants (8.6%) had no follow-up data; hence, final analyses were performed on 7167 participants with complete data, up to March 2012 (median follow-up: 11.94 years; IQ 25–75 8.13–12.50 years) (Fig. 1). The ethics committee of Research Institute for Endocrine Sciences of Shahid Beheshti University of Medical Sciences approved this study. Written informed consent was obtained from all participants.

2.2. Clinical and laboratory measurements

At each phase of TLGS, trained personnel interviewed all participants using a standard questionnaire to collect demographic information. Anthropometric measurements were taken without shoes and participants wearing light clothing. Weight and height were determined using a digital electronic weighing scale (Seca 707; range 0.1–150 kg, Hanover, MD) with an accuracy of up to 100 gr and a tape meter, respectively. BMI was calculated as weight in kilograms divided by height in meters squared. Waist circumference (WC) was measured at the level of umbilicus using an unstretched tape meter.

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured twice in a seating position (after a 15-min rest) on the right arm, using a standard mercury sphygmomanometer. The mean of two measurements was considered as the participant's blood pressure. Blood samples were drawn after 12–14 h overnight fasting and all analyses were undertaken at the TLGS research laboratory on the day of blood collection, using selectra 2 auto-analyzer (Vital Scientific, Spankeren, the Netherlands). Fasting blood sugar (FBS) was measured by the enzymatic colorimetric method using glucose oxidase. For lipid measurements, total cholesterol (TC) and triglyceride (TG) levels were assayed by relevant kits (Pars Azmoun, Tehran, Iran) using enzymatic colorimetric tests with cholesterol esterase and cholesterol oxidase, and glycerol phosphate oxidase, respectively. High density lipoprotein cholesterol (HDL-C) was measured with phosphotungstic acid. All samples were analyzed when internal quality control met the acceptable criteria. Inter- and intra-assay coefficients of variations at baseline were 2.2% for serum glucose, 2.0% and 0.5% for HDL-C

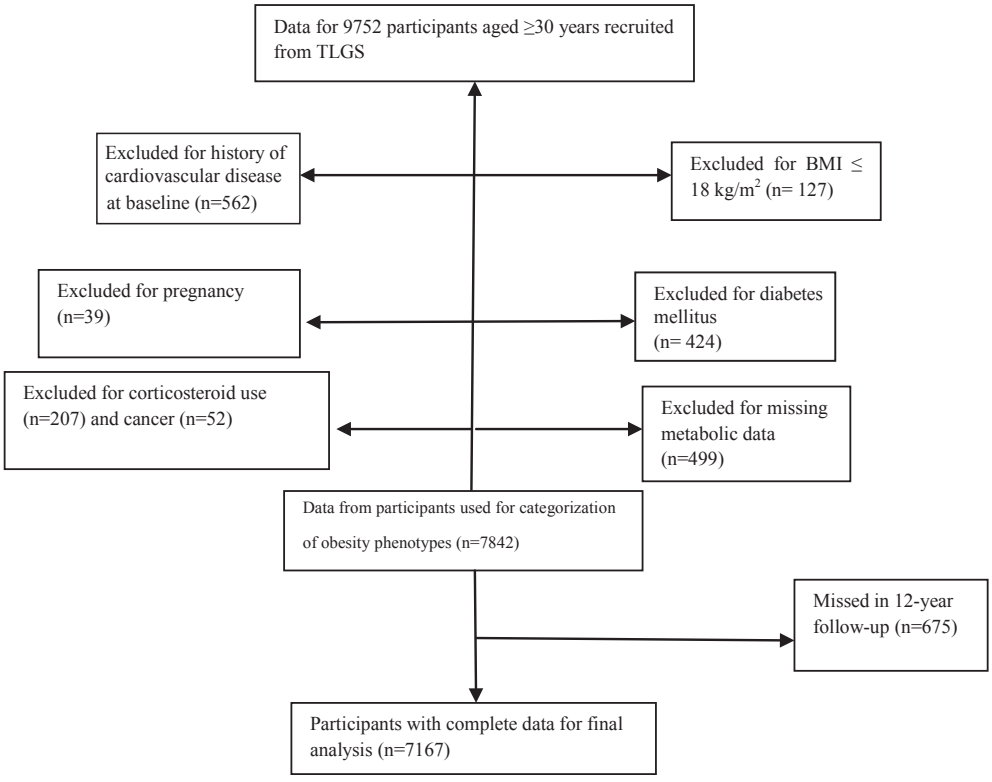

Fig. 1. Diagram showing the selection process of study participants.