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Incidence of type 2 diabetes, hypertension, and dyslipidemia in metabolically healthy obese and non-obese

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Abstract *Background and aims:* Metabolically healthy obese (MHO) individuals are devoid of many metabolic abnormalities, but how this condition is maintained over time remains debated. We assessed the prevalence of MHO over time and the incidence of hypertension (HTN), dyslipidemia, and type 2 diabetes mellitus (T2DM) in MHO as compared with metabolically healthy non obese (MHNO).

Methods and results: Prospective, population-based study including 3038 participants (49.9 ± 9.9 years; 1753 women) free from metabolic syndrome and cardiovascular disease at baseline and examined after a follow-up of 5.6 years and 10.9 years on average. At each follow-up, prevalence of MHO, MHNO, metabolically unhealthy not obese (MUNO), and metabolically unhealthy obese (MUO), as well as of HTN, dyslipidemia, and T2DM, was calculated and stratified by sex, age group, and education.

At baseline, 179 (5.7%) MHO participants were identified, of which 62 (34.6%) and 79 (44.1%) remained MHO at 5.6 and 10.9 years follow-up, respectively. At 5.6 years follow-up, MHO participants were more likely to develop low HDL or be on hypolipidemic medication [multivariable-adjusted OR (95% CI): 1.56 (1.02–2.38)], to have dyslipidemia [1.94 (1.33–2.82)], and high triglycerides [2.07 (1.36–3.14)] than MHNO. At 10.9 years follow-up, MHO participants were significantly more likely to develop T2DM [3.44 (1.84–6.43)], dyslipidemia [1.64 (1.14–2.38)], and low HDL or be prescribed hypolipidemic medication [1.57 (1.08–2.27)] than MHNO. Conversely, no differences were found regarding hypertension.

Conclusion: A considerable fraction of MHO individuals lose their status over time, and in metabolically healthy adults, obesity confers a higher risk of developing cardiovascular risk factors.

Introduction

Despite efforts to combat obesity, its prevalence, along with the prevalence of its associated cardiovascular risk factors (CVRFs), such as dyslipidemia, type II diabetes mellitus (T2DM), and hypertension (HTN), remains high [1]. In fact, such CVRFs continue to be responsible for an overwhelming number of deaths worldwide [2,3]. Recent studies have identified various obesity phenotypes, notably metabolically healthy obese (MHO) individuals,

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who are devoid of multiple CVRFs, and metabolically unhealthy obese (MUHO), who present with many CVRFs [4–6]. However, the prevalence of MHO, as well as the comparative incidence of CVRFs and mortality, depends on the Definition of metabolic syndrome applied, as there is little consensus on gold standard criteria for categorizing individuals as metabolically healthy or unhealthy obese [7,8]. Indeed, in a previous study on a Caucasian cohort, we showed that the prevalence of the MHO phenotype ranged between 3.3 and 32.1% in men and between 11.4 and 43.3% in women [7]. Further work has also found a substantial prevalence of MHO in other ethnic groups [9,10].

Several studies have suggested that MHO is an unstable condition, commonly leading to the development of metabolic abnormalities, but results have been inconsistent [4,5,11–13]. In fact, few prospective studies have focused on the natural course of MHO. The bulk of these studies focused primarily on endpoints of cardiovascular disease (CVD), T2DM, and all-cause mortality but reported contradictory results [12,14–17]. Even fewer have examined the evolution of MHO as it concerns the incidence of dyslipidemia, T2DM, and HTN for MHO in comparison to that for metabolically healthy non-obese (MHNO) individuals. Clearly, the MHO state, along with its implications, remains poorly understood.

Thus, the aims of this study were to assess the prevalence of metabolically healthy obesity and the incidence of HTN, dyslipidemia, and T2DM in the MHO as compared with that in the MHNO after a 10-year follow-up in an adult Swiss population-based sample.

Participants and methods

Participants

Participants were from the CoLaus study, a prospective study intended to evaluate the prevalence of CVRFs and to identify genetic determinants of these risk factors in a Swiss population aged between 35 and 75 years at baseline [18]. Sampling was performed as follows: the source population was defined as all subjects within the age range of interest registered in the population register of the city of Lausanne, Switzerland. The register includes all subjects living in this city for more than 90 days. A simple, non-stratified random sample of 19′830 subjects (corresponding to 35% of the source population) was drawn and the selected subjects were invited to participate by letter. If no answer was obtained, a second letter was sent, and if no answer was obtained, the subjects were contacted by phone.

Inclusion criteria were: (a) written informed consent; (b) willingness to take part in the examination and to provide blood samples; (c) Caucasian origin; (d) French language ability. For this study, we added the following inclusion criteria: (a) participants who completed the baseline, first, and second follow-up examinations and (b) availability of all variables analysed. For eligibility, we excluded (a) metabolically unhealthy participants (obese and non-obese) at baseline, as defined by Joint Interim Statement (JIS) criteria (see below for more details) and (b) type 1 diabetics at baseline. We further excluded (a) participants with cardiovascular disease at baseline; (b) participants with missing data at baseline; (c) participants without follow-up and (d) participants with missing data at follow-up.

Recruitment began in June 2003 and ended in May 2006, enrolling 6733 participants who underwent an interview, a physical exam, and a blood analysis. The first follow-up was performed between April 2009 and September 2012, 5.6 years on average after the collection of baseline data. The second follow-up was performed between May 2014 and July 2016, 10.9 years on average after the collection of baseline data. The information collected was similar to that collected in the baseline examination but contained questions regarding food consumption and detailed physical activity information.

Methods

All participants were examined in the morning after a fast of at least 8 h. They were probed about their personal and family history of CVD, CVRFs, and cardiovascular treatment. CVD status at baseline was confirmed by further checking the available information provided by the participants (i.e. doctors, hospital registers, etc.). Smoking status was defined as never, former (no matter how long before the interview) and current. Educational level was categorized as low (primary), middle (apprenticeship), upper middle (high school), and high (university) for highest completed level of education. Physical activity was defined by answering positively to exercising 2 or more times per week for at least 20 min per session.

Body weight and height were measured while participants stood without shoes in light indoor attire. Body weight was measured in kilogrammes to the nearest 100 g using a Seca® scale (Hamburg, Germany) that was frequently calibrated. Height was measured to the nearest 5 mm using a Seca® (Hamburg, Germany) height gauge. Waist circumference was measured mid-way between the lowest rib and the iliac crest using a non-stretchable tape. The average of two measurements was taken and rounded to the nearest 0.5 cm. Blood pressure (BP) was measured thrice using an Omron® HEM-907 automated oscillometric sphygmomanometer after at least a 10 min rest in a seated position, and the average of the last two measurements was used.

Venous blood samples (50 mL) were drawn in the fasting state. Most biological assays were performed at the clinical laboratory of the Lausanne university hospital (CHUV) within 2 h of blood collection on fresh samples. Glucose was assessed by glucose dehydrogenase with a maximum inter- and intra-assay CV of 2.1% and 1.0%, respectively; total cholesterol by CHOD-PAP (1.6%–1.7%); HDL-cholesterol by CHOD-PAP + PEG + cyclodextrin (3.6%–0.9%) and triglycerides by GPO-PAP (2.9%–1.5%).

Definition of variables and outcomes

Obesity was defined per World Health Organization (WHO) guidelines and convention as having a body mass

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