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Letter to the Editor

Is there a definition of Metabolically Healthy Obese Pediatric Patients?

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We have clearly explained in the first articles of this special issue that pediatric obesity increases the risk for metabolic diseases, including T2DM, HTN, dyslipidemia and many other chronic disorders. We have also explained that pediatric obesity is associated with the risk of developing cardiovascular disease (CVD) later in life. However, it is also clear that not all obese pediatric patients develop these disorders. Therefore we have a clear evidence that a unique subset of obese pediatric patients who appear to be protected from the development of metabolic disturbances and CVD. In adults, Plourde and Karelis have been able to provide a definition of a subgroup of adult obese patients considered as metabolically healthy obese (MHO) [1].

This definition is now used internationally under the term of (PK definition; Plourde and Karelis definition) and is used to determine the prevalence of MHO vs the prevalence of metabolically unhealthy obese patients (MUHO) [2]. As in adults, identifying obese pediatric patients with this potential protective profile could help us determine which part of the obese pediatric population needs to be only periodically observed and which needs to have early therapeutic interventions [1]. However, as in adults important questions on the MHO profile remain unanswered: do we have consensus on the definition and do they remain metabolically healthy over the course of their lifetime?

Obviously, for the purpose of this article, we will limit our discussion to the adolescent age group i.e., those more at risk of developing T2DM. We limit to this age group for the purpose of being more easily able to compare to the adult population. Also because many questions still remained to be answered having different age group will increase difficulties finding an appropriate definition of MHO. We will not be able to get definitive answers to the questions raised, but we hope that this letter will generate scientific discussion around the topic of pediatric patients with MHO.

Identifying MHO individuals

Adults defined as MHO are characterized for their low metabolic abnormalities such as: insulin resistance (IR), pro-atherogenic lipoprotein profile, pro-inflammatory state, or hypertension. In addition, they present lower visceral, hepatic, muscle fat accumulation and gene expression-encoding markers of adipose cell differentiation [3]. However, it is important to note that MHO individuals may also have multiple intermediate metabolic risk factors that may signal increased risk for T2DM and CVD (3). In general, insulin sensitivity indices and a cluster of metabolic risk factors (i.e. blood pressure, triglycerides, HDL-cholesterol and glycaemia) with specific thresholds are used in the identification of MHO subjects.

As discussed in the review by Plourde and Karelis [1], the complexity of techniques to determine insulin sensitivity and the use of different surrogate indexes to determine metabolic risk factors has led to different definitions of MHO. Therefore, without an expert consensus on the definition of MHO patients, findings and/or conclusions on MHO subjects are difficult to interpret. Accordingly, we considered appropriate to provide simple clinical criteria for the identification of MHO individuals.

We first believed that waist circumference of ≥80 cm for women and ≥94 cm for men should be used to identify adults MHO subjects instead of a BMI of ≥30 kg/m^2. We then suggested the following metabolic markers with their cut-points: glycemia <5.6 mmol/l, HDL ≥1.3 mmol/l for women and ≥ 1.03 mmol/l for men, triglycerides <1.7 mmol/l, and blood pressure <120/80 mm Hg. The proposed choice of these clinical markers was based from the criteria for the identification of the metabolic syndrome in adults from the International Diabetes Federation [5]. It should be noted that the cut-point for blood pressure was set at <120/80 mmHg since there is evidence to suggest that pre-hypertension may increase the risk of cardiovascular disease [6]. We propose that adults MHO individuals may be identified when all four of the metabolic markers are met. We seek to apply a strict method because our goal is to identify a "true" MHO population which could be different from a non-metabolic syndrome population.

We feel this represents a good first step for a consensus of a standard definition for MHO individuals. We understand that this definition is open to criticism and that the list of criteria could be modified and that the cut-points may be refined. However, according to Truthmaan J et al, (2016) [2], the PK criteria, which define MHO by the fulfilment of all included PK criteria may be more appropriate to determine ªtrueº MHO. However, in the adolescent age group, it seems that the definition of abdominal obesity is particularly lacking and need to be challenged by the medical and scientific community.

Potential definition for MHO adolescent

In a recent study performed in a district school in Bangladesh they assess the prevalence of obesity and abdominal obesity by means of body mass index (BMI) and waist-to-height ratio (WHtR), respectively, in adolescent girls [7]. Based on age and sex specific BMI percentiles, the students were classified as normal weight (5^{th}–$<85^{th}$ percentile), overweight (85^{th}–$<95^{th}$ percentiles), and obese ($\geq 95^{th}$ percentile). Central obesity was categorized as WHtR ≥ 0.5. Adolescent girls (aged 9–17 years) attending the sixth to twelfth grades (n = 501) in a Bengali medium school participated in the study. The prevalence of obesity and overweight were 23% and 14% among the girls. The prevalence of central obesity was 26%. Around 14% of girls in the normal weight group were centrally obese. Which reinforce the rationale for measuring abdominal obesity in adolescents? There was a significant relationship between WHtR and BMI status (P = 0.0001) [7].

The importance of measuring waist circumference is strongly supported by the results of the 2007–2009 Canadian Measures Health Survey where 2.6% of adults with normal weight, 35.3% of adults with overweight and 93.0% of adults with obesity had waist circumferences suggesting abdominal obesity [8]. Furthermore, although BMI data suggest that 24% of Canadian adults are at high risk for obesity-related illness or death, 37% of Canadian adults are at high risk when waist circumference is taken into consideration [8]. Thus, using both measures increases the threshold for identifying patients at risk for health problems and as mentioned above, adolescent are not different on that aspect [7]. Therefore, the risks for all medical conditions associated with obesity increase with higher BMIs and larger waist circumferences in both adults and adolescent patients [7, 9].

The current International Diabetes Federation definition of metabolic syndrome in pediatric patients recommends the use of WC as a mandatory diagnostic component [10]. Evidence suggested that compared to general obesity, abdominal obesity is associated with greater cardiovascular risks. Recently, the use of BMI as a cardiovascular risk factor has been questioned and WC received increasing attention in clinical practice [10]. Considering the high prevalence of pediatric obesity, we suggest that more attention should be paid to the monitoring aspects of abdominal obesity among children and adolescents and that prevention strategies should be more focused on abdominal obesity [11].

According to the IDF [10, 12], in adolescent ages 10 to 16 years-old, MUHO is defined as: abdominal obesity with the ≥90th percentile for age and sex (or adult cut-off if lower) as assessed by waist circumference; triglycerides ≥1.7 mmol/L; HDL-cholesterol <1.03 mmol/L; Blood pressure ≥130 mm Hg systolic or ≥85 mm Hg diastolic and Glucose ≥5·6 mmol/L (oral glucose tolerance test recommended) or known T2DM.

For the adolescent aged higher than 16, it is recommended to use the existing criteria for adults. Accordingly, we considered appropriate to provide the same clinical criteria for the identification of adults with MUHO. We first retain the same waist circumference of ≥80 cm for women and ≥94 cm that we used to identify adults MUHO subjects [1]. We then suggest the following metabolic markers with their cut-points: glycemia <5.6 mmol/l, HDL ≥1.3 mmol/l for girls and ≥ 1.03 mmol/l for boys, triglycerides <1.7 mmol/l, and blood pressure <120/80 mm Hg. I believe that, at this point, that this definition is the best definition of MHO especially considering that being obese at a young age and for a longer period of time is associated with a high risk of T2DM and CVD risk factors later in life (see article # 2). However, we do not think that this one is the final definition of pediatric MHO and again we hope that the scientific community will be open to discuss this definition.

Conclusion

As in adults, data on the lifestyle profile of adolescents MHO subjects is rather limited. Indeed, there is evidence to suggest that physical activity levels and the dietary profile of MHO individuals are not similar to MUHO subjects [1]. Thus, currently, it is difficult to elaborate on relevant clinical practice guidelines for both surveillance and treatment of MHO patients. There is no evidence that these subjects are permanently protected from the risk of developing obesity, T2DM and their related comorbidities. Also, adolescent MHO individuals may present other obesity-related comorbidities such as sleep apnea, knee osteoarthritis, poorer body image and many others comorbidities. Moreover, there is no evidence that MHO adolescents could tolerate a further increase of their fat mass, without any consequences on their cardio-metabolic profile as it is well established that worsening of body weight is strongly associated with the deterioration of risk factors for CVD [13]. Therefore, on the basis of this evidence or until future evidence can state otherwise, a prudent attitude would be to regularly monitor cardio-metabolic risk factors in obese adolescent MHO patients (especially elevated triglycerides, glycaemia, HOMA and C-reactive protein as well as low HDL), in order to detect as early as possible a negative evolution of their cardio-metabolic profile as recommended in the Clinical Practice Guidelines for the Management of Obesity [14]. In particular, a special surveillance should be applied to prevent any increase in body weight, and waist circumference (WC) as it was previously concluded that the MHO phenotype may be maintained by promoting lower WC [15]. Furthermore, it seems difficult to prescribe the optimal weight loss program in MHO individuals since the potential benefits of a weight loss treatment are still a matter of debate. Studies assessing the effects of lifestyle interventions, including diet and/or physical activity in MHO have led to divergent results [1]. Thus, we would suggest that prioritization for weight loss treatment may be given to MUHO patients. Achieving permanent weight reduction is a difficult challenge for any obese person and the risk of weight regain is elevated. For this reason, any weight loss program in MHO individuals should be preceded by a careful evaluation of expected resources, costs and benefits. However, for all obese patients including adolescents our public health message should remain the same about promoting good lifestyle habits and prevention of weight gain.

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