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Review

Metabolically healthy obesity from childhood to adulthood — Does weight status alone matter?☆

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ABSTRACT

Up to 30% of obese people do not display the "typical" metabolic obesity-associated complications. For this group of patients, the term "metabolically healthy obese (MHO)" has been established during the past years and has been the focus of research activities. The development and severity of insulin resistance as well as (subclinical) inflammations seems to play a key role in distinguishing metabolically healthy from metabolically non-healthy individuals. However, an internationally consistent and accepted classification that might also include inflammatory markers as well as features of non-alcoholic fatty liver disease is missing to date, and available data – in terms of prevalence, definition and severity – are heterogeneous, both during childhood/adolescence and during adulthood. In addition, the impact of MHO on future morbidity and mortality compared to obese, metabolically non-healthy as well as normal weight, metabolically healthy individuals is absolutely not clear to date and even conflicting. This review summarizes salient literature related to that topic and provides insight into our current understanding of MHO, covering all age spans from childhood to adulthood.

1. Introduction

Obesity prevalence has nearly doubled worldwide between 1980 and 2008 and still continues to increase. The largest increase in prevalence rates, especially during childhood and adolescence, has been lately seen in the African region as well as Europe [1].

Almost 10% of the world's adult population presents with diabetes, with highest prevalence rates in the Eastern Mediterranean region as well as the American region [1].

Obesity is in general associated with significantly higher all-cause mortality during adulthood [2], and obesity during childhood and adolescence has been shown to significantly increase the risk for morbidity and mortality later in life [3]. Especially visceral obesity, defined as increased waist circumference and accumulation of adipose tissue in the abdomen, significantly increases the risk for cardiovascular or metabolic diseases, starting as soon as during puberty [4]. However, there is emerging evidence that some obese patients do not have the typical obesity-associated metabolic disorders, such

Abbreviations: BMI, body mass index; CRP, C-reactive protein; FFA, free fatty acid; IR, insulin resistance; MHO, metabolically healthy obese; NAFLD, non-alcoholic fatty liver disease; WBC, white blood cell count.

☆ The authors disclose any potential conflict of interest.

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Table 1 – Several definitions of metabolically healthy obesity (MHO) from childhood to adulthood (mean age: years ± standard deviation).

Study	No. of patients	Mean age [range]	Criteria to define MHO	Criteria to define unhealthy obesity	Prevalence of MHO (%)
Pediatric population					
Prince RL et al 2014 [51]	181 overweight (BMI > 85th percentile) youths	[8–17]	Based on: (a) insulin resistance (IR) and (b) cardiometabolic risk (CR) factors (blood pressure, serum lipids, and glucose)	Based on: (a) insulin resistance (IR) and (b) cardiometabolic risk (CR) factors (blood pressure, serum lipids, and glucose)	IR: 31.5 CR: 21.5
Camhi SM et al 2013 [48]	335 obese (BMI > 95th percentile) youths	14.8 ± 0.3 [8–18]	<2 abnormal cardiometabolic risk factors [a]	≥2 abnormal cardiometabolic risk factors [a]	68
Mangge H et al 2013 [50]	299 overweight (>85th percentile)/ obese (>95th percentile) youths	11.7 ± 3.3 [8–18]	No laboratory criterium of definition for metabolic syndrome according to IDF criteria [b] fulfilled	≥3 IDF criteria [b] of metabolic syndrome fulfilled	36
Weghuber D et al, 2013 [52]	299 overweight (>85th percentile)/ obese (>95th percentile) youths	12.6 ± 3.0 [4–18]	No laboratory criterium of definition for metabolic syndrome according to IDF criteria [b] fulfilled	≥3 IDF criteria [b] of metabolic syndrome fulfilled	36
Senecha lM et al 2013 [47]	108 overweight (>85th percentile)/ obese (>95th percentile) youths	15.2 ± 1.5 [13–18]	No elevated triglycerides, glucose, syst./diast. blood pressure, hepatic triglyceride content and no abnormally low HDL-C	≥1 of the following: elevated triglycerides, glucose, syst./ diast. blood pressure, hepatic triglyceride content, low HDL-C	25
Vukovic R et al 2013 [46]	248 obese (BMI > 95th percentile) youths	[5.9–18.9]	Insulin sensitivity: lower quartile of HOMA-IR (≤2.75)	Insulin resistance: upper quartile of HOMA-IR (≥6.16)	25 by design
Adults					
Camhi SM, Katzmarzyk PT 2013 [48]	395 obese adults	[18–68]	<2 MetS risk factors [c]	≥2 MetS risk factors [c]	n.a.
Ortega FB, et al 2013 [33]	43,265 adults (all weight ranges)	44.2 ± 9.9	BMI ≥ 30.0 kg/m^2; ≤2 MetS criteria [c]	BMI ≥ 30.0 kg/m^2; >2 MetS criteria [c]	46
Phillips CM, Perry IJ 2013 [33]	2.047 normal weight/obese adults	[45–74]	BMI ≥ 30 kg/m^2; application of 5 existing metabolic health definitions based on a range of cardiometabolic abnormalities	BMI ≥ 30 kg/m^2; application of 5 existing metabolic health definitions based on a range of cardiometabolic abnormalities	9.7–36.4
Bobbioni-Harsch et al 2012 [19]	152 overweight/ obese adults	45.0 ± 9.0 [30–60]	3 years incidence of cardiometabolic risk factors: no indication for impaired fasting glucose, reduced high-density lipoprotein (HDL)-cholesterol, increased plasma triglycerides or blood pressure as well as impaired glucose tolerance, normal intima media thickness	3 years incidence with ≥3 cardiometabolic risk factors: impaired fasting glucose, reduced high-density lipoprotein (HDL)-cholesterol, increased plasma triglycerides or blood pressure as well as impaired glucose tolerance, normal intima media thickness	17.7
Hamer M et al 2012 [21]	22,203 overweight/ obese adults	54.1 ± 12.7 [30–60]	BMI ≥ 30.0 kg/m^2; <2 MetS criteria [c] including antihypertensive medication, diagnosed diabetes or CRP ≥ 3 mg/L	BMI ≥ 30.0 kg/m^2; ≥2 MetS criteria [c] including antihypertensive medication, diagnosed diabetes or CRP ≥ 3	5.2
Kantarzis K et al 2011 [15]	262 non-diabetic adults	46.8 ± 2.2	BMI ≥ 30.0 kg/m^2; insulin sensitivity based on an OGTT (IS in the upper quartile)	BMI ≥ 30.0 kg/m^2; insulin resistance based on an OGTT (IS in the lower three quartiles)	22.4
Aguilar-Salinas CA et al 2008 [20]	470 obese adults	[18–70]	BMI ≥ 30 kg/m^2; HDL-C of least 40 mg/dL in the absence of type 2 diabetes and arterial hypertension.	BMI ≥ 30 kg/m^2; impaired HDL-C and/or type 2 diabetes and/or arterial hypertension.	36.4
Stefan N et al 2008 [16]	314 adults (all weight ranges)	45 [18–69]	BMI ≥ 30.0 kg/m^2; insulin sensitivity: placement in the upper quartile of an ISI derived from an OGTT	BMI ≥ 30.0 kg/m^2; insulin resistance: placement in the lower 3 quartiles of an ISI derived from an OGTT	25 by design
Wildman RP et al 2008 [16]	5.440 adults (all weight ranges)	45.0 ± 0.4 [18–69]	Overweight (BMI ≥ 25 kg/m^2) or obesity (BMI ≥ 30 kg/m^2); <2 MetS criteria [c] including HOMA > 5, high-sensitivity CRP >0.1 mg/L, HDL <1.3 mmol/L	Overweight (BMI ≥ 25 kg/m^2) or obesity (BMI ≥ 30 kg/m^2); ≥2 MetS criteria [c] including HOMA > 5, high-sensitivity CRP >0.1 mg/L, HDL <1.3 mmol/L	Overweight: 17.9; obese: 9.7

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