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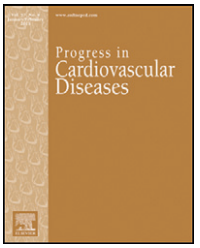

Role of Fitness in the Metabolically Healthy but Obese Phenotype: A Review and Update

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ABSTRACT

Despite the strong and consistent evidence supporting that a high physical fitness (PF) level at any age is a major predictor of a healthier metabolic profile, major studies focused on the metabolically healthy but obese (MHO) phenotype have ignored the role of PF when examining this phenotype and its prognosis. Particularly, the role of its main health-related components such as higher cardiorespiratory fitness (CRF) and muscular fitness in the MHO phenotype needs to be reviewed in depth. The present review aimed to: 1) contribute to the characterization of the MHO phenotype by examining whether MHO individuals are fitter than metabolically abnormal obese (MAO) individuals in terms of CRF and other PF components; 2) review the role of CRF and other PF components in the prognosis of MHO. The studies reviewed suggest that a higher CRF level should be considered a characteristic of the MHO phenotype. Likewise, CRF seems to play a key role in the prognosis of the MHO individuals, yet this statement is based on a single study and future studies need to confirm or contrast these findings. Comparability of studies is difficult due to the different definitions used for MHO; consequently, the present review makes a proposal for harmonizing this definition in adults and in youth. Obesity is still related to an important number of comorbidities; therefore, the public health message remains to fight against both obesity and low CRF in both adult and pediatric populations.

Strong and consistent evidence supports that a higher cardiorespiratory fitness (CRF) level at any age is a major predictor of a healthier metabolic profile, as well as a lower risk for incident cardiovascular disease (CVD) and CVD mortality.[1–4] Based on this evidence, it would be expected that epidemiological studies and reviews focusing on metabolic syndrome and/or CVD would account for CRF in their analyses or if CRF data are not available, would at least mention it as a limitation. The

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Abbreviations and Acronyms

1RM = 1 repetition maximum

ATP III = Adult Treatment Panel III

BF% = body fat percentage

BMI = body mass index

CI = confidence interval

CRF = cardiorespiratory fitness

CVD = cardiovascular disease

ES = effect size

FFM = fat free mass

HDL-C = high-density lipoprotein cholesterol

HE = hyperinsulinemic-euglycemic

MAO = metabolically abnormal obese

MHO = metabolically healthy but obese

MS = muscular strength

NS = not significant

PF = physical fitness

SD = standard deviation

VO_2max = maximal oxygen consumption

VO_2peak = peak oxygen consumption

WC = waist circumference

same would apply when studying the metabolically healthy but obese (MHO) phenotype, a condition in which obesity coexists with a fully healthy metabolic profile. MHO is present in 10–30% of obese adults[5] and in 6–36% of obese children/adolescents,[6,7] with prevalence differences largely due to different definitions of MHO. Unfortunately, many of the major studies on this topic ignored the critical impact of CRF. As an example, Primeau et al.[8] reviewed the existing literature and reported a number of characteristics of the MHO phenotype, including lower visceral fat accumulation, higher birth weight, adipose cell size, and gene expression-encoding markers of adipose cell differentiation; however, CRF was not mentioned. Likewise, Kramer et al.[9] conducted a systematic review and meta-analysis about the prognosis of individuals who are MHO, but again, the potential role of CRF in this prognosis was ignored. Another recent high profile study by Bell and colleagues indicated that a high percentage of those with MHO usually lose their metabolic health over time, much more so than do leaner subjects who are also metabolically healthy[10]; however, we have argued that this analysis also did not assess physical activity much less CRF.[11] On the other hand, the latest literature on this topic does acknowledge that CRF levels should be considered and that CRF could play a central role in the risk of mortality in MHO individuals.[12–14] Moreover, a recent review specifically explored the role of CRF when comparing *healthy obese* with *unhealthy lean*, and concluded that greater emphasis should be placed on improving CRF rather than weight loss *per se* in the primary and secondary prevention of CVD, at least in patients with overweight and class I obesity (body mass index, BMI 25–35 kg/m^2).[15]

Although available information is promising, whether a higher CRF is a characteristic in MHO individuals has not been specifically reviewed. In order to address this question we searched for studies assessing both CRF and the MHO phenotype in adults as well as in youth up to March 31st 2015. We decided to extend the search to other health-related physical fitness (PF) components, such as muscular strength (MS), flexibility and balance. Particularly, there is accumulating evidence supporting that MS is an emerging predictor for CVD mortality, independently of traditional risk factors such as obesity and hypertension, and also independently of CRF[16–19]; however, its role in the MHO phenotype is unknown. Likewise, there is a need for an update on the potential role of PF on the prognosis of MHO individuals. The present review specifically aimed to: 1) contribute to the characterization of the MHO phenotype by examining whether MHO individuals are fitter than metabolically abnormal obese (MAO) individuals in terms of CRF and other PF components; 2) review the role of CRF and other PF components in the prognosis of MHO.

Are MHO individuals fitter than their MAO peers? Current evidence from cross-sectional data

Overall description of the studies reviewed

We found 12 studies in which any of the components of PF were compared between MHO and MAO. The most relevant information from each of these studies is presented in Table 1. In addition, a summary of the characteristics of these studies is shown in Table 2. Surprisingly, 75% of the studies focused exclusively on women[20–22,24,26–30] and only 25% focused on both women and men (no study was focused only in men).[31,33,34] Likewise, all studies[20–22,24,26–30,33,34] but one[31] were conducted in adults or older adults. These two observations inform us that the output and conclusion derived from this review would mainly apply to adult or older adult women.

Most of studies were conducted in Canada (n = 6)[21,22,29–31,33] or in USA (n = 2),[20,34] with both comprising two thirds (50% + 17% = 67%) of the studies published on this topic. The concept of MHO, as indicated by its name, refers to obese individuals. However, 5 out of the 12 studies (42%) also included overweight participants and analyzed them together with the obese participants,[21,27–29,31] so that the results reported in these studies are referring to metabolically healthy but overweight or obese individuals. The definition of MHO differed across studies and could be summarized into 2 groups: 1) those based on meeting 0 or 1 (including or excluding waist circumference) of the metabolic syndrome criteria internationally accepted (yet with slight modifications in some studies),[25] which was used in 75% of the studies[22,24,26–28,30,33,34]; and/or 2) markers of insulin sensitivity (mainly using top/bottom tertiles/quartiles of the hyperinsulinemic-euglycemic clamp), which was used in 33% of the studies.[20,21,29,30]

Although our effort was to search studies assessing any PF component, we found that CRF was the most studied, with 100% of the studies including a measure of CRF, only 2 studies additionally assessing MS[24,29] and one of them, additionally assessing other components of PF, such as flexibility, balance and agility.[24] CRF was assessed mainly using an incremental test in a cycle ergometer (58% of the studies),[21,26–31] followed by treadmill testing (25%),[20,33,34] and expressed as measured/estimated maximal oxygen consumption (VO_2max or VO_2peak; 83% of the studies).