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The Concept of Normal Weight Obesity

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ABSTRACT

Individuals with normal body weight by body mass index (BMI) and high body fat percentage show a high degree of metabolic dysregulation. This phenomenon, defined as normal weight obesity, is associated with a significantly higher risk of developing metabolic syndrome, cardiometabolic dysfunction and with higher mortality. Recently, we have also shown that coronary artery disease patients with normal BMI and central obesity have the highest mortality risk as compared to other adiposity patterns. Therefore, it is important to recognize these high-risk groups for better adiposity-based risk stratification. There is a need for an updated definition of obesity based on adiposity, not on body weight.

The Merriam-Webster dictionary defines obesity as a condition characterized by the excessive accumulation and storage of fat in the body.[1] Obesity is a chronic metabolic disorder characterized by an increase in the number and/or the size of fat cells. Global prevalence of obesity has almost doubled since 1980[2] and has now become an epidemic[3,4] threatening public health. In 2008, more than 1.4 billion adults in the world were overweight, from which approximately 200 million men and 300 million women were obese.[2] Overweight and obesity represent the fifth leading risk for global deaths.[2] Formerly thought as a problem of high-income countries, overweight and obesity are becoming more prevalent in low- and middle-income countries.

The American Heart Association and the American College of Cardiology guidelines labeled obesity as a major modifiable cardiovascular disease (CVD) risk factor. Obesity is associated with higher rates of insulin resistance, type 2 diabetes mellitus (DM), hypertension (HTN), dyslipidemia, coronary heart disease (CHD), gallbladder disease, obstructive sleep apnea, non-alcoholic fatty liver disease and some malignancies including endometrial, breast, and colon cancer.[3,4] Obesity is considered an independent risk factor for CVD[5] and is associated with increased mortality in general healthy populations.[3]

Historic perspective of the concept of obesity

Measurement of height and weight was the initial step in the clinical assessment of overweight and obesity. In 1908, Symonds reported the results of a large prospective study of weight and mortality in New Jersey. He registered weight for a given height and age, and the influence of excess weight on vitality.[6] Subsequently, obesity was defined in relation to desirable weight, taking in consideration the actuarial tables from the Metropolitan Life Insurance Company.[7] The concept used was percent of ideal body weight. Later on, the Diet and Health report questioned the approach of using ideal body weight[8] and suggested that terms like "healthy or good weight ranges" were associated with decreased mortality.[9] Afterwards, body mass index (BMI) substituted the assessment of obesity, calculated as body weight (in kg) divided by height (in

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Abbreviations and Acronyms

BF = body fat

BMI = body mass index

CHD = coronary heart disease

CVD = cardiovascular disease

DM = diabetes mellitus

HDL = high-density lipoprotein cholesterol

HF = heart failure

HOMA = Homeostasis Model Assessment

HTN = hypertension

LDL = low-density lipoprotein

NWO = normal weight obesity

WC = waist circumference

WHO = World Health Organization

WHR = waist-to-hip ratio

meters) squared. The initial use of the index was in 1842 by Quetelet – a Belgian mathematician – who noticed that in people he considered to have a "normal frame" the weight was proportional to the height squared.[10] In the last 3 decades of the 20th century, several epidemiologic studies used BMI to prove the association between adiposity and mortality, CVD, DM and many other obesity-related comorbidities. With the help of experts from around the world who formed The International Obesity Task Force, in 1997 the World Health Organization (WHO) came up with the definition of obesity as a BMI $\geq$30 kg/m^2.[11,12] The definition also described other degrees of adiposity like overweight and obesity grade 1 and 2, although the cutoffs chosen were arbitrary. Fig 1 shows the classification of obesity modified by the National Heart, Lung and Blood Institute task force, along with the associated disease risk with increasing BMI.[13]

Obesity can be also measured using direct and indirect measures of fatness other than BMI. The methods to estimate body fat (BF) include bioelectrical impedance, hydrostatic plethysmography, isotope dilution techniques, dual x-ray absorptiometry, skinfold method, body impedance measures with over the counter scales, and air displacement plethysmography.[14] Epidemiologic studies have also demonstrated that central fat distribution, measured with waist circumference (WC), waist-to-hip ratio (WHR) and weight-to-height ratio, is also an important measure of adiposity-related risk.[15]

Pitfalls of current BF mass measurements

BMI as a measure of BF became popular and widely used because of its simplicity and validation in multiple epidemiologic studies. Surprisingly, even though obesity is defined as excessive adiposity, there is no consensus on how to define obesity using fat mass calculation or fat percentage, other than the effort by the American Society of Endocrinologists who defined obesity by BF percent as >35% in women and >25% in men.[16] Direct measurement of adipose tissue using methods like water-displacement plethysmography or magnetic resonance is too cumbersome to be used in large populations or in clinical practice. Newer methods to measure fat content like air-displacement plethysmography, DEXA or electrical bioimpedance have shown to be valid and not necessarily expensive.

Although several studies have demonstrated a high correlation between BMI and directly-measured BF, the diagnostic performance of BMI is not optimal to identify leanness or excessive BF. We have tested the accuracy of BMI for diagnosing obesity in the adult general population using data from 13,601 individuals from the Third National Health and Nutrition Examination Survey.[17] Using bioimpedance to calculate BF and a BMI >30 kg/m^2 to define obesity, BMI had a very high specificity (97%) but poor sensitivity (42%) to detect obesity[17,18] Therefore, more than half of the individuals with increased BF percentage may be misclassified by BMI. In individuals with BMI of $\geq$25 kg/m^2, the index had 86% sensitivity and a specificity of 73%. A meta-analysis of the diagnostic performance of BMI to detect excessive adiposity using different techniques as the gold standard showed similar results.[18] A recent study demonstrated a wide range of BF % using dual energy x-ray absorptiometry in people with normal BMI, ranging from 5.6 to 31.2% in men and from 4.6 to 51.1% among women.[19] The main limitation of BMI is that it cannot differentiate BF from lean mass, and central from peripheral fat. Therefore, athletes with enhanced body muscle mass may be misclassified as obese when using only BMI to diagnose obesity, whereas people with low lean mass but high BF content may still have a normal BMI.[20]

Challenging the simplistic concept of obesity as defined by BMI

Over the last 30 years, there have been several new concepts challenging the simplistic concept that obesity can be diagnosed based on weight and height. Numerous studies have proposed definitions of the obesity subtypes (Table 1).

Firstly, Ruderman et al[21] challenged the notion that standard weight–height tables were the proper way to determine high-risk groups for obesity associated disorders. They observed normal weight individuals suffering from type 2 DM, premature CHD, HTN and hypertriglyceridemia with associated hyperinsulinemia. They pointed out that these abnormalities could not be explained by skinfold thickness or adipose mass and hypothesized that it was due to larger fat cells. The identified metabolically obese, normal weight individuals had benefits when they went through programs of energy restriction and weight loss. If patients were challenged to a 4–12 week period of diet and exercise there was metabolic improvement.[22] Some studies suggested that the main issue to explain the metabolic abnormalities in individuals not particularly overweight was fat distribution. On the basis of these studies, it was proposed a scoring method to identify a metabolically obese normal weight individual. Depending on the presence of associated diseases or biochemical abnormalities related to insulin resistance, individuals would be assigned a score to base the diagnosis of metabolically obese normal weight. All of these mentioned disturbances predispose the individual to suffer from,[23] as well as making them a susceptible population to suffer