Body Mass Index and Weight Change: The Sixth Vital Sign

Pierre Singer MD[1,2,4], Joelle Attal-Singer MD[3,4] and Haim Shapiro MD[2]

[1]Department of General Intensive Care and [2]Institute for Nutrition Research, and [3]Institute of Endocrinology, Diabetes Services, Rabin Medical Center (Beilinson Campus), Petah Tikva, and [4]Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Key words: body mass index, obesity, cachexia, vital signs

IMAJ 2008;10:523–525

Determining the heart rate, breathing rate, temperature and blood pressure is an essential and fundamental component of western medicine and of the interaction between health care provider and patient. These physiological parameters are easily measured by physical examination or with a diagnostic device. They are normally maintained within a physiological range by homeostatic feedback systems that have powerful compensatory capabilities. Measurements that exceed or drop below a threshold indicate an underlying pathology and are often associated with increased morbidity and mortality. Furthermore, they may serve as a diagnostic criterion, a prognostic factor, and/or as an indication to initiate treatment. In this brief article, we intend to show that body weight/body mass index (weight/height^2 in kg/m^2) is also a vital sign.

Body weight regulation

In adults, body weight is efficiently maintained at a set point. Energy intake and expenditure are regulated by the nervous and hormonal systems, including peptides from the gastrointestinal tract, pancreas and adipose tissue. These modulate multi-level physiological processes from motivation to mitochondrial function in order to match energy intake to energy expenditure. It has been calculated that the accuracy of matching energy intake and expenditure over one year is more than 95.5% in adults [1]. The finding of a BMI beyond the 20–30 range or of significant weight loss in a short period indicates a significant deviation in energy balance and has detrimental health implications.

Epidemiology and pathophysiology of BMI variations and weight loss

Excess weight gain in children and adults is increasingly prevalent worldwide. A large international study found 24% of men and 27% of women to be clinically obese, i.e., having a BMI ≥ 30, although national and ethnic variations exist [2]. Obesity predisposes to type 2 diabetes and atherosclerosis-related disease [3] and is associated with an increased long-term risk of premature death secondary to these disorders and certain cancers [4,5]. These deleterious consequences of excessive weight gain are not due to the physical characteristics of triglycerides and adipose tissue, but rather to the spillover of free fatty acids and inflammatory mediators from the expanded adipose tissue. This leads to insulin resistance, dyslipidemia, non-alcoholic fatty liver disease and atherosclerosis. The intra-abdominal fatty deposit is the leading culprit behind the systemic effect of obesity, probably due to its propensity to attract macrophages, its resistance to insulin's inhibitory effect on lipolysis, its prominent blood supply and its venous drainage to the liver. Conversely, subcutaneous fat in the lower extremities appears to be protective [3]. BMI serves as an imperfect but easily obtained index of excess adiposity. Once obesity is diagnosed, lifestyle and pharmacological or surgical interventions are indicated, as well as the assessment and treatment of associated pathologies [3].

In contrast to obesity, unintentional weight loss is typically the result, rather than the cause of an underlying pathology. Occasionally, however, a cause for weight loss and low body weight is not identified. In addition, weight loss is often associated with nutritional deficiencies that negatively impact any major underlying disease [6,7].

Chronic severe medical disorders such as advanced human immunodeficiency virus infection and cancer, as well as chronic insufficiency of a vital organ (chronic heart or renal failure, chronic obstructive pulmonary disease, etc.) induce a debilitating catabolic state termed cachexia. The latter may be defined as a pathological loss of weight with a disproportionate reduction in skeletal muscle mass. To a certain degree, a reduction in lean body mass is a normal part of aging (sarcopenia). However, the prevalence of chronic organ failure increases with age, and its effect on body weight is superimposed upon sarcopenia. Weight loss in the elderly may also be exacerbated by various psychosocial factors, loss of appetite, malabsorption and musculoskeletal deconditioning [8,9]. Given the growing elderly population and increasing incidence of the chronic diseases mentioned above, cachexia is quite common. Discerning clinically between sarcopenia and cachexia is challenging [9], but the simple finding of significant recent weight loss and/or a reduced BMI is strongly predictive of short-term mortality in hospitalized patients [10],

BMI = body mass index

the elderly dwelling in the community [11] or a nursing home [12], patients with HIV infection, cancer or chronic insufficiency of a vital organ [9], and in the adult population as a whole [13]. Results of a 35 year cohort study of more than 5000 Jewish Israeli adults (the Israel Glucose Intolerance, Obesity and Hypertension study) recently showed that in males, an initial BMI of below 20 or above 30 were significantly associated with increased mortality [14]. In this study females with a low BMI did not exhibit excess mortality.

Associations of mal- and overnutrition with inflammation

Humans, like other organisms, avidly store energy and nutrients that are distributed according to the particular priorities arising during scenarios such as the postprandial state, starvation, exercise, and infection/trauma. Together with the robust inflammatory and immune response to invading pathogens, these capabilities promote survival during times of lack and infection. Inflammation and nutrient supply are also essential for repair and recovery from injury and aseptic tissue damage. Cells involved in metabolism (adipocytes, hepatocytes, myocytes) and inflammation (leukocytes and resident macrophages) share molecular machinery (e.g., pattern recognition and cytokine receptors, stress kinases, peroxisome proliferator-activated receptors), which facilitates dual communication. They become interdependent during infection and trauma: inflammatory cells are dependent on macro- and micronutrients in order to execute an effective innate immune response; hepatocytes require a large quantity of amino acids to synthesize. Acute-phase reactants target pathogens and enhance inflammation. Nutrient re-prioritization during infection and trauma is mediated to a great extent by pro-inflammatory cytokines, with skeletal muscle bearing the burden of proteolysis [15,16].

BMI and weight should be considered the sixth vital sign and should be more widely implemented for the initial diagnosis of malnutrition, obesity and their associated disorders

In the past, and in some third world countries today, malnutrition was a major cause of death from infectious disease and of the short average lifespan. The advantage in having both a robust inflammatory response and a metabolic system gauged for nutrient deficiency becomes apparent during acute infection at times of insufficient food supply; its downside has only recently been uncovered. Prevention and treatment of infectious disease has prolonged life expectancy. Energy-dense, highly palatable foods are now more available and the need to exert physical effort is lower than ever before, leading to an escalating positive energy balance. These changes facilitated the transition from an era of communicable diseases to the present epidemic of obesity and chronic inflammatory disease [16,17].

When excess caloric intake surpasses the body's ability to store energy-providing nutrients, a spillover of glucose and fatty acids to the blood and certain tissues occurs. Elevated levels of glucose and free fatty acids, as seen in obesity, induce oxidative stress and activate stress kinases that lead to inflammation, insulin resistance and cytotoxicity. In the obese state, the liver and visceral adipose tissue produce inflammatory mediators such as tumor necrosis factor-alpha. Inflammation itself reduces insulin sensitivity, permitting increases in glucose and free fatty acid levels. A vicious cycle of chronic inflammation, elevated glucose and fatty acid levels, insulin resistance and organ damage, paves the way to diabetes, atherosclerosis and other diseases [15].

Cachexia and other forms of pathological weight loss are often the result of chronic systemic inflammation. The circulating and tissue levels of inflammatory mediators are increased in disease states in which cachexia is common; mediators such as TNFα (cachectin) and interleukin-1 beta contribute both to protein loss from skeletal muscle and to anorexia [8,9]. Thus, inflammation is a major instigator of the cachectic phenotype, and both obesity and cachexia are causatively associated with inflammation. Given the role of the latter in acute and chronic disease, this association may explain the increased mortality seen in both over- and undernutrition. In other words, there appears to be a J-shaped correlation between BMI and between both mortality and the degree of inflammation [Figure 1]. The J-curve appears to shift to the right in the elderly, in critically ill patients and in those with chronic organ failure (congestive heart failure, chronic obstructive pulmonary disease, chronic renal failure, etc), in whom higher weight appears to be protective. This is partially due to the fact that obesity leads to long-term mortality, whereas it is short-term mortality that is increased in cachectic diseases. However, the precise mechanisms and clinical implications of the

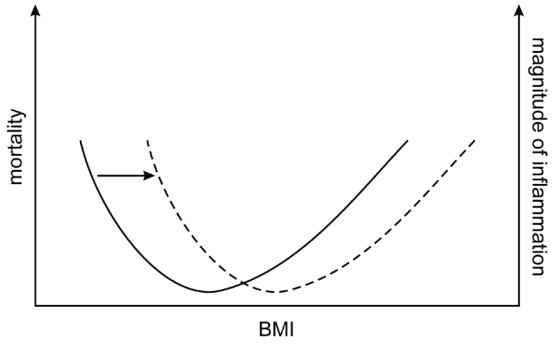

Figure 1. J-curve correlation between BMI and between inflammation and mortality. The magnitude of inflammation and the mortality rate (Y axis) are greater at the extremes of BMI (X axis). Long-term mortality is higher in relatively healthy middle-aged – adults (continuous line curve). The J-curve appears to be shifted to the right (dotted line curve) in the elderly and in patients with severe disease and chronic organ failure, i.e., being overweight appears to actually be protective. This may be because lean body mass, which is reduced in cachexia, contributes to the BMI and is often referred to as the obesity paradox. Still, depending on the clinical scenario, a particular BMI correlates with both inflammation and mortality.

HIV = human immunodeficiency virus

TNFα = tumor necrosis factor-alpha

"obesity paradox," a form of reverse epidemiology, remain to be established, and this phenomenon does not distract from the importance of weight/body mass assessment [18].

BMI and weight change should be, but often are not assessed

Thus, weight measurement supplies us with critical information regarding a patient's overall condition, possible underlying and associated conditions, and the risk of increased morbidity and mortality. Occasionally, it will serve as an indication for therapeutic intervention such as the administration of nutritional support or bariatric surgery. Do these characteristics not accredit weight/BMI the title of vital sign?

Pain is referred to as the fifth vital sign, partially in order to promote awareness of pain recognition and treatment among health care professionals [19]. Pain is also one of the five cardinal signs of inflammation designated by Celsus and Virchow, along with redness, heat, swelling and loss of function [20]. We propose that weight/BMI be considered the sixth vital sign, and emphasize that mass matters and that detecting and treating patients with abnormal measurements is elementary medicine. Also, we suggest that an abnormal BMI/weight loss is the sixth sign of inflammation.

In reality, measuring BMi and assessing weight change are neglected by health care providers. In a recent population-based study of adult Israelis, the body weight of only 40% of obese individuals had been measured in the clinic within the previous 5 years [21]. A recent European survey of 16,456 patients including 198 Israeli patients showed that Israel had one of the lowest rates of weighing patients on admission. This parameter was, however, of importance since it correlated strongly to length of stay [21,22].

Conclusions

Obesity is a health care burden of global dimensions and is being addressed by health organizations, governments, medical associations and medical care systems that emphasize the need to diagnose and treat patients with elevated BMI. But in our age of plenty, of advanced imaging technology and tailor-made molecular therapeutics, the failure to identify malnutrition, the diagnosis of which is simple, safe and cheap, is not excusable. Treatment of malnutrition is an attainable goal and can reduce morbidity, length of hospital stay and possibly mortality [23], further underscoring the need for body mass/weight assessment in health care [24].

References

1. Cota D, Proulx K, Seeley RJ. The role of CNS fuel sensing in energy and glucose regulation. *Gastroenterology* 2007;132(6):2158–68.
2. Balkau B, Deanfield JE, Despres JP, et al. International Day for the Evaluation of Abdominal Obesity (IDEA): a study of waist circumference, cardiovascular disease, and diabetes mellitus in 168,000 primary care patients in 63 countries. *Circulation*. 2007; 116(17):1942–51.
3. Pi-Sunyer FX. The relation of adipose tissue to cardiometabolic risk. *Clin Cornerstone* 2006;8(Suppl 4):S14–23.
4. Adams KF, Schatzkin A, Harris TB, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. N *Engl J Med* 2006;355(8):763–78.
5. McMillan DC, Sattar N, McArdle CS. ABC of obesity. Obesity and cancer. *BMJ* 2006;333(7578):1109–11.
6. Alibhai SM, Greenwood C, Payette H. An approach to the management of unintentional weight loss in elderly people. *CMAJ* 2005;172(6):773–80.
7. Schwartz DB. Malnutrition in chronic obstructive pulmonary disease. *Respir Care Clin North Am* 2006;12(4):521–31.
8. Morley JE, Thomas DR, Wilson MM. Cachexia: pathophysiology and clinical relevance. *Am J Clin Nutr* 2006;83(4):735–43.
9. Thomas DR. Loss of skeletal muscle mass in aging: examining the relationship of starvation, sarcopenia and cachexia. *Clin Nutr* 2007;26(4):389–99.
10. Thomas DR, Kamel H, Azharrudin M, et al. The relationship of functional status, nutritional assessment, and severity of illness to in-hospital mortality. *J Nutr Health Aging* 2005;9(3):169–75.
11. Landi F, Zuccala G, Gambassi G, et al. Body mass index and mortality among older people living in the community. *J Am Geriatr Soc* 1999;47(9):1072–6.
12. Murden RA, Ainslie NK. Recent weight loss is related to short-term mortality in nursing homes. *J Gen Intern Med* 1994;9(11):648–50.
13. Andres R, Muller DC, Sorkin JD. Long-term effects of change in body weight on all-cause mortality. A review. *Ann Intern Med* 1993;119(7 Pt 2):737–43.
14. Dankner R, Haratz D, Segal P. The Israel Glucose Intolerance, Obesity and Hypertension Study – 35 year follow up. Presented at the 3rd Russell Berry Symposium Tel Aviv, Israel, 2007.
15. Hotamisligil GS. Inflammation and metabolic disorders. *Nature* 2006;444(7121):860–7.
16. Santos JI. Nutrition, infection, and immunocompetence. *Infect Dis Clin North Am* 1994;8(1):243–67.
17. Yusuf S, Reddy S, Ounpuu S, Anand S. Global burden of cardiovascular diseases. Part I: General considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation* 2001;104(22):2746–53.
18. Kalantar-Zadeh K, Horwich TB, Oreopoulos A, et al. Risk factor paradox in wasting diseases. *Curr Opin Clin Nutr Metab Care* 2007;10(4):433–42.
19. Graf C, Puntillo K. Pain in the older adult in the intensive care unit. *Crit Care Clin* 2003;19(4):749–70.
20. Scott A, Khan KM, Cook JL, Duronio V. What is "inflammation"? Are we ready to move beyond Celsus? *Br J Sports Med* 2004;38(3):248–9.
21. Kalter-Leibovici O, Atamna A, Lubin F, et al. Obesity among Arabs and Jews in Israel: a population-based study. *IMAJ* 2007; 9(7):525–30.
22. Frishman S, Lustigman H, Gindy L, Rozen G, Hinga M, Hehmesh I, Singer P: Nutrition day 2006 in Israel [Abstract]. *Clin Nutr* 2007;2:S70.
23. Schuetz T, Schindler K, Schlaffer R, Mouhieddine M, Schuh C, Hiesmayr M: Nutrition day 2006: Impact of nutritional state and food intake on length of stay in German hospitals. *Clin Nutr Suppl* 2007;2:10.
24. Stratton RJ, Elia M. Who benefits from nutritional support: what is the evidence? *Eur J Gastroenterol Hepatol* 2007;19(5):353–8.

Correspondence: Dr. P. Singer, Dept. of General Intensive Care, Rabin Medical Center (Beilinson Campus), Petah Tikva 49100, Israel.

Phone: (972-3) 937-6521; Fax: (972-3) 923-2333

email: psinger@clalit.org.il