Measurement of body composition as a surrogate evaluation of energy balance in obese patients

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Abstract

In clinical practice obesity is primarily diagnosed through the body mass index. In order to characterize patients affected by obesity the use of traditional anthropometric measures appears misleading. Beyond the body mass index, there are overwhelming evidences towards the relevance of a more detailed description of the individual phenotype by characterizing the main body components as free-fat mass, muscle mass, and fat mass. Among the numerous techniques actually available, bioelectrical impedance analysis seems to be the most suitable in a clinical setting because it is simple, inexpensive, noninvasive, and highly reproducible. To date, there is no consensus concerning the use of one preferred equation for the resting energy expenditure in overweight and/or obese population. Energy restriction alone is an effective strategy to achieve an early and significant weight loss, however it results in a reduction of both fat and lean mass therefore promoting or aggravating an unfavourable body composition (as sarcobesity) in terms of mortality and comorbidities. Therefore the implementation of daily levels of physical activity should be simultaneously promoted. The major role of muscle mass in the energy balance has been recently established by the rising prevalence of the combination of two condition as sarcopenia and obesity. Physical exercise stimulates energy expenditure, thereby directly improving energy balance, and also promotes adaptations such as fiber type, mitochondrial biogenesis, improvement of insulin resistance, and release of myokines, which may influence different tissues, including muscle.

Key words: Obesity; Body composition; Bioelectrical impedance analysis; Energy expenditure; Sarcobesity

Core tip: There are overwhelming evidences towards the relevance of a more detailed description of the individual phenotype by characterizing the main body components as free-fat mass, muscle mass, and fat mass. Among the numerous techniques actually available, bioelectrical impedance analysis seems to be the most suitable in a clinical setting because it is simple, inexpensive, noninvasive, and highly reproducible. To date, there is no consensus concerning the use of one preferred equation for the resting energy expenditure in overweight and/or obese population.
INTRODUCTION

Obesity, defined by excessive adipose tissue, has been shown several deleterious effects on many body organs through thrombogenic, atherogenic, oncogenic, hemodynamic and neurohumoral pathways and has been linked to several chronic diseases, as diabetes, ischemic heart, and musculo-skeletal disorders, together with malignancies. Overweight and obesity represent the fifth leading risk for global death by The World Health Organization on March 2013[1]. At least 2.8 million adults die each year as a result of overweight/obesity. Moreover the 44% of diabetes and 23% of ischemic heart disease burden can be attributable to an abnormal adipose tissue accumulation[1].

Obesity is diagnosed accordingly to the body mass index (BMI). This index has been strongly recommended for use in clinical practice[2,3]. Multiple studies have shown a U or J-shaped relation between BMI, all causes and/or cardiovascular mortality, thus identifying the best survival rate for BMI values in overweight (25-27 kg/m^2) followed by a dramatic increase in risk profile out of these values[4,5].

In a cross-sectional study enrolling 13601 subjects (45.5 ± 17 years; 48% men) from the National Health and Nutrition Examination Survey (NHANES)[10], the BMI cut-off of ≥ 30 kg/m^2 shown an overall low sensitivity and an high specificity to identify obesity such as defined by an excessive body fat percentage at bioelectrical impedance analysis (> 25% in men and > 35% in women, respectively, thus according to the gold standard definition proposed by the World Health Organization)[5]. The BMI-based definition of obesity has important limitations on diagnostic performance, particularly in men and elderly, missing more than 50% of people with excessive fat mass. In men, BMI showed a more reliable association with lean mass and all-cause mortality rate (HR = 1.033, 95%CI: 1.09-1.17) for men and 1.21 (1.17-1.25) vs 1.20 (1.16-1.24) for women, respectively[15].

In the NHANES I and NHANES II longitudinal prospective cohort studies, performed in 10169 male subjects a continuous positive relationship between fat-mass and all-cause mortality rate (HR = 1.033, 95%CI: 1.09-1.17, P = 0.0213) have been reported, together with a preponderant significantly negative relationship between free-fat mass and all-cause mortality (i.e., protective; HR = 0.923, 95%CI: 0.906-0.941, P < 0.0001)[16].

Furthermore, BMI and weight loss rate may not be linked to clinical improvement of health-related outcomes, in comparison to different body composition measures by simple and non-invasive methods, which demonstrated a strong relationship between mortality, body lean mass and adipose tissue[17-24].

In conclusion beyond the BMI, there are overwhelming evidences towards a more detailed description of the individual phenotype by characterizing the main body components as free-fat mass (FFM), muscle mass (MM), and fat mass (FM).

BODY COMPOSITION MEASUREMENTS:
TECHNOLOGICAL ADVANCES AND CURRENTLY AVAILABLE NON INVASIVE TECHNIQUES

Numerous techniques for body composition analysis are currently available: anthropometry, including the 4-skinfold method, hydrostatic weighing, in vivo neutron activation analysis, anthropogammammetry from total body 40K, nuclear magnetic resonance, dual-energy X-ray absorptiometry (DEXA), computerized tomography (CT), and bioelectrical impedance analysis (BIA). Evaluating complexity, invasiveness, and cost only DEXA, CT, and BIA may represent the methods of choice to assess body composition in clinical practice whereas the other techniques are limited to scientific
pursposes.

DEXA estimates body fat and lean mass percentage through a tissue-specific model (fat, lean tissues, and bone) based on X-ray (dose 1-3 mrad) tissue-dependent attenuation[28]. The largest sample (n = 22000 participants) have been analyzed by the NHANES[26]. DEXA systems currently available for scanning whole-body tissue composition are capable to analyze a wide range of weights including severe obese subjects (> 150 kg). DEXA scans can be subdivided into different body regions, i.e., trunk, arms, and legs, thus identifying and estimating both android and gynoid fat distribution. DEXA can detect only abdominal adipose tissue accumulation without any distinction between visceral and subcutaneous fat because of their similar X-ray attenuation properties and tissue overlapping[27]. DEXA is the gold standard technique for the evaluation of body composition in clinical research[28-30], although limited in clinical practice by the radiation exposure, availability and cost. The use of the same DEXA instruments and analysis software are of relevant importance for longitudinal studies, since they could influence body composition measurements[31].

In patients affected by malignancies, the analysis at the level of the 3rd lumbar vertebra by CT strongly predicted whole body fat and FFM as compared with DEXA[32]. CT provided an accurate evaluation of body composition, not provided by DEXA or BIA and a X-ray exposition similar to a chest radiography. Although not validated, also CT images of the right thigh halfway showed to be significantly related to overall mortality rate in chronic obstructive pulmonary disease patients[33]. Despite its wide use at diagnosis and follow-up in severely ill patients, CT scan at the 3rd lumbar vertebra cannot be considered a feasible method to assess body composition in obese population requiring expensive equipment, trained operators and exposure to ionizing radiation.

BIA is based on the capacity of hydrated tissues to conduct electrical energy. The BIA methodology have been described in two ESPEN position papers[34,35]. The analysis of total body impedance is based on the estimation of total body water. From total body water, prediction equations allow the calculation of FM and FFM. BIA equations have been validated for chronic obstructive pulmonary disease, AIDS, transplant patients and elderly individuals[36]. A prediction equation for FFM estimation by BIA in adults (age: 20-94 years; BMI: 17.0-33.8 kg/m2) has been proposed[37] as well as reference values of FFM and FM for a Caucasian population[38]. Previously reported data showed no significant differences between DEXA and BIA for the assessment of fat mass in overweight and/or obese patients with a significantly good linear correlation[39,40]. However several factors could limit the validity of BIA in severe obesity[41].

**ENERGY BALANCE IMPLICATIONS FOR ADDRESSING OBESITY: AVAILABLE ENERGY EXPENDITURE MEASUREMENTS**

Energy balance is constituted by three major components including energy intake, energy expenditure (EE) and energy storage. Energy expenditure is expressed by resting energy expenditure (REE), as the amount of energy required for the endogenous metabolic activity separated from the metabolic effects of food and physical activity, the food-related thermic effects (TEF), as energy need to absorb and metabolize ingested food, and energy expenditure associated to physical activity (EEfa). EEfa is the most inter-individual variable component of energy expenditure and consists of the amount of physical activity performed multiplied the energy requirement of that activity. The REE is proportional to body mass, particularly to the FFM[42]. The REE prediction equations evaluate the energy expenditure of 2 different body compartments as the adipose tissue or FM and the lean mass or FFM. FM is the main source for REE and is commonly considered as a surrogate measure of metabolically active tissues. Brain, liver, heart, and kidney account for approximately the 60% of REE, despite a combined weight < 7% of FFM. In comparison to the skeletal muscle, the metabolic rate of heart and kidney is approximately 30-fold higher; and the later approximately 2-fold higher in comparison to brain and liver. The skeletal muscle represents the major contributor to the FFM (50%), but accounts for only the 21% of the REE. Adipose tissue has a low energy expenditure, however its body rate varies significantly according to the dramatic increase of overweight and obesity. Then it is notable that FM represent an important source for the REE in all prediction models. Among adults, REE is lower in elderly, almost in part explained by the change in body composition[27].

Advantage and limitations of currently available non invasive techniques for the estimation of EE are summarized in Table 1.

Indirect calorimetry represents the gold standard technique to evaluate REE. This method used the rates of oxygen consumption (V02) and/or carbon dioxide production (VCO2) to calculate EE according to the Weir predictive equation, derived from studies comparing indirect calorimetry with direct calorimetry[43]. The complexity and cost, together with the requirement of the patient isolation for at least 24 h limit the feasibility of the direct calorimetry in humans.

The indirect calorimetry consists in a gas collector, a canopy and a system that measures the volume and concentrations of O2 and CO2 minute by minute. Through a unidirectional valve located in the ventilated canopy, the calorimeter collect and quantify the volume and concentration of O2 inspired and of CO2 expired. A systematic literature review aimed to determine the
optimal conditions for obtaining reliable measures of REE by indirect calorimetry recommends fasting for at least 6 h, avoiding caffeine during the night, nicotine and alcohol for at least 2 h, moderate physical activity for at least 2 h, and vigorous physical activity for 14 h before[44]. Despite methodological, environmental and individual limitations indirect calorimetry represents a non-invasive and very accurate method to estimate REE[46,47]. However this method is widely limited in most of clinical settings by the requirement of expensive equipment, and trained operators, then many efforts are spent to identify the most accurate predictive equation to determine REE in overweight and obesity.

Predictive equations have generally been calculated from experimental studies performed in healthy subjects on the basis of regression analysis of bodyweight, height, sex, and age as independent variables and REE by indirect calorimetry as a dependent variable. On the basis of a review of available evidences from Harris and Benedict[46], FAO/WHO/UNU weight or weight and height equations[47], and the equations of Mifflin et al[40] and Owen et al[49], Frankenfield et al[50] proposed the use of the Mifflin equation both for overweight and obese subjects. All the available predictive equations have been further validated with indirect calorimetry from adults aged 18-65 years with a BMI of 25 to 40 kg/m² in order to identify the most accurate and precise REE predictive equation in specific overweight and obese groups of United States and Dutch subjects: the results of this study were similar to the data of Frankenfield et al[50], then supporting the use of Mifflin equation in the United States. However for overweight and obese Dutch adults, there appears to be no accurate equation[51]. This discrepancy for the Dutch than for the United States adults could be explained by the difference about weight and height values, even within sex and BMI subgroups, thus limiting the validity of this equation in similar taller populations. Numerous studies contributed to further evaluate the currently available predictive equations in overweight and obese subjects[52-55] and/or in extremely obese subjects[56,57]. There is some evidences supporting the Mifflin[59], the FAO/WHO[56,58] and the Harris Benedict[60], the Siervo equations[61] in extremely obese subjects. More recently a new equation, using FFM, Horie-Waitzberg, and Gonzalez equations, have been validated and proposed in Brazilian severely obese subjects[62]. The most commonly proposed equation for the measurement of REE have reported in Table 2.

To date there is no consensus about the use of one REE equation compared to others, in overweight and/or obese population. This might be related to differences about group composition, methods, or statistical analysis, at least in part.

In order to estimate EE including EEₜₐ, a practical multi-sensor device, the SenseWear Armband (BodyMedia, Inc., Pittsburgh) has been recently developed. This device contains four sensors to detect heat flux, accelerometry, galvanic skin reaction, skin temperature. Despite excellent results by comparison with energy expenditure measured using the doubly labeled water in overweight/obese children[63] and lactating women[64], other evidences underline the need of obesity-specific equations[65,66].

A meta-analysis of randomized clinical trial suggest that pedometer use is associated with a significant decrease of body weight and blood pressure[67]. However a recent review assessing different accelerometers to measure daily physical activity as a surrogate of EE in comparison with the doubly labeled water only few available devices have been proven to adequately correlate with the reference method[68].

### TABLE 1: Advantages and limitations of available techniques the measurement of Energy Expenditure

| Technique                        | Advantages                                                                 | Limitations                                                                 |
|----------------------------------|-----------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| Direct calorimetry               | The gold standard method for measure EE in animal models                      | High complexity, high cost, need to confine the subject for almost 24 h     |
| Indirect calorimetry             | The gold standard to measure REE in humans. Non invasive, adequately accurate, highly reproducible | High cost, relatively complex, need of trained personnel                    |
| Bioelectrical impedance analysis | Non invasive, simple, adequately accurate for body composition analysis, relatively inexpensive | The estimation of EE is limited by the need of obesity-specific predictive equations |
| Multi-sensor device              | Easy and practical to use                                                    | The estimation of EE is limited by the need of obesity-specific predictive equation |

EE: Energy expenditure; REE: Resting energy expenditure.

### BEYOND THE ADIPOSE TISSUE EXCESS: THE IMPORTANCE OF MUSCLE MASS IN OBESITY

Skeletal muscle plays a critical role in the glucose metabolism and peripheral insulin sensitivity as well as musculoskeletal performance. The importance of lean mass on energy balance has been widely recognized by the rising prevalence of the combination of two condition as sarcopenia and obesity[69]. Two major consensus documents provide different definition of sarcopenia. The European consensus, the Working Group on Sarcopenia in Older People, defines sarcopenia as generalized loss of skeletal muscle mass and strength[70]. The International consensus, the International Working Group on Sarcopenia, requires a decline in muscle mass and walking speed to diagnose sarcopenia[71]. Although sarcopenic obesity is commonly used to define the coexistence of diminished muscle mass and increased adipose tissue, a standard...
definition of sarcopenic obesity is still lacking. Several clinical studies have indicated that obesity and/or insulin resistance may underlie the development of sarcopenia[72]. A possible role of vitamin D in sarcopenia has been postulated in two studies demonstrating that serum 25-hydroxy vitamin D was negatively correlated with appendicular (legs and arms) fat mass and positively associated with appendicular muscle mass, both evaluated through DEXA analysis[73,74].

Fat mass excess may induce and/or worsen sarcopenia because the increase of lipid depot reduces both amino acid utilization and protein synthesis in muscle fibers. Evaluating 3132 elderly male subjects without diabetes the highest quartile of homeostasis model assessment of insulin resistance showed the highest risk for a decrease in lean body mass and appendicular mass[75]. On the counterpart, skeletal muscle is the main target of insulin, then loss of muscle mass may cause insulin resistance. A previous study identified sarcopenia as a risk factor for exacerbating insulin resistance in obese subject with dysglycemia[76].

Skeletal muscle fibers can be classified into different categories: from slow (type I) fibers with low contractile abilities, numerous mitochondria and high oxidative energy metabolism, to type IIa and type II d/x, and eventually fast (type II b) fibers able to contract rapidly and predisposed toward glycolytic processes. In obese and diabetic population skeletal muscle commonly contains more type II b fibers, while slow muscle fiber percentage and skeletal muscle glucose transport are significantly reduced. Sarcopenic individuals have been shown to be associated with a further impairment of muscle fiber content, predominantly of type I[77]. Recent studies have shown that exercise is able to increase the content of type I and type II a fibers[78]. Furthermore, in skeletal muscle with ageing both the number and morphology of mitochondria are changed with an impaired function and an associated reduced oxidative capacity[79]. In particular since the primary role of mitochondria is to maintain the cellular energy balance, shifts in mitochondria respiratory activity can lead to a reduced maximal capacity of the tricarboxylic acid cycle and the electron transport chain together with an incomplete lipid-induced upregulation of β-oxidation rates, thus inducing a significant accumulation of intramyocellular lipids and further impairing whole body insulin resistance[79]. Physical exercise has been demonstrated to induce mitochondria biogenesis, upregulates skeletal muscle gene expression and protein synthesis, and increases skeletal muscle oxidative capacity both in older and sedentary populations[80].

Moreover, recent evidences promote the hypothesis of cross talk between muscle and different tissues mediated by cytokines and other peptides called myokines[81] which are involved both in acute exercise-induced metabolic reactions, as well as in the long-term metabolic benefits induced by exercise[82]. Irisin is one of the most recently identified myokines. Following regular physical activity, Irisin increases two-fold its circulating levels and promotes the shift of white adipocytes into “brite” cells: white adipocytes with a brown-fat-like phenotype. Brown adipocytes activate thermogenesis via the mitochondria uncoupling protein UCP-1 (Figure 1). Overexpression of irisin
determined through a gene therapy approach mediated by adenoviral particles, and leading to a modest approximately 3 fold increase in circulating levels, induced browning of subcutaneous white adipose tissue, stimulating a 10-20 fold increase in UCP1, thus increasing energy expenditure and improving glucose tolerance of high fat fed mice[83]. Despite more recent in vitro evidences against the possible translation of the beneficial effects observed in mice to humans, the major role of muscle mass in the energy balance has been definitively established.

In conclusion, physical exercise increases EE and stimulates muscle adaptation mechanisms with potential benefits on different tissues.

**ENERGY BALANCE, PHYSICAL ACTIVITY AND DIETARY RESTRICTION**

Analysis from the NHANES database describes an average daily intake increase of 168 kcal/d for men and of 335 kcal/d for women, from 1971 to 2000[84]. On the counterpart, examining in 2004, the physical activity patterns in a typical agrarian population in the United States through pedometers an average of about 18000 steps per day in men and of about 14000 steps per day have been reported[85], whereas an average American adult walked about 5000 steps per day[86].

An energy balance flipping point between energy intake and energy expenditure could be recognized in United States around 60’ years, thereafter followed by energy intake continuously driving energy expenditure, together with a worldwide burden in the incidence of obesity and type 2 diabetes[87].

The most frequently proposed strategy for treating obesity is food restriction. Energy restriction alone is an effective strategy to achieve a rapid and substantial weight loss, however it results in a reduction of both fat and muscle mass therefore promoting or aggravating an detrimental body composition (as sarcopeny) in terms of mortality and comorbidities. Specifically, approximately 25% of weight loss obtained through short-term low energy diets is lean muscle mass[88-92]. Moreover, the lack of success in weight loss maintenance after low-energy regimen and the subsequent weight regained comprising of up to 80% fat mass compound a further detrimental body composition impairment[93,94]. Weight loss should not be considered the sole focus of therapeutic approach aimed to decrease obesity-related disease risk profile. A systematic review by Chaston et al[95] demonstrates that very low calories regimens (VLCD) result in significant greater loss of FFM (lean) in comparison to low-calories diets[96]. Current evidences sustained that the most beneficial long-term outcomes are achieved with a modest energy deficit (2000-4000 kJ/d)[97]. Therefore increased levels of daily physical activity should be simultaneously promoted. Although resistance training retains or improves the relative percentage of lean mass to total body, current evidence failed to detect a loss of fat mass of a similar magnitude to aerobic training which promotes fat mass loss together with beneficial changes in muscle tissue[98-99].

Studies evaluating efficacy of dietary restriction together with exercise program showed more favorable results (as weight loss rate and body composition improvement) compared to diet or exercise prescription alone[100]. Emerging data suggest that the combination of resistance and aerobic exercise with a modest energy restriction was successful for preserving skeletal muscle concomitantly with a significant decrease of fat mass[100].

**CONCLUSION**

In order to characterize patients affected by obesity the use of traditional anthropometric measures appears misleading. A systematic and deep phenotyping of these patients, thus integrating data from body composition analysis and energy expenditure should be used in a dynamic rather than only basal approach to define and periodically verify the efficacy of the therapeutic regimen proposed. Among the numerous techniques evaluated in this paper, BIA seems to be the most suitable in a clinical setting because it is simple, inexpensive, noninvasive, and highly reproducible. Moreover, a recent paper by our research group showed that the FM and MM percentage estimated by BIA at baseline should be considered as predictors of success (weight loss > 5% at 6 mo from baseline) in a individual cognitive-behavioral program[40].

**REFERENCES**

1 World Health Organization. Fact Sheet No 311. Available from: URL: http://www.who.int/mediacentre/factsheets/fs311/en/index.html.
2 World Health Organization. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995; 854: 1-452 [PMID: 8594834]
3 Seidell JC, Kahn HS, Williamson DF, Lissner L, Valdez R. Report
Rotella CM et al. Body composition and energy balance evaluation in obesity

from a Centers for Disease Control and Prevention Workshop on use of adult anthropometry for public health and primary health care. Am J Clin Nutr 2001; 73: 123-126 [PMID: 11124761]

Ronero-Corral A, Montori VM, Somers VK, Korinek J, Thomas RJ, Allison TG, Mookadam F, Lopez-Jimenez F. Association of bodyweight with total mortality and with cardiovascular events in coronary artery disease: a systematic review of cohort studies. Lancet 2006; 368: 666-678 [PMID: 16920472]

Franzosi MG. Should we continue to use BMI as a cardiovascular risk factor? Lancet 2006; 368: 624-625 [PMID: 16920449]

McGee DL. Body mass index and mortality: a meta-analysis based on person-level data from twenty-six observational studies. Ann Epidemiol 2005; 15: 87-97 [PMID: 15652713]

Flegal KM, Graubard BI, Williamson DF, Gail MH. Cause-specific excess deaths associated with underweight, overweight, and obesity. Jama 2007; 298: 2028-2037 [PMID: 17986696]

Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumberdt Z, Onen CL, Lisheng L, Tanomsup S, Wuytack F, Faiz A, Sharma AM, Anand SS, Islam Q, Pogue J, Saeed N, Hajnal JV, Brynes A, Goldstone AP, Frost GS, Doré CJ, Thomas EL, Parkinson JR, Frost GS, Adunsky A, Doré CJ, Kyle UG, Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, Baracos VE. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol 2008; 9: 629-635 [PMID: 18539529 DOI: 10.1016/S1470-2045(08)70153-0]

Kimagaros S, Kild R, Levenkrohn S, Fleissig Y, Kopol B, Arad M, Adunsky A. Body mass index (BMI), body composition and mortality of nursing home elderly residents. Arch Gerontol Geriatr 2010; 51: 227-230 [PMID: 19939476 DOI: 10.1016/j.jarchger.2009.10.013]

Leonard CM, Rozza MA, Barr RD, Webber CE. Reproducibility of DXA measurements of bone mineral density and body composition in children. Pediatr Radiol 2009; 39: 148-154 [PMID: 19052738 DOI: 10.1007/s00247-008-0617-7]

Kelly TL, Wilson KE, Heymsfield SB. Dual energy X-ray absorptiometry body composition reference values from NHANES. PLoS One 2009; 4: e7038 [PMID: 19753111 DOI: 10.1371/journal.pone.0007038]

Baracos V, Caserotti P, Earleman CP, Fields D, Gallagher D, Hall KD, Heymsfield SB, Müller MJ, Rosen AN, Pichard C, Redman LM, Shen W, Shepherd JA, Thomas D. Advances in the science and application of body composition measurement. JPN J Parenter Enteral Nutr 2012; 36: 96-107 [PMID: 22235108 DOI: 10.1111/j.1365-3016.2011.04748.x]

Slosman DO, Casez JP, Pichard C, Rochat T, Ferry F, Rizzoli R, Pichard C, Redman LM, Shen W, Shepherd JA, Thomas D. Bioelectrical impedance analysis in patients with chronic heart failure. Eur Heart J 2011; 32: 794-801 [PMID: 18478025 DOI: 10.1093/eurheartj/2008.35]

Genton L, Haus D, Kyle UG, Pichard C. Dual-energy X-ray absorptiometry and body composition: differences between devices and comparison with reference methods. Nutrition 2002; 18: 66-70 [PMID: 11827768]

Ellegård LH, Ahlén M, Körner U, Lundholm KG, Plank LD, Bosaeus IG. Bioelectrical impedance spectroscopy underestimated fat-free mass compared to dual-energy X-ray absorptiometry. Radiology 1992; 185: 593-598 [PMID: 1410379]

Steiner MC, Barton RL, Singh SJ, Morgan MD. Bedside methods versus dual energy X-ray absorptiometry for body composition measurement in COPD. Eur Respir J 2002; 19: 626-631 [PMID: 11998990]

Ellegård LH, Ahlén M, Körner U, Lundholm KG, Plank LD, Bosaeus IG. Bioelectrical impedance spectroscopy underestimated fat-free mass compared to dual-energy X-ray absorptiometry in incurable cancer patients. Eur J Clin Nutr 2009; 63: 794-801 [PMID: 18478025 DOI: 10.1093/eurheartj/2008.35]

Genton L, Haus D, Kyle UG, Pichard C. Dual-energy X-ray absorptiometry and body composition: differences between devices and comparison with reference methods. Nutrition 2002; 18: 66-70 [PMID: 11827768]

Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab 2008; 33: 997-1006 [PMID: 18923576 DOI: 10.1139/H08-075]

Marquis K, Debigaré R, Lacasse Y, LeBlanc P, Jobin J, Carrier G, Maltais F. Midthigh muscle cross-sectional area is a better predictor of mortality than body mass index in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2002; 166: 809-813 [PMID: 12231489]

Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez JM, Heitmann BL, Kent-Smith L, Melchior JC, Pirlich
Rotella CM et al. Body composition and energy balance evaluation in obesity

M, Scharfetter H, Schols AM, Pichard C. Bioelectrical impedance analysis—part I: review of principles and methods. Clin Nutr 2004; 23: 1226-1243 [PMID: 15380917]

35 Kyle UG, Bosaeus I, De Lorenzo AD, Deurenberg P, Elia M, Gómez LP, Janssen I, Lohmann A, Luik A, Money D, Pichard C, Schols AM, Sjöström M, Steiniger J, Topinková E, Vandewoude M, Zamboni M. Sarcopenia: European consensus on definition and diagnosis: Report of the European Evidence-Based Consensus Workgroup on Sarcopenia in Older People. Age Ageing 2013; 42: 393-401 [PMID: 23380190 DOI: 10.1093/ageing/afa031]

36 de Luis DA, Aller R, Izazoa O, Romero E. Prediction equation of resting energy expenditure in an adult Spanish population of obese adult population. Ann Nutr Metab 2006; 50: 193-196 [PMID: 16407645]

37 Das SK, Saltzman E, McCrory MA, Hsu LK, Shikora SA, Dolnikowski G, Kehayas JJ, Roberts SB. Energy expenditure is very high in extremely obese women. J Nutr 2004; 134: 1412-1416 [PMID: 15173405]

38 Huang KC, Kormas N, Steinbeck K, Loughnan G, Caterson ID. Resting metabolic rate in severely obese diabetic and nonobese subjects. Obes Res 2004; 12: 840-845 [PMID: 15166305]

39 Lazzer S, Agosti F, Resnik M, Marazzi N, Mornati D, Santorio A. Prediction of resting energy expenditure in severely obese Italian males. J Endocrinol Invest 2007; 30: 754-761 [PMID: 17993767]

40 Dobratz JR, Sibley SD, Beckman TR, Valentine BJ, Kellogg TA, Ikramuddin S, Earthman CP. Predicting energy expenditure in extremely obese women. J Parenter Enteral Nutr 2007; 31: 217-227 [PMID: 17463148]

41 Boulatta J, Williams J, Cottrell F, Hudson L, Compher C. Accurate determination of energy needs in hospitalized patients. J Am Diet Assoc 2007; 107: 393-401 [PMID: 17324656]

42 Weis PJ, Vansant GA. Validity of predictive equations for resting energy expenditure in Belgian normal weight to morbid obese women. Clin Nutr 2010; 29: 347-351 [PMID: 19853980 DOI: 10.1016/j.clnu.2009.09.009]

43 Horme LM, Gonzalez MC, Torrinhas RS, Giovannoni I, Wattez DL. New specific equation to estimate resting energy expenditure in severely obese patients. Obesity (Silver Spring) 2013; 21: 2231-2235 [PMID: 23512821 DOI: 10.1002/oby.20363]

44 Papazoglou D, Augello G, Tagliaferri M, Savia G, Marzullo P, Maltezos E, Liuzzi A. Evaluation of a multisensor armband in estimating energy expenditure in obese individuals. Obes Rev 2004; 5: 115-116 [PMID: 15007020]

45 Slinde F, Bertz F, Winkvist A, Ellegård L, Olausson H, Brekke HK. Energy expenditure by multisensor armband in overweight and obese subjects. Obes Rev 2003; 4: 377-388 [PMID: 17644692]

46 Compher C, Frankenfield D, Keim N, Roth-Yousey L. Best practice methods to apply to measurement of resting metabolic rate in adults: a systematic review. J Am Diet Assoc 2006; 106: 881-903 [PMID: 16752029]

47 Klein TR, Ockene IS, Yancey AK, Proctor L, Nelson SE, Weisner C, Teutsch SM, Sorensen G, Levine DM. Development and testing of a clinical prediction rule for estimating energy expenditure in adults aged 20–94 years. Am J Clin Nutr 2004; 80: 1379-1390 [PMID: 15531690]

48 Fielding RA, Vellas B, Evans WJ, Bhasin S, Morley JE, Newman AB, Abellan van Kan G, Andrius S, Bauer J, Breuleix D, Cederholm T, Chandler J, De Meynard C, Donini L, Harris T, Kannen A, Keime G, Sarafand J, Schols AM, Sjöström M, Steiniger J, Topinková E, Vandewoude M, Zamboni M. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010; 39: 412-423 [PMID: 20392703 DOI: 10.1093/ageing/afq034]
Guibert F, Onder G, Papanicolaou D, Rolland Y, Roosk D, Sieber C, Souhami E, Verlaan S, Zamboni M. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc 2011; 12: 249-256 [PMID: 21527165 DOI: 10.1016/j.jamda.2011.01.003]

Steholm S, Harris TB, Rantanen T, Visser M, Kritchevsky SB, Ferrucci L. Sarcopenic obesity: definition, cause and consequences. Curr Opin Clin Nutr Metab Care 2008; 11: 693-700 [PMID: 18827572 DOI: 10.1097/MCO.0b013e328312e37d]

Kim MK, Baek KH, Song KH, Il Kang M, Park CY, Lee WY, Oh KW. Vitamin D deficiency is associated with sarcopenia in older Koreans, regardless of obesity: the Fourth Korea National Health and Nutrition Examination Surveys (KNHNES IV) 2009. J Clin Endocrinol Metab 2011; 96: 3250-3256 [PMID: 21832109 DOI: 10.1210/jc.2011-1602]

Seo JA, Cho H, Eun CR, You HJ, Kim SG, Baik SH, Choi DS, Park MH, Han C, Kim NH. Association between visceral obesity and sarcopenia and vitamin D deficiency in Koreans: the Ansan Geriatric Study. J Am Geriatr Soc 2012; 60: 700-706 [PMID: 22316290 DOI: 10.1111/j.1532-5415.2012.03887.x]

Lee CG, Boyko EJ, Strotmeyer ES, Lewis CE, Cawthon PM, Hoffman AR, Everson-Rose SA, Barrett-Conner E, Orwoll ES. Association between insulin resistance and lean mass loss and fat mass gain in older men without diabetes mellitus. J Am Geriatr Soc 2011; 59: 1217-1224 [PMID: 21718263 DOI: 10.1111/j.1532-5415.2011.03472.x]

Srikanthan P, Hevener AL, Karlamangla AS. Sarcopenia exacerbates obesity-associated insulin resistance and dysglycemia: findings from the National Health and Nutrition Examination Survey III. PLoS One 2010; 5: e10085 [PMID: 22421977 DOI: 10.1371/journal.pone.0010085]

Harrison BC, Leinwand LA. Fighting fat with muscle: bulking up to slim down. Cell Metab 2008; 7: 97-98 [PMID: 18249167 DOI: 10.1016/j.cmet.2008.01.003]

Eckardt K, Taube A, Eickel J. Obesity-associated insulin resistance in skeletal muscle: role of lipid accumulation and physical inactivity. Rev Endocr Metab Disord 2011; 12: 163-172 [PMID: 21336841 DOI: 10.1007/s11154-011-9166-2]

Kohara K. Sarcopenic obesity in aging population: current status and future directions for research. Endocrine 2014; 45: 15-25 [PMID: 23821364]

Peterson CM, Johannsen DL, Ravussin E. Skeletal muscle mitochondria and aging: a review. J Aging Res 2012; 2012: 194821 [PMID: 22888430 DOI: 10.1155/2012/194821]

Pedersen L, Hojman P. Muscle-to-organ cross talk mediated by myokines. Adipocyte 2012; 1: 164-167 [PMID: 23700527 DOI: 10.4161/adip.20344]

Pedersen BK. Muscle as a secretory organ. Compr Physiol 2013; 3: 1337-1362 [PMID: 23897689]

Boström P, Wu J, Jedrychowski MP, Korde A, Ye L, Lo JC, Raskoch K, Boström EA, Choi JH, Long JZ, Kajimura S, Zingaretti MC, Vind BF, Tu H, Cinti S, Højhjuld K, Gygi SP, Spiegelman BM. A PGC1α-dependent myokine that drives brown-fat-like development of white fat and thermogenesis. Nature 2012; 481: 463-468 [PMID: 22227023 DOI: 10.1038/nature10777]

Centers for Disease Control and Prevention. National Health and Nutrition Examination Survey. Available from: URL: http://www.cdc.gov/nchs/nhanes.htm

Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. Med Sci Sports Exerc 2004; 36: 79-85 [PMID: 14707772]

Bassett DR, Wyatt HR, Thompson H, Peters JC, Hill JO. Pedometer-measured physical activity and health behaviors in U.S. adults. Med Sci Sports Exerc 2010; 42: 1819-1825 [PMID: 20305579 DOI: 10.1249/MSS.0b013e3181de2e54]

Swinnburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML, Gortmaker SL. The global obesity pandemic: shaped by global drivers and local environments. Lancet 2011; 378: 804-814 [PMID: 21872749 DOI: 10.1016/S0140-6736(11)60813-1]

Nicklas BJ, Wang X, You T, Lyles MF, Demons J, Easter L, Berry MJ, Lenchik L, Carr J. Effect of exercise intensity on abdominal fat loss during calorie restriction in overweight and obese postmenopausal women: a randomized, controlled trial. Am J Clin Nutr 2009; 89: 1043-1052 [PMID: 19211823 DOI: 10.3945/ajcn.2008.26938]

Hoie LH, Bruusgaard D, Thom E. Reduction of body mass and change in body composition on a very low calorie diet. Int J Obes Relat Metab Disord 1993; 17: 17-20 [PMID: 8383636]

Ballor DL, Katch VL, Beadle ME, Marks CR. Resistance weight training during calorie restriction enhances lean body mass maintenance. Am J Clin Nutr 1998; 47: 19-25 [PMID: 3337037]

Campbell WW, Haub MD, Wolfe RR, Ferrando AA, Sullivan DH, Apolzan JW, Iglay H. Resistance training preserves fat-free mass without impacting changes in protein metabolism after weight loss in older women. Obesity (Silver Spring) 2009; 17: 1332-1339 [PMID: 19247271 DOI: 10.1038/oby.2009.2]

Foster-Schubert KE, Alfano CM, Duggan CR, Xiao L, Campbell KL, Kong A, Bain CE, Wang CY, Blackburn GL, McTiernan A. Effect of diet and exercise, alone or combined, on weight and body composition in overweight-to-obese postmenopausal women. Obesity (Silver Spring) 2012; 20: 1628-1638 [PMID: 21942229 DOI: 10.1038/oby.2011.176]

Newman AB, Lee JS, Visser M, Goodpaster BH, Kritchevsky SB, Tylavsky FA, Nevitt M, Harris TB. Weight change and the conservation of lean mass in old age: the Health, Aging and Body Composition Study. Am J Clin Nutr 2005; 82: 872-878; quiz 915-916 [PMID: 16207191]

Beavers KM, Lyles MF, Davis CC, Wang X, Beavers DP, Nicklas BJ. Is lost lean mass from intentional weight loss recovered during weight regain in postmenopausal women? Am J Clin Nutr 2011; 94: 767-774 [PMID: 21795437 DOI: 10.3945/ajcn.110.004895]

Chaston TB, Dixon JB, O’Brien PE. Changes in fat-free mass during significant weight loss: a systematic review. Int J Obes (Lond) 2007; 31: 743-750 [PMID: 17075583]

Strychar I. Diet in the management of weight loss. CMAJ 2006; 174: 56-63 [PMID: 16392440]

Willis LH, Stentz CA, Bateman LA, Shields AT, Piner LW, Iglay HB. Effects of aerobic and/or resistance training on body mass and fat mass in overweight or obese adults. J Appl Physiol (1985) 2012; 113: 1831-1837 [PMID: 23019316 DOI: 10.1152/japplphysiol.01370.2011]

Ismail I, Keating SE, Baker MK, Johnson NA. A systematic review and meta-analysis of the effect of aerobic vs. resistance exercise training on visceral fat. Obes Rev 2012; 13: 68-91 [PMID: 21951360 DOI: 10.1111/j.1467-789X.2011.00931.x]

Rolland Y, Czerwinski S, Abellan Van Kan G, Morley JE, Cesari M, Onder G, Woo J, Baumgartner R, Pillard F, Boirie Y, Chumlea WM, Vellas B. Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. J Nutr Health Aging 2008; 12: 433-450 [PMID: 18652255]

Frime TN, Pinidare DR, Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. Med Sci Sports Exerc 2008; 40: 1213-1219 [PMID: 18580399 DOI: 10.1249/MSS.0b013e3181b6a5ce]

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