The Evaluation of Body Composition: A Useful Tool for Clinical Practice

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Introduction

Chronic undernutrition is characterized by a progressive reduction of the fat-free mass (FFM) and fat mass (FM) which has deleterious consequences on health. Undernutrition is insufficiently screened and treated in hospitalized or at-risk patients despite its high prevalence and negative impact on mortality, morbidity, length of stay (LOS), quality of life, and costs [1–4]. The risk of underestimating hospital undernutrition is likely to worsen in the next decades because of the increasing prevalence of overweight, obesity, and chronic diseases and the increased number of elderly subjects. These clinical conditions are associated with FFM loss (sarcopenia). Therefore, an increased number of patients with FFM loss and sarcopenic obesity will be seen in the future.

Sarcopenic obesity is associated with decreased survival and increased therapy toxicity in cancer patients [5–10], whereas FFM loss is related to decreased survival, a negative clinical outcome, increased health care costs [2], and impaired overall health, functional capacities, and quality of life [4–11]. Therefore, the detection and treatment of FFM loss is a major issue of public health and health costs [12].

Weight loss and the body mass index (BMI) lack sensitivity to detect FFM loss [13]. In this review, we support the systematic assessment of FFM with a method of body composition evaluation in order to improve the detection of FFM loss and sarcopenic obesity.

Key Words
Fat-free mass • Fat mass • Undernutrition • Bioelectrical impedance analysis • Sarcopenic obesity • Drug toxicity

Abstract

Undernutrition is insufficiently detected in in- and outpatients, and this is likely to worsen during the next decades. The increased prevalence of obesity together with chronic illnesses associated with fat-free mass (FFM) loss will result in an increased prevalence of sarcopenic obesity. In patients with sarcopenic obesity, weight loss and the body mass index lack accuracy to detect FFM loss. FFM loss is related to increasing mortality, worse clinical outcomes, and impaired quality of life. In sarcopenic obesity and chronic diseases, body composition measurement with dual-energy X-ray absorptiometry, bioelectrical impedance analysis, or computed tomography quantifies the loss of FFM. It allows tailored nutritional support and disease-specific therapy and reduces the risk of drug toxicity. Body composition evaluation should be integrated into routine clinical practice for the initial assessment and sequential follow-up of nutritional status. It could allow objective, systematic, and early screening of undernutrition and promote the rational and early initiation of optimal nutritional support, thereby contributing to reducing malnutrition-induced morbidity, mortality, worsening of the quality of life, and global health care costs.

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Fig. 1. Conceptualization of the expected impact of early use of body composition for the screening of fat-free loss and undernutrition in sarcopenic overweight and obese subjects. An increased prevalence of overweight and obesity is observed in all Western and emerging countries. Simultaneously, the ageing of the population, the reduction of the level of physical activity, and the higher prevalence of chronic diseases and cancer increased the number of patients with or at risk of FFM impairment, i.e., sarcopenia. Thus, more patients are presenting with ‘sarcopenic overweight or obesity’. In these patients, evaluation of nutritional status using anthropometric methods, i.e., weight loss and calculation of BMI, is not sensitive enough to detect FFM impairment. As a result, undernutrition is not detected, worsens, and negatively impacts morbidity, mortality, LOS, length of recovery, quality of life, and health care costs. On the contrary, in patients with ‘sarcopenic overweight or obesity’, early screening of undernutrition with a dedicated method of body composition evaluation would allow early initiation of nutritional support and, in turn, improvements of nutritional status and clinical outcome.

Rationale for a New Strategy for the Screening of Undernutrition

Screening of Undernutrition Is Insufficient

Academic societies encourage systematic screening of undernutrition at hospital admission and during the hospital stay [14]. The detection of undernutrition is generally based on measurements of weight and height, calculations of BMI, and the percentage of weight loss. Nevertheless, screening of undernutrition is infrequent in hospitalized or nutritionally at-risk ambulatory patients. For example, in France, surveys performed by the French Health Authority [15] indicate that: (i) weight alone, (ii) weight with BMI or percentage of weight loss, and (iii) weight, BMI, and percentage of weight loss are reported in only 55, 30, and 8% of the hospitalized patients’ records, respectively. Several issues, which could be improved by specific educational programs, explain the lack of implementation of nutritional screening in hospitals (Table 1). In addition, the accuracy of the clinical screening of undernutrition could be limited at hospital admission. Indeed, patients with undernutrition may have the same BMI as sex- and age-matched healthy controls but a significantly decreased FFM hidden by an expansion of the FM and the total body water which can be measured by bioelectrical impedance analysis (BIA) [13]. This example illustrates that body composition evaluation allows a more accurate identification of FFM loss than body weight loss or BMI decrease. The lack of sensitivity and specificity of weight, BMI, and percentage of weight loss argue for the need for other methods to evaluate the nutritional status.

Changes in Patients’ Profiles

In 2008, twelve and thirty percent of the worldwide adult population was obese or overweight; this is two times higher than in 1980 [16]. The prevalence of over-
weight and obesity is also increasing in hospitalized patients. A 10-year comparative survey performed in a European hospital showed an increase in patients’ BMI, together with a shorter LOS [17]. The BMI increase masks undernutrition and FFM loss at hospital admission. The increased prevalence of obesity in an ageing population has led to the recognition of a new nutritional entity: ‘sarcopenic obesity’ [18]. Sarcopenic obesity is characterized by increased FM and reduced FFM with a normal or high body weight. The emergence of the concept of sarcopenic obesity will increase the number of situations associated with a lack of sensitivity of the calculations of BMI and body weight change for the early detection of FFM loss. This supports a larger use of body composition evaluation for the assessment and follow-up of nutritional status in clinical practice (fig. 1).

**Body Composition Evaluation for the Assessment of Nutritional Status**

Body composition evaluation is a valuable technique to assess nutritional status. Firstly, it gives an evaluation of nutritional status through the assessment of FFM.
Body Composition in Practice

Body Composition Techniques for FFM Measurement

Body composition evaluation allows measurement of the major body compartments: FFM (including bone mineral tissue), FM, and total body water. Table 2 shows indicative values of the body composition of a healthy subject weighing 70 kg. In several clinical situations, i.e. hospital admission, chronic obstructive pulmonary disease (COPD) [21–23], dialysis [24–26], chronic heart failure [27], amyotrophic lateral sclerosis [28], cancer [5, 29], liver transplantation [30], nursing home residence [31], and Alzheimer’s disease [32], changes in body compartments are detected with the techniques of body composition evaluation. At hospital admission, body composition evaluation could be used for the detection of FFM loss and undernutrition. Indeed, FFM and the FFM index (FFMI) [FFM (kg)/height (m²)] measured by BIA are significantly lower in hospitalized patients (n = 995) than in age-, height-, and sex-matched controls (n = 995) [3]. Conversely, clinical tools of nutritional status assessment, such as BMI, subjective global assessment, or mini-nutritional assessment, are not accurate enough to estimate FFM loss and nutritional status [30, 32–34]. In 441 patients with non-small cell lung cancer, FFM loss determined by computerized tomography (CT) was observed in each BMI category [7], and in young adults with all

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<th>Table 1. Main reasons for the lack of nutritional screening at hospitals</th>
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<th>Table 2. Mean values of body composition compartments (adapted from Pichard and Kyle [19] and Wang et al. [20])</th>
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<td>Whole-body compartments</td>
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ACM = Active cell mass; ECW = extracellular water; ICW = intracellular water; TBW = total body water.
types of cancer, an increase in FM together with a decrease in FFM were reported [29]. These findings reveal the lack of sensitivity of BMI to detect FFM loss. Moreover, the FFMI is a more sensitive determinant of LOS than a weight loss over 10% or a BMI below 20 [3]. In COPD, the assessment of FFM by BIA is a more sensitive method to detect undernutrition than anthropometry [33, 35]. BIA is also more accurate at assessing nutritional status in children with severe neurologic impairment than the measurement of skinfold thickness [36].

**Body Composition for the Evaluation of Prognosis and Clinical Outcome**

FFM loss is correlated with survival in different clinical settings [5, 21-28, 37]. In patients with amyotrophic lateral sclerosis, an FM increase, but not an FFM increase, measured by BIA, was correlated with survival during the course of the disease [28]. The relation between body composition and mortality has not yet been demonstrated in the intensive care unit. The relation between body composition and mortality has been demonstrated with anthropometric methods, BIA, and CT. Measurement of the mid-arm muscle circumference is an easy tool to diagnose sarcopenia [38]. The mid-arm muscle circumference has been shown to be correlated with survival in patients with cirrhosis [39, 40], HIV infection [41], and COPD in a stronger way than BMI [42]. The relation between FFM loss and mortality has been extensively shown with BIA [21-28, 31, 37], which is the most used method. Recently, very interesting data suggest that CT could evaluate the disease prognosis in relation to muscle wasting. In obese cancer patients, sarcopenia as assessed by CT measurement of the total skeletal muscle cross-sectional area is an independent predictor of the survival of patients with bronchopulmonary [5, 7], gastrointestinal [5], and pancreatic cancers [6]. FFM assessed by measurement of the mid-thigh muscle cross-sectional area by CT is also predictive of mortality in COPD patients with severe chronic respiratory insufficiency [43]. In addition to mortality, a low FFMI at hospital admission is significantly associated with an increased LOS [3, 44]. A bicentric controlled population study performed in 1,717 hospitalized patients indicates that both loss of FFM and excess of FM negatively affect the LOS [44]. Patients with sarcopenic obesity are most at risk of increased LOS. This study also found that excess FM reduces the sensitivity of BMI to detect nutritional depletion [44]. Together with the observation that the BMI of hospitalized patients has increased during the last decade [17], these findings suggest that FFM and FFMI measurement should be used to evaluate nutritional status in hospitalized patients.

BIA measures the phase angle [45]. A low phase angle is related to survival in oncology [46-50], HIV infection/AIDS [51], amyotrophic lateral sclerosis [52], geriatrics [53], peritoneal dialysis [54], and cirrhosis [55]. The phase angle threshold associated with reduced survival is variable: less than 2.5 degrees in amyotrophic lateral sclerosis patients [52], 3.5 degrees in geriatric patients [53], from less than 1.65 to 5.6 degrees in oncology patients [47-50], and 5.4 degrees in cirrhotic patients [55]. The phase angle is also associated with the severity of lymphopenia in AIDS [56], and with the risk of postoperative complications among gastrointestinal surgical patients [57]. The relation of phase angle with prognosis and disease severity reinforces the interest in using BIA for the clinical management of patients with chronic diseases at high risk of undernutrition and FFM loss.

In summary, FFM loss or a low phase angle is related to mortality in patients with chronic diseases, cancer (including obesity cancer patients), and elderly patients in long-stay facilities. A low FFM and an increased FM are associated with an increased LOS in adult hospitalized patients. The relation between FFM loss and clinical outcome is clearly shown in patients with sarcopenic obesity. In these patients, as the sensitivity of BMI for detecting FFM loss is strongly reduced, body composition evaluation appears to be the method of choice to detect undernutrition in routine practice. Overall, the association between body composition, phase angle, and clinical outcome reinforces the pertinence of using a body composition evaluation in clinical practice.

**Which Technique of Body Composition Evaluation Should Be Used for the Assessment of Nutritional Status?**

Numerous methods of body composition evaluation have been developed: anthropometry, including the 4-skinfold method [58], hydrodensitometry [58], in vivo neutron activation analysis [59], anthropogammammetry from total body potassium-40 [60], nuclear magnetic resonance [61], dual-energy X-ray absorptiometry (DEXA) [62, 63], BIA [45, 64-66], and more recently CT [7, 43, 67]. DEXA, BIA, and CT appear to be the most convenient methods for clinical practice (fig. 2), while the other methods are reserved for scientific use.

Compared with other techniques of body composition evaluation, the lack of reproducibility and sensitivity of the 4-skinfold method limits its use for the accurate measurement of body composition in clinical practice [33,
evaluate FFM by measuring the muscle cross-sectional area from L3 to the iliac crest by use of Hounsfield unit (HU) thresholds (–29 to +150) [5, 7]. The muscles included in the calculation of the muscle cross-sectional area are psoas, paraspinal muscles (erector spinae, quadratus lumborum), and abdominal wall muscles (transversus abdominis, external and internal obliques, rectus abdominis) [6]. CT also provided detail on specific muscles, adipose tissues, and organs not provided by DEXA or BIA. L3-targeted CT images could be theoretically performed solely, since they result in X-ray exposition similar to that of a chest radiography.

In summary, DEXA, BIA, and L3-targeted CT images could all measure body composition accurately. The technique selection will depend on the clinical context, hardware, and knowledge availability. Body composition evaluation by DEXA should be performed in patients having a routine assessment of bone mineral density. Also, analysis of L3-targeted CT is the method of choice for body composition evaluation in cancer patients. Body composition evaluation should also be done for every abdominal CT performed in patients who are nutritionally at risk or undernourished. Because of its simplicity of use, BIA could be widely implemented as a method of body composition evaluation and follow-up in a great number of hospitalized and ambulatory patients. Future research will aim to determine whether a routine evaluation of body composition would allow early detection of the increased FFM catabolism related to critical illness [75].

Body Composition Evaluation for the Calculation of Energy Needs

The evaluation of FFM could be used for the calculation of energy needs, thus allowing the optimization of nutritional intakes according to nutritional needs. This could be of great interest in specific situations, such as severe neurologic disability, overweight, and obesity. In 61 children with severe neurologic impairment and intellectual disability, an equation integrating body composition had good agreement with the doubly labeled water method. It gave a better estimation of energy expenditure than did the Schofield predictive equation [36]. However, in 9 anorexia nervosa patients with a mean BMI of 13.7, prediction formulas of resting energy expenditure including FFM did not allow accurate prediction of the resting energy expenditure measured by indirect calorimetry [76]. In overweight or obese patients, the muscle catabolism in response to inflammation was the same as that observed...
Body Composition Evaluation for the Follow-Up and Tailoring of Nutritional Support

Body composition evaluation allows a qualitative assessment of body weight variations. The evaluation of body composition may help to document the efficiency of nutritional support during a patient’s follow-up of numerous clinical conditions, such as surgery [59], anorexia nervosa [76, 80], hematopoietic stem cell transplantation [81], COPD [82], ICU [83], lung transplantation [84], ulcerative colitis [59], Crohn’s disease [85], cancer [86, 87], HIV/AIDS [88], and acute stroke in elderly patients [89]. Body composition evaluation could be used for the follow-up of healthy elderly subjects [90]. Body composition evaluation allows characterization of the increase in body mass in terms of FFM and FM [81, 91]. After hematopoietic stem cell transplantation, the increase in BMI is the result of the increase in FM, but not of the increase in FFM [81]. Also, during recovery after an acute illness, weight gain 6 months after ICU discharge could be mostly related to an increase in FM (+7 kg) while FFM only increased by 2 kg; DEXA and air displacement plethysmography were used to measure the FM and FFM [91]. These two examples suggest that body composition evaluation could be helpful to decide the modification and/or the renewal of nutritional support. By identifying the patients gaining weight but reporting no or insufficient FFM, body composition evaluation could contribute to influencing the medical decision of continuing nutritional support that would have been stopped in the absence of body composition evaluation.

In summary, body composition evaluation is of the utmost interest for the follow-up of nutritional support and its impact on body compartments.

Body Composition Evaluation for Tailoring Medical Treatments

In clinical situations when weight and BMI do not reflect the FFM, the evaluation of body composition should be used to adapt drug doses to the FFM and/or FM absolute values in every patient. This point has been recently illustrated in oncology patients with sarcopenic obesity. FFM loss was determined by CT as described above. In cancer patients, some therapies could affect body composition by inducing muscle wasting [92]. In patients with advanced renal cell carcinoma [92], sorafenib induces a significant 8% loss of skeletal muscular mass at 12 months. In turn, muscle wasting in patients with BMI less than 25 was significantly associated with sorafenib toxicity in patients with metastatic renal cancer [8]. In metastatic breast cancer patients receiving capcitabine treatment, and in patients with colorectal cancer receiving 5-fluoro-uracile, using the convention of dosing per unit of body surface area, FFM loss was the determinant of chemotherapy toxicity [9, 10] and time to tumor progression [10]. In colorectal cancer patients administered 5-fluoro-uracil, low FFM is a significant predictor of toxicity only in female patients [9]. The variation in toxicity between women and men may be partially explained by the fact that FFM was lower in females. Indeed, FFM represents the distribution volume of most cytotoxic chemotherapy drugs. In 2,115 cancer patients, the individual variations in FFM could change by up to three times the distribution volume of the chemotherapy drug per body area unit [5]. Thus, administering the same doses of chemotherapy drugs to a patient with a low FFM compared to a patient with a normal FFM would increase the risk of chemotherapy toxicity [5]. These data suggest that FFM loss could have a direct impact on the clinical outcome of cancer patients. Decreasing chemotherapy doses in case of FFM loss could contribute to improving cancer patients’ prognosis through the improvement of the toler-
ance of chemotherapy. These findings justify the systematic evaluation of body composition in all cancer patients in order to detect FFM loss, tailor chemotherapy doses according to FFM values, and then improve the efficacy-tolerance and cost-efficiency ratios of the therapeutic strategies [93]. Body composition evaluation should also be used to tailor the doses of drugs which are calculated based on patients’ weight, e.g. corticosteroids, immunosuppressors (infliximab, azathioprine or methotrexate), or sedatives (propofol).

In summary, measurement of FFM should be implemented in cancer patients treated with chemotherapy. Clinical studies are needed to demonstrate the importance of measuring body composition in patients treated with other medical treatments.

Towards the Implementation of Body Composition Evaluation in Clinical Practice

The implementation of body composition evaluation in routine care presents a challenge for the next decades. Indeed the concomitant increases in elderly subjects and patients with chronic diseases and cancer, and in the prevalence of overweight and obesity in the population, will increase the number of patients nutritionally at risk or undernourished, particularly those with sarcopenic obesity. Body composition evaluation should be used to improve the screening of undernutrition in hospitalized patients. The results of body composition should be based on the same principle as BMI calculation, towards the systematic normalization for body height of FFM (FFMI) and FM [FM (kg)/height (m)² = FM index] [94]. The results could be expressed according to previously described percentiles of healthy subjects [95, 96]. Body composition evaluation should be performed at the different stages of the disease, during the course of treatments and the rehabilitation phase. Such repeated evaluations of body composition could allow assessment of the nutritional status, adjusting the calculation of energy needs as kilocalories/kilogram FFM, following the efficacy of nutritional support, and tailoring drug and nutritional therapies. BIA, L3-targeted CT, and DEXA represent the techniques of choice to evaluate body composition in clinical practice (fig. 2). In the setting of cost-effective and pragmatic use, these three techniques should be alternatively chosen. In cancer, undernourished, and nutritionally at-risk patients, an abdominal CT should be completed by the analysis of L3-targeted images for the evaluation of body composition.

In other situations, BIA appears to be the simplest most reproducible and less expensive method, while DEXA, if feasible, remains the reference method for clinical practice. By allowing earlier management of undernutrition, body composition evaluation can contribute to reducing malnutrition-induced morbidity and mortality, improving the quality of life and, as a consequence, increasing the medico-economic benefits (fig. 1). The latter needs to be demonstrated. Moreover, based on a more scientific approach, i.e. allowing for printing reports, objective initial assessment and follow-up of nutritional status, and the adjustment of drug doses, body composition evaluation would contribute to a better recognition of the activities related to nutritional evaluation and care by the medical community, health care facilities, and health authorities (fig. 2).

Conclusion

Screening of undernutrition is insufficient to allow for optimal nutrition care. This is in part due to the lack of sensitivity of BMI and weight loss for detecting FFM loss in patients with chronic diseases. Methods of body composition evaluation allow a quantitative measurement of FFM changes during the course of disease and could be used to detect FFM loss in the setting of an objective, systematic, and early undernutrition screening. FFM loss is closely related to impaired clinical outcomes, survival, and quality of life, as well as increased therapy toxicity in cancer patients. Thus, body composition evaluation should be integrated into clinical practice for the initial assessment, sequential follow-up of nutritional status, and the tailoring of nutritional and disease-specific therapies. Body composition evaluation could contribute to strengthening the role and credibility of nutrition in the global medical management, reducing the negative impact of malnutrition on the clinical outcome and quality of life, thereby increasing the overall medico-economic benefits.

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Disclosure Statement

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Body Composition in Practice

Drugs Affecting Fat Distribution and Body Composition


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