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NARRATIVE REVIEW

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# Revisiting the beyond BMI paradigm in excess weight diagnosis and management: A call to action

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## Abstract

Adolphe Quételet, a 19th-century Belgian sociologist and statistician, pioneered the incorporation of statistics into social sciences. He initiated the development of anthropometry since he was interested in identifying the proportions of the 'ideal man'. He devised a ratio between weight and height, originally termed the *Quételet Index*, and today widely known and used as the body mass index or BMI. In 1835, he demonstrated that a normal curve accommodates the distribution of human traits articulating his reasoning on human variance around the average. Quételet's long-lasting legacy of the establishment of a simple measure to classify people's weight relative to an ideal for their height endures today with minor variations having dramatically influenced public health agendas. While being very useful, the limitations of the BMI are well known. Thus, revisiting the beyond BMI paradigm is a necessity in the era of precision medicine with morphofunctional assessment representing the way forward via incorporation of body composition and functionality appraisal. While healthcare systems were originally designed to address acute illnesses, today's demands require a radical rethinking together with an original reappraisal of our diagnosis and treatment approaches from a multidimensional perspective. Embracing new methodologies is the way forward to advance the field, gain a closer look at the underlying pathophysiology

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of excess weight, keep the spotlight on improving diagnostic performance and demonstrate its clinical validity. In order to provide every patient with the most accurate diagnosis together with the most appropriate management, a high degree of standardization and personalization is needed.

**KEYWORDS**

adiposity, morphofunctional assessment, muscle mass and function, obesity phenotypes, precision medicine, sarcopenic obesity

## 1 | INTRODUCTION AND HISTORICAL BACKGROUND

Ancestors of current humans evolved under the pressure of having to adapt to rapidly changing precarious circumstances. This empowered the development of complex and numerous cultures allowing settlements and, subsequently, colonization of most habitable areas of the earth. In parallel, the blending of particular genetic features and tangible morphological differences is deeply rooted in the constitution of a specific body built enabling survival and development of distinct body composition characteristics with relevant functional consequences. Genetic variants emerging in the human lineage determined the heritage of today's individuals underlying the biological differences that shape modern human phenotypes.[1] Nonetheless, how and to what extent single changes or the combination of several ones interacting with environmental conditions may influence a phenotype has not been fully uncovered.

Obesity prevalence has increased at a rate impossible to be explained by genetics, thereby posing the focus rather on environmental factors as likely drivers.[2,3] In this context, the nurture versus nature concept is a frequently put forward opposition.[4] Undoubtedly, biology exerts a pivotal role in energy homeostasis with genetic susceptibility underlying the potential development of obesity in the middle of an obesogenic environment that can drive body weight variation.[5] Thus, it is important to weigh up the relative contribution of both nurture and nature in excess weight regulation. While genes underlie the expression of many of the phenotypic traits, environmental influences and nurture certainly play a relevant role. While the genetic pool has not changed over the last decades, in this time, the prevalence of obesity has increased rapidly, thereby showing that genetics can not be solely blamed for the current excess weight pandemic. In this scenario, epigenetics, which explains gene function alterations without genetic code changes or any genome modification also needs to be considered.[6,7] Genetic susceptibilities together with epigenetic modifications and the wider influence of the exposome impact on ageing within a given environmental milieu.[2,8] Thus, modern humans are engulfed by a surrounding obesogenic environment in which energy-dense foods are readily available and opportunities for physical activity succumb in a sedentary habitat favour that currently every person can easily put on excess weight. Moreover, a higher prevalence of excess weight is observed in socioeconomically disadvantaged people with a clear socioeconomic gradient being established by low educational level and decreased income.[4,5]

In spite of the worldwide interest in deaccelerating the numbers of people living with obesity (PwO), its prevalence continues to increase in adults as well as in adolescents and children.[3,9–14] Noteworthy, obesity is a multifactorial, chronic, progressive and frequently relapsing non-communicable disease accompanied by increased morbi-mortality and decreased quality of life.[15,16] Interestingly, the practice of sorting people out by their

**Key message**

- Obesity needs to be redefined and reframed to reflect both current physiological research and more evidence-based clinical person-centred management.
- While being a simple, easy, useful and cheap method, the BMI is only a surrogated measure of total adiposity.
- It is imperative to expand the focus beyond the BMI to quantitatively and qualitatively ponder adiposity as well as the musculoskeletal system.
- Morphofunctional assessment encompasses a set of imaging and functional techniques aimed at achieving a more precise assessment of body composition and functionality.
- Embracing new processes and technologies is the way forward to advance the field, gain a closer look at the underlying pathophysiology and improve diagnostic performance as well as clinical management.

weight dates back to the metric devised initially as a curiosity. It was Adolphe Quételet, a 19th-century Belgian astronomer, sociologist, mathematician and statistician, who pioneered the incorporation of statistics to analyse social sciences.[17,18] He initiated the development of anthropometry since he was interested in identifying the values of the 'ideal man'. To that end, he collected data from Scottish and French soldiers, which can hardly be viewed as a representative sample of the world's population, to calculate the average man. He devised a ratio between the weight and height, originally termed the *Quételet Index*, and today widely known and applied for diagnostic purposes as the body mass index or BMI. Everyone outside those parameters was defined as either under- or overweight. Thereafter, in 1828 Adolphe Quételet initiated and led the Royal Observatory, an influential institution incorporating statistical methodology to the social sciences. In 1835 he demonstrated that a normal curve accomodates the distribution of human traits articulating his reasoning on human variance around the average Subsequently, around the 1970s, Ancel Keys, an American physiologist enshrined Quételet's index by endorsing the BMI as an obesity indicator. Quételet's long-lasting legacy of the establishment of a simple measure to classify people's weight relative to their height endures today with minor variations having dramatically influenced public health agendas.

Apparently, specific cut-off points for BMI to define obesity were established over 60 years ago according to data collected by the Metropolitan Life Insurance Company.[19] Their statistics identified that health started to decline with a BMI ≥25 $kg/m^2$. Thus, the decision to adopt this figure as the 'normal weight' upper limit was based on the association with health markers. However, does this value actually identify all people at risk of premature death or ill health? Given the current existence of more precise measurements should persistence of the BMI as the only criterion be maintained? The present narrative review focuses on analysing how the application of a simple metric like the BMI has been tremendously useful during a certain period of time but in the context of precision medicine and in view of novel scientific developments both in technology and understanding of the pathophysiology of the disease the adoption of new tools and ways of evaluating excess weight is required.

## 2 | REDEFINING AND REFRAMING OBESITY

Several scientific societies are currently working on developing new working frameworks to better capture the reality of excess weight and its appropriate management.[5,20–23] On the one hand, the simplicity of the measurement of weight, height, waist, hip and combinations to derive anthropometric indices makes it useful in clinical as well epidemiological settings. On the other hand, being a mere surrogate of adiposity the right balance between usefulness and meaningfulness needs to be struck. While consensus on the heterogeneity of the nature of obesity has been achieved, the tools used for its definition beyond BMI are more difficult to reach agreement upon.

To redefine and reframe obesity to reflect both current physiological research and more evidence-based clinical person-centred management is desperately needed.[24] In this scenario, it is important to go beyond the prevailing focus on body weight as the only health outcome.[25] Both the theoretical underpinnings and the day-to-day practicalities of the evaluation have to be thoroughly considered. A multidimensional perspective of the main compartments of the human body encompassed by adipose tissue, skeletal muscle, bone and water will be analysed and their contribution to the current modern-day epidemic will be contemplated. The current purpose of practicing specialists is to examine our understanding of the topic in the context of clinical management approaches to excess weight as well as to mention potential strengths and limitations of the presently applied methodology.

### 2.1 | Measuring what matters

Expansion of adipose tissue takes place in the context of sustained energy surplus that is accomodated in fat cells in the form of triacylglycerols. The perpetuation over time of this dysbalance translates into metabolic, mechanic, endocrine and inflammatory alterations.[26–29] The deranged secretory profile of proinflammatory factors and adipokines elicits an often subclinical low-grade inflammation together with a milieu characterized by increased oxidative stress and hypoxic conditions associated with the adipocyte enlargement that ultimately lead to pyroptosis and necrosis of the surrounding cells.[30]

In order to warrant movement and the performance of a wide range of activities, skeletal muscles are encountered all over the body. Not surprisingly, it does account for as much as 50% of the total body mass being a hugely plastic tissue actively involved in energy homeostasis and overall health. Relevant functions include maintaining body position, balance and posture, joint stabilization, organ protection, locomotion, respiration, body temperature maintenance, oxygen consumption, turnover of substrates as well as storage of glycogen, amino acids and energy. Therefore, alterations in skeletal muscle may entail only trivial problems to chronic insidious limitations

in everyday performance that decrease quality of life up to serious life-threatening conditions.

Expanding the focus beyond merely body weight and adiposity necessarily implies quantitatively and qualitatively pondering the musculoskeletal system. Determination of muscle mass, strength and quality incontrovertibly form part of comprehensively analysing a key body compartment. Quantification of skeletal muscle size is key in identifying increased frailty, decreased quality of life and morbi-mortality.[31] Beyond the mechanical, anatomical and physiological connection between bone and muscle, a dynamic crosstalk between metabolically active tissues like muscle, fat and bone takes place at organ, tisular and cellular level[32] mediated by autocrine, paracrine and endocrine communication via cytokines, myokines, adipokines and osteokines.[33–36] This complex relationship underlies the pathophysiological health triangle of obesity, sarcopenia and osteoporosis that needs to be considered in every thorough assessment.

The importance of hydration has been acknowledged, among others, in metabolism control, obesity, diabetes and chronic disease development,[37] thereby representing a body compartment gaining recognition in health outcomes also in the long term. Water balance is subject to homeostatic influences aimed at maintaining body volume, intra- and extracellular fluid composition and osmolality.

## 2.2 | Current frames obscure a precise diagnosis

While being a simple, easy, useful and cheap method, the BMI is only a surrogated measure of total adiposity. However, the World Health Organization (WHO) defines obesity 'as an abnormal or excessive fat accumulation that presents a risk to health'.[38] Unassailable evidence for the misdiagnosis of the BMI as opposed to actual body fat assessment shows that 29% of the people within the normal BMI range and 80% of those within the overweight category actually exhibit adiposity in the obesity domain.[39–41] Furthermore, the BMI-based classification of excess weight does not reckon the diverse obesity subtypes.[16,19,42–46] In fact, a range of other anthropometric determinations that more precisely captures adiposity, fat distribution, musculoskeletal system and hydration may better provide the means to assess the health status. Innumerable pathways implying morphological, structural, mechanical, functional, neural, endocrine and hemodynamic influences, among others, directly and indirectly impinge on the onset and development of the disease with body composition characteristics lying at its heart.[15] Moreover, the BMI further reinforces barriers to an adequate health approach, thereby narrowing diagnostic possibilities, management alternatives as well as useful preventive initiatives.

## 2.3 | Morphofunctional assessment: Theoretical framework

The concept of morphofunctional assessment brings together a set of imaging and functional techniques aimed at achieving a more precise assessment of body composition and functionality of the different compartments that comprise it. It pursues greater accuracy in the clinical management of patients with chronic adipose metabolic disease, studying the quantity, distribution and dysfunctionality of adipose tissue, and muscle mass. The estimation of morphological parameters, together with biochemical and dynamic tests, using tools available to the clinician, will allow a more accurate phenotyping of the body composition and functional status of the individual.[47] This global evaluation is necessary to complete a precision diagnosis that will allow us to carry out a more precise and personalized therapy and monitoring of the patient's evolution. The analysis of body composition has so far served to establish the relative proportions of the compartments in different pathophysiological situations and also for the assessment of changes during follow-up. A morphofunctional assessment of patients is important in the evaluation of chronic metabolic disease, encompassing, in its broadest concept, adipose and muscle tissue. To this end, the assessment must integrate anthropometric and biochemical parameters together with imaging techniques and body composition analysis tools, aimed at quantifying the quantity and distribution of body tissues, adding batteries of tests that estimate muscle functionality.[47] What is most interesting is that all these methodologies are already in use in daily clinical practice, to a greater or lesser degree of development and are highly accessible. The concept of morphofunctional assessment aims to group them together and use them for a more global pathophysiological estimation of the patient.

## 2.4 | Practicalities and tools

Healthcare professionals are slowly but progressively becoming cognizant of the relevance of body composition to predict a broad scope of health outcomes and circumstances. The implementation of direct adiposity measures has been suggested for decades to more truthfully quantify body fat.[32] Other anthropometric determinations like skin-fold thickness measurements, the waist and hip circumferences as well as combinations of them like the waist-to-hip or the waist-to-height

ratio have been proposed.[48–50] Moreover, the focus on the contribution of the fat-free mass and other compartments is driving the interest in other instruments and devices. The advent and introduction of novel methodologies and imaging biomarkers of adiposity, muscle and bone attained by bioimpedance, dual-energy X-ray absorptiometry (DEXA), air-displacement plethysmography (Bod-Pod), ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI) is profoundly changing the field.[32,51,52]

Figure 1 illustrates the powerful armamentarium of currently available equipment for the morphofunctional assessment of patients together with their progressive incorporation heralded by the technological development of new measuring devices. Already in the mid-1990s, surgical patients who reportedly had a low food intake and suffered from obvious nutritional deficiencies exhibited deranged biochemical parameters. Although the variables used to assess the nutritional status of patients have varied over the years, no single reference parameter that is altered solely by poor nutritional status has been identified. The C-reactive protein-to-prealbumin ratio has emerged in this scenario as the laboratory parameter currently employed that combines a marker of inflammation with a marker of nutritional status to aid in diagnosis and prognosis.[53]

The determination of anthropometric parameters is simple, low-cost and non-invasive having served for decades to obtain ranges of fat and muscle mass from the measurement of perimeters and skinfolds. The arm or calf circumference in the elderly, is the most commonly used assessment to estimate muscle mass, whereas the tricipital skinfold is the most applied estimate of fat mass.

Underwater weighing or hydrodensitometry is traditionally considered the gold standard for assessing body fat. This technique can estimate the body density and the percentage of body fat. Displaced water by the body is measured while the volunteer is completely submerged

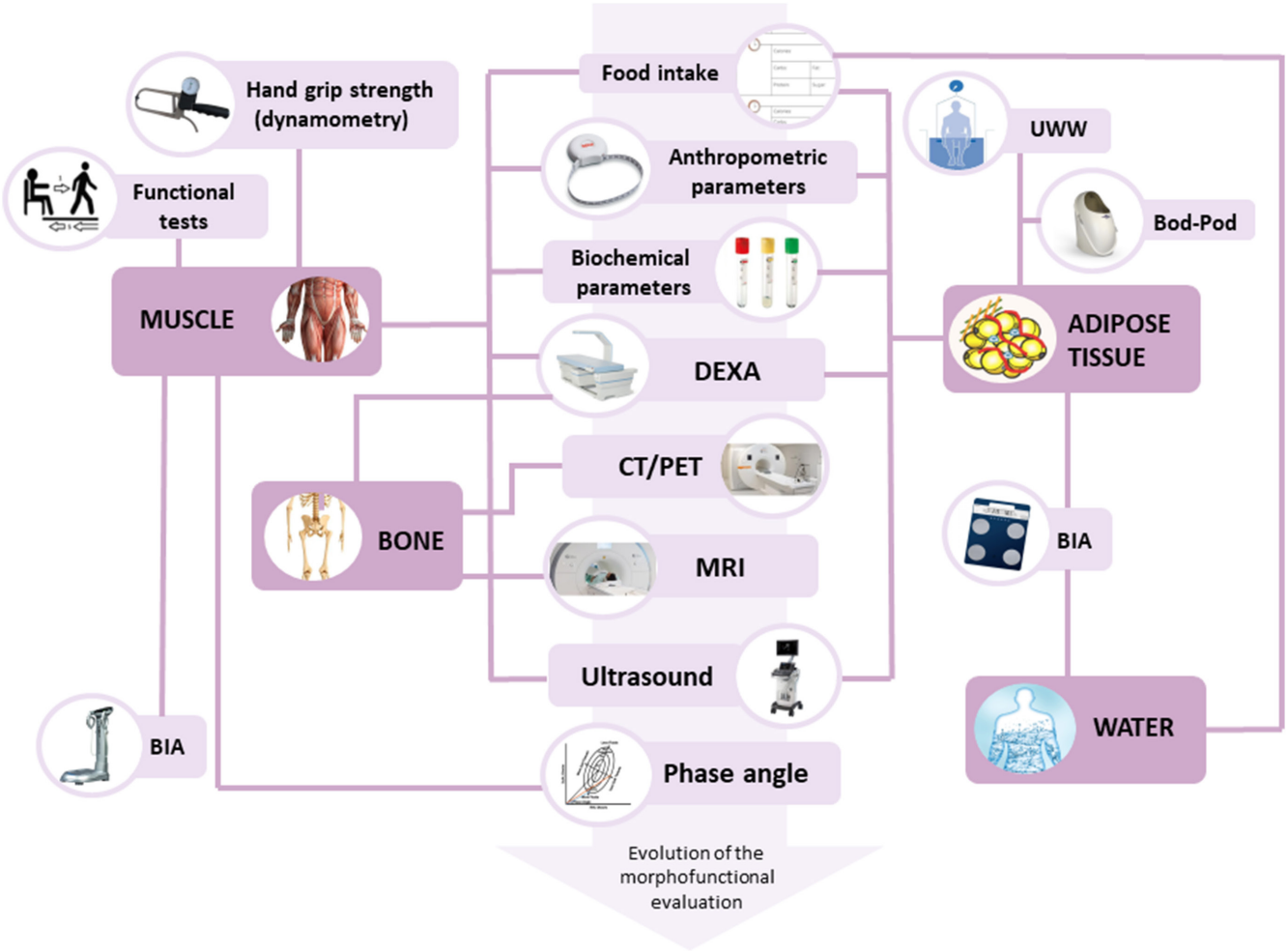


FIGURE 1 Development of morphofunctional evaluation tools and body compartment addressed. BIA, bioelectrical impedance; CT, computed tomography; DEXA, dual-energy X-ray absorptiometry; MRI, magnetic resonance imaging; PET, positron emission tomography; UWW, underwater weighing.

at the same time as residual lung volume assessment aids in obtaining a precise measurement of body volume, in order to derive the person's body density.[54] However, this technique has some disadvantages such as discomfort for individuals and its duration, making its use not common nowadays in the clinical setting.

To overcome the cumbersome practicalities of underwater weighing, the Bod-Pod started to be used to assess body fat by changing the water by air by means of air-displacement plethysmography.[41,43,51,55] This technique closely agrees with underwater weighing at the same time as being much easier and relatively faster to perform. It uses classic general gas equation laws based on the pressure-volume relationship in two separate chambers connected by a diaphragm, to calculate body density from mass and volume in order to obtain the body composition. However, the Bod-Pod is expensive, thereby not being accessible in most centres.

Bioelectrical impedance analysis (BIA) is a method used to determine the approximate composition of a body since the mid-1980s.[51,56–58] This technique has been widely used due to its simplicity, device portability and reasonable cost in comparison to other methods of body composition analyses. BIA depends on measuring resistance opposed by the body to the passage of a current, but this technique is not the most accurate as it rules out many variables that influence the final result. The estimation of fat mass and fat-free mass values according to electrical conductance has been tried to be validated by MRI-derived measurements with the added advantage of performance at the point of care when compared to imaging techniques.

DEXA is the gold standard method for bone density determination using X-rays. It thus entails exposure to a low radiation to yield bone mineral as well as fat and lean tissue mass, thereby representing a three-compartment model. Whole-body DEXA determinations are usually performed to measure body composition.[59] It delivers fat-free mass, including muscles, organs and appendicular lean mass, together with fat mass, and body fat percentage.

CT is an imaging device involving X-ray exposure that allows precise determination of fat depots.[60] However, being expensive it is only available in hospitals with access to sophisticated technology. CT enables examination of adipose tissue quality, quantity and distribution. Differences between visceral and subcutaneous adiposity can be readily identified in a reproducible and reliable way. Moreover, other fat depots, such as perirenal, perivascular or epicardial fat, can also be quantified. In addition, some specialized studies can quantitate intermuscular adipose tissue, an indicator of myosteatosis.[61] MRI has been equally applied for muscle mass quantification and determination of muscle fat infiltration. Identically, MRI distinguishes between subcutaneous and visceral fat.[60]

The limitations of these unwieldy imaging techniques have led to the incorporation of other measuring devices already present in the hospital setting like a specific BIA and echography. In this context, novel techniques have emerged, due to their availability in health centres and straightforward reproducibility, namely phase angle (PhA) retrieved from bioelectrical impedance vector analysis (BIVA) and nutritional ultrasound. BIVA emerged as a helpful method to track changes in hydration, cellular integrity and health via PhA quantitation, a compound of two raw BIA determinations, resistance and reactance, removing the potential bias introduced by the use of predictive equations.[62] Since oxidative stress and chronic inflammation have the potential to damage cellular structures, PhA can be viewed as an expeditious index of cellular integrity, health and hydration, thereby being useful in inflammation identification and prediction of adverse health outcomes.[63] Sex, age, extra- to intracellular water ratio, fat-free mass and BMI reportedly affect PhA values as do obesity-associated multimorbidity.[64]

The advent of nutritional US, a surging technique in clinical nutrition to analyse morphology and structure of muscle mass and adipose tissue with the advantage of low cost, portability and lack of radiation is really welcome.[51,52,65] However, no standardized way of assessment and no reliable cut-off points for discrimination have been firmly established. Usually, midthigh rectus femoris thickness is measured. Moreover, the thickness of the thigh muscle reportedly correlates with the speed of walking, an independent indicator of muscle loss and functionality. Further variables like muscle echogenicity, fascicle length and pennation angle have been analysed with less reproducibility.[47]

Handheld dynamometry to measure hand grip strength represents the most frequently used, validated and suitable functional technique for muscle strength assessment in clinical practice.[66] Correlation with calf muscles cross-sectional area, leg power and functional disability has been shown. Handgrip strength is considered a phenotypic indicator of malnutrition diagnosis. Gait speed determination over a short distance of several meters is also often used to assess physical performance. The Timed Up and Go test represents a customary method to screen aged adults for problems in maintaining balance and potential falls. The Short Physical Performance Battery, evaluating the individual's ability to stand, walk 8 feet, return to the chair, and sit five times adds useful information to predict adverse health events.[67]

All methodological approaches exhibit specific peculiarities and limitations as regards cost, complexity, availability, radiation and portability that health professionals

need to ponder when evaluating their inclusion into everyday practice. Both theoretical foundations and practice issues of currently available non-invasive equipment with a patient-centred focus should drive the comprehensive decision-making process.

## 2.5 | Translation to clinical application

Excess weight is steadily being acknowledged as a recognizable disease with distinctive clinical features, biological risk factors and overall behavioural influences. In view of an increasingly ageing population and the unabating rise of non-communicable diseases (NCDs) novel operating frameworks are awaiting the acquisition of compelling evidence. Amidst the obesity field, the coherent integration of understanding, and discovery followed by research translation into clinical provision should be chased. Due to the enormous potential of body composition analysis to improve the diagnosis and care of patients, its routine incorporation and implementation in practice is urgently needed and prompts this call to action to enrich the classical anthropometric determinations and BMI-centric approach with morphofunctional assessment whenever possible (Figure 2). PhA is a composite appraisal combining resistance and reactance to operate as a global marker that reflects a patient's nutritional and inflammatory state.[62,64] Furthermore, it is a real-time, low-cost, reliable surrogate marker of cell membrane integrity for oxidative and inflammatory alteration screening.[63]

The lack of standardization in the acquisition and processing of images represents a concern. Notable efforts to develop carefully designed protocols will be needed. Moreover, the establishment of clinically meaningful cut-off thresholds applied to frame what is considered low skeletal muscle size, physiological variation and pathological alterations is pending. While thresholds for both muscle mass and physical performance do change depending on the definitions applied, association to a pleiad of diverse adverse health outcomes has been reported.[64,68] It will be imperative that both researchers and clinicians collaborate to develop diagnostic reference values based on accuracy of the determination, clinical relevance of the diagnosis and functional impact of the finding.

In the clinical scenario sarcopenic obesity particularly attracts attention due to the demographical changes of a population that is ageing surrounded by an obesogenic environment.[69] The concurrent decline of skeletal muscle mass and function together with simultaneously increased adiposity characterizes sarcopenic obesity.[69–71] Nevertheless, sarcopenic obesity persists flagrantly underdiagnosed, probably in relation to its anodyne symptomatology as well as the lack of

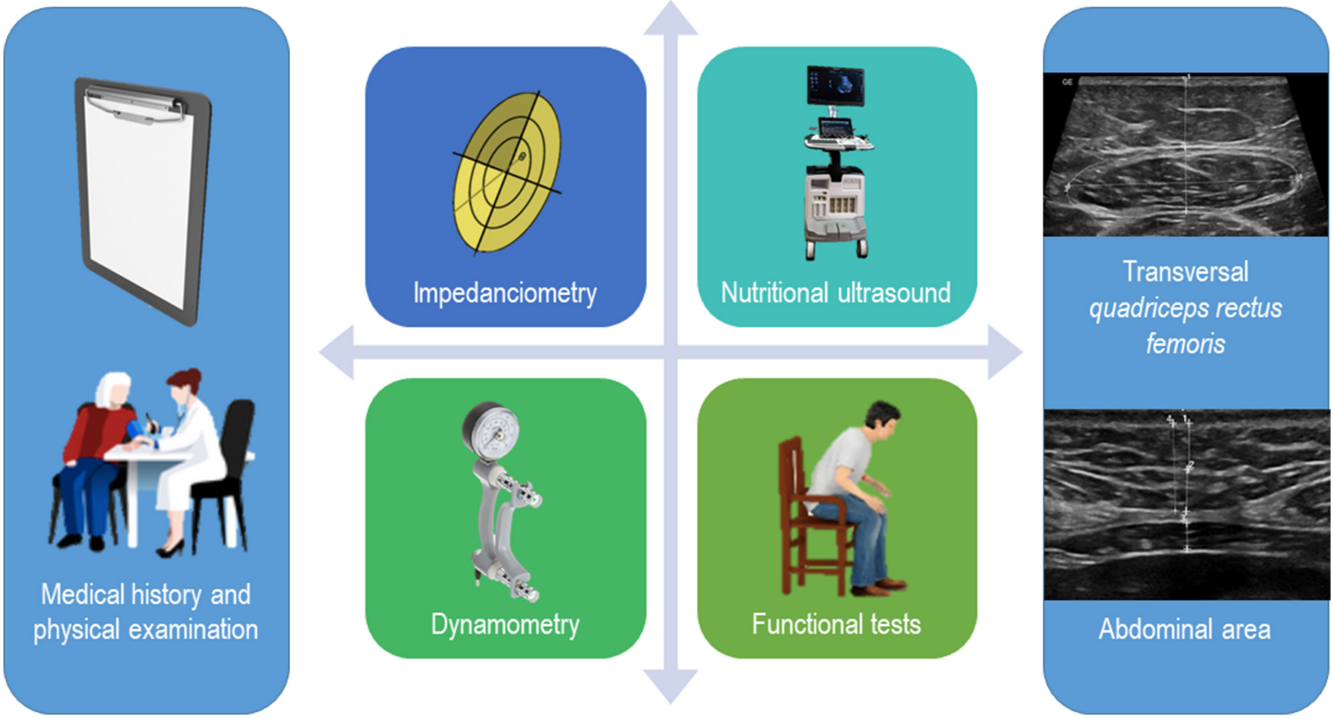


FIGURE 2 Features of morphofunctional assessment. Schematic representation of a comprehensive evaluation of morphofunctional characteristics of the patient.

recognition by practicing physicians.[72] In addition, the abscence of widely recognized diagnostic criteria and a taxonomic standardization further hamper a correct identification.[73,74]

In addition to a more accurate diagnosis, the relevance of precise follow-up is equally paramount. Thus, detailed pre- and post-interventional assessments are required to thruthfully monitor success as well as to minimize potential adverse consequences. Rapid weight loss may be particularly harmful in patients with sarcopenic obesity, given the blend of diminished muscle mass, augmented fat mass and weakened muscular function. This potential circumstance needs to be particularly contemplated in marked weight reduction attainable with bariatric surgery and contemporary antiobesity medication[20] in the context of excess muscle wasting and muscular strength drop because of disrupted energy homeostasis.

Analysis of opportunistic imaging examinations derived from routine clinical indications has yielded relevant information on tissue health as regards fat, muscle and bone. In practice, characteristics underlying adipose tissue integrity, biology and functioning will need to be addressed.[75–77] Amidst the precision medicine era the dynamic interplay between adipogenesis,[78–80] lipolysis,[29,81–84] inflammation,[28,85–87] secretory profile,[88–90] and fibrosis[91,92] determines individualized responses that shape a holistic understanding of energy homeostasis,[93–95] which needs to be contemplated.[46,96] On the other hand, knowledge needs to be expanded as regards the active crosstalk among metabolically relevant organs like skeletal and myocardial muscles, liver, kidneys, pancreas, gastrointestinal system, bone and the vasculature within an internal milieu characterized by inflammation and oxidative stress (Figure 3).

A number of obstacles still prevents a broader application in clinical practice, which can be summarized in two main areas, workflow and scientific understanding. Workflows involving a thorough description of protocols for each methodology should be pursued. Undoubtedly, detailed clinical practice guidelines and consensus statements will need to be developed to warrant outright optimization.

The proposed approach is primarily aimed at specialized centers. In the short consultation time available, currently primary care professionals and other clinicians lack the equipment and skills to carry out the proposed examinations. However, as has happened throughout the history of medicine, what in many fields initially started as specialized determinations limited only to specialists has subsequently been extended to the incorporation into routine practice over time. Moreover, the advancement in technology together with the increasing availability of medical devices at the tip of our hands through mobile phones will make previously unconceivable explorations readily available for health care professionals working in primary care or other settings.[97–99]

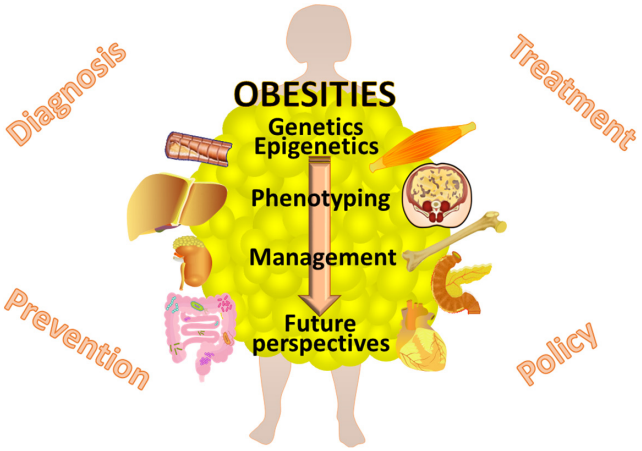


**FIGURE 3** Ways to revisit the beyond BMI paradigm. In order to better characterize people living with excess weight, a thorough phenotyping that encompasses adiposity together with all relevant body compartments, their function and interactions is required to ensure a better diagnosis and treatment that will further translate into prevention efforts and policy changes.

## 3 | FUTURE PERSPECTIVES

How to reframe obesity needs to be discussed and reconsidered. A renovated approach to body composition analysis is needed to foster advances in this field. A broader range of strategies has to be invoked. Alternative systems to examine how we define obesity are under way. To advance in this field, reconsiderations are required, novel ways will have to be adopted, and lessons of already identified mistakes applied from a wide perspective. While technological advances inspire and promote new ways to move forward, the focus necessarily needs to be kept on improving clinical practice and health promotion.

A comprehensive attitude towards the management of PwO should always guide physicians. Undoubtedly, a better understanding which implies challenging the current medical inertia will need to be in place. In the future extensive and diverse, large populations of varied age, gender and health state will need to be analysed to further validate different devices and their accuracy as potential indicators of oxidative stress and inflammation in the clinical setting.

Automation by means of deep learning techniques, 3D body scanning, segmentation of tissues of interest in imaging technologies as well as the reporting of the

diverse parameters measured will surely help to further drive progress in the field.[98,100] In particular, patient phenotyping with disease-specific profiling is of utmost importance as is the adequate choice of the main elucidative outcomes.[68] Although still at an early stage, the implementation of artificial intelligence analysis automation will permeate the clinical workflow in the near future. It can be foreseen that in the future morphofunctional assessment may be carried out automatically at the click of a button. An interim transition time during which technological advances are finally adopted and automated will be witnessed.

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The structure and contents were agreed upon by all authors. Each author contributed part of his/her main expert area to produce the first draft, which was then critically revised by all until reaching the final version. The authors did not use generative AI or AI-assisted technology to write the manuscript.

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The authors declare no conflicts of interest.

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