Clinical Evaluation

15

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15.1 Introduction

Obesity is a complex chronic disease with extended and highly variable effects on individual health and function. As for any chronic disorder, a cure of the condition is the ultimate goal, but difficult to achieve. We can manage obesity but to date have no cure, and we need to use a range of partially effective long-term therapies. Combining interventions and scaling up therapy for serious or resistant disease are usual parts of the continuum of care for chronic diseases. All interventions have a range of benefits and risks, and this need to be balanced for each individual health burden and risk. This clinical balance requires a precise and complete evaluation of any individual obese patient, covering both the severity of obesity itself and the effects that obesity has on critical body systems and functions. This large body of information needs to be integrated in a general scheme guiding the therapeutic choices at the individual level.

15.2 Body Composition and Fat Distribution

A crude measure of overweight and obesity is the *body mass index* (BMI), a person's weight (in kilogrammes) divided by the square of his height (in metres). Height and weight should be measured by appropriate and calibrated scales with the subject wearing only light clothes without shoes. BMI (kg/m^2) is used in epidemiology and in clinical practice to define underweight, normal weight, overweight (pre-obesity) and severity of obesity [1]. At a population level, different and progressively increasing risks of comorbidity are observed for increasing BMI values (Table 15.1). BMI

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Table 15.1 The classification of weight category by BMI in adults

Classification	BMI (kg/m^2) cut-off points	Comorbidity risk
Underweight	<18.5	–
Normal range	18.5–24.9	Normal
Pre-obese	25.0–29.9	Increased
Obese class I	30.0–34.9	Moderate
Obese class II	35.0–39.9	High
Obese class III	≥40.0	Very high

Source: Adapted from WHO [1]

cut-offs in adults are independent from age and similar in both genders. However, different cut-off points have been introduced for some particular ethnic groups, notably Asian populations, in which the relationship between BMI and risk of morbidity seems to be steeper than in Caucasian, with an increase of metabolic derangements appearing at lower BMI levels [2].

The use of BMI as a proxy for adiposity, the true determinant of the obese state, has been criticised, given that body weight is the sum of individual organs and tissues and therefore it includes adipose tissue, skeletal muscle mass and organs mass. On a population level, a strong positive correlation between BMI and overall body fat content has been reported [3]. However, at an individual level, a substantial variation in percentage body fat may be observed for any given BMI value [4]. Therefore, a high BMI may correspond to a low *fat-free mass* and a substantial fat accumulation in an obese patient, or to a large skeletal muscle mass and normal *fat mass* in a healthy athlete, in which high BMI simply reflects increased muscle mass, which has nothing to do with obesity and associated diseases. Visual inspection is usually sufficient to discriminate these extremes in body composition, but in some subjects the distinction may be more subtle, and a more precise determination of body composition may be requested. Fat mass and fat-free mass may be reliably distinguished and measured by direct densitometric methods (underwater weighing; total body densitometry). *Dual-energy X-ray absorptiometry (DEXA)* has a good reproducibility for total body fat mass (coefficient of variation: 2–3 %) and total body fat-free mass or lean soft tissue (1–2 %), and it is sensitive in assessing minimal changes in body composition [5]. Unfortunately, DEXA is not applicable in routine office practice; it is costly and exposes patients to a low dose of radiations. *Bioelectrical impedance analysis (BIA)* is an indirect method that derives body composition values from electrical data (reactance, resistance, impedance) measured during the passage of a small electrical current through the patient's body [6]. The method is applicable also in the outpatient setting and does not have virtually potential side effects, and it is relatively not expensive. However, the reliability of BIA in the accurate determination of fat mass and fat-free mass may be questioned. BIA measurements must be standardised in order to obtain reproducible results (reported mean coefficients of variation for within-day measurements: 1–2 %), and overall reproducibility/precision is estimated around 2.7–4.0 %, with prediction errors for FFM ranging from 3 % to 8 % [7]. These large errors may be even larger in obese patients and limit the utility of BMI in clinical evaluation.

A further important limitation for BMI is that this index does not convey any information on *fat distribution* (e.g. visceral fat accumulation and fatty infiltrations in individual organs) that is considered now an important determinant of metabolic and cardiovascular risk [8]. A clear evidence in favour of the inclusion of fat distribution in the clinical evaluation comes from the observation of normal-weight or slightly overweight subjects with low subcutaneous but increased visceral fat mass. This TOFI (thin-on-the-outside fat-on-the-inside) sub-phenotype has been observed in both male and female subjects and increases an individual's risk of metabolic disease [4]. The elevated *visceral fat* found in individuals classified as TOFI is accompanied by increased levels of ectopic fat deposition both in the liver and in the skeletal muscle. Lipid accumulation in non-adipose cells (ectopic fat) may impair the normal function of some tissues through a process known as "lipotoxicity". Ectopic storage of excess lipids in organs such as the liver, skeletal muscle, and pancreatic beta cells may be the causative link between fat distribution and the metabolic syndrome or cardiovascular diseases [9]. Similar findings have been already reported in obese individuals, where obese subjects with a disproportionate accumulation of visceral fat had increased incidence of metabolic disorders and cardiovascular events [10].

Visceral fat accumulation may be measured precisely with CT and MRI, but it may be difficult to quantify at a clinical level, and surrogate anthropometric indexes have been proposed. In particular, the *waist circumference* has been selected as a reliable clinical indicator of visceral fat accumulation, and having a large waist is associated to a higher prevalence of metabolic disorders and cardiovascular diseases [11]. Therefore, the measurement of the waist circumference is suggested for the determination of cardiovascular risk of overweight and obese patients, and the integration of BMI and waist values may be used to better stratify their health risk [11] (Table 15.2). Waist circumference should be measured with a plastic stretch-resistant tape on the subject in the standing position, at the end of a gentle expiration, without constricting the abdomen. Different anatomic landmarks have been suggested for waist measurement [12]. According to WHO guidelines, waist circumference should be measured at the approximate midpoint between the lower

Table 15.2 Classification of overweight and obesity by BMI, waist circumference and associated disease risk

		Disease risk relative to normal	
		Men waist <102 cm	Men waist >102 cm
BMI	Obesity class	Women waist <88 cm	Women waist >88 cm
<18.5	Underweight	–	–
18.5–24.9	Normal range	–	–
25.0–29.9	Overweight	Increased	High
30.0–34.9	Obese class I	High	Very high
35.0–39.9	Obese class II	Very high	Extremely high
≥40.0	Obese class III	Extremely high	Extremely high

Source: Adapted from NIH [11]

margin of the last palpable rib and the top of the iliac crest [13]. The US National Institutes of Health (NIH), by applying the same method used for the US National Health and Nutrition Examination Survey (NHANES) III, indicates that waist circumference measurement should be made at the top of the iliac crest [11]. The two methods did not produce the same results, with the WHO method underestimating waist values in respect to the NIH method, particularly in women [12]. It should be emphasised that the cut-off values proposed for "at-risk" waist values (Table 15.2) and utilised for the original ATP-III definition of the *metabolic syndrome* are those proposed by the NIH. The simple measurement of waist circumference has replaced the use of the *waist-to-hip circumference ratio (WHR)*, originally proposed as a powerful marker of fat distribution. More recently, on the basis of several epidemiological studies showing that having a large hip circumference may confer some BMI-independent protection from metabolic and cardiovascular diseases, particularly in women, a return to the measurement of hip circumference has been proposed [14]. The reliability of waist circumference in assessing visceral fat accumulation may be reduced in obese women, particularly at higher BMI levels [15]. Other anthropometric indexes have been therefore suggested as more effective than waist circumference for the prediction of visceral fat depots, with the *sagittal abdominal diameter (SAD)* being the more promising one [16]. SAD is determined at the highest point of the abdominal surface with the subject in the supine position and during normal breathing by means of a specifically made instrument. Abdominal ultrasonography is another reliable, repeatable and less expensive method which has been proposed to detect visceral fat deposition without radiation exposure [17]. *Peritoneal fat thickness* is considered the gold standard echographic index for visceral fat prediction in abdominal ultrasonography, and it corresponds to the distance from the internal face of the recto-abdominal muscle and the anterior wall of the aorta, measured with the echographic probe transversely placed perpendicular to the skin in the midline of the abdomen [17]. The increasing availability of portable low-cost ultrasonographic instruments will probably stimulate the applicability of ultrasonographic measurements of visceral fat accumulation in clinical practice.

The presence of *ectopic fat deposition* in the relevant organs may be even more difficult to quantify than visceral fat accumulation in clinical practice. However, liver fat infiltration (hepatic steatosis) may be roughly, albeit imprecisely, estimated by ultrasound [18]. An alternative approach to the quantification of ectopic fat accumulation may be represented by the ultrasonographic measurement of epicardial fat, which has been suggested as a further marker of metabolic and cardiovascular risk [19].

15.3 Metabolic Status and Cardiovascular Risk

Several epidemiologic studies confirmed the strict relationships between BMI and type 2 diabetes, and 65–75 % of the cases of type 2 diabetes may be attributed to the presence of overweight and obesity [1]. According to American Diabetes Association's (ADA) Standards of Medical Care, adults of any age who

Table 15.3 Criteria for the diagnosis of diabetes and prediabetes in adults

Method	Diabetes	Prediabetes
FPG	FPG > 126 mg/dL (7.0 mmol/L)	FPG 100–125 mg/dL (5.6–6.9 mmol/L) (impaired fasting glucose or IFG)
2-h PG during OGTT	2-h PG >200 mg/dL (11.1 mmol/L)	2-h PG 140–199 mg/dL (7.8–11.0 mmol/L) (impaired glucose tolerance or IGT)
A1C	A1C > 6.5 %	A1C 5.7–6.4 %
Random PG	Random PG > 200 mg/dL (11.1 mmol/L) in a patient with classic symptoms of hyperglycaemia or hyperglycaemic crisis	–

Source: Adapted from ADA [20]
FPG fasting plasma glucose defined as no caloric intake for at least 8 h. *OGTT* oral glucose tolerance test performed using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. A1C, glycosylated haemoglobin performed in a laboratory using certified and standardised assay

are overweight or obese and who have one or more additional risk factors for diabetes should be tested to detect type 2 diabetes and prediabetes [20]. Additional risk factors for diabetes include physical inactivity, first-degree relative with diabetes, high-risk ethnicity, previous delivery of a macrosomic baby or previous gestational diabetes, hypertension, low HDL cholesterol level, hypertriglyceridaemia, polycystic ovarian syndrome in women, other clinical conditions associated with insulin resistance (e.g. severe obesity, acanthosis nigricans), and history of cardiovascular disease [20]. The glycosylated haemoglobin (A1C), the fasting plasma glucose (FPG) or a 2-h 75-g oral glucose tolerance test (OGTT) are all considered appropriate for testing [20]. However, the three tests do not necessarily detect diabetes in the same individuals. In particular, many obese patients may have normal FPG, but abnormal post-load glucose levels. More frequent retesting should be considered in patients testing positive for prediabetes in previous occasions. The diagnostic criteria for diabetes and prediabetes are summarised in Table 15.3. In case of diabetes, a complete screening for macro- and microvascular complications should be scheduled [20].

The association between *arterial hypertension* and obesity is very well documented. The prevalence of hypertension in adults with obesity is three to five times higher than in normal-weight subjects [1]. Arterial hypertension in obese patients is frequently unrecognised or suboptimally treated. The office measurement of systolic and diastolic blood pressure with a sphygmomanometer with a normal cuff size can grossly overestimate blood pressure levels in obese patients. The use of an appropriate cuff size is therefore of paramount importance in obese patients. In practice, a large adult size 16×36 cm should be used for arm circumferences ≥35 cm and an adult thigh size 16×42 cm for arm circumferences ≥45 cm [21]. Diagnostic criteria for arterial hypertension in overweight and obese patients did not differ from those used in the general population, and hypertension may be therefore defined as a systolic

blood pressure ≥140 mmHg, or a diastolic blood pressure ≥90 mmHg or the use of any anti-hypertensive drug [22].

Obese patients, in particular in the presence of abdominal obesity or visceral fat accumulation, are frequently characterised by a particular *dyslipidaemia* with high *triglycerides* and low *HDL cholesterol* levels. LDL cholesterol levels are usually not particularly affected, but there is an increase in the proportion of a particular class of *small dense LDL particles* [1] that are considered highly atherogenic. Small dense LDL are not measured in normal clinical practice, but their presence may be indirectly estimated trough the measurement of *apo-B lipoprotein* and the ratio between apo-B lipoprotein and LDL cholesterol [1]. An alternative and more simple way to assess atherogenic dyslipidaemia in patients with abdominal obesity is the calculation of the *non-HDL-cholesterol* levels (total cholesterol minus HDL cholesterol). Non-HDL cholesterol may be used as an estimation of the total number of atherogenic particles in plasma [VLDL + intermediate-density lipoprotein (IDL) + LDL] and relates well to apo-B levels [23]. *Treatment targets for dyslipidaemia* in overweight and obese patients, as well as in the general population, are primarily based on results from clinical trials and are modulated according to the level of *total cardiovascular risk* (see below). Primary target for cardiovascular disease prevention should be a reduction in LDL cholesterol. Treatment targets for LDL cholesterol are set to less than 70 mg/dl in patients with very high cardiovascular risk, to less than 100 mg/dl in patients with high cardiovascular risk and to less than 115 mg/dl in patients with moderate cardiovascular risk [23]. Once the primary LDL target is achieved, the level of non-HDL cholesterol should be checked and targeted. Treatment targets for non-HDL cholesterol are set 30 mg/dl higher than the corresponding target for LDL cholesterol [23].

Prediabetes/diabetes, hypertension, hypertriglyceridaemia and low HDL cholesterol levels are frequently clustered in patients with abdominal obesity. This cluster of metabolic abnormalities has been labelled as the *metabolic syndrome,* and specific diagnostic criteria have been proposed [24] (Table 15.4).

Table 15.4 Clinical identification of the metabolic syndrome

Risk factor	Defining level
Abdominal obesity (waist circumference)	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/85 mmHg
Fasting glucose	≥110 mg/dL

The metabolic syndrome is identified by the presence of three or more of the components listed in the table
Source: Adapted from ATP III panel [24]

The superiority of the metabolic syndrome over the combined evaluation of the single risk factors as an indicator of cardiovascular risk has been criticised, but the diagnosis of metabolic syndrome still remains useful in clinical practice for the rapid identification of overweight and obese patients with a worse cardiovascular and metabolic fate. Patients with the metabolic syndrome frequently have other accompanying metabolic abnormalities, like insulin resistance, low-grade chronic inflammation and a prothrombotic state. However, the routine measurement of insulin resistance (e.g. plasma insulin), proinflammatory state (e.g. high-sensitivity C-reactive protein) or prothrombotic state (e.g. fibrinogen or PAI-1) is not yet supported by adequate evidence, and it is not recommended [24].

All current guidelines for the prevention of cardiovascular disease in clinical practice recommend the assessment of *total cardiovascular risk*, because in most patients atherosclerotic disease is usually the product of multiple cardiovascular risk factors. Total cardiovascular risk is usually defined as the probability of having a fatal or nonfatal cardiovascular event in a given time frame (usually 10 years), and it may be estimated by using a wide array of risk assessment systems based on the occurrence of cardiovascular events in large population longitudinal studies. No specific instruments for the calculation of total cardiovascular risk has been produced for overweight and obesity, and therefore general instruments should be applied also for the clinical evaluation of these patients. In Europe, the use of the *systemic coronary risk estimation (SCORE)* system should be recommended, because it is based on a very large and representative European data set [23]. The SCORE system estimates the 10-year risk of a first fatal atherosclerotic event, and it is based on specific charts for low (Belgium, France, Greece, Italy, Luxembourg, Spain, Switzerland and Portugal) and high-risk regions in Europe. The SCORE charts are based on gender, age, smoking status, systolic blood pressure, total cholesterol and HDL cholesterol. Patients may be considered to have a very high risk when having a calculated 10-year risk SCORE $\geq$10 %, a high risk when having a 5–10 % SCORE, a moderate risk when having a 1–5 % SCORE and a low risk when having a risk SCORE <1 %. Patients with established cardiovascular disease, diabetes type 2 or type 1 with microalbuminuria or chronic renal disease should be considered high-risk patients independently from the SCORE. Patients with very high levels of individual risk factors (familial dyslipidaemia, severe hypertension) should be considered as high-risk patients independently from the SCORE. Risk will also be higher than indicated in the charts in socially deprived individuals, sedentary subjects and patients with abdominal obesity, individual with diabetes, patients with pre-clinical evidences of atherosclerosis, patients with impaired renal function or patients with positive family history of premature cardiovascular disease [23]. Considering that SCORE system estimates the 10-year risk of fatal events, the risk for total (fatal and nonfatal) events may be calculated multiplying the SCORE risk by 3.0 in men and by 4.0 in women. Alternative systems for total cardiovascular risk calculation are the Framingham Risk Score or the PROCAM Risk Score [23].

15.4 Hepatic Function

Patients with abdominal overweight or obesity and with related metabolic syndrome frequently have liver fat infiltration. *Nonalcoholic fatty liver disease (NAFLD)* corresponds to a spectrum of liver histologic findings. In most patients NAFLD is represented by a simple and uneventful steatosis, but in a proportion of cases, NAFLD may progress to *nonalcoholic steatohepatitis (NASH)*, cirrhosis and hepatocellular carcinoma [25]. Liver fat infiltration (*hepatic steatosis*) may be easily detected and, albeit imprecisely, estimated by standard abdominal ultrasonography [18]. Accompanying biochemical abnormalities are usually represented by a mild elevation of liver enzymes, with *alanine transaminase (ALT)* usually higher than *aspartate transaminase (AST)*.

The most important clinical question in the evaluation of the liver of obese patients is the distinction between the simple relatively benign hepatic steatosis and the progressive and more harmful NASH. This question remains to date substantially unresolved. The only reliable means of proving a diagnosis of NASH and separating it from simple fatty liver is a *liver biopsy*. NASH is diagnosed when histologic examination shows fat along with ballooning of hepatocytes, lobular inflammation and fibrosis. Given the rising obesity epidemic and the very large number of subjects potentially affected by NAFLD, the need for non-invasive alternative testing is rising. In the last few years, *liver stiffness measurement* (LSM) by transient elastography, with *FibroScan*® (Echosens, Paris, France), has emerged as a non-invasive test for liver fibrosis [26]. However, the reliability of LSM and its levels of correlations with histologic findings remain still debated.

15.5 Respiratory Function

The impairment of respiratory function produced by obesity is known since many years. Obese patients are affected by a restrictive respiratory impairment, with the most characteristic pulmonary function abnormality being a reduction of the *expiratory reserve volume* (ERV) [27]. The decrease of ERV and *functional vital capacity* (FVC) associated with obesity has been attributed to a mechanical effect played by visceral fat accumulation, and it is indeed more relevant in patients with abdominal fat deposition [28]. Obesity-related impairments of lungs volumes may be easily detected by standard spirometry. However, the clinical utility of spirometric testing in overweight or obese patients without respiratory symptoms may be questioned, given that the results usually do not change significantly the management of these patients.

Obstructive sleep apnoea (OSA) is a common sleep disorder characterised by repetitive episodes of apnoea and hypopnoea during sleep, accompanied by hypoventilation, oxygen desaturation, sympathetic arousal and wakening. The diagnosis of OSA is confirmed if the number of obstructive events is greater than

Table 15.5 The STOP-BANG questionnaire for the screening of obstructive sleep apnoea (*OSA*)

S = Snoring	Do you snore louder than talking or loud enough to be heard through closed doors?
T = Tiredness	Do you often feel tired, fatigued, or sleepy during daytime?
O = Observed apnoea	Has anyone observed you stop breathing during your sleep?
P = Pressure	Do you have or are you being treated for high blood pressure?
B = BMI >40 kg/m^2	
A = Age >50 years	
N = Neck circumference >40 cm	
G = Male gender	

Modified by Ref. [24]
High risk of OSA is considered if answering yes to three or more questions of the questionnaire

15 events/h of sleep or greater than 5 events/h in a patient reporting at least one of the following symptoms: unintentional sleep episodes during wakefulness; daytime sleepiness; unrefreshing sleep; fatigue; insomnia; waking up breath-holding, gasping or choking; or the bed partner describing loud snoring, breathing interruptions or both during the patient's sleep [29]. OSA severity is defined as mild for events/h ≥5 and <15, moderate for events/h ≥15 and ≤30, and severe for events/h >30 [29]. OSA is highly prevalent in the obese population and may be present in at least 40 % of patients with severe visceral obesity [28]. The screening for OSA in overweight and obese patients is therefore mandatory, given that OSA is associated with important health consequences, such as increased cardiovascular disease risk and mortality, and that these consequences can be prevented by adequate OSA management [29].

Full night *polysomnography* (PSG) is considered the gold standard for the diagnosis of OSA and sleep-disordered breathing [29]. However, PSG is a lengthy and expensive procedure and requires inhospital staying. Portable sleep monitoring devices designed for use at home have been implemented, but availability limitation frequently causes long waiting times for testing. Several screening questionnaires have been therefore proposed in order to predict which patients have the higher probability of OSA and will need PSG. The most popular of these questionnaires (Berlin Questionnaire, American Society of Anesthesiologists Checklist and STOP Questionnaire) have been recently compared and found to have a moderately high level of sensitivity and a negative predictive value [30]. The *STOP-Bang questionnaire* (Table 15.5), an extended version of the STOP Questionnaire with eight instead of four items, has a high specificity to detect moderate and severe OSA, thereby identifying the patients in which PSG is needed [31]. No screening test is perfect, and the sensitivity and specificity of these predictive tools have been criticised. However, the application of a standardised screening tool for OSA, with confirmatory PSG if screening tests are positive, should be recommended [32].

15.6 Staging

Obesity is a complex disease with extended clinical implications. Evaluation and management of any individual obese patient should be therefore based on a comprehensive characterisation of the patient's global health and on a reliable prediction of its future disease risk. On the basis of the above considerations, a more precise phenotypization of obese patients should include a determination of body composition with a reliable technique (DEXA), particularly in cases where the BMI value may be misleading, and an estimation of fat distribution and ectopic fat deposition (waist circumference, hip circumference, hepatic steatosis, epicardial fat, etc.). Phenotyping should obviously be completed by the determination of cardiovascular and metabolic risk factors and by the assessment of obesity-related comorbidities. A list of all the clinical data that should potentially be integrated in the comprehensive evaluation of the obese patients beyond BMI values is reported in Table 15.6.

Table 15.6 A list of clinical factors that should be included in a comprehensive clinical evaluation of the obese patient

Body composition	BMI (% body fat, as determined by DEXA)
Fat distribution	Waist circumference
	Hip circumference
	Visceral fat accumulation (ultrasonography)
Ectopic fat deposition	Liver fat infiltration (hepatic steatosis)
	Epicardial fat
Cardiovascular risk factors	LDL cholesterol, HDL cholesterol, triglycerides
	Fibrinogen
	hs-PCR
Obesity-related comorbidities	Type 2 diabetes
	Hypertension
	Obesity-related cardiomyopathy
	Sleep apnoea syndrome
	Obesity/hypoventilation syndrome
	Disabling weight-bearing joint disease
	Obesity-related infertility
	Urinary stress incontinence
	Severe gastro-oesophageal reflux disease
High risk for type 2 diabetes	Family history of type 2 diabetes
	Previous gestational diabetes
	Polycystic ovary syndrome
	Impaired glucose tolerance/impaired fasting glucose
	Hyperinsulinaemia/insulin resistance
Early markers of atherosclerosis	Plaques or increased intima-media thickness at carotid ultrasonography
	Low ankle-brachial index
	High coronary artery calcium score
Initial signs of organ damage	Left-sided cardiac hypertrophy
	Micro-albuminuria/proteinuria

The integration of this large set of clinical information in a comprehensive picture would be highly facilitated by the adoption of an obesity scoring system. The use of a score that could quantitatively represent the actual and future health burden that obesity induces in every single patient would be an important tool for clinicians for the phenotypization of the patients and for guiding therapeutic choices. A scoring system should also be helpful for prioritisation and resource allocation in a health system with limited resources. An integrated rating scale for the determination of the initial level of care (outpatient, partial hospitalisation, residential rehabilitation centre, inpatient hospitalisation) needed by the obese patients has been proposed by a multidisciplinary group of Italian obesity experts [33]. However, this scale has never been validated in other countries or other clinical settings. An alternative option would be the use of a more simple but integrated staging system. The *Edmonton Obesity Staging System* (EOSS) has been proposed as a clinical staging system for obesity [34]. EOSS classified obesity in five stages (0–4) accordingly to worsening clinical and functional status (Table 15.7) [34]. EOSS stage has been shown to be a more stringent predictor of total mortality than BMI levels in large epidemiological databases [35, 36]. The validation and application of EOSS or other alternative staging systems for the phenotypization of obese patients should be a focus of future clinical research in the field of overweight and obesity.

Table 15.7 Edmonton obesity scoring system: a proposed clinical and functional staging of obesity

Stage	Description
0	No apparent obesity-related risk factors (e.g. blood pressure, serum lipids, fasting glucose, etc., within normal range), no physical symptoms, no psychopathology, no functional limitations and/or impairment of well-being
1	Presence of obesity-related subclinical risk factors (e.g. borderline hypertension, impaired fasting glucose, elevated liver enzymes, etc.), mild physical symptoms (e.g. dyspnoea on moderate exertion, occasional aches and pains, fatigue, etc.), mild psychopathology, mild functional limitations and/or mild impairment of well-being
2	Presence of established obesity-related chronic disease (e.g. hypertension, type 2 diabetes, sleep apnoea, osteoarthritis, reflux disease, polycystic ovary syndrome, anxiety disorder, etc.), moderate limitations in activities of daily living and/or well-being
3	Established end-organ damage such as myocardial infarction, heart failure, diabetic complications, incapacitating osteoarthritis, significant psychopathology, significant functional limitations and/or impairment of well-being
4	Severe (potentially end-stage) disabilities from obesity-related chronic diseases, severe disabling psychopathology, severe functional limitations and/or severe impairment of well-being

Modified by Ref. [34]

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