Chapter 7
Clinical Definition of Overweight and Obesity

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Pearls of Wisdom

- BMI inter-relates height and weight and is not a direct measure of adiposity. It is useful in screening patients but must be interpreted when used to diagnose overweight or obesity in the context of a physical exam that confirms increased adipose tissue mass.
- BMI does indicate the degree to which adiposity or the development of adiposopathy adversely impact health, as manifest by weight-related complications.
- Best practices require a careful evaluation for the presence and severity of weight-related complications in all patients presenting with overweight and obesity.
- Key weight-related complications can be identified during an initial patient evaluation consisting of physical examination, history, clinical laboratory testing, and an obesity-focused review of systems.
- In bariatric endocrinology an optimal diagnostic framework incorporates an anthropometric measure of increased adiposity (i.e., BMI) together with an assessment of the presence and severity of weight-related complications (including adiposopathy).

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7.1 Introduction

Body mass index (BMI) is widely used in the screening, diagnosis, and classification of overweight and obesity. The World Health Organization (WHO) criteria shown in Table 7.1 are widely accepted, with BMI 25–29.9 kg/m^2 indicative of overweight and BMI ≥ 30 kg/m^2 indicative of obesity, designated as class I (BMI = 30–34.9 kg/m^2), class II (35–39.9 kg/m^2), or severe class III (≥40 kg/m^2). BMI is an anthropometric measurement that inter-relates height and weight (kg/m^2) and does not provide a direct measure of adipose tissue mass. Furthermore, BMI does not indicate the degree to which excess adiposity can lead to adiposopathy, or adversely affects the health of individual patients. The risk, presence, and severity of multiple weight-related complications vary markedly among patients at any given BMI level. It is the presence and severity of complications that indicate whether any degree of excess adiposity has caused adiposopathy and is adversely affecting the health of individual patients. While the likelihood of weight-related complications generally increases as a function of progressive obesity, there can be a poor correlation between BMI and the emergence of complications. Patients with overweight or obesity need not have weight-related complications and can be free of disease-related morbidity and mortality. For these reasons, the diagnostic evaluation of obesity extends beyond BMI and requires a careful clinical assessment for weight-related complications. This is consistent with the genetic model for chronic disease where the interaction between susceptibility genes and the environment produces the disease, and additional and perhaps overlapping subsets of genes interacting with the environment determine the severity of the disease and the emergence and severity of complications.

This chapter will discuss the advantages and limitations of BMI when used in the diagnosis of overweight or obesity. While BMI can suffice as a screening tool for obesity, the need for clinical interpretation is required in the use of BMI as a mea-

Table 7.1 Classification of overweight and obesity by BMI and waist circumference

	BMI		Waist	
			Waist circumference and comorbidity risk	
Classification	BMI (kg/m^2)	Comorbidity risk	Men ≤40 inches Women ≤35 inches	Men >40 inches Women >35 inches
Underweight	<18.5	Low but other problems		
Normal weight	18.5–24.9	Average		
Overweight	25–29.9	Increased	Increased	High
Obesity class I	30–34.9	Moderate	High	Very high
Obesity class II	35–39.9	Severe	Very high	Very high
Obesity class III	≥40	Very severe	Extremely high	Extremely high

Adapted from: World Health Organization (WHO) (1998); used with permission

sure of adiposity for diagnosis of the disease. In addition, the careful clinical assessment of the risk, presence, and severity of weight-related complications will be emphasized as an integral component of best practices in obesity management. As will be discussed, this assessment can be accomplished with a "new patient" history, physical examination, and laboratory testing in addition to an obesity-focused review of systems (ROS). Thus, the optimal diagnostic framework has two components: the assessment of adipose tissue mass and the impact of excess adiposity on health as manifest by disease complications. This diagnostic framework is clinically actionable since it provides an indication of disease severity and can help guide clinical decisions regarding the modality and intensity of therapy.

7.2 The Anthropometric Component of the Diagnosis of Obesity

7.2.1 BMI and the Assessment of Adipose Tissue Mass

Adolphe Quetelet first proposed the Quetelet Index, body mass (kg)/height (m^2), as a measure of obesity in 1859. He was a Belgian astronomer and mathematician who developed an interest in quantifying individual variation in human traits and behaviors, a discipline he termed "social physics." In 1972, the Quetelet Index was renamed the BMI by Ancel Keys, a polymath, nutritionist, epidemiologist, and inventor, after "validating" BMI against skin fold thickness in his Seven Countries Study, which established a relationship between serum cholesterol and heart disease and the first endorsement of the "Mediterranean Diet." Other approaches used to assess obesity include the Ponderal Index (weight/$height^3$) first proposed by Ridolpho Livi in 1898 but popularized by F. Rohrer in 1921 as the Corpulence Index and applied to newborns (weight/$crown\text{-}to\text{-}heel\text{-}length^3$). The rationale for the Ponderal Index was that a cubic function was more appropriate for an obesity measurement that essentially represents a volume. Another approach is the relative body weight using actuarial tables of the Metropolitan Life Insurance Company to assess relative weight for a given height after adjusting for a small, medium, or large frame. Relative body weight has the disadvantage of not providing an absolute value of body mass and uses actuarial standards from 1959 that do not reflect the average increments in average body weight that have occurred over the past three decades.

The WHO adopted BMI for the clinical classification of obesity in 1998. The WHO promulgated the widespread application of BMI in epidemiology and medicine (Table 7.1). The National Institutes of Health adopted BMI as the measure for obesity classification and interventional recommendations soon thereafter, as delineated in Table 7.2. Subsequently, BMI cut-offs have predominated in the diagnosis of obesity and in the clinical classification of the severity of obesity. BMI is widely employed in epidemiological and physiological scientific investigations, guidelines for obesity management advocated by multiple health care organizations, by the

Table 7.2 NHLBI obesity treatment guidelines

	BMI category (kg/m^2)				
Treatment	25–26.9	27–29.9	30–34.9	35–39.9	≥40
Diet, physical activity, and behavior	Appropriate NHLBI guidelines	+	+	+	+
Pharmacotherapy	No	With comorbidities	+	+	+
Surgery[a]	No	No	No[a]	With comorbidities	+

Adopted from: Summary of recommendations in the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. National Institutes of Health/National Heart, Lung and Blood Institute; 1998. http://www.nhlbi.nih.gov/guidelines/obesity/ob_gdlns.pdf
No = not indicated, + = clinically indicated for consideration
[a]US Food and Drug Administration (FDA)-approved gastric banding surgery for patients with BMI of at least 30 kg/m^2 and one weight-related medical condition (February 2011)

FDA in setting indications for weight loss medications, and in the clinical evaluation of patients as the basis for the diagnosis of obesity. In children and adolescents, obesity is defined as ≥ 95% percentile of BMI, as a function of age and gender, using the Centers for Disease Control growth charts.

The use of BMI in screening and diagnosis of obesity has advantages and disadvantages. Height and weight are easily measured, and BMI generally correlates with adipose tissue mass in population studies. It is useful for the initial screening to detect excess body fat, and higher BMI levels are associated with increased risk of complications of obesity. There is a large body of evidence correlating higher BMI with diabetes, gestational diabetes, and atherosclerotic cardiovascular disease (CVD), including stroke and recurrent coronary events in those with coronary artery disease. BMI confers increasing risk of coronary artery disease beyond 25 kg/m^2 in both genders. Mortality generally correlates with increasing BMI above 25 kg/m^2. The mortality correlation carries varying degrees of consistency among different populations and is partly explained by a correlation between BMI and certain types of cancer. In the general population and in patients with type 2 diabetes mellitus (T2DM), there is a J-shaped curve relating BMI with mortality. In those individuals who have never smoked cigarettes, BMI values >30 kg/m^2 are consistently associated with higher mortality. In these individuals, the increased risk of mortality is not as clearly defined for the BMI range 25–30 kg/m^2. The increases in metabolic diseases and CVD are conferred more directly by other risk factors that may be associated with obesity. The impact of BMI is diminished when these risk factors are accounted for in multivariate analyses.

BMI cut-offs for identifying excess adiposity and risk of metabolic and cardiac diseases are lower for some Asian-Pacific populations and should be taken into account when screening. Based upon the evidence that lower BMI values are correlated with the risk of T2DM, the American Diabetes Association recommends that screening for diabetes should be considered for all Asian American adults who present with a BMI of ≥23 kg/m^2. The body of evidence addressing this issue, including

meta-analyses performed by the Working Group on Obesity in China, suggests that using a BMI cut-off of ≥23 kg/m^2 would be the optimal single criterion for screening all Asian ethnicities.

Regarding the limitations of BMI, it is important to consider that BMI is an anthropometric measure that inter-relates the height and weight of individuals. The weight measurement used in the calculation incorporates lean mass, fat mass, bone mass, and fluid status; all of these body components contribute to weight. Therefore, BMI is only an indirect measure for the estimation of total body fat mass. Lean mass and body water can vary independently from fat mass, and, for this reason, BMI alone cannot identify excess adiposity and establish a diagnosis of overweight or obesity in all instances. BMI may have poor inter-individual consistency for estimating body fat percentage and distribution. BMI will overestimate adiposity in athletes with high muscle mass and low percent body fat and underestimate adiposity in elderly patients with sarcopenia. The degree of adiposity is also overestimated in patients with edema. The imprecision of BMI as a measure of adiposity weakens the association of BMI with health risks and impairs its utilization as a risk factor. For example, BMI inadequately predicts the risk of metabolic and vascular diseases in those with sarcopenic obesity. Waist circumference is a more accurate predictor than BMI of the high mortality rates that characterize these patients. Along these same lines, low lean mass index predicts mortality in the elderly better than BMI.

The limitations in BMI as a measure of adiposity have important clinical ramifications. While BMI can be used to screen for the presence of obesity, it cannot by itself be used to diagnose overweight or obesity. For diagnosis, the BMI measurement must be clinically interpreted based on medical history and physical examination of the patient. It will be important to ascertain whether the patient has edema or sarcopenia, or is an athlete with high muscle mass, or other conditions listed in Table 7.3. Clinical judgment must then be used to identify those with a low BMI but with excess adiposity, as well as those with high BMI but normal or low percent body fat.

Additional approaches are available that primarily estimate body fat mass as shown in Table 7.4. Some methods involve high-cost equipment. Others are more feasibly conducted in the research arena, such as magnetic resonance imaging, three-dimensional photonic scanning, and total body water dilution techniques. Other measures can be applied in patient care venues. There are several commercially available bioelectric impedance plethysmography devices that are inexpensive and which can estimate body fat. Bioelectric impedance analyses are dependent on the state of hydration of the patient and become less accurate at high degrees of adiposity. Other methods entail more expensive equipment but provide measures that are more highly correlated with results using underwater weighting as the "gold standard." These include air displacement plethysmography and dual-energy X-ray absorptiometry (DXA). DXA has the advantages of providing measures of bone mass and density, lean mass, and fat mass in addition to regional fat distribution (i.e., limbs versus trunk). DXA can quantify intra-abdominal fat by subtracting subcutaneous fat estimates from total trunk adipose. Body fat percentage cut-off points for obesity have been proposed by the WHO to be 25% and 35% for men and women, respectively. One measurement available from a DXA scan is the fat mass

Table 7.3 Limitations of BMI in the screening and diagnosis of obesity

1. BMI inter-relates height and weight but does not directly measure adiposity
2. When applied as an index of adiposity, BMI requires interpretation based on individual clinical assessment with attention to the following: Muscularity Volume status – edema and dehydration Sarcopenia Age Gender Pregnancy Third space fluid accumulation (e.g., ascites) Large tumors (e.g., uterine leiomyosarcomas) Lipodystrophy Loss of muscle mass due to denervation or intrinsic myopathy
3. BMI does not indicate location or distribution of fat Intracellular Extracellular but within the tissue (e.g., "marbling") Peri-organ (mesenteric, pericardial, and perinephric) Subcutaneous versus intra-abdominal Adipose tissue depots (omentum and gluteal) Brown fat versus white fat
4. BMI does not indicate the degree to which excess adiposity is adversely affecting the health of the patient.

Table 7.4 Methods for quantifying adipose tissue mass

Feature measured	Advantages	Method	Limitations
Total body water Extracellular and intracellular fluid spaces	Ease of use Low cost Speed (fast)	Bioelectrical impedance analysis (BIA)	Population specific Poor accuracy in individuals
Total and regional body fat Total and regional lean mass	Ease of use Low radiation exposure Accurate	Dual-energy X-ray absorptiometry (DXA)	Biased for body size, sex, and fatness High equipment cost Specially trained personnel
Total body water Extracellular fluid	Ease of use OK for all ages	Dilution techniques	Inaccurate in disease High equipment cost Labor-intensive analysis
Total body volume Total body fat	Relatively good accuracy Speed (fast)	Air displacement plethysmography	Less accurate in disease High equipment cost
Total and regional body volume	OK for very obese Ease of use	3D photonic scanning	Limited availability
Total body water Total body fat	Ease of use Safety Speed (fast)	Quantitative magnetic resonance imaging	High equipment cost Limited availability
Total and regional adipose tissue Skeletal muscle	Highly accurate and reproducible	Magnetic resonance imaging (MRI)	Costly

index, which is calculated as total body fat mass (kg) divided by height (m^2). The fat mass index is analogous to the BMI but incorporates only fat mass as the weight measure instead of total body weight.

7.2.2 Waist Circumference and the Importance of Intra-abdominal Fat Mass

Beyond the assessment of BMI, the next consideration is the distribution of body fat. Accumulation of excess fat in different fat depots can have significant implications for disease risk. The accumulation of visceral adipose tissue, which surrounds organs in the intra-abdominal compartment, is central to the pathophysiology of metabolic and vascular diseases. Central to the disease process is insulin resistance, which progresses to dysmetabolic syndrome, prediabetes, and finally to T2DM, CVD, or both, in individual patients. Also integral to disease pathogenesis is adiposopathy, with inflammation and dysregulated secretion of adipocytokines in visceral adipose tissue, which leads to the development of the dysmetabolic syndrome trait complex. On the other hand, a relative distribution of fat to the periphery (i.e., upper and lower extremities and hips) generally occurs in the subcutaneous space. Subcutaneous adipose tissue accumulation carries a lower risk of metabolic or vascular disease, when adjusting for BMI and age.

Waist circumference estimates visceral adipose tissue and is the simplest anthropometric measurement of abdominal adiposity in clinical settings. Waist circumference consistently and strongly predicts components of dysmetabolic syndrome, T2DM, CVD risk factors, and CVD events in cross-sectional studies and prospective cohorts. The predictive value of waist circumference for CVD and all-cause mortality is generally independent of and stronger than BMI and is even evident in lean individuals with BMI < 25 kg/m^2. As shown in Table 7.1, adding waist circumference to BMI more precisely categorizes metabolic and vascular risk in patients with overweight or obesity. Waist circumference should be measured when screening for obesity and obesity-related comorbidities. This is best done in a private setting using a tension-controlled tape measure placed around the waist just above the anterior superior iliac spine, on a plane horizontal to the floor. Threshold values that are indicative of increased risk of diabetes and CVD are delineated in Table 7.5, as recommended in a joint statement from multiple professional organizations attempting to harmonize criteria for the dysmetabolic syndrome.

Three salient points are important concerning the interpretation of waist circumference measurements. First, waist circumference cut-off points for predicting metabolic and vascular diseases exhibit ethnic variation, including a consistently lower threshold in South Asian, Southeast Asian, and East Asian adults. Therefore, population-specific cut-off values should be used as established by epidemiological studies in regional cohorts (Table 7.5). Second, waist circumference measurements are most discriminative of greater chronic disease risk in individuals with BMI ≤ 35 kg/m^2. When the BMI exceeds 35 kg/m^2, most patients will exceed the

Table 7.5 Waist circumference thresholds for abdominal obesity

Population	Organization	Men	Women
Europid	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Caucasian	WHO	≥94 cm (↑ risk) ≥37 inches ≥102 cm (↑↑ risk ≥40 inches	≥80 cm (↑ risk) ≥31 inches ≥88 cm (↑↑ risk) ≥35 inches
United states	AHA/NHLBI (ATPIII)	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Canada	Health Canada	≥102 cm ≥40 inches	≥88 cm ≥35 inches
European	European Cardiovascular Societies	≥102 cm ≥40 inches	≥88 cm ≥35 inches
Asian (including Japanese)	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Asian	WHO	≥90 cm ≥35 inches	≥80 cm ≥31 inches
Japanese	Japanese Obesity Society	≥85 cm ≥33 inches	≥90 cm ≥35 inches
China	Cooperative Task Force	≥85 cm ≥33 inches	≥80 cm ≥31 inches
Middle East, Mediterranean	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Sub-Saharan African	IDF	≥94 cm ≥37 inches	≥80 cm ≥31 inches
Ethnic Central and South American	IDF	≥90 cm ≥35 inches	≥80 cm ≥31 inches

Adapted from: Alberti et al. (2009)
IDF International Diabetes Federation, *WHO* World Health Organization, *AHA* American Heart Association, *NHLBI* National Heart, Lung, and Blood Institute, *ATPIII* Adult Treatment Panel III

waist circumference cut-off value, whether or not they have insulin resistance or have manifestations of metabolic disease. Finally, it is important to understand that risks conferred by waist circumference are continuous despite the use of categorical cut-off values. Thus, at any given BMI (above and below a BMI of 35 kg/m^2), risks of T2DM and CVD increase progressively, with additional increments in waist circumference.

The waist circumference encompasses subcutaneous adipose tissue, trunk musculature, and abdominal organs, and, therefore, it represents only an estimation of intra-abdominal fat. Intra-abdominal fat can be estimated in the analyses of DXA scans by subtracting subcutaneous fat (from fat mass estimates in the lateral flanks) from total abdominal fat. Intra-abdominal fat can be quantified by magnetic resonance imaging or transverse CAT scan, although these measures are primarily relegated to research studies.

It is unclear whether waist circumference or waist-to-height ratio (WHtR) is a better predictor of T2DM and CVD risks. However, WHtR has better discriminatory power for CVD risk variables than BMI. A WHtR cut-off value of 0.5 is optimal for identifying those with a higher CVD risk across different genders and ethnicities.

7.3 The Clinical Component of the Diagnosis of Obesity

7.3.1 Relationship Between BMI and Weight-Related Complications

As an anthropometric measurement, BMI alone does not indicate the impact of adiposity on the health of individual patients. Since BMI alone is not a sufficient indicator of health status in overweight and obesity, all patients should be clinically evaluated for weight-related complications. While the likelihood of weight-related complications generally increases as a function of progressive obesity, there can be a poor correlation between BMI and the emergence of complications. Patients with overweight or obesity need not have weight-related complications and be free of disease-related morbidity and mortality. The variable associations between BMI and weight-related complications are exemplified below for several key complications that can adversely affect the health of patients with overweight or obesity. While it is clear that elevated BMI per se does not ensure that specific complications are present, the important consideration is that weight loss will ameliorate or prevent many weight-related complications, thus justifying a careful evaluation for their presence.

7.3.1.1 Diabetes Risk, Dysmetabolic Syndrome, and Prediabetes

Obesity is a major risk factor for the development of dysmetabolic syndrome and prediabetes (impaired fasting glucose (IFG) or impaired glucose tolerance (IGT)). Obesity is also a risk for progression to overt T2DM and CVD. However, many individuals with metabolic disease with progression to T2DM and/or CVD are lean. In addition, a significant proportion of individuals with obesity are insulin sensitive, do not exhibit dysmetabolic syndrome traits, and have been referred to as "metabolically healthy obese." While obesity can exacerbate insulin resistance, insulin sensitivity largely varies independent of BMI, and the risks of T2DM and CVD are largely conferred by the presence of metabolic traits associated with adiposopathy and insulin resistance (e.g., increased waist circumference, high triglycerides, low HDL-c, elevated blood pressure, and abnormal glucose tolerance) rather than BMI per se. Therefore, overweight or obesity as assessed by BMI are neither sufficient nor necessary as a pathogenic factor in the development of adiposopathy, insulin resistance, dysmetabolic syndrome, and prediabetes.

It is for this reason that the cardiometabolic risk staging was developed as a quantitative clinical tool that stratifies risks for T2DM and CVD in patients with

overweight and obesity. CMDS assigns patients to one of five risk categories using parameters readily available to the clinician, including waist circumference, systolic and diastolic blood pressures, fasting blood glucose, triglycerides, and HDL-C, as well as the 2-h oral glucose tolerance test (OGTT) glucose value. As shown in Fig. 7.1, with advancement from stage 0 to stage 4, there are significant increments in risk and adjusted hazard ratios for diabetes. This is validated by using the Coronary Artery Risk Development in Young Adults (CARDIA) study national cohort. There is also an increased risk and hazard ratios for both all-cause and CVD-related mortality in the National Health and Nutrition Examination Survey (NHANES) cohort. The CMDS staging system is a strong predictor of risk for diabetes, CVD, and all-cause mortality independent of BMI.

More recently, a weighted CMDS system was developed that assigns different weights in the form of integer values to the various risk factors based on their relative contribution to T2DM risk. The range of the sum of integer values for all risk factors was set at 0–100 providing an overall score that was validated to be

Stage	Criteria	Specifications
0	No risk factors	Metabolically healthy obese
1	1 or 2 risk factors	Waist, blood pressure, triglycerides, HDL -c
2	Metabolic syndrome OR prediabetes	Only one of the following: metabolic syndrome or IFG or IGT
3	Metabolic syndrome plus prediabetes	Two or more of the following: metabolic syndrome, IFG, IGT
4	T2DM and/or CVD	End stage cardiometabolic disease

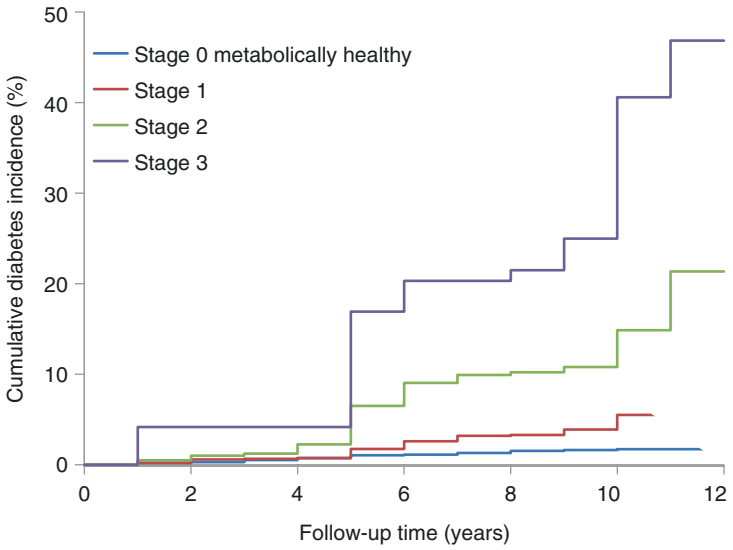

Fig. 7.1 Cardiometabolic disease staging with validation using data from the National CARDIA Study Cohort. (Adapted from: Guo et al. 2014; used with permission)

proportional to the risk of future diabetes. The relative contribution of various traits to diabetes risk varied as a function of gender and race allowing for greater precision of risk quantification in individual patients. This risk engine provides the clinician with the ability to target more aggressive weight loss therapy to those patients at the greatest risk of future T2DM and CVD.

7.3.1.2 T2DM

The proportion of adults who had normal weight at the time of incident diabetes ranged from 9% to 21% (overall 12%) across a substantial number of large cohort studies (ARIC, CARDIA, CHS, Framingham, and MESA). In the Behavior Risk Factor Surveillance System, the prevalence of diabetes is 4.1% in individuals with normal weight, 7.3% in individuals with overweight, 14.9% in class 2 obesity, and 25.6% in class 3 obesity. Thus, the clear majority of individuals with obesity do not have diabetes. While BMI is a strong risk factor for T2DM, the data indicate that BMI is a poor indicator of the presence or absence of diabetes.

7.3.1.3 Hypertension

In the serial NHANES III cross-sectional surveys from 1988 to 1994, there is a strong association between elevated BMI and hypertension. Hypertension is present in 23% of patients with a normal weight, 34–39% in patients with overweight, 48–49% in patients with class 1 obesity, 55–65% in patients with class 2 obesity, and 63–64% in patients with class 3 obesity. Thus, not all patients with overweight or obesity have hypertension. Hypertension has other risk factors independent of obesity, including age, ethnicity/race, sedentary lifestyle, cigarette smoking, high sodium intake, heavy alcohol use, stress, family history, insulin resistance, dysmetabolic syndrome, and genetic factors.

7.3.1.4 CVD Events and CVD Mortality

BMI is associated with an increased risk of CVD events, principally through its association with other risk factors. The independent risk of CVD events conferred by BMI is negated or minimized in multivariate analyses.

7.3.1.5 Nonalcoholic Fatty Liver Disease/Nonalcoholic Steatohepatitis

Seventy percent of patients with obesity have nonalcoholic fatty liver disease (NAFLD), whereas 30% do not. Only 15–20% of patients with obesity have nonalcoholic steatohepatitis (NASH). While the factors that predict which patients with NAFLD will progress to NASH and cirrhosis have not been elucidated, factors other

than generalized obesity, such as insulin resistance and the dysmetabolic syndrome, appear to predominate as major contributors to NAFLD and NASH.

7.3.1.6 Female Infertility and Polycystic Ovary Syndrome (PCOS)

The prevalence rates of PCOS in women who have normal weight, overweight, or class 1 obesity were 9.8%, 9.9%, and 9.0%, respectively, with rates rising to 12.4% when the BMI is >35 kg/m^2. Thus, the majority of women who have overweight or obesity do not experience infertility or PCOS, and these problems also afflict women with a normal weight. Central adiposity and dysmetabolic syndrome are risk factors associated with PCOS independent of BMI.

7.3.1.7 Obstructive Sleep Apnea (OSA)

OSA affects ~70% of patients with obesity, and prevalence rates rise progressively as the BMI exceeds 29 kg/m^2. Clearly, not all patients with obesity have OSA. Insulin resistance, abdominal obesity, enlarged neck circumference, and T2DM are also risk factors for OSA.

7.3.1.8 Osteoarthritis

Increasing BMI is associated with progressive increments in the odds ratio for osteoarthritis of the knee in patients with severe obesity when compared with normal-weight individuals. However, osteoarthritis can afflict both individuals who are lean or who have obesity, and not all patients with overweight or obesity have osteoarthritis. Other independent risk factors for osteoarthritis include age, work history, knee trauma, participation in certain sports, and adiposopathy with elevated adipocytokines.

7.3.1.9 Urinary Stress Incontinence

BMI increases risk for stress urinary incontinence, although the majority of women who have overweight or obesity do not experience incontinence, and this disorder affects individuals with normal weight as well. Other factors in addition to BMI constitute independent risk factors for urinary incontinence, including age, waist circumference, parity, previous hysterectomy, dysmetabolic syndrome, and depression.

7.3.1.10 Gastroesophageal Reflux Disease

While there is an association with elevated BMI, GERD is common in both individuals who are lean and those with obesity. Odds ratios attributable to obesity are somewhat modest in the range of 1.22–2.8. The pathophysiology involves abnormal

functioning of the lower esophageal sphincter, and other risk factors include positive family history, cigarette smoking, hiatal hernia, delayed gastric emptying, *Helicobacter pylori* infection, and alcohol consumption.

In summary, it is clear that the presence of overweight or obesity by BMI is not a good predictor of any weight-related complications. Best practices for obesity management will always necessitate a careful evaluation for the presence or absence of adiposopathy and weight-related complications.

7.3.2 Clinical Evaluation of Patients for Weight-Related Complications

The identification of weight-related complications and the staging of the severity of these complications are important for two reasons in patients with overweight or obesity. First, the presence and severity of weight-related complications will indicate the need for more aggressive therapy to improve the health of individual patients. Second, since these complications can be improved, or reversed by weight loss therapy, the evaluation will establish therapeutic targets for weight loss and the integration of these goals as desired outcomes into the therapeutic plan. For example, if a patient is diagnosed to have the dysmetabolic syndrome or prediabetes and the goal of therapy is to prevent progression to T2DM, then 10% body weight loss is a rational goal, since this represents a threshold for maximal diabetes prevention. Similarly, weight loss of 10% or greater is required to predictably decrease the apnea–hypopnea index in patients with OSA. On the other hand, if the patient has T2DM and the goal of weight loss is to improve glycemia, dyslipidemia, and hypertension, there does not appear to be a threshold of weight loss for maximal clinical benefit. For example, the Look AHEAD study demonstrated that reductions in HbA1c, blood pressure, and triglycerides and increments in HDL-c were progressive as weight loss increased from 5% to >15% body weight in patients with T2DM.

From this perspective, the goals of weight loss therapy are to improve the health of patients with overweight or obesity by treating and preventing weight-related complications. This is consistent with the "complications-centric" approach to obesity management as advocated by the American Association of Clinical Endocrinologists (AACE). In these guidelines, it is not so much the baseline BMI that is important in establishing the indications for the modality and aggressiveness of weight loss therapy but the presence and severity of weight-related complications, as illustrated by the algorithm in Fig. 7.2. This is a medical model for obesity care wherein weight loss therapy is employed to treat or prevent weight-related complications as the endpoint of therapy. This stands in contrast to a "BMI-centric" approach, such as advocated by the National Heart, Lung and Blood Institute (NHLBI) (Table 7.2), where the baseline BMI largely sets the indications for utilization of treatment modalities and where a set decrease in weight or BMI is the endpoint of therapy.

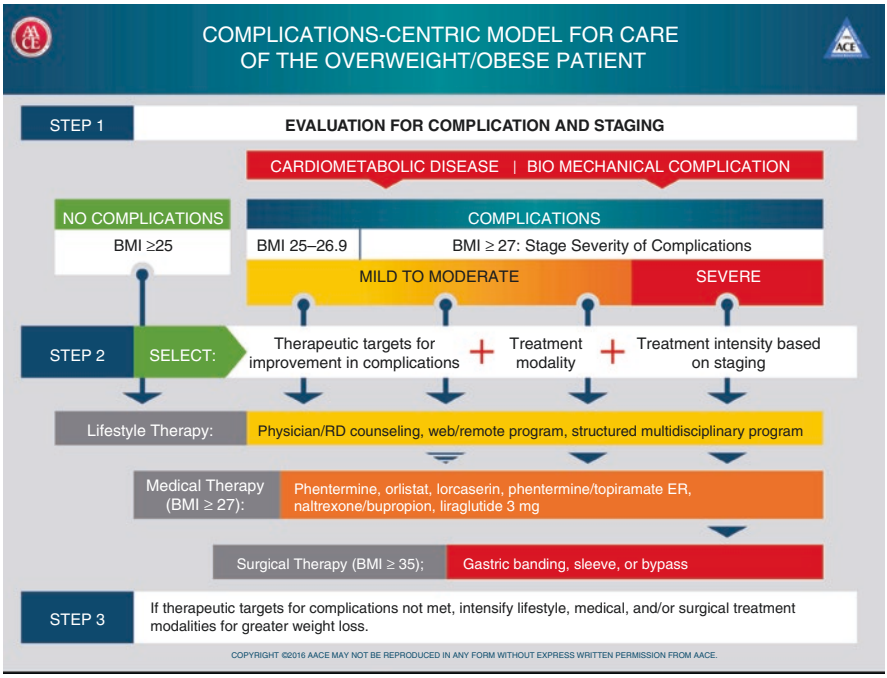

Fig. 7.2 AACE algorithm for obesity management. (Reprinted with permission from American Association of Clinical Endocrinologists © 2018. Endocr Pract. 2018;24:90–120)

The identification of complications does not involve an extensive or extraordinary degree of testing but can be ascertained in the course of an initial patient evaluation consisting of medical history, review of systems (ROS), physical examination, and laboratory studies. In the initial evaluation, the clinician will need to pay particular attention to the relevant aspects of the history and examination and conduct an obesity-focused ROS assessing potential symptomatology of weight-related complications. Clinical data that are important to obtain in the initial evaluation are listed in Table 7.6 for the physical examination, ROS, and clinical laboratory testing. These data can be used to identify the key complications that can be treated or prevented by weight loss. In many cases, the information gathered in the initial examination is sufficient for the diagnosis of certain weight-related complications. For other complications, the initial information augments the degree of suspicion, and additional testing consistent with standards of care is then necessary to confirm the diagnosis and for staging the severity of the complication. Depending on the expertise of the clinician, referral may be indicated for further evaluation and treatment of specific complications. The complications that can be prevented or treated by weight loss therapy are listed in Table 7.7 together with the basis for screening or diagnosis using clinical data obtained at the initial patient evaluation and the follow-up tests that are potentially helpful in confirming certain diagnoses and staging their severity.

Table 7.6 Key clinical data to be obtained at the initial evaluation of patients with overweight or obesity

Initial evaluation	System	Findings	Relevant complication[a]
Physical examination	Anthropometrics	Weight, BMI, waist circumference	Anthropometric component of the diagnosis of obesity, Dysmetabolic syndrome (waist)
		Neck circumference	Obstructive sleep apnea
	Vital signs	Blood pressure	Hypertension, Dysmetabolic syndrome
	General	Mobility and physical ability	Disability secondary to excess weight
	Skin	Acanthosis nigricans	Insulin resistance
		Hirsutism	Polycystic ovary syndrome
	Pulmonary	Wheezing, prolonged expiratory phase	Asthma
	Extremities	Edema	Interpretation of BMI, Edema-forming state
	Joints	Swelling, tenderness, crepitance, decreased range of motion	Osteoarthritis
	Liver	Enlarged, firm	Nonalcoholic fatty liver disease
	Muscle	Increased muscularity	Interpretation of BMI
		Weakness	Sarcopenia
	Endocrine	Thyroid, findings consistent with hypo/hyperthyroidism	Hypo/hyperthyroidism
		Stigmata of hypercortisolism	Cushing's disease
Medication history		Medications predisposing to weight gain	Iatrogenic obesity
Review of systems (obesity focused)	Metabolic	Symptoms of hyperglycemia	Diabetes
	Cardiovascular	For example, chest pain, syncope, palpitations, orthopnea, dyspnea, transient ischemic attacks, stoke history/symptoms, claudication	Cardiovascular disease
	Menstruation	Menstrual history, fertility	Polycystic ovary disease
	Pulmonary	Shortness of breath, wheezing, allergy	Asthma
		Snoring, daytime fatigue, restless sleep	Obstructive sleep apnea
	Gastrointestinal	Heartburn, indigestion	GERD
	Urinary	Leaking, wetting, stress versus urge symptoms	Urinary incontinence
	Skeletal	Joint pain, limited functionality, and range of motion	Osteoarthritis
	Functional capacity	Activities of daily living, weakness	Disability, Sarcopenia
	Psychological complications/ disease	Depression, binge eating, stigmatization	Depression, Binge eating syndrome

(continued)

Table 7.6 (continued)

Initial evaluation	System	Findings	Relevant complication[a]
Clinical laboratory	Fasting glucose, HbA1c, 2-h OGTT glucose	Prediabetes: Fasting 100–125 mg/dl (IFG); 2-h 140–199 mg/dl (IGT); HbA1c 5.7–6.4%	Prediabetes, Dysmetabolic syndrome (IFG), Diabetes
	Total cholesterol, triglycerides, HDL-c, LDL-c, non-HDL-c	Triglycerides ≥ 150 mg/dl; HDL-c < 40 mg/dl men, <50 women; LDL-c ≥100 mg/dl; non-HDL-c ≥ 130 mg/dl	Dyslipidemia, Dysmetabolic syndrome (HDL-c and triglycerides), LDL-c target for CVD risk reduction
	Transaminases (AST, ALT), liver function tests	Transaminase levels above normal	Nonalcoholic fatty liver disease

Notes: The table illustrates key aspects in the evaluation but should not be considered all inclusive
[a]The diagnosis of each "Relevant Complication" may be complete based on findings in the initial evaluation, while other potential complications will be suspected and will require further testing for diagnosis or staging (see Table 7.7)

In this context, an "Advanced Framework for a New Diagnosis of Obesity" emerged from multidisciplinary discussions at the AACE/ACE Consensus Conference on Obesity held in Washington, DC, in March 2014. The consensus was that the diagnosis of obesity based solely on BMI was not medically meaningful or actionable and that this represented an impediment to concerted action to fight obesity among health care professionals, regulators, payers, and employers. BMI may not reflect the impact of weight gain on the health or well-being of the individual, and its significance varies as a function of different ethnicities and body types. An improved medically relevant diagnosis would consist of the continued use of BMI (together with other anthropometrics such as waist circumference) and an assessment of the presence and severity of obesity-related complications. Furthermore, strategy regarding prevention and treatment of obesity should conform to the three classic phases of chronic disease prevention: primary, to prevent the disease in the first place; secondary prevention, once the disease has appeared but before the emergence of complications; and tertiary prevention, after complications develop. Therefore, the new obesity diagnostic algorithm (Table 7.8) incorporates two components: (*1*) an assessment of body mass, including validated ethnicity-adjusted anthropometrics to identify individuals with increased adipose tissue placing them at risk and (*2*) the presence and severity of weight-related complications as shown in Table 7.8. The approach emphasizes risk stratification and complications staging in order to target more aggressive interventions to those patients who will most benefit from weight loss therapy. Each complication is evaluated for severity and impact on the patient's health using complication-specific criteria: stage 0 (no complication is present), stage 1 (complication is mild to moderate), or stage 2 (complication is severe).

Table 7.7 Screening and diagnoses of weight-related complications in patients with overweight/obesity

Weight-related complication	Basis for screening and/or diagnosis	Secondary testing when needed to confirm diagnosis, stage severity, or guide therapy
Prediabetes	Fasting glucose, HbA1c	If fasting glucose is 100–125 mg/dl, a repeat elevated fasting glucose completes diagnosis of IFG; however, 2-h OGTT glucose should also be performed to exclude diabetes and IGT. Fasting and 2-h OGTT glucose should be performed if initial fasting glucose is normal and HbA1c is elevated, or in high-risk patients based on family history or dysmetabolic syndrome
Dysmetabolic syndrome	Waist circumference, blood pressure, fasting glucose, triglycerides, HDL-c	Initial evaluation completes diagnosis
Type 2 diabetes	Fasting glucose, HbA1c, ROS	Overtly elevated (i.e., ≥200 mg/dl) or a repeat fasting glucose ≥126 mg/dl completes diagnosis. If fasting glucose and/or HbA1c is consistent with prediabetes, 2-h OGTT should be performed to test for diabetes. HbA1c should be performed to help guide therapy
Hypertension	Blood pressure	Repeat elevated blood pressure measurements complete diagnosis; home blood pressure or ambulatory blood pressure monitoring may help complete testing
Dyslipidemia	Lipid panel (total cholesterol, HDL-c, triglycerides, LDL-c, non-HDL-c)	Lipid panel completes diagnosis; lipoprotein subclasses, apoB-100 may further define risk
NAFLD/NASH	Physical exam, LFTs	Imaging (e.g., ultrasound, MRI, elastography) and/or liver biopsy needed to complete diagnosis
PCOS	Physical exam, ROS	Hormonal testing (e.g., androgen levels LH/FSH) needed to complete diagnosis
Obstructive sleep apnea	Physical exam, neck circumference, ROS	Polysomnography needed to complete diagnosis
Osteoarthritis	Physical exam, ROS	Radiographic imaging may be needed to complete diagnosis
Urinary stress incontinence	Physical exam, ROS	Urine culture and urodynamic testing may be needed to complete diagnosis
GERD	Physical exam, ROS	Endoscopy and esophageal motility study may be needed to complete diagnosis
Disability	Physical exam, ROS	Functional testing may be helpful
Asthma/ respiratory disease	Physical exam, ROS	Chest X-ray and respirometry studies may be needed to complete diagnosis
Depression/ stigmatization	Physical exam, ROS	Psychological testing and evaluation may be needed to complete diagnosis

(continued)

Table 7.7 (continued)

Weight-related complication	Basis for screening and/or diagnosis	Secondary testing when needed to confirm diagnosis, stage severity, or guide therapy
Obesity secondary to hormonal disorder	Physical exam, ROS	TSH for suspected hypothyroidism; serum/urine cortisol for hypercortisolism, if clinical findings or symptoms are present
Iatrogenic obesity (e.g., secondary to medications)	Review current medications and medication history	Follow-up following withdrawal of offending medication and/or substitution with a weight-neutral alternative may be needed to complete diagnosis
Genetic syndrome	Physical exam, ROS, family history	If clinical findings are suggestive, genetic testing of the patient and perhaps family members may be needed to complete diagnosis

Table 7.8 Two-component diagnostic framework for overweight/obesity consistent with the phases of chronic disease prevention

Diagnosis	Anthropometric component	Clinical component[a]	Phases of prevention/ treatment
Normal	BMI < 25 kg/m^2		Primary
Overweight stage 0	BMI 25–29.9 kg/m^2	No obesity-related complications	Secondary
Obesity stage 0	BMI ≥ 30 kg/m^2	No obesity-related complications	
Obesity stage 1	BMI ≥ 25 kg/m^2	Presence of one or more mild-to-moderate obesity-related complications	Tertiary
Obesity stage 2	BMI ≥ 25 kg/m^2	Presence of one or more severe obesity-related complications	

Adapted from Garvey et al. (2014a)
[a]Staging of complications as mild-to-moderate (Stage 1) or severe (Stage 2) is based on complication-specific criteria

Interventions for primary prevention might include public education or modifications in the built environment to prevent overweight or obesity. Secondary prevention strategies are designed to prevent further weight gain and/or promote weight loss in patients with overweight or obesity and to prevent the emergence of complications. Once complications develop, it is evident that the excess adiposity is adversely affecting the health of the patient, and a more intensive approach to management is indicated. Tertiary prevention/treatment is then required to treat the complications by achieving sufficient weight loss to ameliorate them. Thus, the diagnostic framework that combines a measure of adiposity and an assessment of the presence and severity of weight-related complications is actionable. This diagnostic framework indicates disease severity and aids in therapeutic decisions. It renders a diagnosis that dictates what to treat and why.

7.4 Conclusion

The diagnosis of overweight or obesity based solely on BMI is insufficient for two major reasons. First, overweight and obesity represent a continuum of excess adiposity, and BMI is not a direct measure of adipose tissue mass. Thus, while BMI can be used as a parameter for screening, an evaluation is necessary to interpret the BMI measurement for diagnostic purposes and assure that elevated values reflect fat mass and not excess muscularity, edema, pregnancy, large tumors, third-space fluid collection, etc. Furthermore, BMI does not indicate distribution of fat in different adipose tissue depots. On the other hand, waist circumference is useful in identifying relative accumulation in the intra-abdominal depot, which is an element of adiposopathy, and is central to the development of metabolic and vascular complications. Second, BMI does not indicate the degree to which adiposity adversely impacts health since the presence and severity of adiposopathy and weight-related complications varies tremendously among individual patients at any given BMI value. In bariatric endocrinology, best practices require a careful evaluation for the presence and severity of weight-related complications (including adiposopathy) in all patients presenting with overweight and obesity. Key weight-related complications can be identified during an initial patient evaluation consisting of history, an obesity-focused review of systems, physical examination, and clinical laboratory testing. An optimal diagnostic framework incorporates an anthropometric measure of increased adiposity (i.e., BMI) together with an assessment of the presence and severity of weight-related complications, which provides both an indication of disease severity and the intensity of weight loss therapy required to improve health.

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