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REVIEW ARTICLE

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Evolving perspectives on evaluating obesity: from traditional methods to cutting-edge techniques

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ABSTRACT

Objective: This review examines the evolution of obesity evaluation methods, from traditional anthropometric indices to advanced imaging techniques, focusing on their clinical utility, limitations, and potential for personalized assessment of visceral adiposity and associated metabolic risks.

Methods: A comprehensive analysis of existing literature was conducted, encompassing anthropometric indices (BMI, WC, WHR, WHtR, NC), lipid-related metrics (LAP, VAI, CVAI, mBMI), and imaging technologies (3D scanning, BIA, ultrasound, DXA, CT, MRI). The study highlights the biological roles of white, brown, and beige adipocytes, emphasizing visceral adipose tissue (VAT) as a critical mediator of metabolic diseases.

Conclusion: Although BMI and other anthropometric measurements are still included in the guidelines, indicators that incorporate lipid metabolism information can more accurately reflect the relationship between metabolic diseases and visceral obesity. At the same time, the use of more modern medical equipment, such as ultrasound, X-rays, and CT scans, allows for a more intuitive assessment of the extent of visceral obesity.

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1. Introduction

According to a recent study cited by the WHO (World Health Organization)'s official website, the global obese population has exceeded one billion in 2022, accounting for about one-eighth of the world 's total population [1]. Among them, approximately 159 million obese people are children or adolescents aged 5–19 years, and 879 million are adults. Data analysis estimates that the global obesity rate of children and adolescents in 2022 is four times higher than that in 1990. Among adults, the obesity rate in women has more than doubled, and that in men has almost tripled [1]. This study, makes us pay attention to the fact that obesity has become a worldwide problem, and also emphasizes the importance of preventing and managing obesity from early to adulthood. According to the WHO definition, obesity refers to excessive fat accumulation, which may damage health. It is a chronic metabolic disease that is caused by a combination of genetic, physiological, and environmental factors.

1.1. Different adipose cells

Adipose tissue is a remarkably complex organ with profound physiological and pathophysiological effects. Until the late 1940s [2], adipose tissue was characterized as a form of connective tissue, without linking this fact to the metabolism of the organism in any meaningful way. In the following period, people became aware of the relationship between adipose cells and energy storage, which led to research on the metabolic activity of adipose tissue from rodents to humans [3]. As research progressed, the connection between adipose tissue and glucose metabolism was gradually discovered in the 1980s [4,5]. In 1994, Jeffrey Friedman and his colleagues first discovered leptin, followed by the identification of a series of adipose-derived serum factors that can be secreted by adipocytes, including adiponectin and tumor necrosis factor (TNF) [6]. Since then, research on the developmental, functional, and pathophysiological aspects of adipose tissue has increased.

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Traditionally, placental mammals have two main types of adipocytes: white and brown. Brown adipocytes are highly specialized cells that dissipate stored chemical energy in the form of heat. A specific uncoupling protein-1 (UCP-1) is present in the mitochondria of brown adipocytes. They accumulate densely on mitochondria and catalyze proton leakage through the mitochondrial inner membrane, thus 'uncoupling' fuel oxidation from ATP synthesis [7]. Human infants have a large amount of stored brown fat, which possibly provides heat in the cold environment they encounter at birth. We once thought that adults had little brown fat unless they were stimulated by chronic cold or in a state of excessive catecholamine secretion (such as pheochromocytoma) [8,9]. In a study published in 2009, Cypess et al. [10] analyzed the data of patients who required 18F-FDG PET-CT (Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography) for various diagnoses. PET-CT showed that some patients had a large number of UCP-1 immunopositive multilocular adipocytes in the area extending from the anterior neck to the chest, which is characteristic of brown adipose tissue. In addition, it has been observed in rodents that long-term cold exposure or adrenergic signals can cause the emergence of UCP-1+ cell clusters in white adipocyte (a phenotype considered characteristic of brown adipocyte). In other words, under certain circumstances, white adipocytes can closely resemble brown adipocytes in cellular phenotype. Over the past few decades, these cells have been considered to be poorly characterized, and they are simply called 'beige' or 'brite' adipocytes [11]. Lineage tracing experiments have shown that brown and beige (brite) adipocytes have different developmental origins. Classic brown adipocytes and skeletal muscle cells arise from precursors in the dermomyotome [12], and beige (brite) cells originate from endothelial and perivascular cells within white adipose tissue (WAT) depots [13,14]. Some research groups have conducted this study to determine whether UCP-1+ cells in humans originate from brown adipocytes or are more similar to rodent beige (brite) adipocytes. In humans, 'classic' brown adipocytes exist in the developmentalally committed BAT depot of interscapular cells, and it is the only component of UCP-1+ cells in infancy. In adults, cells with brown and beige properties have been identified, which may depend on a specific sampling depot [15,16]. Due to the unique biological function of brown adipocytes, recent studies have begun to explore their therapeutic potential in obesity and metabolic diseases [17].

White adipocytes, now considered dynamic, malleable, and heterogeneous, are involved in a wide range of biological processes, including energy homeostasis, glucose and lipid processing, blood pressure control, and host defense [18]. White adipocytes usually have a single large lipid droplet occupying most cells and relatively few mitochondria. The main function of white adipocytes is to store and release energy to cope with changes in the body's energy levels. At the same time, WAT is an important endocrine organ that secretes a variety of hormones and other factors, collectively referred to as adipokines. Adipokines play a major role in regulating systemic metabolism, including insulin sensitivity, insulin resistance (e.g. resistin, RBP4, and lipocalin), and inflammatory responses (e.g. TNF-α, IL-6, IL-1b, IL-8, IL-18, and sFRP5) [19]. Since the functions of brown adipocytes and white adipocytes are very different, it is important to clarify that when discussing visceral fat, it is the white adipocytes that are referred to, which is important for understanding the mechanisms of obesity and metabolic diseases.

1.2. Visceral adipose and disease

Figure 1 shows the relationship between accumulated visceral adipose and various diseases.

WAT is roughly divided into visceral adipose tissue (VAT) according to the anatomical site, including adiposity in the greater omentum and mesentery or subcutaneous adipose tissue (SAT) under the skin [20,21]. The main areas of subcutaneous adiposity deposition are the femoro-gluteal regions, back, and anterior abdominal wall. Approximately 80% of all body adiposity occurs in the subcutaneous area [22]. The type of adipocytes, endocrine function, lipolytic activity, and response to insulin and other hormones differ between the SAT and VAT. In the Dallas Heart Study [23], 1200 obese participants who underwent magnetic resonance imaging (MRI) examinations were evaluated for individual adipose distribution differences. By assessing individual adipose differences, studies have found that the number of VAT is associated with more severe metabolism, dyslipidemia, and atherosclerosis than SAT. Other studies [24,25] have found that the quantity of VAT is associated with more severe metabolism, dyslipidemia, and atherosclerosis than SAT. Inflammatory cells (monocytes-macrophages) were more abundant in the VAT than in the SAT.

Type 2 diabetes mellitus (T2DM) is a chronic endocrine and metabolic disease that has become a major global public health concern. From 2000 to 2021, the prevalence of T2DM worldwide has increased by 2.5 times, mainly due to the prevalence of obesity [26]. Obesity, especially visceral obesity, is an independent risk factor for type 2 diabetes, its complications, and

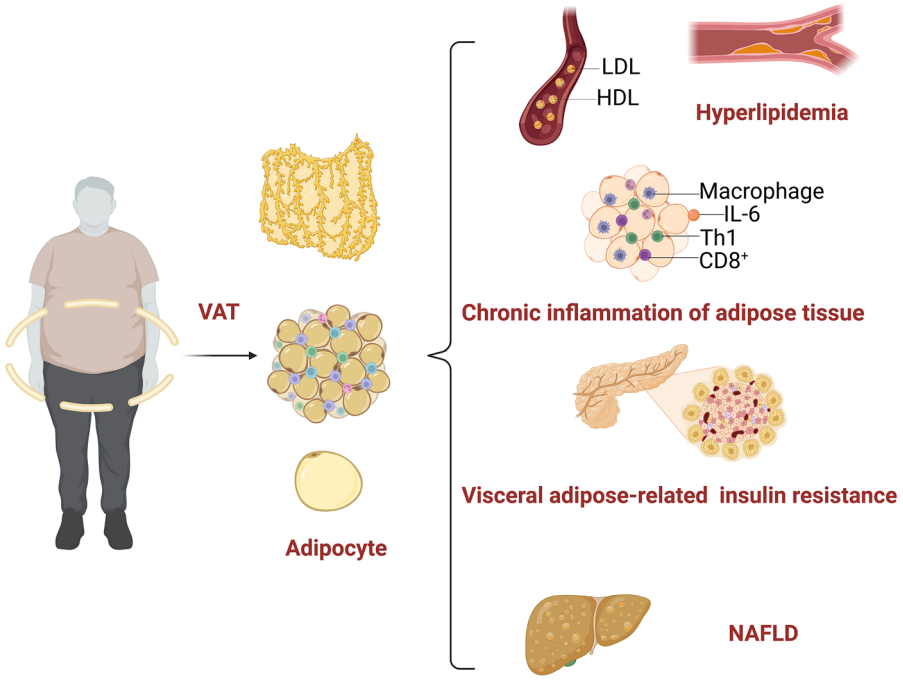

Figure 1. Visceral adipose and disease.
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even all-cause death [27,28]. WAT is not only responsible for sufficient lipid storage by lipogenesis, but also for free fatty acid (FFAs) availability by lipolysis, thereby generating substrates for energy metabolism *via* β-oxidation. FFAs recruit and activate macrophages, stimulate pro-inflammatory factors, leading to a systemic inflammatory response linked with adipose tissue [29,30]. Adipose tissue insulin resistance (IR), which impairs lipolysis inhibition at high insulin levels, is associated with glucose tolerance. Elevated plasma FFAs levels have been shown to impair muscle insulin signaling, promote hepatic gluconeogenesis, and impair glucose-stimulated insulin response [31,32]. Lipolytic activity and insulin sensitivity are different in different compartments of human adipose tissue. Insulin-resistant obese humans show a greater lipolytic response to catecholamines but a decreased sensitivity to the antilipolytic effects of insulin in VAT compared to SAT *in vivo*[33]. The higher response of VAT to catecholamines allows more plasma FFAs to be transported to the liver through the portal vein, which may promote liver and systemic insulin resistance. In contrast, SAT has lower lipolytic activity and higher insulin sensitivity, indicating that SAT can store excess FFAs in the form of triacylglycerols and protect other organs and tissues from lipotoxicity [34,35]. Therefore, people with lower SAT and higher VAT volumes are more likely to show systemic insulin resistance. Several hypotheses explain the mechanisms responsible for IR in obese subjects. These mechanisms include adipose tissue dysfunction/lipotoxicity [36], inflammation [37], mitochondrial dysfunction [38], hyperinsulinemia [39], and endoplasmic reticulum (ER) stress [40].

Fatty liver disease includes alcoholic and non-alcoholic fatty liver disease (NAFLD). NAFLD is considered an exclusionary diagnosis based on alcohol consumption; however, this does not address the key driving factor of the disease, which is metabolic dysfunction. Therefore, the most appropriate name for the disease is 'metabolic associated fatty liver disease (MAFLD)' [41,42]. With the increasing prevalence of obesity, MAFLD has become the most common chronic liver disease worldwide [43]. The spectrum of MAFLD ranges from benign steatosis to metabolic associated steatohepatitis (MASH), fibrosis, and cirrhosis. MASH, previously known as non-alcoholic steatohepatitis (NASH), is a progressive form of MAFLD characterized by hepatic steatosis, inflammation, and fibrosis. Obesity-related inflammation is a key factor in the pathogenesis of MAFLD [44].

The distribution of ectopic fat has been widely studied in the process of atherosclerosis, especially VAT, which is considered the core factor in the pathogenesis of atherosclerosis [45]. A large number of adipocytokines secreted by the VAT promote the occurrence and development of atherosclerosis. In addition, excessive VAT can lead to a hypercoagulable state, and elevated FFA levels in patients with

excessive VAT can affect vascular endothelial function. Together, these factors lead to atherosclerosis [46].

Transplantation studies have put this into a direct test; placing visceral adiposity in a subcutaneous position has very little effect, but transplanting subcutaneous adiposity to the visceral compartment leads to reduced adiposity and improvement in glucose homeostasis [47]. Numerous studies on SAT and VAT differences have led to genetic discussions of fat distribution. The British Biobank was an observational study. The focus of that study was to investigate the genetic architecture of fat distribution independent of the overall size of an individual. Finally, they confirmed that fat distribution is a highly genetic feature [48]. Therefore, it is important to identify reliable indices to evaluate visceral adiposity.

1.3. The evaluation of visceral adiposity

Table 1 shows the advantages and disadvantages of different indicators.

Many attempts have been made in modern medicine to better assess visceral obesity. In clinical practice, we utilize anthropometric methods such as body mass index (BMI), neck circumference (NC), waist circumference (WC), and WC derivative indicators such as waist-to-hip ratio (WHR) and waist-height ratio (WHtR) to assess the patient's body fat status. Not all individuals with obesity have metabolic disorders. Indicators based on lipidomics, demography (age and sex), and anthropometry (BMI and WC) subsequently appeared to assess visceral fat, such as LAP, VAI, CVAI, and mBMI. Although there are various evaluation indicators for abdominal obesity, imaging methods, such as 3D-CT and MRI, are still the gold standard for visceral fat quantification. In addition, to avoid the radiation problems caused by CT and the high cost of MRI, other devices, such as ultrasound and human electrical impedance analysis, are still widely used in clinical practice. All these methods have their own advantages and disadvantages. The purpose of this article is to

Table 1. Advantages and disadvantages of different indicators.

		Advantages	Limitations
Anthropometry	BMI	The calculation method is very simple, can be used across different populations, and is suitable for large-scale screening and assessment. It is the preferred method for evaluating obesity and its related health risks.	Racial differences require the establishment of different standards for use according to various ethnic groups. BMI cannot quantify body fat percentage, fat distribution (VAT or SAT), or the degree of metabolic disorders, while also overlooking the impact of muscle mass.
	WC; WHR; WHtR	More strongly correlated with VAT.	Cannot effectively distinguish between SAT and VAT. The reliability of these measurements for assessing body fat in women is low.
	Neck circumference (NC)	The correlation is similar to or better than WC, and it predicts the risk of OSA more effectively.	Cannot be used for patients with neck enlargement due to disease. Accuracy is low in children. Evaluation is inaccurate for males.
The lipid-related indices	Lipid accumulation product (LAP)	Its sensitivity and specificity in predicting metabolic syndrome and diabetes are higher than traditional indicators.	There is controversy regarding the predictive effect on diabetes.
	Visceral adiposity index (VAI)	Focusing on visceral adiposity, it predicts metabolic syndrome and diabetes more effectively than traditional indicators.	The calculation formula is relatively complex and relies on multiple physiological parameters.
	Chinese visceral adiposity index (CVAI)	It performs well in assessing the risk of metabolic syndrome, diabetes, and cardiovascular diseases in the Chinese population.	It has limitations for other ethnic groups.
	metabolic BMI score (mBMI)	More accurately identify individuals with a normal BMI who have a higher risk of cardiovascular diseases.	More complex than traditional BMI calculations. There is relatively less research, so its effectiveness and reliability need more empirical support.
Equipment detection method	Three-dimensional (3D) body scanning	Data on abdominal volume and body shape can be obtained.	The ability to predict VAT is limited.
	Bioelectrical impedance analysis (BIA)	By combining impedance and abdominal shape information, this method can more comprehensively quantify VAT.	In individuals with higher levels of visceral fat, this analysis may underestimate the extent of visceral fat, leading to significant bias.
	Ultrasound	Convenient, relatively accurate, and radiation-free.	Cannot achieve the accuracy of CT or MRI.
	Dual-energy X-ray absorptiometry (DXA)	There is a strong correlation between the VAT volume estimated by DXA and the results measured by MRI, and it is relatively commonly used.	As a two-dimensional imaging technique, DXA cannot directly differentiate between VAT and subcutaneous fat tissue.
	CT and MRI	It is the reference method for evaluating abdominal obesity.	A certain dose of radiation and higher costs.

review the current VAT evaluation methods, comprehensively analyze various evaluation methods, and try to find a method that can accurately perform individualized evaluation and also has universality.

2. Anthropometry

Anthropometry included physical and body composition analysis. The items of physical measurement mainly include height, weight, skinfold thickness, WC, and hip circumference (HC). Quantitative assessment of the accumulation of potentially harmful visceral fat in the human body by anthropometry is helpful to clarify its role in disease and to predict the risk of disease.

2.1. BMI

BMI is defined as follows: BMI (kg/m^2) = weight (kg)/height^2 (m^2). This simple formula was proposed around the nineteenth century by Belgian mathematician Lambert Adolphe Jacques Quetelet (1835). In the second chapter of Surl'homme, it is first proposed that there is a relationship between height and weight growth. In the 1990s, the expert committee of WHO defined BMI ≥25.0 kg/m^2 as overweight and BMI ≥ 30.0 kg/m^2 as obese [49]. The WHO BMI classifications for overweight and obesity are intended for international use. However, since the classification is mainly based on the observation of BMI and death risk among Caucasian people in Europe and America, it is doubtful whether this threshold is applicable to people of other ethnic groups.

After this view was put forward, studies continued to reveal that for Asian people, even a slight increase in BMI would significantly increase the risk of death [50]. In response to this emerging new evidence, WHO recommended in 2004 that the obesity threshold for obese people in South Asia should be set to 27.5 kg/m^2 [51]. Based on this recommendation, the British National Institute for Health and Care Excellence (NICE) guidelines set the BMI that triggers life intervention for South Asian and Chinese people to 27.5 kg/m^2 [52]; and the American Diabetes Association (ADA) also adjusted BMI based on new evidence. The cutoff points for overweight and obese among Indian Americans dropped to 23.0 kg/m^2 and 25.0 kg/m^2 [53].

Although BMI is an adequate tool for reporting secular trends in the prevalence of obesity at the population level, physicians have been perplexed by the fact that while some obese patients clearly show complications associated with their excess body adiposity, some other equally obese patients do not display expected metabolic abnormalities despite their significant excess body adiposity [53,54]. Another notable example of BMI limitations is associated with metabolic obesity normal weight (MONW), which was first proposed by Delman et al. [55]. For MONW individuals, who have normal BMI values, suffer from metabolic complications commonly found in obese people. The notion of MONW subjects was also documented by St-Onge et al. [56]. These observations suggest that a high CVD risk may be observed even below the normal BMI cutoff of 25 kg/m^2. In contrast, data from independent studies show that a subgroup of individuals with obesity is either shielded from obesity-related cardiometabolic diseases or may be at a significantly lower risk than what would be predicted solely based on the positive association between BMI and cardiometabolic risk [57]. This sub-phenotype is metabolically healthy obesity (MHO). MHO is typically defined as obesity without any metabolic disorders and cardiovascular diseases, as well as type 2 diabetes, dyslipidemia, and hypertension. Note that there is no uniform definition for MHO. More than 30 definitions of metabolic health have been used in clinical studies [58,59]. A key factor underpinning the difference in CVD risk between individuals with MONW and MHO is the likely presence of excess VAT [59,60].

The China Kadoorie Biobank study [61,62], conducted by the Chinese Academy of Medical Sciences and Oxford University, recruited over 500,000 residents from various regions between 2004 and 2008. A follow-up survey on 20,000 participants from 2013 to 2014 examined the impact of BMI and WC on health, focusing on mortality risk. Results showed that participants with BMI <18.5 kg/m^2, 18.5-20.4 kg/m^2, and ≥35 kg/m^2 had higher all-cause mortality risks compared to those with a BMI of 20.5-22.4 kg/m^2. Further study with a large-scale meta-analysis of over 30 million individuals, the correlation between BMI and all-cause mortality in the general population can be described as U-shaped or J-shaped [63]. Mosterd et al. [64] found that increased BMI predicted better survival in heart failure patients during a 6.1-year follow-up. Kalantar et al. [65,66] pointed out that low BMI increases the mortality risk in dialysis patients, while overweight dialysis patients have a higher survival rate. Additionally, coronary artery disease patients with a BMI < 22 kg/m^2 have a higher mortality rate than those who are overweight [67]. In fact, obesity may be linked to reduced mortality risk from heart failure and other conditions [67,68], known as the 'obesity paradox'.

Several mechanisms have been hypothesized to support the existence of the obesity paradox. Body structure and body composition: weight gain may

resist side effects caused by treatment by providing sufficient muscle and fat reserves [69]; high levels of total cholesterol and lipoprotein can improve endotoxin clearance [66]; N-terminal pro-brain natriuretic peptide (NT-proBNP) levels in overweight or obese patients are significantly reduced [70]; and prethrombotic factors (e.g. thromboxane B2) are negatively correlated with BMI and leptin [70]. Additionally, considering that cardiovascular diseases in obese patients typically occur at an earlier age, there may also be factors related to the more timely timing of interventions and the better physical condition of the patients, which contribute to optimal medical care [68]. However, this does not mean that obesity is a good prognostic indicator for these diseases. The obesity paradox seems to be due to the use of BMI to define obesity because BMI cannot quantify body fat percentage and obesity distribution, nor can it quantify the degree of metabolic disorders it can constitute [71]. Simultaneously, the obesity paradox appears to be observed in patients who are classified as obese yet maintain a significant level of 'lean body mass', indicating that their muscle quality remains well preserved [68].

Although the limitations of BMI as an obesity index have been discussed for decades and more assessment indices of obesity-related diseases have been developed, many obesity guidelines [72–74] continue to recommend BMI as the first choice for evaluating the incidence of obesity-related metabolic diseases and risk of death.

2.2. WC, WHR and WHtR

By using BMI, one must rely on the assumption that adipose tissue is distributed evenly over the body, which does not consider the heterogeneity of regional body adiposity deposition. Over 60 years ago [75], it was noted that cardiovascular risk from obesity relates more to abdominal adipose distribution than total adipose. BMI alone is not sufficient to be used as a biomarker for abdominal obesity.

WC is a simple method to evaluate abdominal obesity and is easy to standardize for clinical applications. The WHO states that WC > 94 cm in men and >80 cm in women is associated with an increased risk of metabolic complications [76]. To better reflect the risk of metabolic diseases in the Chinese population, the Chinese Obesity Working Group proposed a new scheme that regards WC ≥ 85 cm in men and female WC ≥ 80 cm in women as abdominal obesity [77]. A large study [78] found that WC (R^2 0.826, $p < 0.0001$) demonstrated a stronger correlation with VAT content measured by MRI compared to BMI (R^2 0.672, $p < 0.0001$). Standardization of WC measurements is crucial, with common methods including the upper iliac crest (WC-C) and mid-iliac crest (WC-mid) [79]. CT measurements showed WC-mid correlates more strongly with VAT than WC-C and is linked to various health markers, especially in women [79]. WC-mid can even predict the development of diabetes, using male >90 cm and female >80 cm to determine the boundaries of diabetes obesity [79]. Overall, WC is a effective predictor of VAT in adults [80] and children [81], but lacks evidence for its association with cancer risk due to insufficient prospective studies [82].

The WHR was obtained by dividing the WC by the HC using the same units of measurement for both. The WHR is an indicator of body fat distribution (apple or pear). According to the WHO, the healthy WHR is ≤0.9 for men and ≤0.85 for women. The higher the WHR, the higher is the health risk. WHR >1.0 is referred to as abdominal obesity [76].

Renal threshold for glucose (RTG) is defined as the plasma glucose concentration at which the kidneys begin to excrete glucose into the urine. Below this level, almost all filtered glucose is reabsorbed. Above this level, glucose is present in the urine. In a study on the relationship between WHR and promoting urinary glucose excretion (UGE) in subjects without a history of diabetes, it was found that high-WHR patients had a risk of UGE reduction. Studies have shown that WHR rather than BMI may be an important factor in UGE [83]. A data analysis of 248 women with normal thyroid, non-diabetic, and normal body weight showed that WHR levels were associated with IR and seemed to be a useful anthropometric indicator for assessing IR in women [84]. However, Wang et al. indicated that WC is more effective than WHR in predicting diabetes [85].

A significant interaction between sex, WHR, and mortality was found ($p < 0.001$) [84]. In women, higher WHR correlated with increased death risk, while no such correlation was observed in men [86]. A multinational study indicated that WHR is three times more strongly related with acute myocardial infarction than BMI [87]. In patients with heart failure (HF) with mid-range ejection fraction (HFmrEF), increased WHR trend patterns were linked to higher all-cause mortality, which underscored the importance of abdominal fat accumulation management during HF progression [88]. Additionally, WHR in obese adolescents significantly correlated with metabolic syndrome [89]. In obstructive sleep apnea (OSA) patients with non-obese males (WHR < 0.9, BMI < 28kg/m^2), WHR is a moderate screening marker for moderate-to-severe OSA and an independent risk factor for OSA severity [90].

The use of the waist-height ratio (WHtR) to detect abdominal obesity and its associated health risks was first proposed in the mid-1990s. WHtR allows the height of each individual to be corrected, so a single threshold can be determined in different populations and genders [91,92]. Compared with BMI, WHtR is significantly associated with obesity-related diabetes in different populations (race, sex, age) [93,94]. A longitudinal study with 1,718 participants aged 39-72 evaluated the relationship between WHtR and hypertension. Participants were divided based on hypertension development from 2005-2011. The follow-up showed that those with hypertension had significantly higher WHtR. After adjusting for various factors, participants in the highest WHtR quartile (≥0.54) were 4.51 times more likely to develop hypertension than those in the lowest quartile [92]. WHtR also outperformed BMI in identifying hypertension risk [95]. In a study of people younger than 60 years in southern China, WHtR was positively correlated with hypertension and its subtypes [96]. WHtR has also been proposed to predict cardiac metabolic risk in children and adolescents across different populations [97]. Lin et al. found that body size assessed by the WHtR is a key factor affecting reduced cardiorespiratory fitness (CRF) and can determine the prognosis of heart failure [98].

The advantage of WC is that it allows a crude estimation of the absolute amount of VAT. However, it also became obvious that variations in WC cannot distinguish SAT from VAT [99,100]. Research on WC, WHR and WHtR has indicated that these measurements are not reliable indicators of body fat in women. Even in cases where there are significant differences in body fat percentages among women, measurements such as WC, WHR and WHtR do not show significant variation [101]. This may be because estrogen generally helps women accumulate fat in subcutaneous areas (such as the hips and thighs) rather than in the abdomen [102]. In addition, WC and WHR also have some limitations, such as limited by certain conditions, such as cultural acceptability, pregnancy, thighs fat and very obese individuals [76,103]. In general, there is no consensus on the value of these three indicators in evaluating VAT, and there is still controversy.

2.3. Neck circumference (NC)

The BMI mainly reflects overall obesity. WC is a classic anthropometric measure for assessing VAT. NC is a reliable alternative for assessing upper body fat, unaffected by external factors (exhalation, posture, abdominal droop, hernia, or ascites [104,105]. Traditionally, NC has been suggested to be more predictive of OSA [106]. NC has been suggested as an alternative measure of central obesity in children and adults, as an index of upper-body adiposity distribution, and to screen for excess body weight in the population. It has been suggested that adiposity in the neck may be more similar to visceral adiposity, which is more strongly related with cardiometabolic risks [107].

Recently, NC showed similar or better associations with metabolic factors than WC [108]. Ben-Noun et al. [109] found that Men with NC ≥ 37 cm and women with NC ≥ 34 cm required additional evaluation of overweight or obesity status. NC is an independent predictor of metabolic syndrome (MetS) burden, with a high association in women. MetS prediction cut-off point was a NC of 39.5 cm for men and 33.3 cm for women [110]. A study performed in China with 4201 patients found a positive association between NC and MetS components individually, such as fasting plasma glucose, blood pressure, and triglycerides, whereas this parameter was inversely associated with high-density lipoprotein (HDL) [111]. This anthropometric parameter can be used as an additional marker for screening MetS and cardiovascular risk diseases.

NC has certain limitations when assessing obesity. It is not applicable for patients with cervical enlargement, such as those suffering from lymphadenopathy or thyroid disease, and it can be affected by the rapid growth rates observed in young children, resulting in reduced accuracy for those under 6 years old. Furthermore, due to higher muscle mass in males, NC may not provide sufficiently accurate evaluations for this group [112]. Although NC can better reflect conditions in females, it is still influenced by other factors. Anatomical variability, including differences in neck shape (such as slender or stocky), muscle mass, and fat distribution, also plays a role. Generally, an NC greater than 40 cm in men and greater than 36 cm in women is considered a marker of increased risk for cardiovascular disease [112,113].

3. The lipid-related indices

In recent years, new anthropometric indicators have emerged, and ongoing research has continuously explored the relationships between various indicators and health. These new metrics incorporate more blood lipid-related levels, further highlighting the importance of VAT.

3.1. Lipid accumulation product (LAP)

Kahn first described the LAP to estimate lipid accumulation in adults [114]. The LAP is based on a combination of two safe and inexpensive measurement methods.

One is WC, which is measured by including the visceral storage of fat. The other is the fasting concentration of circulating triglycerides (TG). LAP = [WC(cm)−65]×TG (mmol/L) for men and LAP = [WC(cm)−58]×TG (mmol/L) for women. To our knowledge, this is the first study to introduce lipid metabolism indicators based on anthropometry. However, the author only compared its effectiveness with BMI, and at that time, there had been indicators such as WC were used to measure visceral obesity, which the author did not evaluate.

Since the emergence of LAP, an increasing number of studies have complemented the evaluation of LAP with other anthropometric or visceral obesity indicators. Marcadenti et al. [115] evaluated the independent correlations between T2DM and LAP, NC, and body adiposity index (BAI) in patients with hypertension. In hypertensive women, obesity phenotypes such as LAP and NC were independently associated with T2DM. A study of the relationship between traditional/non-traditional lipid profiles and MetS in a total sample of 1112 adolescents aged 13–18 years (564 boys and 548 girls) found that all our lipid profiles were closely related to MetS ($p < 0.05$), and the LAP index was most closely related to MetS [116]. The LAP index is a simple and efficient tool for identifying individuals with MetS among Chinese adolescents [116]. Recent studies have also found that the sensitivity and specificity of LAP in predicting MetS and diabetes are significantly higher than those of BMI and WC [117,118].

However, some scholars believe that LAP can only help to identify the prevalence of diabetes rather than predict its occurrence [119]. It can be seen that LAP is a simple and effective clinical indicator to evaluate the risk of diabetes, CVD, MetS and other diseases, but its predictive efficacy is still controversial, which needs to be further demonstrated by high-quality follow-up studies. It is undeniable that the metabolic disorder information captured by LAP is not related to BMI, which provides an opportunity to identify individuals at risk of MetS to carry out targeted management interventions.

3.2. Visceral adiposity index (VAI)

In a retrospective study, TG (mmol/L) and HDL (mmol/L) levels were used to correct the actual effects of adiposity in the adiposity distribution model (MOAD). Thus, a new sex-specific index was developed based on WC, BMI, TG, and HDL, which was defined as VAI [120]. Compared to classical parameters (such as WC, BMI, and lipids), VAI has higher sensitivity and specificity. Initially, it was used as a reliable indicator to assess visceral adiposity function associated with cardiac metabolic risk. Subsequently, because of the simplicity of WC and BMI measurements and TG and HDL assessments, it became a simple indicator to assess visceral adiposity dysfunction [120].

VAI was determined and calculated using the following formulas, where WC is expressed in cm, and TG and HDL are expressed in mmol/L [120].

$$\text{Males}: \left[\text{WC} / \left(39.68 + \left(1.88^{*}\text{BMI}\right)\right)\right]^{*} \left(\text{TG} / 1.03\right)^{*} \left(1.31 / \text{HDL}\right);$$

$$\text{Females}: \left[\text{WC} / \left(36.58 + \left(1.89^{*}\text{BMI}\right)\right)\right]^{*} \left(\text{TG} / 0.81\right)^{*} \left(1.52 / \text{HDL}\right).$$

Over the past decade, numerous publications have highlighted the ability of the VAI to indicate potential dysfunction of adipose tissue and assess cardiometabolic risk across various age groups [121–123]. One study indicated that the VAI has superior predictive ability for the risk of developing type 2 diabetes compared to other common anthropometric measures such as WC, BMI and WHtR [124]. Additionally, VAI is recognized as an important risk factor for the development of CVD [125]. Research on VAI primarily focuses on cardiovascular and metabolic diseases, highlighting its role as an indicator of adipose distribution and function [121].

3.3. Chinese visceral adiposity index (CVAI)

Table 2 shows the efficacy of CVAI in assessing obesity-related diseases within the Chinese population.

There is a consensus has been reached that there are differences in body indicators between Asian, European, and American populations. The VAI is based on the equation established for Caucasian populations. In order to better assess the degree of visceral adiposity in Asians, Xia et al. [126] developed a new surrogate index, the Chinese visceral adiposity index (CVAI). This index combines demographic (age), anthropometric (BMI and WC), and metabolic characteristics (TG and HDL-C), and was verified by CT. It was found to be a reliable index for the evaluation of visceral adiposity dysfunction in a cross-sectional study with 485 subjects conducted in the Lianqian Community, Xiamen, China, and was further validated in a study with 6,495 subjects recruited from Changfeng, Shanghai [126].

Wu et al. found that CVAI had a higher predictive value than VAI, BMI, WC, WHR, and WHtR for early T2DM identification [127]. Han et al. confirmed CVAI's positive correlation with T2DM risk in a large prospective study [127]. CVAI has the best performance in predicting the incidence of T2DM, therefore, it may be a

Table 2. The efficacy of CVAI in the evaluation of obesity-related diseases in the chinese population.

Authors (Years)	Diseases	Evaluation effectiveness		References
Wu et al. [127]	T2DM	Early identification	Higher than that of VAI, BMI, WC, WHR and WHtR.	129
Han et al. [128]		Predicting the incidence of T2DM	Has the best performance in predicting the incidence of T2DM.	130
Han et al. [129]	Hypertension	The predictive value of CVAI for hypertension was significantly better than that of VAI, WC and BMI regardless of gender.		131; 132
Li et al. [130]				
Zhang et al. [132]	Stroke	The highest risk of new stroke was associated with the fourth quartile (Q4) of CVAI.		134
Duan et al. [133]	MetS	There are gender differences in the ability of CVAI to diagnose MetS, and CVAI is superior to VAI in women. VAI is superior to CVAI in men.		135

reliable and applicable index to identify high-risk groups for T2DM [128].

Han et al. [129] conducted a six-year follow-up of 10,304 Chinese adults, finding that each 1.0-standard deviation increase in CVAI raised the hypertension risk by 9% in males and 14% in females after adjustments. CVAI's predictive value for hypertension was significantly better than VAI, WC, and BMI (all $p < 0.05$). Additionally, Li et al. [130] reported that the highest quartile of CVAI increased prehypertension risk by 1.7 times and hypertension risk by 2.5 times in a study of over 30,000 people, with CVAI showing a stronger correlation than other measures like VAI, BMI, and WC.

In China, there are approximately two million new stroke cases each year, with a growth rate of 8.7% [131]. CVAI can be used to observe the risk of diseases caused by mechanisms such as dyslipidemia and insulin resistance. In view of the fact that inflammation and thrombosis are key factors in the pathogenesis of stroke, Zhang et al. [132] hypothesized that higher CVAI may affect the incidence of new stroke. Their multivariate logistic regression analysis indicated that the highest new stroke risk correlated with the top quartile of CVAI (OR 2.33, 95% CI 1.67-3.28). In hypertensive patients, a CVAI ≥83 and CRP ≥1.1 mg/L increased stroke risk, highlighting CVAI's significance in predicting strokes.

Duan et al. [133] explored the diagnostic ability of the CVAI for MetS in 1452 Chinese subjects. ROC analysis showed that there were sex differences in the ability of CVAI and VAI to diagnose MetS, and CVAI was superior to VAI in women. In men, the VAI was superior to the CVAI. In general, these two indicators are highly accurate for the diagnosis of MetS. For assessing MAFLD within obesity studies, CVAI proved effective. A cross-sectional study [134] showed CVAI had the strongest association with MAFLD risk among six obesity metrics, indicating its robust diagnostic capability for metabolic dysfunction-related fatty liver.

3.4. Metabolic BMI score (mBMI)

A series of studies have shown that the risk of many metabolic diseases, including diabetes and cardiovascular diseases, is significantly associated with metabolites (including lipids) related to BMI, but this metabolic disease risk is unrelated to BMI itself [135,136]. These results suggest that BMI-related metabolic phenotype analysis may provide a more accurate prediction of obesity and related diseases. Cirulli et al. [137] analyzed the metabolic levels of 1007 substances in 2396 volunteers, screened 49 substances related to the BMI of volunteers, and obtained comprehensive metabolic data, named mBMI (metabolic BMI). These 49 metabolites included peptides, lipids, amino acids, and sugars. They believed that mBMI is more predictive of a person's health than BMI. In most cases, mBMI and BMI are positively correlated; that is, the metabolic level of overweight people is often worse than that of normal-weight people. However, 20% of the population's mBMI and BMI did not match. The predicted mBMI of these populations was significantly lower than the actual BMI or significantly higher than the actual BMI. Individuals with mBMI that was significantly lower than the actual BMI had similar levels of insulin resistance, total triglycerides, high-density lipoprotein, blood pressure, WHR, body fat percentage, visceral fat percentage, and subcutaneous fat percentage in metabolically healthy normal-weight individuals. The levels of these characteristics in individuals with mBMI prediction significantly higher than the actual BMI were similar to those of obese individuals with an obese metabolome. These characteristic levels of individuals with an mBMI predicted to be significantly higher than the actual BMI were similar to those of obese individuals with an obese metabolome.

Metabolomic analysis and the emergence of BMI further confirmed the clinically significant heterogeneity in obesity. Furthermore, in a study by Wang et al. mBMIΔ was established using the difference between mBMI and BMI [138]. The research article [138] developed a new mBMIΔ score prediction model using plasma lipidomics data from the Australian large cohort AusDiab and quantified its relationship with the incidence of cardiovascular disease and type 2 diabetes. To assess mBMIΔ's relationship with cardiometabolic risk factors, AusDiab participants were grouped into quintiles. Q5 showed poorer lipoprotein profiles, increased insulin resistance, and higher blood pressure

despite similar BMI values compared to Q1-Q4. Wang et al. also evaluated the odds of T2DM and prediabetes in the quintile of mBMIΔ, with Q1 as a reference. According to the quintile analysis, the odds ratio of T2DM gradually increased from the lowest mBMIΔ range (Q1) to the highest mBMIΔ(Q5). People in Q5 were more than four times more likely to have T2DM than those in Q1 were [138].

We are pleased to see the participation of more metabolic indicators, which reflect the importance of obesity as an epidemic disease. However, systematic horizontal studies of different indicators for the evaluation of metabolic diseases are still limited, and it is hoped that continued enthusiasm for obesity research will lead to further research.

4. Equipment detection method

Despite the vigorous development of anthropometric indicators, imaging methods remain the gold standard for quantifying adipose tissue.

4.1. Three-dimensional (3D) body scanning

Three-dimensional (3D) body scanning is a rapidly evolving technology that projects lasers and other forms of light onto the body surface and uses a camera system to capture the body 's reflective contours [139]. In a study of 473 children and adolescents, the consistency correlation coefficient between the 3D laser scanner, WC, and HC was higher than 0.937 [140]. The use of 3D scanning applications may be a future direction for assessing abdominal obesity. Three-dimensional body scanning can be used to obtain more central obesity indices such as abdominal volume and body shape. Future studies are needed to compare the differences between abdominal volume, body shape measurements, and WC in predicting visceral obesity and obesity-related health risks.

4.2. Bioelectrical impedance analysis (BIA)

Double abdominal bioelectrical impedance analysis quantifies VAT by combining impedance and abdominal-shape information. The ability of bioelectrical impedance analysis to estimate total abdominal fat is higher than that of VAT [141]. Some studies have shown that bioimpedance can estimate VAT equivalently or better than WC [142,143]. However, other studies have found the opposite result. When the VAT is high, double-abdominal bioimpedance analysis may underestimate the degree of VAT, in other words, there is a relatively large deviation[144].

4.3. Ultrasound

Ultrasound can be used to measure the thickness of tissues on different planes, measure from multiple points around the abdomen, and evaluate the VAT stereoscopically [145]. There is a high correlation between the VAT evaluated using ultrasound and the VAT calculated using CT [145]. At present, there is no consistent evidence to prove that ultrasonic assessment of VAT is more accurate than WC [146,147]. Currently, b-mode ultrasound is more commonly used than a-mode ultrasound in obesity research. In an anatomical study of six human subjects [148], the differences between the thickness of anatomical tissue and the thickness of different ultrasound detectors were compared. The average difference between the thickness of subcutaneous adipose tissue in the abdomen, thighs, and abdomen of types a and b was less than 0.7 mm. Both methods provide the same subcutaneous fat thickness measurements. The advantages of ultrasonic method are that it is easy to use, does not involve radiation exposure, has high safety, and can be repeated many times in a short period of time.

4.4. Dual-energy X-ray absorptiometry (DXA)

Because DXA is a two-dimensional imaging technique, it cannot directly distinguish VAT from subcutaneous adipose tissue, but the VAT volume estimated by DXA is closely related to the VAT volume measured by MRI. In a cohort study of elderly men, Deming regression and Bland-Altman plots showed strong correlation between VAT measured by DXA and MRI ($r = 0.90$, $p < 0.0001$) [149]. It should not be ignored that there are some defects in DXA assessment of VAT, DXA performs poorly in subjects with low body mass index, while the correlation is slightly reduced in subjects with high WC [78].

4.5. CT and MRI

CT and MRI directly measure the area or volume of the VAT and are considered reference methods for assessing abdominal obesity. Compared with MRI, CT is less susceptible to respiratory artifacts. Nevertheless, ionizing radiation from CT limits its application in children and longitudinal studies. Currently, the commonly used MRI equipment is affected by the caliber of the equipment and may not be able to accommodate severely obese individuals. Now, with the use of large-caliber equipment, it can accommodate all patients [150,151]. PET-CT, MRI, and dual-energy CT can distinguish brown adipose tissue from white adipose tissue [152]. Epidemiological studies over the past 30 years have shown that VAT accurately measured using CT or MRI is an independent

risk marker for cardiovascular and metabolic morbidity and mortality [153].

It is worth noting that we discuss the accuracy of CT or MRI based on the use of a three-dimensional full-volume VAT. The reliability of single-slice CT in evaluating VAT still needs to be further analyzed using statistical methods, and a study was conducted to evaluate the correlation between VAT estimated by single-slice CT at different levels and the whole VAT volume constructed by CT [78]. When using the single-slice method, the predictive performance was best at L3 and L4. When slices were combined at the level of a single vertebral body, their predictive ability improved. For example, combining CT scans of the entire lumbar spine (L1-L5) or two levels, such as L2-L3, showed a strong correlation [78].

CT and MRI allow noninvasive and accurate measurements of body composition. Still, owing to the complex anatomical structure of the abdominal compartment, the automatic segmentation technique for distinguishing adipose tissue from different compartments still needs to be manually corrected [154]. Therefore, it is important to develop an automatic segmentation technique for VAT and SAT measurements in abdominal CT or MRI images. Artificial intelligence (AI), including machine learning and deep learning, has recently been proposed as a solution for obtaining automatic and reliable abdominal adipose tissue analysis [155,156]. In recent years, an increasing number of studies have evaluated automatic abdominal adipose tissue segmentation on CT and MRI scans using machine learning and deep learning algorithms. Because the performance of an algorithm depends on the quality of the training data, it is not surprising that these algorithms [157,158] have achieved better performance in the case of soaring obesity rates and increased interest in obesity research.

Previous studies have compared the accuracy of BIA with DXA and MRI for body composition assessment, but typically in small populations without intra-subject comparisons across all three models. One large-scale study [78] analyzed data from 4588 participants, using CT or MRI 3D full-volume VAT as a reference to evaluate BIA, DXA, and single-slice CT methods. The study found that VAT volume obtained by DXA had a stronger correlation with MRI (R^2 0.94, $p < 0.0001$) than total body fat mass (R^2 0.27, $p < 0.0001$) and trunk fat mass (R^2 0.49, $p < 0.0001$) obtained by BIA.

5. Discussion

We are pleased that the study of obesity has shifted from body weight to adipose to visceral adipose. Still, it is also regrettable that for a long time, although anthropometric indicators have emerged vigorously, a large number of studies have fallen into the research dilemma of 'statistical evaluation of a certain indicator has advantages over certain problems'. A large amount of research' stacking, and no particularly innovative discoveries. BMI status is still unshakable for the evaluation of obesity and metabolic diseases, and indicators of lipid metabolism have not been widely used in clinical practice. Perhaps VAI and CVAI have been widely recognized for their ability to evaluate most metabolic diseases, but there is still a long way to go to clinical practice.

At the same time, with the progress in equipment and the development of computer technology and big data, imaging methods have made rapid progress. Machine learning algorithms, such as deep learning, can be used for the automatic identification and quantification of visceral adiposity regions. For example, CT or MRI images can be utilized to accurately calculate the area of visceral adiposity, thereby enhancing measurement accuracy and efficiency. Radiomics, a new image analysis technology, has been successfully used in the diagnosis and prognosis evaluation of cancer in recent years. It aims to describe the characteristics and heterogeneity of tissues or lesions by extracting a large number of features from medical images, including texture, shape, and intensity distribution. In the future, it may be used to identify and interpret visceral adiposity radiomic textures, which could be closely related to the accumulation of visceral adiposity and associated disease risks. Overall, machine learning provides new tools and methods for the assessment and research of visceral adiposity, and with the advancement of technology and the accumulation of data, more innovative applications are likely to emerge in the future.

Authors contributions

Heyue Wang: Conceptualization, Data Curation, Visualization, Writing-Original Draft Preparation, Writing-Review & Editing. Yaxin Qin, Jinzhu Niu, Haowen Chen, Xinda Lu, and Rui Wang, Data Curation, Visualization, Writing-Original Draft Preparation, Writing-Review & Editing. Jianli Han, Supervision. All authors have contributed to the manuscript and approved the submitted version.

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