REVIEW

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Recognition of visceral obesity beyond body fat: assessment of cardiovascular risk in chronic kidney disease using anthropometry

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Abstract

Evaluation of body fat and its distribution are important because they can predict several risk factors, mainly cardiovascular risk. Imaging techniques have high precision and accuracy for body fat measurement. However, trained personnel are required and the cost is high. Anthropometric indices might be used to evaluate body fat and its distribution in general population. In chronic kidney disease patients, studies have been indicating that overweight status improves survival rates. On the other hand, visceral fat accumulation is associated with inflammatory responses and insulin resistance. This narrative review discusses particularities of fat distribution in metabolic context and the relevance of available methods for abdominal adiposity evaluation in chronic kidney disease and end-stage renal disease patients.

Keywords: Anthropometry, Chronic kidney disease, Hemodialysis, Obesity, Visceral fat

Background

Until the 1990s, adipose tissue was considered an inert organ and its known roles were energy storage, thermal insulation, and mechanical protection [1]. With subsequent recognition of leptin and other mediators secreted by the adipose tissue, it was suggested that it is an endocrine and active organ [1, 2].

Today, it is well established that body fat and its distribution exerts a relevant influence on metabolic risk factors. Imaging scans, such as computed tomography and magnetic resonance, are substantial tools to assess fat quantity and its distribution on clinical research situations [3]. These assessments measure both visceral and subcutaneous abdominal fat accurately. Ultrasound and dual energy X-ray absorptiometry (DXA) may also be used to assess abdominal fat, although subcutaneous and visceral fat cannot be distinguished [4]. However, the use of image exams on clinical practice is limited, due to

high cost, requiring trained personnel and availability of such expensive equipment [3, 4].

On the other hand, anthropometric measurements are also good parameters to assess obesity. Evaluation of nutritional status using anthropometry should be valorized because of its main advantages, as low cost, safety, and simplicity in its execution. Association between anthropometrical indices and metabolic risk factors has been vastly studied, mainly as indicators for cardiovascular risk factor assessment in both epidemiological research and clinical practice [5–15].

In this review, anthropometric indices to evaluate obesity and results of researches associating those indices with cardiometabolic risk factors in general population and chronic kidney disease (CKD) are presented. Moreover, more recent information about types of adipose tissue (brown and white) is briefly discussed.

Anthropometrical indices of obesity

Anthropometric parameters may be analyzed according to the type of obesity (Table 1): central obesity, which represents the accumulation of fat in the abdominal region; generalized obesity, which includes fat accumulation, both peripheral and central; and body fat distribution.

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Table 1 Anthropometric indices and respective formula categorized according to type of obesity

Type of obesity	Indices	Formulas	Reference
Fat quantity (general and central obesity)	Conicity index	Waist circumference (cm)/0.109 × √ body weight (kg)/height (cm)	[5]
	Abdominal circumference	–	[17]
	Sagittal abdominal diameter	–	[16]
	Neck circumference	–	[6]
	Waist-to-height ratio	Waist circumference (cm)/height (cm)	[7]
	Body mass index	Body weight (kg)/height^2 (m)	[18]
	Body fat percentage	%body fat = (4.95/body density) − 4.50 × 100	[19, 20]
Fat distribution	Waist-to-hip ratio	Waist circumference (cm)/hip circumference (cm)	[17]
	Waist-to-thigh ratio	Waist circumference (cm)/thigh circumference (cm)	[8]
	Sagittal index	Sagittal abdominal diameter (cm)/thigh circumference (cm)	[28]

Body fat quantity

Parameters to evaluate central obesity are sagittal abdominal diameter [16], waist circumference (WC) [17], neck circumference [6], conicity index [5], and waist-to-height ratio (WHtR) [7]. The anatomical points to measure the anthropometric indices are showed in Figure 1. To assess generalized obesity, body mass index (BMI) [18] and body fat percentage [19, 20] are usually used.

Usually, the most used parameters in clinical practice are BMI and WC. BMI is a relatively simple index, which is calculated dividing body weight by height squared. WC is the measurement of abdominal perimeter, and according to the World Health Organization [17], it should be measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest (Fig. 1). However, this measurement may be obtained from other anatomic points, as at the top of the iliac crest, at the level of the umbilicus or navel, and at the point of the minimal waist [17].

Another index to assess general obesity is body fat percentage. This index can be estimated using a complex set of formulas, according to sex and age group and including body density as a variable [20]. Body density is obtained through the sum of four skinfold thickness: tricipital, bicipital, supra iliac, and subscapularis [19]. The equations of Weltman et al. [21, 22], which uses WC, body weight, and height, have been used to estimate body fat percentage in obese individuals in CKD patients. In CKD patients at stages 3–4, the estimated body fat percentage was associated with systemic inflammation.

Changes in BMI, body fat percentage, and WC were positively associated with changes in inflammatory markers in 1-year follow-up of stage 3 and 4 CKD patients [23].
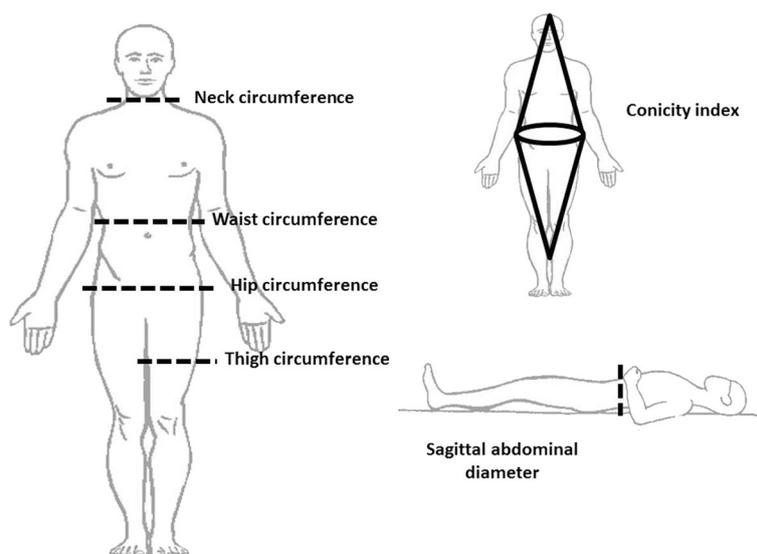

Fig. 1 Anatomical points to measure the anthropometric indices

WHtR is an indicator of central obesity which has the same cutoff for all populations. This indicator represents the ratio between WC and height, and it is based on the assumption that, for a given height, there is an acceptable degree of fat stored in the upper portion of the body [11]. A meta-analysis, which included data from more than 300,000 individuals from different ethnic groups, showed that WHtR was the best predictor of cardiometabolic risk compared to BMI and WC [13]. The use of WHtR is defended because it is simpler to measure and to calculate than BMI, and the use of the same reference value for men and women and for various ethnic groups is allowed. Maintaining the WC below the value corresponding to half the height represents a simple and effective message for entire population, in order to prevent metabolic syndrome [24].

It has become evident that assessment of visceral adiposity is important due to its role in the development of cardiometabolic disarrangements. Computed tomography and magnetic resonance are currently the recommended methods to directly assess visceral fat. However, their use on clinical practice is limited, as aforementioned. There are several anthropometrical indexes with the objective to evaluate abdominal fat, which have been associated with cardiovascular risk factors.

Conicity index is a simple estimate derived from easily available measures of height, weight, and waist circumference (Fig. 1). It is an estimate of abdominal fat deposition that models the relative accumulation of abdominal fat as the deviation of body shape from a cylindrical towards a double-cone shape (i.e., two cones with a common base at the waist level) [5]. Conicity index proved to be one of the most accurate in discrimination of the visceral obesity, especially in men. It detects the changes in fat distribution, allowing comparisons between individuals that had different measurements of body weight and height [9]. Studies have shown that this index is a good predictor of high coronary risk [25].

Conicity index has been assessed in many studies. Roriz et al. [26] showed that conicity index was one of the best anthropometric clinical indicators that had higher accuracy in visceral obesity discrimination using computed tomography measurement in an adult population as a gold standard. Pitanga and Lessa [25] showed this index is a good measurement to identify coronary risk, and Vidigal et al. demonstrated that conicity index has great ability to detect higher levels of inflammatory markers in adult men [27].

Sagittal abdominal diameter is the measurement of abdominal height, which can be assessed with the patient on supine position or standing (Fig. 1). When it is measured in the supine position, subcutaneous fat located in abdomen tends to displace sideways due to gravity. Therefore, abdominal height would correspond to visceral fat only [11]. Recently, Pajunen et al. [15] showed sagittal abdominal diameter and BMI are strong predictor of diabetes incidence, and Pimentel et al. [12] found positive association between sagittal abdominal diameter and serum triglycerides and glycaemia and negative association with HDL-c. In this study, WC was not associated with those risk factors.

Neck circumference is measured using a metric tape horizontally around the neck above the cricothyroid cartilage (Fig. 1). Laakso et al. [6] tested the association between neck circumference and abdominal and general obesity, and metabolic disarrangements related to insulin resistance. They conclude that neck circumference is related to all those factors and this measurement may be useful for subjects screening with increased risk for IR [6]. It is cheaper and easier to reproduce than WC, which may vary during the day [11].

Body fat distribution

To evaluate body fat distribution, the used indices are waist-to-hip ratio (WHR) [17], waist-to-thigh ratio [8], and sagittal index [28].

To assess body fat distribution, WHR may be used. This ratio is calculated dividing WC by hip circumference. WC and hip circumference reflect different aspects of body composition and exert independent and opposite effects in determining cardiovascular risk and its risk factors. Narrower waist and larger hip are associated with protection against cardiovascular disease. This relationship is explained by the following theory: narrower hips reflect reduced amount of muscle mass; on the other hand, larger hips have more muscle tissue [29]. However, the use of WHR as visceral fat predictor has been reduced due to its limitations. The interpretation of the independent effects of each circumference and the influence of the pelvic structure may be confused. Moreover, this ratio may not properly evaluate changes in visceral fat in the case of body weight variations [30]. WC might over- or under-evaluate central obesity prevalence for tall or short individuals with similar waist circumference, while WHR has a limitation in case of weight loss when both sizes decrease and the changes in ratio remain rather small [10].

WC and WHR measurements are recommended by the World Health Organization. Nevertheless, the differences in body composition of the several age and ethnical groups hamper the adoption of universal cutoffs [17].

Sagittal index and waist-to-thigh ratio are other indices used to evaluate fat distribution. However, these indices are less widespread and less used in clinical practice. Sagittal index was proposed as an alternative to WHR to estimate body fat distribution and morbidity prediction. It is represented by the ratio between sagittal abdominal diameter and mid-thigh perimeter. The principle is the

sagittal abdominal diameter and the mid-thigh perimeter measurements would be more representative of the tissue of interest, compared to WC and hip circumference, respectively [28]. Waist-to-thigh ratio presents principle similar to the sagittal index regarding the advantages of the use of thigh circumference replacing hip circumference. It is represented by the ratio between WC and thigh perimeter, which is measured in the midpoint between the inguinal fold and the proximal border of the patella [11].

Recently, Krakauer and Krakauer [14] developed a Body Shape Index based on WC that is approximately independent of height, weight, and BMI. It is a risk factor for premature mortality in the general population [14, 31].

Anthropometric indices and risk of chronic kidney disease

Abdominal obesity is widely thought to be an important predictor of the development of kidney disease [32]. Thomas et al. [33] performed a meta-analysis and showed that abdominal obesity assessed by WC had a positive association with the development of estimated glomerular filtration rate <60 ml/min/1.73 m^2 (nine studies; $n = 28,897$). Elsayed et al. [34] showed WHR but not BMI was associated with incident CKD and mortality among 13,324 individuals. WHR was also a predictor of cardiac events in stage 3 CKD patients, while increasing BMI was not associated with cardiac events [35]. BMI might not be an effective measurement to predict risk factors because it decreases with aging. Patients' mean age in Elsayed et al.'s study was 70.3 years. WHR did not decrease with increasing age, suggesting that it is a better marker of obesity in elderly population [36].

Noori et al. [37] compared the predictive power of BMI, WC, and WHtR in CKD development in a cohort of 3.107 adults followed up for 7 years. Largest WC values, in other words, more abdominal fat accumulation was independently and positively associated with risk of developing CKD. General obesity, assessed by BMI, was also associated with risk of developing CKD. However, this association was weaker than the association with WC, and waist-to-hip ratio was not significantly associated. Therefore, anthropometric measures of abdominal obesity seem to be better predictors of CKD development and cardiovascular risk than BMI.

WHtR, rather than BMI, was a predictor of CKD in a multicenter study which enrolled 41,600 Taiwanese subjects. CKD occurrence increased in both male and female by every 0.1 unit increase in WHtR [38]. Evans et al. [36] showed anthropometric measurements that include a measure of central fat distribution (WC, waist-to-hip ratio, WHtR, and conicity index) were significantly associated with more risk factors for CKD progression and CVD than increased BMI in stage 3 CKD patients .

Obesity prevalence is growing also among CKD subjects. Kramer et al. [39] analyzed data of 662,639 incident dialysis patients in the USA between 1995 and 2002 using US Renal Data System. They showed that mean BMI increased from 25.7 to 27.5 kg/m^2 among those patients. In the same period, obesity I prevalence risen 32% and obesity II and III risen 63%. However, the main limitation of BMI is that it is not able to distinguish fat and muscle, and body fat distribution. Moreover, BMI is influenced by volume overload, which is frequent in patients with CKD [40].

Anthropometric indices and cardiovascular risk

Nutritional status assessment in CKD is of paramount importance. While malnutrition has been associated with higher risk of poor outcomes in this population [41], overweight status improves the survival rates in these patients [42]. On the other hand, abdominal obesity is a source of inflammatory mediators, increasing the inflammatory profile of CKD patients [43, 44] which overlaps with malnutrition status and mortality risk. Circulating inflammatory mediators and free fatty acids released by adipose tissue, mainly by visceral fat, seems to be the key that associate obesity to insulin resistance. The dysregulation of inflammatory cytokine production in obese individuals leads to chronic low-grade inflammation status and may promote several metabolic disorders, which increase cardiovascular risk [1, 45]. Thus, body composition and body fat distribution evaluation are indispensable.

Cardiovascular disease is the main cause of mortality in CKD patients. A significant proportion of CKD patients on dialysis are not obese and present insulin resistance at the same time, indicating that insulin resistance in CKD does not exclusively depend on obesity [46]. Moreover, CKD patients have multiple metabolic abnormalities that may accelerate atherosclerosis, such as hypertension, dyslipidemia, and insulin resistance, as well as non-traditional risk factors associated to uremia and dialysis therapy [47].

Postorino et al. [48] followed a cohort of 537 end-stage renal disease patients (ESRD) and showed the relationship between waist circumference and the incidence rate of all-cause and CV mortality was closely dependent on BMI. The incidence rate of overall and CV death was maximal in patients with relatively lower BMI (less than median 24.8 kg/m^2) and higher waist circumferences (at least median 94 cm) and minimal in patients with higher BMI (at least median) and small waist circumferences (less than median). They suggest a redefinition of nutritional status by combining the metrics of abdominal obesity and BMI may refine prognosis in the ESRD population.

Recently, our group has published a study assessing the association of anthropometric indices with metabolic syndrome in maintenance hemodialysis patients [49].

Anthropometric indices evaluated were BMI, percent standard of triceps skinfold thickness and of middle-arm muscle circumference, WC, sagittal abdominal diameter, neck circumference, WHR, waist-to-thigh ratio, WHtR, sagittal and conicity indexes, and body fat percentage. Among the anthropometric indices, WHtR was the index that showed the best association with metabolic syndrome followed by WC and BMI. Besides BMI, those that characterize central obesity (WC, neck circumference, sagittal abdominal diameter, conicity index, and WHtR) showed the best association with metabolic syndrome. The cutoff of waist-to-height ratio that better predicts metabolic syndrome was 0.56, with a sensitivity of 73% and a specificity of 89%. Percent standard of middle-arm muscle circumference and sagittal index did not have significant association with metabolic syndrome.

Silva et al. [50] showed waist-to-height ratio was a good index to evaluate abdominal adiposity in non-dialyzed patients with CKD. It was better correlated with trunk fat evaluated by DXA compared with WC, waist-to-hip ratio, and conicity index. In addition, waist-to-height ratio predicts increased values of HOMA-IR.

Conicity index is another index which is associated with risk factors in CKD patients. In dialysis patients, Ruperto et al. [51] and Cordeiro [43] used conicity index as a measurement of central obesity and showed abdominal fat was directly linked to inflammation and protein energy wasting, which represent mortality risk factors.

In a relative small study with patients on hemodialysis, Afsar et al. [52] did not find association between body shape index and mortality, as well as BMI, WC, and waist-to-hip ratio. In this study, increased age, presence of diabetes, hemoglobin, and albumin were independently related with mortality.

Therefore, it is relevant to assess obesity in these patients using a feasible method for clinical practice. Furthermore, interventions aiming body composition changes or even shift on body fat distribution in CKD and ESRD are necessary.

Novel issues regarding body fat

Besides body fat distribution, the type of the adipose tissue is also significant. There are two main types of adipose tissue in our body, white adipose tissue (WAT) and brown adipose tissue (BAT) that may coexist throughout the adipose tissue sites [53].

BAT is found in less quantity than WAT. It is located along vessels (e.g., aorta, carotid, and coronary arteries), neck, supraclavicular region, axilla, abdominal wall, retroperitoneum, inguinal fossa, and muscle [53, 54]. BAT has an important thermogenic function due to the large mitochondria content. It is essential to dissipate energy through the regulation of thermogenesis in response to food intake and cold, sympathetic activation, and hormones released by the muscle [53]. Moreover, BAT activity is inversely associated with diabetes, BMI, and fasting glucose level in observational studies [55–57], and it seems to have a role in systemic lipid metabolism [58]. Therefore, perhaps lower quantity and activity of BAT exerts a role in the pathogenesis of metabolic syndrome and type 2 diabetes and BAT accumulation is protective [54]. The presence and quantity of metabolically activated BAT can be measured using imaging techniques, mainly 18 fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) [59].

To the best of our knowledge, there are no studies about BAT quantity or activity in CKD patients. It would be valuable to evaluate if there is any association of this type of fat with cardiometabolic risk factors and whether there is a protective role of BAT accumulation in this population.

An interesting and novel concept is sarcopenic obesity. It is defined as the co-occurrence of obesity and reduced muscle mass (sarcopenia). In other words, excess fatness is present and, at the same time, there is a misclassification by BMI cutoffs because BMI does not differentiate body composition (muscle mass and fat mass) [60]. Therefore, sarcopenic obesity may confuse the interpretation of data showing the protective effect of overweight on survival rates in CKD patients and ESRD patients [61].

Conclusions

Anthropometrics are feasible and cost-effective to evaluate fat quantity and distribution. Considerable advances in understanding the distribution of fat in different clinical situations has been interpreted in light of insulin resistance understanding. However, the validation of anthropometric indices is still needed for several clinical situations. Body fat distribution, more than the total amount of fat, is relevant to assess the risk of developing metabolic disorders associated with insulin resistance.

As BMI is inversely associated with mortality in CKD and dialysis patients, various other measures of central obesity and body fat distribution, such as WC, waist-to-hip ratio, WHtR, and conicity index, appear to be options to predict cardiovascular risk factors and mortality. Moreover, each index may reflect different aspects of fat mass, so it would help understanding patient's situation complementary. The role of visceral fat on CKD and ESRD should be highlighted, as well as practical, innocuous, effective, and low-cost methods to identify the subjects with high visceral adiposity and higher cardiovascular risk. The role of BAT activity in CKD and dialysis patients

has not been explored yet, and it would be an interesting topic to provide knowledge about cardiovascular risk and energy metabolism.

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