World Journal of
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Anthropometric indicators of visceral adiposity as predictors of non-alcoholic fatty liver disease: A review

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Abstract

The objective was to critically analyze studies that evaluated the predictive capacity of indicators of visceral adiposity in non-alcoholic fatty liver disease (NAFLD). The bibliographic research was carried out using the electronic database PubMed, LILACS and SciELO, references of selected articles. Although we found few studies, they have already used several indicators of visceral adiposity as waist circumference, waist-to-hip ratio, waist-to-height ratio, Lipid accumulation product, Body Shape Index, Body Roundness Index and most them were good predictors of NAFLD. Thus, the anthropometric indicators may contribute for the diagnosis of NAFLD in a simple, low-cost and non-invasive way, allowing early therapeutic measures to prevent the evolution to non-alcoholic steatohepatitis.

Key words: Anthropometry; Adiposity; Non-alcoholic fatty liver disease; Abdominal fat; Pediatrics; Predictive value

Core tip: Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide and presents evolutional potential for more severe forms of the disease such as cirrhosis and hepatocellular carcinoma. The most effective treatment is based on changes in lifestyle, diet and exercise; however, this presents the challenge of having to be performed for

a long time. The diagnosis, especially of non-alcoholic steatohepatitis (NASH), requires invasive examination such as liver biopsy. The anthropometric clinical indicators of visceral obesity, of easy applicability and low cost, have been very promising in the prediction of NAFLD. Thus, future studies could be conducted to use them in the prediction of NASH, besides assisting in the therapeutic and preventive conduction NASH.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a relevant metabolic disorder with a high evolutional potential, including from isolated hepatic steatosis to non-alcoholic steatohepatitis (NASH), and if left untreated, can progress to fibrosis, cirrhosis and even liver failure[1].

Excess weight, mainly the accumulation of visceral fat, is considered the main risk factor for NAFLD, being closely related to the severity of the disease[2-4]. Currently, clinical anthropometric indicators such as waist-to-height ratio (WHtR) and lipid accumulation product (LAP) are described in the literature as the most sensitive and specific for discriminating visceral fat compared to the classic parameters as waist circumference (WC) and body mass index (BMI)[5].

Some formulas recommended in the literature for NAFLD prediction already use anthropometric indicators such as BMI and WC[6,7]. However, there are few studies that have evaluated predictive capacity as well as the cutoff points of these new indicators in individuals with NAFLD[8-11]. This review aimed to critically analyze studies that assessed the ability of anthropometric indicators of adiposity to predict NAFLD.

LITERATURE SEARCH

To perform the search and retrieval of scientific articles, we used the PubMed (National Library of Medicine), Scielo (Scientific Eletronic Library Online) and LILACS (Literatura Latino-Americana e do Caribe em Ciências da Saúde) databases. The "OR" and "AND" connectors were used to combine the descriptors: ("non-alcoholic fatty liver disease" or "non-alcoholic steatohepatitis" or "fatty liver" or "NAFLD") and ("adult") and ("waist circumference" or "body mass index" or "waist-to-height ratio" or "conicity index" or "lipid accumulation product") and ("discriminatory performance" or "optimal cutoff points"). The articles of interest listed in the references have also been identified and reviewed.

Inclusion criteria were: the availability of the full text in the database; publication in the last ten years (Feb 2008-Feb 2018); written in Portuguese, English or Spanish. Exclusion criteria were: review studies, repeated studies in more than one database, research outside the previously determined context.

After analyzing the titles and abstracts, according to the eligibility criteria, the studies were selected for reading in full. One thousand eight hundred and sixty-three studies were found in the databases. After completing the selection of the studies based on the reading of the titles and abstracts, 1858 studies were excluded: 1845 did not meet the eligibility criteria; 1 duplicated, 1 Chinese, 1 cohort study; 1 evaluated individuals with hepatitis B and C virus, and 2 studies were included after the screening of the references.

Thus, eleven articles were included in the review. The main information of the studies as authorship and year of publication, where the study was conducted, the study population characteristics (number of individuals and age), anthropometric indicators evaluated BMI, WC, WHtR, LAP, Waist-To-Hip Ratio (WHR), Body Shape Index (ABSI), Body Roundness Index (BRI) and diagnosis criteria of NAFLD (Table 1).

CLINICAL ANTHROPOMETRIC INDICATORS OF VISCERAL ADIPOSITY

Classical anthropometric indicators, such as BMI and WC, are disseminated in clinical practice to assess nutritional status, since they are relatively simple and inexpensive tools[12,13]. Visceral obesity is the most important risk factor for NAFLD[2-4] and recent studies have been investigating the relevance of WC and other new clinical indicators of visceral adiposity (WHtR and LAP) in NAFLD diagnosis (Table 2).

In the studies selected here it is observed that different methods were used to identify hepatic steatosis: liver biopsy[9], computed tomography[14], proton magnetic resonance spectroscopy[8,15] being that the great majority realized abdominal ultrasonography[10,11,16-20].

Most of these methods such as ultrasonography, computed tomography and magnetic resonance imaging are important in the diagnosis of NAFLD, however these techniques cannot distinguish benign steatosis from steatohepatitis, severity of inflammation and grade and degree of fibrosis or stage of disease[21]. The liver biopsy, although not used in routine clinical practice remains the only available procedure to grade and to stage NAFLD and to exclude other causes of liver disease. It has been considered a gold standard method[22].

WAIST CIRCUMFERENCE

The WC is an anthropometric indicator widely used

Table 1 Studies evaluating the anthropometric indicators as predictors of non-alcoholic fatty liver disease

Ref.	Country	Population (*n*)	Age (yr)	Anthropometric indicator	NAFLD diagnosis
Yoo *et al*[14]	South Korea	NAFLD (77)	20-88	WC and WHtR	Tomography
		Non-NAFLD (379)			
Zheng *et al*[9]	China	NAFLD (250)	36.6 ± 11.1	WHR, BMI, WC and WHtR	Liver biopsy
		Non-NAFLD (240)	37.3 ± 10.2		
Ju *et al*[10]	South Korea	NAFLD (2553)	42.5 ± 5.1	BMI and WC	Ultrasonography
		Non-NAFLD (6606)	41.6 ± 4.9		
Cuthbertson *et al*[8]	England and	NAFLD (168)	50.3 ± 11.9	LAP	Proton magnetic resonance
	Germany	Non-NAFLD (168)	48.6 ± 10.9		spectroscopy
Monteiro *et al*[16]	Brazil	Obese with NAFLD (45)	11-17	WC	Ultrasonography
		Obese without NAFLD (100)			
Zhang *et al*[17]	China	NAFLD (362)	7-18	WHtR, BMI and WC	Ultrasonography
		Non-NAFLD (6867)			
Motamed *et al*[11]	Iran	NAFLD (2048)	48.6 ± 12.7	WHtR, WHR, ABSI, BRI	Ultrasonography
		Non-NAFLD (2824)	39.0 ± 15.4		
Özhan *et al*[18]	Turkey	Obese without NAFLD (130)	11.6 ± 2.7	WHtR	Ultrasonography
		Obese with NAFLD (202)	12.1 ± 2.6		
Lin *et al*[19]	Taiwan	NAFLD (167)	18.8 ± 1.9	WHtR, WHR	Ultrasonography
		Non-NAFLD (1043)	15.1 ± 2.8		
Lee *et al*[15]	United States	Black (94) and White (58)	14.7 ± 1.8	WC	Proton magnetic resonance
		overweight and obese adolescents	14.5 ± 1.5		spectroscopy
Dai *et al*[20]	China	NAFLD (12150)	18-94	LAP	Ultrasonography
		Non-NAFLD (28309)			

NAFLD: Non-alcoholic fatty liver disease; WHR: Waist-to-hip ratio; BMI: Body mass index; WC: Waist circumference; WHtR: Waist-to-height ratio; ABSI: Body shape index; BRI: Body roundness index; LAP: Lipid accumulation product.

in population studies and in clinical practice to assess central obesity, better reflecting the content of visceral fat, in addition to having a good relationship with total body fat[14,23]. However, it presents important limitations when used alone as a predictor of visceral fat[24].

WC and BMI indicators are widely used in the evaluation of individuals with NAFLD[2,8,25]. However, it is known BMI limitations in the evaluation of the composition and distribution of body fat, considering that this indicator only evaluates total body mass[26]. In most studies, the WC was assessed by WHO[26] (midpoint between the iliac crest and the last rib)[9,14,17]. Only Ju *et al*[10] performed the measurement of WC in the umbilical line. Yoo *et al*[14], in an observational cohort study, investigated the WC in 456 adults and elderly Koreans, with BMI of 26.5 ± 2.5 kg/m^2 in men NAFLD group and 27.3 ± 3.3 kg/m^2 in women NAFLD group and found a cutoff point of 89.0 cm for men and 84.0 cm for women, with sensitivity above 74%, in the prediction of NAFLD. Ju *et al*[10] investigated the WC in 9159 adults Koreans in a cross-sectional study with BMI of 22.4 ± 2.5 kg/m^2 in Non-NAFLD group and 25.6 ± 2.61 kg/m^2 in NAFLD group and identified with better levels of sensitivity and specificity, the WC cutoff of 84.9 cm for men and 80.4 cm for women. They observed that WC and BMI showed similar predictive capacity in both sexes, showing that there is still controversy about the best anthropometric parameter to predict NAFLD. In the study conducted by Zheng *et al*[9] in a cross-sectional study with 490 patients

Chinese, between 15-56 years, which included 96 patients with liver disease, 86 hepatitis, 19 hepatic hemangioma, and 39 autoimmune liver disease, with BMI 24.8 ± 10.1 kg/m^2 in Non-NAFLD group and 36.8 ± 10.1 kg/m^2 in NAFLD group, BMI and WC had AUC above 0.84 in the total sample.

In children, the WC AUC was 0.94, with the cutoff point at the 80th percentile for age, in the study by Zhang *et al*[17], a cross sectional study with 7229 students in China. Lee *et al*[15] evaluated white and black obese adolescents in the United States and found an optimal WC cutoff point for predicting NAFLD of 101.5 cm, AUC: 0.847, 93% sensitivity and 80% specificity in white obese women, and with no statistical difference between the values found between the blacks. The cross-sectional study by Monteiro *et al*[16], which evaluated 145 obese children and adolescents in Brazil, found higher WC (AUC: 0.720) when compared to trunk fat mass (AUC: 0.661), estimated by Dual-energy X-ray absorptiometry, however lower than the intra-abdominal adipose tissue (AUC: 0.741), measured by ultrasound examination. It should be noted that the authors did not present the cut-off points of the indicators. It is observed that most of these studies were developed in Asian populations[9,14,17], considering that WC cutoff points may differing between racial and ethnic groups more studies are needed for this identification.

WAIST-TO-HIP RATIO

The Waist-To-Hip Ratio (WHR) is determined by dividing

Table 2 Cut-offs and areas under the ROC curve, sensitivity and specificity of anthropometric indicators to determine non-alcoholic fatty liver disease

Ref.	Indicator	Total				Women				Men			
		AUC (95%CI)	Cut-offs point	Sens (%)	Spec (%)	AUC (95%CI)	Cut-offs point	Sens (%)	Spec (%)	AUC (95%CI)	Cut-offs point	Sens (%)	Spec (%)
Yoo et al[14]	WHtR					0.80 (0.74-0.86)	0.53	90	63	0.72 (0.63-0.81)	0.52	71	65
	WC					0.79 (0.73-0.86)	84	84	62	0.74 (0.65-0.83)	89	75	64
Zheng et al[9]	WHR	0.916 (0.86-0.97)	0.89	99	66								
	BMI	0.854 (0.78-0.93)	24.22	96	64								
	WC	0.876 (0.81-0.94)	82.5	95	68								
	WHtR	0.878 (0.82-0.94)	0.49	96	64								
Ju et al[10]	WC					0.821 (0.801-0.840)	80.395			0.759 (0.746-0.773)	84.945		
	BMI					0.83 (0.811-0.850)	22.715			0.76 (0.747-0.773)	24.465		
Cuthbertson et al[8]	LAP	0.78 (0.73-0.83)				0.77 (0.69-0.85)				0.74 (0.66-0.82)			
Monteiro et al[16]	WC	0.72 (0.636-0.804)		66.7	64			0.733	0.704			0.567	0.6
Zhang et al[17]	WHtR	0.95 (0.94-0.96)	0.47	85.2	92.5								
	WC	0.94 (0.92-0.95)	80[1]	86.2	87.4								
	BMI	0.93 (0.91-0.94)	80[1]	86.2	87.6								
Motamed et al[11]	WHtR	0.8566 (0.8419-0.8714)				0.8566 (0.8419-0.8714)	0.58	83.3	71.7	0.8457 (0.8320-0.8593)	0.533	82.7	70.8
	BRI	0.8566 (0.8419-0.8714)				0.8566 (0.8419-0.8714)	5	83.3	71.7	0.8457 (0.8320-0.8593)	4	82.7	70.8
	WHR	0.7673 (0.7487-0.7860)				0.7673 (0.7487-0.7860)				0.8018 (0.7862-0.8173)			
	ABSI	0.6598 (0.6382-0.6814)				0.6598 (0.6382-0.6814)				0.6539 (0.6351-0.6727)			
Özhan et al[18]	WHtR	0.80 (0.76-0.83)	0.62	48.4	73.8								
Lin et al[19]	WHtR	0.755 (0.714-0.795)	0.469	70.1	76.9								
	WHR												
†Lee et al[15]	WC	0.847	101.5	93	80								
Dai et al[20]	LAP					0.887 (0.882-0.892)	23	82	79	0.843 (0.837-0.849)	30.5	77	75

[1]Data shown for white obese adolescents only. AUC: Area under ROC curve; Sens: Sensitivity; Spec: Specificity; WHtR: Waist-to-height ratio; WC: Waist circumference; WHR: Waist-to-hip ratio; BMI: Body mass index; LAP: Lipid accumulation product; BRI: Body roundness index; ABSI: Body shape index.

the waist circumference by the circumference of the hip. This indicator is used to characterize how body fat is distributed, if it is concentrated in the central region or in body extremities. Sometimes the gain or loss of weight causes similar alterations in waist and hip circumferences, without altering the final ratio, so in these cases, WHR is not so useful to evaluate body mass changes[27].

Few studies have evaluated the WHR in predicting NAFLD. However, the WHR was the indicator with the highest predictive capacity (AUC: 0.91) for NAFLD in the study by Zheng et al[9], as a cutoff point of 0.89 for the total sample. Motamed et al[11], in a cross-sectional study with Iranian adults, reported an AUC above 0.70 of the WHR in both sexes to predict NAFLD, but cut points were not presented. Despite the limited amount of studies found in the literature that addressed the predictive capacity of WHR in NAFLD, the results found in both studies show that this indicator can be considered as a good predictor of NAFLD.

WAIST-TO-HEIGHT RATIO

The WHtR is an indicator of abdominal obesity that has been used in several studies to evaluate metabolic disorders[28-30]. The analysis of the WHtR suggests that a person WC should not exceed half the height value, presenting a better sensitivity in the evaluation of the health risk when compared to the measurement of isolated WC in different populations[31].

Yoo *et al*[14], Zheng *et al*[9] and Motamed *et al*[11] reported an AUC above 0.71 of the WHtR to detect NAFLD. Yoo *et al*[14] identified cutoff points of 0.53 (sens: sensitivity 90%, spec: specificity 63%) for women and 0.52 (sens: 71%, spec: 65%) for men. The cutoff points found in the study conducted by Motamed *et al*[11] with Iranians were similar for men 0.533 (sens: 82.7%, spec: 70.8%), but not for women which was 0.580 (sens: 83.3%, spec: 71.7%). Already Zheng *et al*[9] did not stratify the results by sex.

In children, the WHtR was the indicator that presented the highest AUC 0.95 and with cutoff points of 0.47 (sens: 95%, spec: 96%) in Zhang *et al*[17]. Lin *et al*[19] evaluated 1210 children aged 10-19 years in Taiwan and identified that WHtR had AUC higher than that of WHR. The cutoff point of WHtR to predict NAFLD in the study population was 0.499 (sens: 70.1%, spec: 76.9%). Özhan *et al*[18], evaluated 332 obese children with and without NAFLD, and the WHtR presented an optimal cutoff point for the prediction of NAFLD of 0.62, but with low sensitivity (48.5%) and high specificity (73.8%). In all this study WC was measured according to WHO[26].

In adults, the advantage of this indicator is related to the ability to neutralize the differences between the heights, allowing to individualize the interpretation of the fat concentration for different ages, since only a change in the value of the indicator occurs if the modification comes from the WC. In addition to be a low-cost indicator, it uses traditional and simple body measurements, and is a non-invasive method, being easily interpreted and reproducible[29,30].

LIPID ACCUMULATION PRODUCT

LAP is a proposed indicator for estimating lipid concentration in adults. Its formula includes data from WC and the serum concentration of triglycerides in the fasted state. The indicator proposes to investigate if the concentration of lipids exerts effect in the evaluation of the cardiovascular risks, better than the BMI[32].

Only two studies used LAP in the prediction of NAFLD[8,20]. Cuthbertson *et al*[8] evaluated 4 cohorts in Germany and England and although it has demonstrated an AUC of 0.78, the authors did not calculate cutoff points for NAFLD. Already a large cross-sectional study[20] that evaluated 40459 Chinese, the LAP showed high accuracy for diagnosing NAFLD in both men and women (AUC 0.843 and 0.887, respectively), with cutoff points of 30.5 (sens: 77%, spec: 75%) and 23.0 (sens: 82%, spec: 79%), respectively, and especially in the younger population between 18 and 44 years old.

Therefore, further studies are needed to confirm its usefulness in predicting this condition in other population groups since it is an excellent predictor of NAFLD in the Asian population. In addition, it is important to highlight a limitation in the clinical practice of this indicator, which requires application of complex formula and serum triglyceride values[33].

OTHER INDICATORS

Two new indicators of obesity, Ody Shape Index (ABSI) e Body Roundness Index (BRI) were described in literature. The ABSI was proposed by Krakauer *et al*[34] and it is calculated with the values of WC, BMI and height. Their analysis suggests that the ABSI allows to evaluate the excess risk of high WC. And Thomas *et al*[35] developed BRI to predict body fat and percentage of visceral adipose tissue, calculated with WC and height data.

Motamed *et al*[11] evaluated the ability of two new obesity indicators to predict NAFLD. In this study BRI and WHtR presented the same discriminatory power (AUC above 0.84) for NAFLD. However, ABSI was not a good indicator to predict NAFLD. Because BRI is an indicator of obesity that is still recent and little studied, the use in clinical practice to assess the discriminatory capacity of NAFLD deserves caution.

Of all the articles studied only one study, Ju *et al*[10], stratified the population in NAFLD and NASH. However, this study did not evaluate the predictive capacity of these indicators in NASH, only in NAFLD, besides NASH classification was evaluated by the presence of steatosis associated with elevation of alanine aminotransferase. Therefore, these studies that investigated the anthropometric indicators of visceral adiposity can only predict NAFLD. In addition, we can highlight in these studies the predictive capacity of the anthropometric clinical indicators for NAFLD that the main limitations were the different diagnostic methods used to detect NAFLD, the different ethnicities and different age groups, such as the inclusion of the elderly in some samples.

CONCLUSION

There are still few studies that evaluated anthropometric indicators of visceral obesity in the prediction of NAFLD, and these already have promising results. The identification of these indicators, with specific cutoff points considering the ethnic and racial groups, for use in the prediction of NAFLD, and especially NASH, may help in the early diagnosis, allowing a therapeutic and preventive approach to this population.

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