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Metabolic Dysfunction-Associated Steatotic Liver Disease: Is Body Mass Index the Most Relevant Measure for Evaluation?

Claudineia A de Souza[1], Raquel Rocha[2], Helma P Cotrim[1]*

[1]Graduate Program in Medicine and Health, Federal University of Bahia, Salvador (BA), Brazil.

[2]Sciences of Nutrition, Federal University of Bahia, Salvador (BA), Brazil.

***Correspondence to:** Helma Pinchemel Cotrim, Programa de Pós-Graduação em Medicina e Saúde, Complexo Universitário Prof. Edgar Santos- 5º. Andar , Rua Padre Feijó, S/N – Canela, Salvador – Bahia, Brasil. E-mail: helmacotrim@gmail.com.

Received: 10 August 2024 | **Approved**: 12 August 2024 | **Online**: 13 August 2024

ABSTRACT

Anthropometry has been used to assess health and nutrition status and is considered a simple, universally applicable, and low-cost method. The body mass index (BMI) is the anthropometric indicator most used in studies and clinical practice. However, there are limitations regarding its use. Thus, this review aimed to evaluate the use of BMI as a risk predictor for metabolic dysfunction-associated steatotic liver disease (MASLD). The selected articles were published in PubMed (National Library of Medicine) between July 2014 to July 2024, and we also included a manual search of reference articles in English. While BMI is commonly employed in diagnosing obesity, few studies have established it as an independent predictor for MASLD, the primary risk factor being. Assessing other anthropometric indicators as risk predictors for MASLD is significant because they effectively evaluate body fat distribution and muscle mass. The limitations of using only BMI in MASLD are evident, particularly in patients with eutrophic BMI, commonly referred to as thin, where body composition becomes crucial. Therefore, a deeper understanding of the role of

DOI: 10.20517/scierxiv202408.0409.v1 https://www.scierxiv.com/

anthropometric measurements is essential for assessing the risk and prognosis of MASLD development.

Keywords: body mass index, steatotic liver disease associated with metabolic dysfunction, MASLD, body composition.

INTRODUCTION

The body mass index (BMI) has been adopted by the World Health Organization (WHO) and is used universally to define individuals as underweight, normal weight, overweight and obese. However, this classification has its limitations. The diverse range of body morphologies and physical biotypes around the world presents a challenge for anthropometry, as attempts to impose a universal standard based on a reference population that does not fully represent the global population[1].

BMI has also been used in clinical practice for screening cardiometabolic diseases and metabolic dysfunction-associated steatotic liver disease (MASLD). While being overweight plays a significant role in the initial stages and progression of fatty liver disease, other factors such as fat distribution, adipose tissue functionality, and insulin resistance are crucial in the development of this metabolic disorder[2]. Therefore, understanding the role of excess weight in the pathophysiology and prognosis of MASLD necessitates identifying body indicators that more accurately predict obesity[3].

This scientific literature review aimed to evaluate the utility of BMI as a risk predictor for MASLD.

LITERATURE REVIEW

The PubMed database (National Library of Medicine) was used to search for scientific articles. The “OR” and “AND” connectors were combined with the descriptors “body mass index”, “anthropometry”, and “non-alcoholic fatty liver disease”. Articles of interest listed in the references through the manual search were also identified and examined.

Observational studies published in the last ten years (July 2014 to July 2024) were included in the database without language restriction and full-text availability. Review studies and

studies that did not meet the eligibility criteria were excluded.

After reading the title and abstract, the articles were selected for reading in full, and the main information, such as authors, year of publication, the place where the study was carried out, characteristics of the population, and anthropometric indicators were extracted for further analysis. A total of 129 articles were selected, of which six evaluated anthropometric parameters as a prognosis for MASLD.

Body Mass Index in the MASLD History

Despite the controversies in the natural history of hepatic steatosis, pathogenesis has been better understood throughout the 20th century. Ludwig et al., in 1980, based on a case series of predominantly female patients with obesity and diabetes, characterized steatohepatitis, which was then included in the MASLD spectrum in 1986[4,5].

Thus, obesity has always been a condition frequently associated with MASLD, with the prevalence described by several studies ranging from 30% to 100%, and with an increased risk of 4.6 for obese people who are those determined to have a BMI of at least 30 kg/m^2[6]. Based on the combination of several risk factors, both genetic and environmental, the physiopathogenesis of MASLD has been described, reinforcing the stigma of the relationship with excess weight[7].

Currently, obesity remains the most common and documented risk factor for MASLD, as it is a disease that affects about 20%-30% of the general population and presents an exponential growth parallel to the global obesity epidemic[8]. In a systematic review with meta-analysis, the prevalence of MASLD in the overweight population was 69.5% (95% CI 65.40-74.21 I^2 = 99.10%) and 75.3% (95% CI 70.90-79.18; I^2 = 98.50%) in the obese[9].

The dose-response relationship between MASLD and BMI has a 3.5 times greater risk of developing MASLD in obese patients, and this risk increases by approximately a 1.2 per unit increment in BMI[10].

Body Mass Index as a MASLD predictor

One of the main characteristics of patients with MASLD is high BMI, and increased BMI

DOI: 10.20517/scierxiv202408.0409.v1

appears to be a risk factor for liver fibrosis[11,12]. However, few studies have related BMI as an independent predictor for MASLD[13-15]. Studies conducted in China[13] (OR 8.494, 95% CI 5.58 to 12.92) and Asia[14] (OR 1.09, 95% CI: 0.98–1.23) found that the higher the BMI, the greater the risk of developing MASLD. In a study in Israel[15], the risk of MASLD was correlated with an increase in BMI. However, after multivariate analysis, this association was not maintained (OR: 2.2; 95% CI: 0.9 - 5, p=0.07) [Table 1].

DOI: 10.20517/scierxiv202408.0409.v1

Table 1. Anthropometric indicators as metabolic dysfunction-associated steatotic liver disease predictor

Author	Country/Year	N	Method used to assess body composition	Anthropometric indicators classification	MASLD diagnosis	Main results
Hu, et al	China, 2018	1,479	BMI	Obesity ≥ 28 kg/m²	Abdominal USG, exclusion of other liver diseases or liver biopsy and alcohol consumption, use of steatogenic drugs	BMI (OR 8.494, 95% CI 5.581- 12.928; P<0.001) independent MASLD predictor
Kim, et al	Ásia, 2014	2,307	BMI	Non-obese < 25 kg/m² Obese ≥ 25 kg/m²	Abdominal USG, exclusion of other liver diseases or liver biopsy and alcohol consumption, use of steatogenic drugs	MASLD prevalence: - Non-obese group: 22.4% - Obese group: 60.9% BMI was an independent MASLD risk factor (OR 1.09, CI 95% 0.98–1.23)
Zelber-Sagi, et al	Israel, 2006	352	BMI, WC, WHR	BMI Normal weight ≤ 25 kg/m²	Abdominal USG, exclusion of other liver diseases or liver	The chances of MASLD increased with increasing BMI.

				Overweight 25 ≤ 30 kg/m² Obesity ≥ 30 kg/m² WC (abdominal obesity) Women >88cm Men > 102 cm	biopsy and alcohol consumption, use of steatogenic drugs	For overweight (OR 3.3; CI 95% 1.6–6.8), obesity (OR 14.0; CI 95% 6.4–30.7), abdominal obesity (OR 5.5; CI 95% 3.3–9.1). Abdominal obesity was considered an independent risk factor for MASLD in the multivariate analysis (OR 2.9; 95% CI 1.3-6.4; p=0.007), while BMI did not show a statistically significant association (OR 2.2; 95% CI: 0.9-5, p=0.07).
Atri, et al	Índia, 2020	106	BMI, WC, WHR, WHtR	Overweight ≥ 23 kg/m² Obesity ≥ 25 kg/m²	Abdominal USG, exclusion of other liver diseases or liver biopsy and alcohol consumption, use of	WC (AUC 0.69, 95% CI 0.572–0.810, p=0.003) WHR (AUC 0.7, 95% CI 0.598–0.831, p=0.001) WHR (AUC 0.63, 95% CI

					steatogenic drugs	0.572–0.810, p=0.003) were better predictors as a screening tool for MASLD
Zeng, et al.	China, 2020	2,715	BMI, WC, WHR, WHtR	BMI Obesity > 25 kg/m² Overweight 23 - 25 kg/m² Lean < 23 kg/m² WC (normal) Women < 80 cm Men < 90 cm	Abdominal USG, exclusion of other liver diseases or liver biopsy and alcohol consumption	40.5% with MASLD Prevalence of MASLD: - 61.7% in the obese group - 39.1% in the overweight group - 21.4% in the lean group - 17.5% in the lean group with normal WC WHtR was associated with MASLD in lean patients with normal WC (OR: 4.275; 95% CI: 2.242-5.167; P = 0.003) and represents a risk factor for this population (OR: 3.934; 95% CI: 2.543-5.854; P = 0.004)

Almeida, et al	Brazil, 2021	107	BMI, WC, WHtR, C Index, LAP	Was not specified	Abdominal USG, exclusion of other liver diseases or liver biopsy and alcohol consumption, use of steatogenic drugs	MASLD individuals adopted higher values of BMI, WC, C index, LAP, and WHtR ($p<0.05$) when compared to those without the disease.

BMI: body mass index; CC: waist circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio; MASLD: non-alcoholic fatty liver disease; USG: ultrasonography; OR: odds ratio; FLI: fatty liver index; AUC: area under the curve; CI: conicity index, LAP: lipid accumulation product.

MASLD also develops in eutrophic patients, called lean patients, which has stimulated the need to understand the role of BMI in this liver disease since these individuals have normal BMI[1,16]. A systematic review with meta-analysis estimated a prevalence of 11.2% of eutrophic patients with MASLD in the general population. However, more than 50% of the included studies were in the Asian population[17].

As the highest prevalence of MASLD occurs in patients who are overweight and obese, tracking this disease in *lean* patients is a major challenge in clinical practice. A meta-analysis[18] that evaluated the risk factors for MASLD in 22 studies with lean patients (BMI <25 kg/m²) identified that lean MASLD patients had higher BMI (MD 1.40 kg/m², 95% CI 0.63–2.18) and waist circumference (WC) (MD 5.39 cm, CI 95% 4.58-6.20) that individuals without the disease. Meta-analyses have shown that MASLD in lean and non-lean individuals are anthropometrically different but metabolically similar[18,19].

Regarding the definition of thin patients with MASLD, a recent position of the American Gastroenterological Association (AGA) recommends that thin patients with MASLD should be considered those with BMI < 25 kg/m² for non-Asians and < 23 kg/m² for Asians, recognizing that different populations may present metabolic risk with a lower BMI[20].

However, this definition requires some considerations about the terminology used to classify BMI in the MASLD. A eutrophic person is different from a person with low weight (thinness), and the cutoff points considered for BMI in the MASLD encompass both groups, eutrophic and thin. Another point under discussion is that a eutrophic person can have a BMI close to the upper limit of normality but with an accumulation of visceral fat, which differs from a lower BMI. Thus, the most coherent would be to use the term *without excess weight* to encompass the entire cutoff point established by BMI, eutrophy, and thinness, thus reducing possible discrepancies in the interpretations of BMI classifications.

With these limitations, it is once again evident that interpreting BMI values defined only by the cutoff point can be misleading since BMI is an imperfect index of body adiposity[21]. Using other parameters to assess the body composition of these patients may be a more assertive alternative.

Differences in body composition in MASLD in both sexes

Body composition differs between men and women regarding muscle mass and fat distribution. Women generally have a lower muscle mass reserve and more body fat than men[22] (Karastergiou *et al.* 2012). Additionally, women tend to store fat in subcutaneous and femoral regions, whereas men store more fat in abdominal and visceral regions[23] (Lumish et al. 2020). Women undergo hormonal changes, particularly estrogen, which declines after menopause, promoting increased fat deposition in the visceral region[24] (Lovejoy *et al.* 2008).

This difference between genders is also reflected in the prevalence of MASLD, which is lower in women of reproductive age but starts to increase in postmenopausal women, approaching or even exceeding the prevalence of MASLD in men[25] (DiStefano et al. 2020).

When assessing body composition between men and women with MASLD, indicators such as WC, WHR, and WHtR gain prominence over the isolated use of BMI. WC demonstrated significantly better predictive performance for MASLD than BMI, suggesting that abdominal obesity might be a more accurate and important predictor for hepatic steatosis than excess weight measured by BMI[26] (Pang *et al.* 2023). Men tend to have higher fat-free mass and appendicular muscle mass, while premenopausal women have a higher percentage of body fat and visceral fat[27] (Cao *et al.* 2023). It is noteworthy that WHtR appears to be higher among women and is also a predictive indicator for MASLD[28,29] (Mansour-Ganaei *et al.* 2018; Arefhosseini *et al.* 2024) [Table 2].

Other studies have shown that, regardless of gender, the progression of MASLD is associated with a high percentage of fat, suggesting that the pathophysiology of MASLD may be more dependent on fat accumulation than on muscle mass loss[30] (Miyake *et al.* 2021). Conversely, individuals with a good muscle mass reserve and lower fat levels are at reduced risk for MASLD[31] (Xu *et al.* 2024).

Table 2. Difference between body composition and gender in individuals with metabolic dysfunction-associated steatotic liver disease predictor

Author	Country/year	*N*	Male	Female
Mansour-Ganaei, *et al.*	Irã, 2018	960 (M: 62.2% / F: 37.8%)	↓WC, WHR, WHtr when compared to females (p<0.001)	↑WC, WHR, WHtr, when compared to males (p<0.001)
Peng, *et al.*	EUA, 2023	809 (M: 47.43% / F: 52.57%)	TyG-WC: higher AUC (0.900, IC95%: 0.867 – 0.927)	TyG-WHtR: higher AUC (0.845, IC95%: 0.806 – 0.979)
Cao, *et al.*	China, 2023	880	TyG-WC: statistically different from WC and BMI (p<0.05)	TyG-WC: statistically different from WC (p<0.05)
Arefhosseini, *et al.*	Irã, 2024	238 (M: 62.2% / F: 37.8%)	↑WC, ↑ASMI, ↓FFM/FM: associated with the most severe degree of steatosis (p<0.001) There was no difference regarding BMI (p=1.000)	↑PBF, ↑VFA, ↑FM: associated with the most severe degree of steatosis (p<0.001) There was no difference regarding BMI (p=1.000)

	↑WC (p=0.001) e ↑ WHR (p<0.001)	↑BMI (p=0.015) e ↑WHtR (p<0.001)

M: male; F: female; WC: waist circumference; WHR: waist-to-hip ratio; WHtR: waist-to-height ratio; TyG: triglyceride and glucose index; AUC: area under the curve; BMI: body mass index; ASMI: fat free mass index; FFM/FM: ratio of fat-free mass and fat mass; PBF: visceral fat percentage; VFA: visceral fat area; FM: fat mass.

Limitations in using BMI as a Predictor for MASLD

Even though BMI is widely used to diagnose obesity, this application has been questioned. Weight represents the total body mass, so high weight means overweight and not necessarily obesity, which is considered a disease by the international classification of diseases (ICD E66). A parameter alone cannot diagnose a disease, and this also applies to the diagnosis of obesity. Therefore, not all patients above the BMI limit can be considered “sick”, and not all patients below this BMI are free from health problems. Even so, BMI is an important screening tool for cardiometabolic diseases, but it needs other anthropometric, biochemical, clinical, and imaging indicators to define the diagnosis of obesity[32].

In an attempt to expand the criteria for the diagnosis of obesity, the consensus of the Brazilian Society of Endocrinology and Metabolism (SBEM) and the Brazilian Society for the Study of Obesity and Metabolic Syndrome (ABESO), aimed at adults between 18 and 65 years old and BMI between 30 and 50 kg/m², considers the history of the maximum weight already achieved as an indicator for the diagnosis of obesity. Understanding what BMI represents in people's health is still challenging in clinical practice. There are limitations in different demographic, sociocultural, economic, and ethnic-racial contexts[33].

One of the limitations regarding using BMI is the recommended cutoff point. The National Institutes of Health (NIH) and WHO use BMI classifications for white, Hispanic, and black individuals. However, the cutoffs underestimate the risk of obesity in Asian and South Asian populations, so these populations adapted the cutpoints for their use[34].

Another limitation that must be considered is the use of BMI for the elderly population. Body composition is an aspect that changes with aging, and therefore the reference values for interpretation are not the same as those used for the adult population. When

DOI: 10.20517/scierxiv202408.0409.v1 https://www.scierxiv.com/

28 ≤ BMI < 30 Kg/m² indicates overweight according to the Pan American Health Organization (PAHO, 2003) or BMI ≥ 27 Kg/m² considering excess weight as proposed by the Nutrition Screening Initiative (NSI)[35,36,37]. It seems that a better state of health in the elderly is related to a higher range of BMI[38]. In the MASLD, elderly patients seem to have a lower BMI when compared to non-elderly patients, but the cutoff point for this population has not been defined[39].

Other Anthropometric Indicators at MASLD

WC is a relatively simple measure and provides information about the accumulation of abdominal fat, which cannot be identified only using BMI[40]. Patients with an accumulation of fat in the abdominal region, also called central or visceral adiposity, are at greater risk for cardiometabolic diseases, and MASLD is one of them[40-43].

Studies that evaluated the use of WC as a predictor for MASLD demonstrated that abdominal obesity is a risk factor and a prognostic indicator for MASLD [15,43,44] [Table 1]. Thus, BMI and WC have been recommended to assess risk factors and prognosis in these patients[45,46]. However, in patients with very high BMI, WC measurements are less useful to identify whether excess abdominal fat is due to abdominal, subcutaneous, or visceral fat, and the high inter-individual and intra-individual variability in measuring WC[46-48].

A recently published consensus on the use of WC in clinical practice noted that although the prevalence of obesity according to BMI has stabilized in some countries, the prevalence of abdominal obesity is increasing. This result demonstrates that it is necessary to be careful when assessing obesity considering only BMI, recommending the assessment of WC and BMI as risk indicators for cardiometabolic diseases[46].

Other anthropometric indicators have been studied as risk predictors for MASLD, among which stand out the waist-to-height ratio (WHR), waist-to-hip ratio (WHR), conicity index (C Index), and lipid accumulation product (LAP). All these

anthropometric indicators can be used as screening tools and predictors for MASLD[43,44]. In lean MASLD patients, WHtR was better associated with MASLD than WC[49] [Table 1].

However, although these anthropometric parameters, such as LAP and C-index, are effective, their use in clinical practice may be limited since serum triglyceride levels and complex formulas are required. On the other hand, the BMI, WC, and WHtR are easy to perform, being more applicable[49].

Another indicator that has been gaining prominence for the body assessment of MASLD individuals is muscle mass (MM) reserve. There seems to be a connection between the liver, adipose tissue, and muscle through the expression of insulin receptors, favoring protein catabolism, resulting in MM depletion and, consequently, sarcopenia, in which sarcopenic patients seem to present an approximately 1.5 times greater risk for MASLD[50].

In a study carried out with 56 MASLD individuals in Brazil, 62.5% of the patients had MM depletion, and BMI, WHtR, and WC values were higher in the group with MM depletion when compared to the group without depletion[51]. In another cross-sectional study with 157 Japanese MASLD patients, the authors observed that fibrosis in the MASLD was associated with a higher index of fat mass than of MM, with the results remaining significant after adjustments for possible confounding factors. It is essential to consider that the body composition of the Japanese differs between races, and it is impossible to generalize these results to other races[12].

Thus, it is important to consider that in addition to excess weight at the expense of body fat and visceral fat accumulation as predictors for MASLD, another indicator that should be highlighted is the depletion or low reserve of muscle mass[52,53]. Some studies have observed that MM depletion affects the severity of liver disease, with the

worsening of fibrosis regardless of obesity[54-56]. Therefore, increased skeletal muscle mass over time may be a protective factor for developing MASLD and help resolve the existing disease[57] [Figure 1].

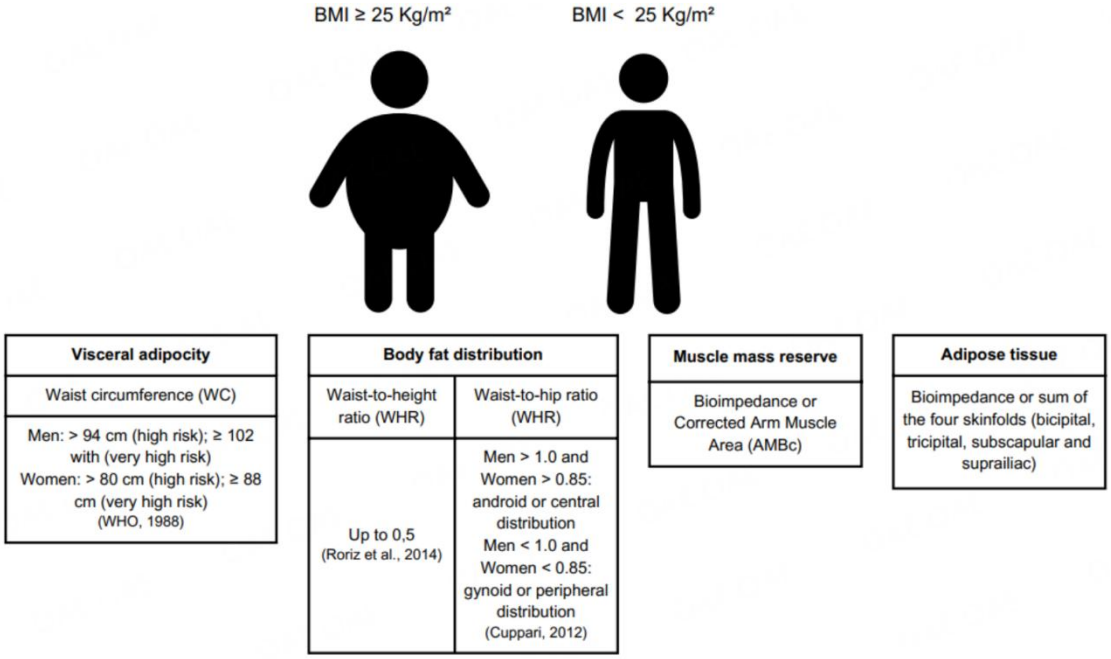

Figure 1. Other anthropometric markers as risk predictors for lMASLD.

CONCLUSION

Despite its widespread use in clinical practice, the BMI has several limitations, ranging from the cutoff points used and its application for diagnosing and prognosticating diseases. When used alone, BMI may not effectively screen for MASLD. Therefore, additional studies are needed to evaluate combined anthropometric indicators and their potential effectiveness as risk predictors for MASLD when associated with clinical indicators.

DECLARATIONS

Authors' contributions:

Writing original draft:de Souza CA

Paper revision and Supervision: Rocha R, P Cotrim H

Availability of data and materials

Not applicable.

Financial support and sponsorship

Not applicable.

Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

REFERENCE

1. WHO Expert Committee on Physical Status: the Use and Interpretation of Anthropometry (1993: Geneva, Switzerland) & World Health Organization. (1995). Physical status: the use of and interpretation of anthropometry, report of a WHO expert committee. World Health Organization. Available from https://iris.who.int/handle/10665/37003
2. Polyzos SA, Kountouras J, Mantzoros CS. Obesity and nonalcoholic fatty liver disease: From pathophysiology to therapeutics. *Metabolism* 2019;92:82-97.

[PMID: 30502373 DOI: 10.1016/j.metabol.2018.11.014]

3. Miyake T, Miyazaki M, Yoshida O, et al. Relationship between body composition and the histology of non-alcoholic fatty liver disease: a cross-sectional study. *BMC Gastroenterol* 2021;21:170. [PMID: 33849437 DOI: 10.1186/s12876-021-01748-y]
4. Ayonrinde OT. Historical narrative from fatty liver in the nineteenth century to contemporary NAFLD – Reconciling the present with the past. *JHEP Reports* 2021;*3*: 100261. [PMID: 34036255 DOI: 10.1016/j.jhepr.2021.100261]
5. Alomari M, Rashid MU, Chadalavada P, et al. Comparison between metabolic-associated fatty liver disease and nonalcoholic fatty liver disease: From nomenclature to clinical outcomes. *World J Hepatol* 2023;15:477-496. [PMID: 37206648 DOI: 10.4254/wjh.v15.i4.477]
6. Angulo P. Nonalcoholic fatty liver disease. *N Engl J Med* 2002;346:1221-21. [PMID: 11961152 DOI: 10.1056/NEJMra011775]
7. Cobbina E, Akhlaghi F. Non-Alcoholic Fatty Liver Disease (NAFLD) - Pathogenesis, Classification, and Effect on Drug Metabolizing Enzymes and Transporters. *Drug Metab Rev* 2017;42:197-221. [PMID: 28303724 DOI: 10.1080/03602532.2017.1293683]
8. Arab JP, Dirchwolf M, Álvares-da-Silva MR, et al. Latin American Association for the study of the liver (ALEH) practice guidance for the diagnosis and treatment of non-alcoholic fatty liver disease. *Ann Hepatol* 2020;19:674-90. [PMID: 33031970 DOI: 10.1016/j.aohep.2020.09.006]
9. Quek J, Chan KE, Wong ZY, et al. Global prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in the overweight and obese population: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2023;8:20-30. [PMID: 36400097 DOI: 10.1016/S2468-1253(22)00317-X]
10. Li L, Liu DW, Yan HY, et al. Obesity is an independent risk factor for non-alcoholic fatty liver disease: evidence from a meta-analysis of 21 cohort studies. *Obesity Comorbidity* 2016;17:510-9. [PMID: 27020692

DOI: 10.1111/obr.12407]

11. Sheng G, Lu S, Xie Q, Peng N, Kuang M, Zou Y. The usefulness of obesity and lipid-related indices to predict the presence of Nonalcoholic fatty liver disease. *Lipids in Health and Disease* 2021;20:134. [PMID: 34629059 DOI: 10.1186/s12944-021-01561-2]
12. Miyake T, Miyazaki M, Yoshida O, et al. Relationship between body composition and the histology of non-alcoholic fatty liver disease: a cross-sectional study. *BMC Gastroenterol* 2021;21(1):70. [PMID: 33849437 DOI: 10.1186/s12876-021-01748-y]
13. Hu XY, Li Y, Li LQ, et al. Risk factors and biomarkers of non-alcoholic fatty liver disease: an observational cross-sectional population survey. *BMJ Open* 2018;8(4):e019974. [PMID: 29626047 DOI: 10.1136/bmjopen-2017-019974]
14. Kim NH, Kim JH, Kim YJ, et al. Clinical and metabolic factors associated with development and regression of nonalcoholic fatty liver disease in nonobese subjects. *Liver International* 2014;34:604-11. [PMID: 24382309 DOI: 10.1111/liv.12454]
15. Zelber-Sagi S, Nitzan-Kaluski D, Halpern Z, Oren R. Prevalence of primary non-alcoholic fatty liver disease in a population-based study and its association with biochemical and anthropometric measures. *Liver International* 2006;26:856–63. [PMID: 16911469 DOI: 10.1111/j.1478-3231.2006.01311.x]
16. Chalasani N, Younossi Z, Lavine JE, et al. The Diagnosis and Management of Nonalcoholic Fatty Liver Disease: Practice Guidance From the American Association for the Study of Liver Diseases. *Gastroenterology* 2018;67:328-57. [PMID: 28714183 DOI: 10.1002/hep.29367]
17. Young S, Tariq R, Provenz J, et al. Singal Prevalence and Profile of Nonalcoholic Fatty Liver Disease in Lean Adults: Systematic Review and Meta-Analysis. *Hepatology Communications* 2020;4:953-72. [PMID: 32626829 DOI: 10.1002/hep4.1519]
18. Sookoian S, Pirola CJ. Systematic review with meta-analysis: risk factors for

non-alcoholic fatty liver disease suggest a shared altered metabolic and cardiovascular profile between lean and obese patients. *Aliment Pharmacol Ther* 2017;46:85–95. [PMID: 28464369 DOI: 10.1111/apt.14112]

19. Gnatiuc L, Alegre-Diaz J, Wade R, et al. General and Abdominal Adiposity and Mortality in Mexico City: A Prospective Study of 150 000 Adults. *Ann Intern Med* 2019;171:3. [PMID: 31404923 DOI: 10.7326/M18-3502]
20. Long MT, Noureddin M, Lim JK. AGA Clinical Practice Update: Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Lean Individuals: Expert Review. *Gastroenterology* 2022;163:764-74. [PMID: 35842345 DOI: 10.1053/j.gastro.2022.06.023]
21. Younes R, Bugianesi E. NASH in Lean Individuals. *Semin Liver Dis* 2019;39:86-95. [PMID: 30654392 DOI: 10.1055/s-0038-1677517]
22. Karastergiou K, Smith SR, Greenberg AS, et al. Sex differences in human adipose tissues - the biology of pear shape. *Biol Sex Differ* 2012;3:13. [PMID: 22651247 DOI: 10.1186/2042-6410-3-13]
23. Lumish HS, O'Reilly M, Reilly MP. Sex Differences in Genomic Drivers of Adipose Distribution and Related Cardiometabolic Disorders: Opportunities for Precision Medicine. *Arterioscler Thromb Vasc Biol* 2020;40(1):45-46. [PMID: 31747800 DOI: 10.1161/ATVBAHA.119.313154]
24. Lovejoy JC, Champagne CM, de Jonge L, et al. Increased visceral fat and decreased energy expenditure during the menopausal transition. *Int J Obes (Lond)* 2008;32:949–958. [PMID: 18332882 DOI:10.1038/ijo.2008.25]
25. DiStefano JK. NAFLD and NASH in Postmenopausal Women: Implications for Diagnosis and Treatment. *Endocrinology* 2020;161:bqaa134. [PMID: 32776116 DOI: 10.1210/endocr/bqaa134]
26. Peng H, Pan L, Ran S, et al. Prediction of MAFLD and NAFLD using different screening indexes: A cross-sectional study in U.S. adults. *Front Endocrinol (Lausanne)* 2023;14. [PMID: 36742412 DOI: 10.3389/fendo.2023.1083032]
27. Cao Y, Zhang W, Lou Y, et al. Sex- and reproductive status-specific relationships

between body composition and non-alcoholic fatty liver disease. *BMC Gastroenterology* 2023;(23):364. [PMID: 37875811 DOI: 10.1186/s12876-023-02997-9]

28. Mansour-Ghanaei R, Mansour-Ghanaei F, Naghipour M, et al. The role of anthropometric indices in the prediction of non-alcoholic fatty liver disease in the PERSIAN Guilan Cohort study (PGCS). *J Med Life* 2018;11:194-202. [PMID: 30364682 DOI: 10.25122/jml-2018-0031]
29. Arefosseini A, Aghajani T, Tutunchi H, et al. Association of systemic infammatory indices with anthropometric measures, metabolic factors, and liver function in non- alcoholic fatty liver disease. *Scientifc Reports* 2024;14:12829. [DOI: 10.1038/s41598-024-63381-5]
30. Miyake T, Miyazaki M, Yoshida O, et al. Relationship between body composition and the histology of non-alcoholic fatty liver disease: a cross-sectional study. *BMC Gastroenterol* 2021;21:170. [DOI: 10.1186/s12876-021-01748-y]
31. Xu G, Wu Y, Chen J, et al. The relationship between muscle mass and fat content in body composition and non-alcoholic fatty liver disease in the Chinese general population: a cross-sectional study. *Frontiers in Medicine* 2024;11:1384366. [DOI: 10.3389/fmed.2024.1384366]
32. Sharma AM, Campbell-Scherer DL. Redefning obesity: Beyond the numbers. *Obesity (Silver Spring)* 2017;25:660-1. [PMID: 28349662 DOI: 10.1002/oby.21801]
33. Halpern B, Marcini MC, Melo ME, et al. Proposal of an obesity classification based on weight history: an official document by the Brazilian Society of Endocrinology and Metabolism (SBEM) and the Brazilian Society for the Study of Obesity and Metabolic Syndrome (ABESO). *Arch Endocrinol Metab* 2022;66:139-51. [PMID: 35420271 DOI: 10.20945/2359-3997000000465]
34. BMI Classification Percentile And Cut Off Points. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541070/ [Last accessed on 02 June 2024].

35. Duarte ACG. Nutritional assessment, clinical and laboratory aspects. 1ª ed. Atheneu: São Paulo, 2007.
36. ORGANIZACIÓN PANAMERICANA DE LA SALUD. Salud Bienestar y Envejecimiento (Sabe) En América Latina Y El Caribe. Available from: https://www1.paho.org/Spanish/HDP/HDR/CAIS-01-05.PDF [Last accessed on 02 June 2024].
37. Lipschitz DA. Screening for nutritional status in the elderly. *Prim Care* 1994;21(1):55-67. [PMID: 8197257]
38. Childers DK, Allison DB. The 'Obesity Paradox:' a parsimonious explanation for relations among obesity, mortality rate, and aging? *Int J Obes (Lond)* 2010;34:1231–1238. [PMID: 20440298 DOI: 10.1038/ijo.2010.71]
39. Noureddin M, Yates KP, Vaughn IA, et al. Clinical and histological determinants of nonalcoholic steatohepatitis and advanced fibrosis in elderly patients. *Hepatology* 2013;58:1644-1654. [PMID: 23686698 DOI: 10.1002/hep.26465]
40. Janssen I, Katzmarzyk PT, Ross R. Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 2004;79:379-84. [PMID: 14985210 DOI: 10.1093/ajcn/79.3.379]
41. Simpson JA, MacInnis RJ, Peeters A, Hopper, J.L.; Giles, G.G.; English, D.R. A comparison of adiposity measures as predictors of all-cause mortality: the Melbourne Collaborative Cohort Study. *Obesity (Silver Spring)* 2007;15:994-1003. [PMID: 17426335 DOI: 10.1038/oby.2007.622]
42. Tsai AG, Wadden TA. In the clinic: obesity. *Ann Intern Med* 2013;159:ITC 3-1-ITC 3-15. [PMID: 24026335 DOI: 10.7326/0003-4819-159-5-201309030-01003]
43. Atri A, Jiwanmall SA, Nandyal MB, et al. The Prevalence and Predictors of Non-alcoholic Fatty Liver Disease in Morbidly Obese Women – A Cross-sectional Study from Southern India. *Eur Endocrinol* 2020;16:152-5. [PMID: 33117448 DOI: 10.17925/EE.2020.16.2.152]
44. Almeida NS, Rocha R, Daltro C, et al. Anthropometric clinical indicators of visceral adiposity as predictors of nonalcoholic fatty liver disease. *Rev Assoc Med*

Bras 2021;67:1544-9. [PMID: 34909876 DOI: 10.1590/1806-9282.20210316]

45. Rocha R, Cotrim HP, Carvalho FM, et al. Body mass index and waist circumference in non-alcoholic fatty liver disease. *J Hum Nutr Dietet* 2005;18:365-70. [PMID: 16150132 DOI: 10.1111/j.1365-277X.2005.00634.x]
46. Ross R, Neeland IJ, Yamashita S, et al. Waist circumference as a vital sign in clinical practice: a Consensus Statement from the IAS and ICCR Working Group on Visceral Obesity. *Nat Rev Endocrinol* 2020;16:177-89. [PMID: 32020062 DOI: 10.1038/s41574-019-0310-7]
47. Ardern CI, Janssen I, Ross R, Katzmarzyk PT. Development of health-related waist circumference thresholds within BMI categories. *Obes Res* 2004;12:1094-103. [PMID: 15292473 DOI: 10.1038/oby.2004.137]
48. Mason C, Katzmarzyk PT. Variability in waist circumference measurements according to anatomic measurement site. *Obesity (Silver Spring)* 2009;17:1789-95. [PMID: 19343017 DOI: 10.1038/oby.2009.87]
49. Zeng J, Yan, R-X, Sun C, et al. Prevalence, clinical characteristics, risk factors, and indicators for lean Chinese adults with nonalcoholic fatty liver disease. *World J Gastroenterol* 2020;26:1792-1804. [PMID: 32351294 DOI: 10.3748/wjg.v26.i15.1792]
50. Wijarnpreecha K, Panjawatanan P, Thongprayoon C, Jaruvongvanich V, Ungprasert P. Sarcopenia and risk of nonalcoholic fatty liver disease: A meta-analysis. *Saudita J Gastroenterol* 2018;24:12-17. [PMID: 29451179 DOI: 10.4103/sjg.SJG_237_17]
51. Barreto IS, Santos RO, Rocha R, et al. Muscle mass and cellular membrane integrity assessment in patients with nonalcoholic fatty liver disease. *Rev Assoc Med Bras* 2021;67:1233-1239. [PMID: 34816913 DOI: 10.1590/1806-9282.20201016]
52. Cai C, Song X, Chen Y, Chen X, Yu C. Relationship between relative skeletal muscle mass and nonalcoholic fatty liver disease: a systematic review and meta-analysis. *Hepatol Int* 2020;14:115-126. [PMID: 31290072

DOI: 10.1007/s12072-019-09964-1]

53. Kang MK, Park JG, Lee HJ, Kim MC. Association of low skeletal muscle mass with advanced liver fibrosis in patients with non-alcoholic fatty liver disease. *Hepatology* 2019;34:1633-40. [PMID: 30667551 DOI: 10.1111/jgh.14607]
54. Petta S, Ciminnisi S, Di Marco V, et al. Sarcopenia is associated with severe liver fibrosis in patients with non-alcoholic fatty liver disease. *Aliment Pharmacol Ther* 2017;45:510-8. [PMID: 28028821 DOI: 10.1111/apt.13889]
55. Hsieh YC, Joo SK, Koo BK, Lin HC, Kim W. Muscle alterations are independently associated with significant fibrosis in patients with nonalcoholic fatty liver disease. *Liver Int* 2021;41:494-504. [PMID: 33164304 DOI: 10.1111/liv.14719]
56. Koo BK, Kim D, Joo SK, et al. Sarcopenia is an independent risk factor for non-alcoholic steatohepatitis and significant fibrosis. *J Hepatol* 2017;66:123-31. [PMID: 27599824 DOI: 10.1016/j.jhep.2016.08.019]
57. Gyuri K, Seung-Eun L, You-Bin L, et al. Relationship Between Relative Skeletal Muscle Mass and Nonalcoholic Fatty Liver Disease: A 7-Year Longitudinal Study. *Hepatology* 2018;68:1755-68. [PMID: 29679374 DOI: 10.1002/hep.30049]