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METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE - ASSESSMENT OF PATIENTS WITH OBESITY AND METABOLIC SYNDROME - GUIDELINE FROM THE BRAZILIAN SOCIETY OF BARIATRIC AND METABOLIC SURGERY

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Position Paper

METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE - ASSESSMENT OF PATIENTS WITH OBESITY AND METABOLIC SYNDROME - GUIDELINE FROM THE BRAZILIAN SOCIETY OF BARIATRIC AND METABOLIC SURGERY

Doença Hepática Esteatótica Associada à Disfunção Metabólica - Avaliação de pacientes portadores de obesidade e síndrome metabólica - Guideline da Sociedade Brasileira de Cirurgia Bariátrica e Metabólica

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RESUMO

Introdução: A Doença Hepática Esteatótica Associada à Disfunção Metabólica (MASLD) é a doença hepática crônica mais prevalente no mundo e foi recentemente renomeada para enfatizar seu componente metabólico. Este artigo busca preencher a lacuna de diretrizes específicas para pacientes portadores de obesidade e MASLD que irão ser submetidos à cirurgia bariátrica.

Método: Foi realizado uma busca sistemática por guidelines nas plataformas PubMed e Embase.

Resultados: Foram encontrados 544 artigos, dos quais 11 foram selecionados conforme critérios de inclusão/exclusão. Todos os 11 *guidelines* são de

sociedades clínicas, portanto, não contemplam algumas interpretações necessárias para o paciente bariátrico.

Conclusões: Recomendamos que seja feito o rastreio de todo paciente que será submetido a cirurgia bariátrica e metabólica inicialmente com o score Fibrosis-4 (FIB-4), seguido da elastografia hepática transitória *(Vibration-controlled Transient Elastography - VCTE)*, principalmente para aqueles com FIB4> 1,3. No entanto, a interpretação dos resultados do VCTE em pacientes obesos necessita de mais estudos para delimitar os reais valores de cortes. O *Enhanced Liver Fibrosis*® (ELF®) mostra-se promissor, mas sua disponibilidade é limitada. A indicação da biópsia hepática durante a cirurgia, precisa ser individualizada, porém é recomendada para aqueles com alteração do FIB4 e/ou da VCTE. O rastreio familiar é recomendado para parentes de pacientes jovens já com fibrose avançada. O transplante hepático é uma opção para pacientes com MASLD avançada, mas o momento ideal para a cirurgia bariátrica em relação ao transplante ainda não está claro. O acompanhamento regular e o exame VCTE são recomendados para monitorar a progressão da doença após a cirurgia.

DESCRITORES: Cirurgia Bariátrica. Fígado Gorduroso. Síndrome Metabólica. Obesidade.

ABSTRACT

Introduction: Metabolic Dysfunction Associated Steatotic Liver Disease (MASLD) is the most prevalent chronic liver disease in the world and has recently been renamed to emphasize its metabolic component. This article seeks to fill the gap in specific guidelines for patients with obesity and MASLD who will undergo bariatric surgery. **Methods:** A systematic search for guidelines was carried out on the PubMed and Embase platforms.

Results: Were found 544 articles, of which 11 were selected according to inclusion/exclusion criteria. All 11 guidelines are from clinical societies and therefore do not include some necessary interpretations for bariatric patients.

Conclusions: We recommend that every patient undergoing bariatric and metabolic surgery be screened initially with the Fibrosis-4 (FIB-4) score, followed by transient hepatic elastography (Vibration-controlled Transient Elastography - VCTE), especially for those with FIB4 > 1.3. However, the interpretation of VCTE

results in obese patients requires further studies to define the real cutoff values. Enhanced Liver Fibrosis® (ELF®) shows promise, but its availability is limited. The indication for liver biopsy during surgery needs to be individualized but is recommended for those with changes in FIB4 and/or VCTE. Family screening is recommended for relatives of young patients with advanced fibrosis. Liver transplantation is an option for patients with advanced MASLD, but the optimal timing for bariatric surgery in relation to transplantation is still unclear. Regular follow-up and VCTE examination are recommended to monitor disease progression after surgery.

KEYWORDS: Bariatric Surgery. Fatty Liver. Metabolic Syndrome. Obesity.

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Central message

The significant increase in the prevalence of obesity in recent decades has been accompanied in recent years by advanced liver disease, including advanced fibrosis, cirrhosis, liver cancer, and an increase in the number of transplants due to MASLD (Metabolic Dysfunction Associated Steatotic Disease), considered the most common chronic liver disease in the world. Scientific evidence indicates that bariatric and metabolic surgery is the primary and best treatment for MASLD in patients with obesity, showing improvement in steatosis and progressive regression of fibrosis in the long term, likely associated with weight loss. To date, there are no studies or guidelines specifically focused on the population of obese patients who will undergo bariatric and metabolic surgery.

Perspectives

Currently, screening for MASLD in patients with obesity and metabolic syndrome in the preoperative phase of bariatric and metabolic surgery should be conducted according to available resources. The FIB-4 index is a simple and easily accessible screening tool and should therefore be the first approach; however, it should not be used for patient follow-up. VCTE is a useful tool for a second evaluation after FIB-4, but more studies are needed to better define the cutoff points for the obese population. Although the ELF® test is a highly accurate method for screening and follow-up, it is not yet widely available in most centers. Bariatric and metabolic surgery should always be considered in the treatment plan for MASLD in patients with a BMI >35. Liver biopsy remains the gold standard for diagnosis and should be strongly recommended during surgery when there is uncertainty about the stage of fibrosis during screening. Patients with signs of advanced disease need to halt the bariatric surgery process and be evaluated by a hepatologist.

INTRODUCTION

Metabolic Dysfunction Associated Steatotic Disease (MASLD) has an estimated global prevalence of 38.7%, making it the most common chronic liver disease worldwide [6]. Its prevalence is estimated at 69.9% in the overweight population and 75.3% in the obese population [25]. The significant increase in the prevalence of obesity in recent decades has been accompanied by advanced liver disease, including advanced fibrosis, cirrhosis, liver cancer, and an increase in the number of transplants due to MASLD[14,15].

In 2023, a multi-society consensus was published, conducted by the American Association for the Study of Liver Diseases (AASLD) and the European Association for the Study of the Liver (EASL), in collaboration with the Asociación Latinoamericana para el Estudio del Hígado (ALEH), which introduced the new nomenclature: replacing the term Non-Alcoholic Fatty Liver Disease (NAFLD) with MASLD [13,26]. According to the opinion of the majority of specialists consulted at the meeting, the use of the term "metabolic" instead of "fatty" and "non-alcoholic" would help healthcare professionals better explain and understand the disease and avoid stigmatizing terms. Thus, patients diagnosed with hepatic

steatosis, who present any evidence of metabolic dysfunction, are diagnosed with MASLD, provided there are no other identifiable origins for chronic liver disease [28].

The important progress in addressing this disease will enable bariatric surgeons and hepatologists to identify, even in the preoperative phase of bariatric and metabolic surgery (BMS), patients at high risk of advanced liver disease and plan the best approach (technique and the need for liver biopsy for better staging of the disease) [31]. There is scientific evidence that bariatric and metabolic surgery is the primary and best treatment for MASLD in patients with obesity, showing improvement in steatosis and progressive regression of fibrosis in the long term, likely associated with weight loss [20,33].

However, it is worth noting that all recently published studies and guidelines were based on population studies (including obese and non-obese individuals) focused on patients with chronic liver disease who will not necessarily undergo bariatric surgery [26]. To date, there are no studies or guidelines specifically focused on the population of obese patients who will undergo BMS. Considering this scenario, the Brazilian Society of Bariatric and Metabolic Surgery discusses some important care points and proposes a guideline to assist the bariatric surgeon in approaching obese patients with a potential risk for associated MASLD.

METHODS

A systematic search for guidelines was conducted in the PubMed and Embase databases that included analyses and/or recommendations directed at the obese population. There were no restrictions regarding publication date or language. The search terms used were: "("Non-alcoholic Fatty Liver Disease"[Mesh] OR "metabolic dysfunction fatty liver disease" OR "MAFLD" OR "metabolic dysfunction associated steatotic liver disease" OR "MASLD") AND ("Obesity, Abdominal"[Mesh] OR "Obesity"[Mesh] OR "Abdominal obesity metabolic syndrome" [Supplementary Concept] OR "Metabolic Syndrome"[Mesh] OR "Body Mass Index"[Mesh]) AND ("Guideline Adherence"[Mesh] OR "Guideline" [Publication Type] OR "Guidelines as Topic"[Mesh] OR "guideline"[All

Fields])" in the PubMed tool and ('nonalcoholic fatty liver'/exp OR 'nonalcoholic fatty liver' OR MASLD OR 'metabolic dysfunction associated steatotic liver disease'/exp OR 'metabolic dysfunction associated steatotic liver disease') AND ('abdominal obesity'/exp OR 'abdominal obesity' OR 'morbid obesity'/exp OR 'morbid obesity' OR 'metabolic syndrome x'/exp OR 'metabolic syndrome x' OR 'body mass'/exp OR 'body mass') AND ('protocol compliance' or 'practice guideline') in the Embase tool.

We searched for studies on screening, diagnosis, treatment, or follow-up for MASLD aimed at the obese population. Exclusions included: studies that were not guidelines; guideline review articles; publications not from associations or scientific societies; studies restricted to the pediatric population; studies restricted to underweight or malnourished populations; guidelines for liver diseases other than MASLD.

RESULTS

A total of 544 articles were identified in the described database. After applying the inclusion and exclusion criteria, eleven guidelines remained for discussion (Figure 1). Three of the articles are from American societies; two from Brazilian societies; two from Italian societies; one from a British society; two from grouped European societies; and one from Asian and Pacific societies. Six are publications from the last five years, and none are from surgical societies.

DISCUSSION

MASLD is closely associated with obesity and metabolic syndrome. Bariatric and metabolic surgery (BMS) is proven to be the best treatment for the disease in the medium and long term. Clinicians, gastroenterologists, hepatologists, and bariatric surgeons should consider screening for MASLD in all patients with obesity and/or metabolic syndrome, particularly those preparing for BMS. However, the literature lacks a guideline for the diagnostic approach, management, treatment (surgical), and follow-up exclusively for this population.

Recommendation for screening all adults with obesity and/or metabolic syndrome for the risk of advanced fibrosis associated with MASLD using the Fibrosis-4 (FIB-4) index.

As suggested by the majority of societies, due to ease, cost, and practicality, fibrosis screening should begin with the calculation of the FIB-4 score [29]. The index is calculated by the mathematical formula that divides the product of age and AST by the product of platelet count and the square root of ALT. Various websites, platforms, and some laboratories already offer the calculation automatically. The score has an AUROC of 0.801 for detecting advanced fibrosis in people with obesity [24]. The AACE [9] also highlights that the FIB-4 can stratify future morbidity and mortality from liver disease. Most guidelines, although not exclusively designed for obese individuals, consider values up to 1.3 as excluding advanced fibrosis. With this cutoff, there is a sensitivity of 84.4% and a specificity of 68.5% in the general population for identifying advanced fibrosis [30]. For patients with values greater than 2.67, it is understood that they are at high risk of advanced fibrosis and thus require more in-depth investigation. The AISF [17] uses a combination of FIB-4 and NFS for screening, with the latter having a cutoff value of 0.1455. We strongly suggest that all patients with obesity and/or metabolic syndrome with a FIB-4 greater than 1.3 continue screening for active hepatic fibrosis via another non-invasive method. For patients with values above 2.67, we recommend referral and evaluation by a hepatologist for appropriate staging (CHILD and MELD) and follow-up.

Recommendation for Vibration-Controlled Transient Elastography (VCTE)

Vibration-controlled transient elastography (VCTE) is the most validated non-invasive technology for liver fibrosis stratification according to current guidelines [1]. The risk classification for advanced fibrosis in nearly all guidelines is based on the following values: low-risk group VCTE < 8.0 kPa; indeterminate risk group VCTE = 8.0 to 12 kPa; and high-risk group those with VCTE > 12.0 kPa. However, it is important to note that there is still no consensus regarding these cutoff points in patients with obesity. In clinical practice, some

discrepancies have been observed between VCTE readings and histopathological findings from biopsies performed during bariatric surgery. One possible hypothesis is that cirrhotic livers resulting from, for example, viral hepatitis are rigid. In contrast, cirrhotic livers associated with MASLD may be less hard due to the presence of some degree of fat accumulation, which could lead to misleading VCTE readings, as VCTE primarily measures liver stiffness. Thus, the cutoff values might be higher in patients with obesity. More validation studies correlating biopsies and VCTE in the obese population are needed to confirm the best cutoff points for fibrosis stratification in this population.

Magnetic resonance elastography could be an alternative for those obese patients in whom VCTE with the XL probe is not feasible. Alongside VCTE, the Controlled Attenuation Parameter (CAP score) can be measured using elastography equipment. As defined by AISF [17], this test is a good non-invasive tool, particularly for post-treatment steatosis follow-up. However, EASL, EASD, and EASO [12] highlight the limitation in discriminating histological grades of steatosis by CAP. A meta-analysis cited by ABESO, SBH, and SBEM [21] indicated from 61 studies that the AUROC of CAP in the obese population is 0.88 for the diagnosis of steatosis ≥ S1 [4]. We therefore recommend that CAP be considered whenever there is doubt in the diagnosis of steatosis, given that the CAP score can be measured alongside VCTE. We consider CAP a useful tool for monitoring the improvement or even resolution of steatosis after bariatric and metabolic surgery.

The initial screening by the ABESO, SBH, and SBEM [21] guidelines should be conducted through an imaging method (USG, VCTE, or MRI). This can be understood as a protocol for the general population with overweight, initially seeking hepatic steatosis, where the prevalence is lower compared to the obese population. We recommend that all patients with obesity and/or metabolic syndrome with an altered FIB-4 be evaluated with VCTE if possible, as most patients with obesity already have some degree of steatosis and a smaller proportion already have fibrosis. For patients already screened and with FIB-4 greater than 1.3, evaluation with VCTE should be recommended. If the VCTE reading is above 8 kPa, referral for evaluation by a hepatologist should always

be considered. Centers without VCTE may use other serum scores for fibrosis stratification or other ultrasound elastography equipment. If no imaging test is possible, a biopsy during bariatric surgery should be considered if the FIB-4 is above 1.3.

Recommendation for the Use of Enhanced Liver Fibrosis® (ELF®) for Diagnosis of Liver Fibrosis

This non-invasive test for the evaluation of liver fibrosis derives from the combination of plasma levels of three matrix renewal proteins. The ELF® test has an AUROC of 0.90 for detecting advanced fibrosis in the general population [2]. NICE [22] refers to ELF® as having the best cost-effectiveness ratio in identifying patients with advanced stages of fibrosis in the general population. The guidelines from AACE [9] and ABESO, SBH, and SBEM [21] position the test as an alternative to VCTE in fibrosis stratification. A meta-analysis of 16 studies showed that ELF® values above 7.70 had a negative predictive value of 0.99 for identifying advanced fibrosis [32]. AACE [9] classifies the following groups for the risk of advanced fibrosis: low-risk group when ELF® < 7.7; indeterminate risk group for ELF® between 7.7 and 9.8; and high-risk group those with ELF® > 9.8. According to NICE's protocol [22], screening starts with ELF®, and they consider higher cutoff values: for advanced fibrosis, they consider a value > 10.51. Interestingly, the guideline does not include any imaging tests for follow-up, thus considering ELF® as the sole diagnostic method due to its sufficient sensitivity for diagnosing advanced fibrosis. We understand that ELF® may not yet be a reality in all centers, and therefore, despite its accuracy, it should be reserved as an alternative or as a confirmation of a positive VCTE result [18].

Recommendation for Liver Biopsy

All guidelines agree that liver biopsy is the gold standard for diagnosing MASLD. However, considering that it is an invasive procedure, subject to interpretation errors, and difficult to apply to the entire obese population,

percutaneous biopsy is not routinely recommended for diagnosis or as a screening method. We understand that since our patients are in the preoperative phase for BMS, the biopsy, when indicated, should be performed during the surgical procedure. AASLD [5,27] recommends biopsy in patients with suspected MASLD associated with consistently elevated serum ferritin levels or increased iron saturation. In its most recent guideline, biopsy should be considered when there is diagnostic uncertainty, such as may occur with discordant or indeterminate results from non-invasive tests [27]. AACE [9] suggests routine biopsy during bariatric surgery due to the possibility of identifying other liver diseases. We believe that indiscriminate liver biopsy for all patients undergoing bariatric surgery is not appropriate, as the extremely high volume of surgeries performed worldwide each year would result in an increased absolute number of patients with complications such as bleeding, hematoma, bilioma, biliary fistula, etc., despite the low complication rate of liver biopsy [35]. We recommend that patients with FIB-4 and/or VCTE and/or ELF® values suggestive of advanced fibrosis should undergo liver biopsy during bariatric surgery. If VCTE or ELF® cannot be performed, we also recommend biopsy during bariatric surgery, especially for FIB-4 values > 2.67 or in patients whose liver appears suspicious macroscopically.

Recommendation for Family Screening (First-Degree Relatives) in Patients with Obesity and Metabolic Syndrome with Advanced Fibrosis

AASLD [27] notes that differences in the presentation of MASLD can also be explained by different ethnicities and are associated with variations in the gene encoding patatin-like phospholipase domain-containing protein 3 (PNPLA-3) [11]. However, routine clinical practice currently does not recommend testing for PNPLA-3 variants, even though their association with advanced fibrosis in MASLD patients has been proven. Additionally, the guideline highlights that certain genetic polymorphisms, such as PNPLA-3, are also associated with a higher susceptibility to hepatocellular carcinoma (HCC). AISF [17] suggests that high-impact prospective studies should investigate the use of genetic risk profiles

in reference centers for individual risk stratification of MASLD-HCC, as well as for stratifying the risk of progression and sub-phenotyping of MASLD.

Despite the genetic variability of the disease, there is sufficient evidence to support family screening for first-degree relatives, especially for individuals with obesity and metabolic syndrome at high risk of advanced fibrosis: FIB-4 > 2.67; VCTE > 8 KPa; ELF® > 9.8. The active search for relatives at risk for the severe form of the disease is justified mainly as an important public health measure that can prevent the progression of patients with incipient MASLD to cirrhosis, HCC, and liver transplantation. Young patients with advanced liver disease should also have their families investigated due to the higher risk of disease progression. This measure is also justified by the lower positive predictive value of FIB-4 in this age group. In the future, determining the PNPLA-3 genotype may become a useful tool for risk stratification of relatives, allowing for earlier intervention. Currently, access to PNPLA-3 testing is not a reality in most of the hepatology or bariatric and metabolic surgery centers. However, in the future, this could have an impact on disease screening with the aim of earlier diagnosis.

Recommendation for Surgical Treatment of MASLD

Bariatric and metabolic surgery is an effective treatment for the remission of MASLD and liver fibrosis in the medium and long term, as well as for optimizing cardiometabolic health in patients with obesity and metabolic syndrome [33,35]. APASL [8,34] emphasizes careful patient selection for bariatric surgery, highlighting its potential to improve MASLD histology and reduce long-term mortality, especially in patients with class II obesity. AASLD [5] and AISF [17] caution about the possibility of increased morbidity and mortality in patients with decompensated cirrhosis, although some studies have shown good outcomes for BMS in cirrhotic patients. All guidelines recommend an individualized approach for patients with obesity and metabolic syndrome undergoing BMS.

According to a meta-analysis cited by ABESO, SBH, and SBEM [21], both vertical sleeve gastrectomy and Roux-en-Y gastric bypass are similarly effective in controlling MASLD [10]. It is worth noting that patients with advanced liver disease may need a liver transplant in the future [7]. Therefore, we consider vertical

sleeve gastrectomy the most appropriate technique, as it maintains intestinal transit, removes the gastric fundus (a site with variceal risks), does not leave blind loops, and functions as an azygo-portal disconnection, contributing to reduced portal flow and porto-mesenteric system hypertension.

MASLD, Bariatric Surgery, and Liver Transplantation

MASLD is already one of the leading causes of liver transplantation worldwide [3]. ABESO, SBH, and SBEM [18] highlight that the presence of liver fibrosis is directly related to disease progression, hepatic decompensation, and mortality or the need for liver transplantation. Any patient with FIB > 2.67, VCTE > 20 kPa, and/or ELF® > 9.8 should be evaluated by a hepatologist and the transplant team before undergoing BMS. Cases where patients require both BMS and liver transplantation are becoming increasingly common [7]. However, there is still no evidence for the optimal timing of BMS: before, during, or after transplantation. This decision requires further investigation in the coming years. Published studies on this subject are currently case reports or case series with small samples [4]. Most articles describe BMS after transplantation, likely because patients are advised to seek bariatric surgery centers for weight loss to avoid graft wear. Chieric et al.[34] showed in their meta-analysis that simultaneous procedures have low morbidity and mortality, while BMS after transplantation presents increased morbidity. However, performing BMS before liver transplantation is a viable option that can improve the clinical liver function of patients awaiting transplantation. It is important to note that many centers do not perform liver transplantation in patients with BMI > 30, so BMS before transplantation may be the only chance for these patients.

Follow-Up After Biopsy Results

Most guidelines emphasize the importance of follow-up and monitoring with a specialist in patients with MASLD, especially those with advanced fibrosis and at risk of cirrhosis and hepatocellular carcinoma (HCC). ABESO, SBH, and SBEM [18] and EASL [13,16] suggest performing blood tests and VCTE every 3 years for patients with F0, F1, and F2 fibrosis; and every 6 months for patients with F3 and F4 fibrosis. NICE [10] recommends the use of ELF® for regular monitoring and

detection of advanced liver disease in high-risk patients. FIB-4 should not be used for follow-up, as age interferes with its absolute value, increasing the number of false positives. Percutaneous biopsy for follow-up after BMS can be considered for those patients with advanced fibrosis at the time of diagnosis or for patients with worsening VCTE and/or ELF® values. After ruling out the possibility of associated HCC, surveillance needs to be continued with a specialist, as suggested by AASLD [19].

CONCLUSIONS

Screening for MASLD in patients with obesity and metabolic syndrome in the preoperative phase of bariatric and metabolic surgery should be conducted according to available resources. However, the FIB-4 index is a simple and easily accessible screening tool and should be the first approach in all bariatric patients before surgery; but, it should not be used for patient follow-up. VCTE is a useful tool for a second evaluation after FIB-4, but more studies are needed to better define the cutoff points for the obese population. Family screening and counseling can have a significant impact on the natural history of the disease and should be performed in patients with advanced disease, particularly in the children of relatives with advanced liver disease. Although the ELF® test is highly accurate for screening and monitoring, it is not yet widely available in most centers. Bariatric and metabolic surgery should always be considered in the treatment plan for MASLD in patients with a BMI >35. Liver biopsy remains the gold standard for diagnosis and should be strongly recommended during surgery when there is uncertainty about the stage of fibrosis during screening. Patients with signs of advanced disease need to halt the bariatric surgery process and be evaluated by a hepatologist. In cases where liver transplantation is indicated, bariatric and metabolic surgery should not be immediately dismissed but rather discussed to determine the best approach for each patient and each specific center.

REFERENCES

1. Altamirano J, Qi Q, Choudhry S, Abdallah M, Singal AK, Humar A, et al. Non-invasive diagnosis: non-alcoholic fatty liver disease and alcoholic liver disease. Transl Gastroenterol Hepatol. 2020;5:31. doi: 10.21037/tgh.2019.11.14.

2. Angulo P, Hui JM, Marchesini G, Bugianesi E, George J, Farrell GC, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. Hepatology. 2007;45(4):846-54. doi: 10.1002/hep.21496.

3. Association for the Study of the Liver (AISF), the Italian Society of Diabetology (SID) and the Italian Society of Obesity (SIO). Eat Weight Disord. 2022;27(5):1603-1619. doi: 10.1007/s40519-021-01287-1.

4. Cao YT, Xiang LL, Qi F, Zhang YJ, Chen Y, Zhou XQ. Accuracy of controlled attenuation parameter (CAP) and liver stiffness measurement (LSM) for assessing steatosis and fibrosis in non-alcoholic fatty liver disease: A systematic review and meta-analysis. EClinicalMedicine. 2022;51:101547. doi: 10.1016/j.eclinm.2022.101547.

5. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2018;67(1):328-357. doi: 10.1002/hep.29367.

6. Chan KE, Koh TJL, Tang ASP, Quek J, Yong JN, Tay P, et al. Global Prevalence and Clinical Characteristics of Metabolic-associated Fatty Liver Disease: A Meta-Analysis and Systematic Review of 10 739 607 Individuals.

J Clin Endocrinol Metab. 2022;107(9):2691-2700. doi: 10.1210/clinem/dgac321.

7. Chierici A, Alromayan M, De Fatico S, Drai C, Vinci D, Anty R, et al. Is bariatric surgery safer before, during, or after liver transplantation? A systematic review and meta-analysis, Journal of Liver Transplantation 2023;9;100139. https://doi.org/10.1016/j.liver.2023.100139.

8. Chitturi S, Wong VW, Chan WK, Wong GL, Wong SK, Sollano J, et al. The Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 2: Management and special groups. J Gastroenterol Hepatol. 2018;33(1):86-98. doi: 10.1111/jgh.13856.

9. Cusi K, Isaacs S, Barb D, Basu R, Caprio S, Garvey WT, et al. American Association of Clinical Endocrinology Clinical Practice Guideline for the Diagnosis and Management of Nonalcoholic Fatty Liver Disease in Primary Care and Endocrinology Clinical Settings: Co-Sponsored by the American Association for the Study of Liver Diseases (AASLD). Endocr Pract. 2022;28(5):528-562. doi: 10.1016/j.eprac.2022.03.010.

10. de Brito E Silva MB, Tustumi F, de Miranda Neto AA, Dantas ACB, Santo MA, Cecconello I. Gastric Bypass Compared with Sleeve Gastrectomy for Nonalcoholic Fatty Liver Disease: a Systematic Review and Meta-analysis. Obes Surg. 2021;31(6):2762-2772. doi: 10.1007/s11695-021-05412-y.

11. Dongiovanni P, Anstee QM, Valenti L. Genetic predisposition in NAFLD and NASH: impact on severity of liver disease and response to treatment. Curr Pharm Des. 2013;19(29):5219-38. doi: 10.2174/13816128113199990381.

12. European Association for the Study of the Liver (EASL); European Association for the Study of Diabetes (EASD); European Association for the Study of Obesity (EASO). EASL-EASD-EASO Clinical Practice Guidelines for the management of non-alcoholic fatty liver disease. Diabetologia. 2016;59(6):1121-40. doi: 10.1007/s00125-016-3902-y.

13. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; Clinical Practice Guideline Panel; Chair:; EASL Governing Board representative:; Panel members:. EASL Clinical Practice

Guidelines on non-invasive tests for evaluation of liver disease severity and prognosis - 2021 update. J Hepatol. 2021;75(3):659-689. doi: 10.1016/j.jhep.2021.05.025.

14. Eslam M, El-Serag HB, Francque S, Sarin SK, Wei L, Bugianesi E, et al. Metabolic (dysfunction)-associated fatty liver disease in individuals of normal weight. Nat Rev Gastroenterol Hepatol. 2022;19(10):638-651. doi: 10.1038/s41575-022-00635-5.

15. Fernandes ESM, de Mello FPT, Pimentel LS, Andrade RO, Girão C, César C, et al. Combined liver transplantation with sleeve gastrectomy: a pioneer case series from Brazil. Updates Surg. 2022;74(1):81-86. doi: 10.1007/s13304-021-01230-0.

16. Godoy-Matos AF, Valério CM, Silva Júnior WS, de Araujo-Neto JM, Bertoluci MC. 2024 UPDATE: the Brazilian Diabetes Society position on the management of metabolic dysfunction-associated steatotic liver disease (MASLD) in people with prediabetes or type 2 diabetes. Diabetol Metab Syndr. 2024;16(1):23. doi: 10.1186/s13098-024-01259-2.

17. Italian Association for the Study of the Liver (AISF). AISF position paper on nonalcoholic fatty liver disease (NAFLD): Updates and future directions. Dig Liver Dis. 2017;49(5):471-483. doi: 10.1016/j.dld.2017.01.147.

18. Karlas T, Dietrich A, Peter V, Wittekind C, Lichtinghagen R, Garnov N, et al. Evaluation of Transient Elastography, Acoustic Radiation Force Impulse Imaging (ARFI), and Enhanced Liver Function (ELF) Score for Detection of Fibrosis in Morbidly Obese Patients. PLoS One. 2015;10(11):e0141649. doi: 10.1371/journal.pone.0141649.

19. Khaitan L, Shea BJ. Laparoscopic vertical sleeve gastrectomy, long and short-term impact on weight loss and associated co-morbidities. Ann Transl Med. 2020;8(Suppl 1):S5. doi: 10.21037/atm.2020.01.89.

20. Lassailly G, Caiazzo R, Ntandja-Wandji LC, Gnemmi V, Baud G, Verkindt H, et al. Bariatric Surgery Provides Long-term Resolution of Nonalcoholic Steatohepatitis and Regression of Fibrosis. Gastroenterology. 2020;159(4):1290-1301.e5. doi: 10.1053/j.gastro.2020.06.006.

21. Moreira RO, Valerio CM, Villela-Nogueira CA, Cercato C, Gerchman F, Lottenberg AMP, et al. Brazilian evidence-based guideline for screening, diagnosis, treatment, and follow-up of metabolic dysfunction-associated steatotic liver disease (MASLD) in adult individuals with overweight or obesity: A joint position statement from the Brazilian Society of Endocrinology and Metabolism (SBEM), Brazilian Society of Hepatology (SBH), and Brazilian Association for the Study of Obesity and Metabolic Syndrome (Abeso). Arch Endocrinol Metab. 2023;67(6):e230123. doi: 10.20945/2359-4292-2023-0123.

22. National Guideline Centre (UK). Non-Alcoholic Fatty Liver Disease: Assessment and Management. London: National Institute for Health and Care Excellence (NICE); 2016 Jul. PMID: 27441333.

23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. doi: 10.1136/bmj.n71.

24. Park H, Yoon EL, Kim M, Lee J, Kim JH, Cho S, et al. Comparison of diagnostic performance between FIB-4 and NFS in metabolic-associated fatty liver disease era. Hepatol Res. 2022;52(3):247-254. doi: 10.1111/hepr.13737.

25. Quek J, Chan KE, Wong ZY, Tan C, Tan B, Lim WH, 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(1):20-30. doi: 10.1016/S2468-1253(22)00317-X.

26. Rinella ME, Lazarus JV, Ratziu V, Francque SM, Sanyal AJ, Kanwal F, et al. A multi-society Delphi consensus statement on new fatty liver disease nomenclature. Hepatology, 2023;78(6):1966-1986. doi: 10.1097/HEP.0000000000000520

27. Rinella ME, Neuschwander-Tetri BA, Siddiqui MS, Abdelmalek MF, Caldwell S, Barb D, et al. AASLD Practice Guidance on the clinical assessment and management of nonalcoholic fatty liver disease. Hepatology. 2023;77(5):1797-1835. doi: 10.1097/HEP.0000000000000323.

28. Silva MBBE, Tustumi F, Dantas ACB, Miranda BCJ, Pajecki D, DE-Cleva R, Santo MA, Nahas SC. Obesity and severe steatosis: the importance of biochemical exams and scores. Arq Bras Cir Dig. 2022;34(4):e1626. doi: 10.1590/0102-6720202210002e1626.

29. Sterling RK, Lissen E, Clumeck N, Sola R, Correa MC, Montaner J, et al. Development of a simple noninvasive index to predict significant fibrosis in patients with HIV/HCV coinfection. Hepatology. 2006;43(6):1317-25. doi: 10.1002/hep.21178.

30. Sun W, Cui H, Li N, Wei Y, Lai S, Yang Y, et al. Comparison of FIB-4 index, NAFLD fibrosis score and BARD score for prediction of advanced fibrosis in adult patients with non-alcoholic fatty liver disease: A meta-analysis study. Hepatol Res. 2016;46(9):862-70. doi: 10.1111/hepr.12647.

31. Valezi AC, Campos ACL, Bahten LCV. Brazilian multi-society position statement on emerging bariatric and metabolic surgical procedures. Arq Bras Cir Dig. 2023;36:e1759. doi: 10.1590/0102-672020230041e1759.

32. Vali Y, Lee J, Boursier J, Spijker R, Löffler J, Verheij J, et al. Enhanced liver fibrosis test for the non-invasive diagnosis of fibrosis in patients with NAFLD: A systematic review and meta-analysis. J Hepatol. 2020;73(2):252-262. doi: 10.1016/j.jhep.2020.03.036.

33. Verrastro O, Panunzi S, Castagneto-Gissey L, De Gaetano A, Lembo E, Capristo E, et al. Bariatric-metabolic surgery versus lifestyle intervention plus best medical care in non-alcoholic steatohepatitis (BRAVES): a multicentre, open-label, randomised trial. Lancet. 2023;401(10390):1786-1797. doi: 10.1016/S0140-6736(23)00634-7.

34. Wong VW, Chan WK, Chitturi S, Chawla Y, Dan YY, Duseja A, et al. Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 1: Definition, risk factors and assessment. J Gastroenterol Hepatol. 2018;33(1):70-85. doi: 10.1111/jgh.13857.

35. Zhou F, Stueck A, McLeod M. Liver biopsy complication rates in patients with non-alcoholic fatty liver disease. Can Liver J. 2022;5(2):106-112. doi: 10.3138/canlivj-2021-0019.

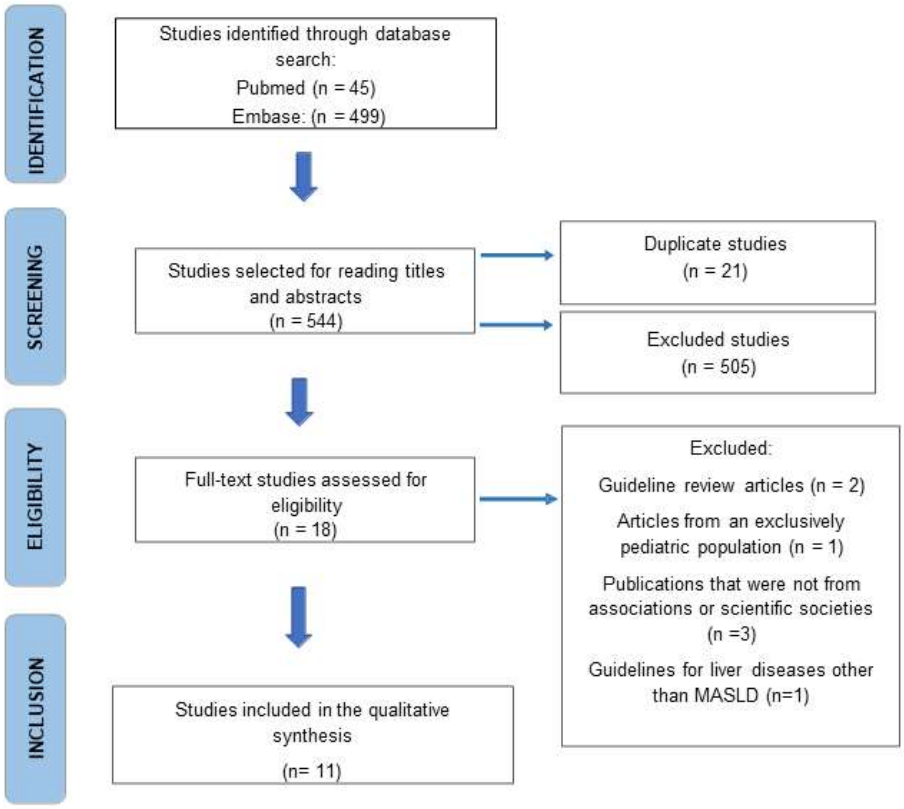

Figure 1. Adapted Prisma Flowchart [23]

Table 1. Included Articles

GUIDELINES	YEAR
European Association for the Study of the Liver - (EASL), European Association for the Study of Diabetes - (EASD) and European Association for the Study of Obesity - (EASO) [12]	2016
National Institute for Health and Care Excellence – (NICE) [22]	2016
Italian Association for the Study of the Liver (AISF) [17]	2017
Asia–Pacific Working Party on Non-alcoholic Fatty Liver Disease (APASL) [8,34]	2017
Association for the Study of Liver Diseases - (AASLD) [5]	2018
Italian Association for the Study of the Liver - (AISF), Italian Society of Diabetology - (SID) and Italian Society of Obesity - (SIO) [3]	2021
EASL clinical practice guidelines: non-invasive liver tests for evaluation of liver disease severity and prognosis [13]	2021
American Association of Clinical Endocrinology - (AACE) [9]	2022
Brazilian Society of Endocrinology and Metabolism - (SBEM), Brazilian Society of Hepatology - (SBH), and Brazilian Association for the Study of Obesity and Metabolic Syndrome - (Abeso) [21]	2023
Association for the Study of Liver Diseases - (AASLD) [27]	2023
Brazilian Diabetes Society – (BDS) [16]	2024

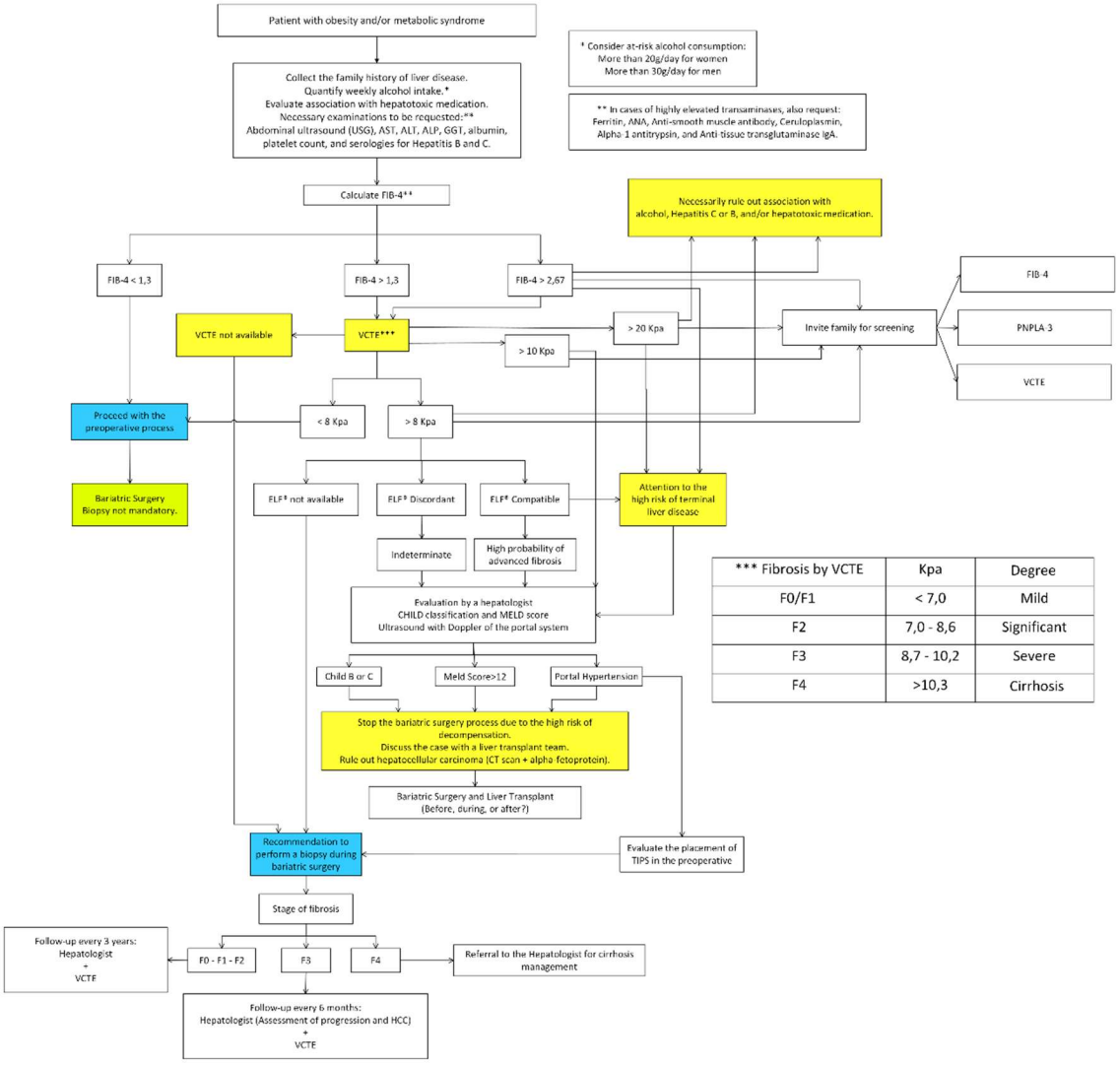

Figure 2. Flowchart for Patients with Obesity and Metabolic Syndrome Undergoing Bariatric and Metabolic Surgery. (F**IB-4=Fibrosis 4; VCTE=Vibration Controlled Transient Elastography; ELF=Enhanced Liver Fibrosis; PNPLA-3=patatin-like phospholipase domain-containing protein 3; CHILD=classificação de Child Pugh; MELD=Model for End-stage Liver Disease)**

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