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Review Article

Steatotic Liver Disease: Review of Diagnosis and Treatment of Sarcopenia

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ABSTRACT

Despite being a prevalent disease, Steatotic Liver Disease (SLD) is not as well recognized by clinicians as other metabolic diseases. The high prevalence of SLD and the associated high morbidity and mortality require an early diagnosis of the disease because of its potential evolution to malignancy.

Sarcopenia is present in 22%-62% of patients with cirrhosis. Given the overlapping pathophysiology between SLD and sarcopenia, it is difficult to determine whether sarcopenia is a genuine pathogenic factor in the development of SLD or a complication of it. Diagnostic methods have been developed to assess muscle mass in patients with SLD, but neither are they standardized nor is there a definite pharmacological therapy for treating sarcopenia or cachexia at the clinical level.

Nutritional assessment should be a fundamental part of the initial approach to the patient with SLD and their subsequent follow-up.

Keywords: Steatotic Liver Disease (SLD); Non-alcoholic steatohepatitis; Fibrosis; Sarcopenia; Muscle; Muscle mass

Abbreviations: SLD: Steatotic Liver Disease; NASH: Non-Alcoholic Steatohepatitis; DM: Diabetes Mellitus; BMI: Body Mass Index; HCC: Hepato-Cellular Carcinoma; GH: Growth Hormone; IGF-1: Insulin-like Growth Factor-1; FFA: Free Fatty Acids; MRE: Magnetic Resonance Elastography; CT: Computed Tomography; SMI: Skeletal Muscle Index; PMI: Psoas Muscle Index, BIA: Bioelectrical Impedance Analysis; DEXA: Dual-Energy X-ray Absorptiometry; MUFA: Mono-Unsaturated Fatty Acids; HMB: β-Hydroxy β-Methyl-Butyrate.

INTRODUCTION

Steatotic Liver Disease (SLD) is defined as the presence of macro vesicular steatosis in ≥ 5% of hepatocytes in the absence of a secondary cause, such as alcohol or drugs. It encompasses a spectrum of diseases ranging from non-alcoholic fatty liver to Non-Alcoholic Steato Hepatitis (NASH), fibrosis and cirrhosis [1].

Steatotic liver disease is one of the leading causes of chronic liver disease worldwide. The global prevalence is around 25%, with a prevalence of 23% in Europe [2-4]. Early diagnosis is of great importance to avoid progression and possible development of oncologic disease [3]. Risk factors for disease progression include genetic variations, weight gain and the presence of metabolic syndrome (central adiposity, hyperglycemia, dyslipidemia and hypertension). It also appears to be more frequent and progressive in the context of insulin resistance and Diabetes Mellitus (DM), with the latter being a predictor of moderate to severe fibrosis. Additionally, an increased risk has been demonstrated in diets high in Tran's fats, red meat, high fructose content, highly refined carbohydrates and low fiber, all of which are exacerbated by a sedentary lifestyle [3].

Although Non-Alcoholic Fatty Liver Disease (NAFLD) is strongly associated with obesity and metabolic comorbidities, a proportion of normal-weight subjects can also develop it. This is known as lean NAFLD, which is divided into two main categories. The first and most common includes non-obese patients who may be overweight, with or without increased waist circumference and adipose tissue, while the second category includes thin individuals without excess visceral fat mass. Several secondary causes have been implicated in this latter category, such as high fructose intake, protein

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malnutrition (Kwashiorkor disease), as well as the use of steatogenic drugs (amiodarone, tamoxifen, methotrexate, prednisolone, etc.), and genetic predisposition [5,6].

Paradoxically, most studies report a worse prognosis of the disease in normal-weight persons compared to persons with obesity. This discrepancy could be explained because usually in the studies the classification of thin or obese people is based on the Body Mass Index (BMI) and not on visceral fat levels [5,6]. The isolated BMI is not a sufficient predictor of the negative impact of obesity. Central obesity (according to the WHO: Waist circumference greater than or equal to 102 cm in men and greater than or equal to 88 cm in women in the Caucasian population) provides a better estimate of abdominal fat, considered a primary determinant of metabolic complications associated with an increased risk of cardiovascular disease [7,8].

Regarding the evolution of the disease, only a small percentage of patients will develop complications typical of chronic liver disease, 4-8% will die from cirrhosis-related complications and 1-5% from Hepato-Cellular Carcinoma (HCC). However, the most common cause of death in these patients is cardiovascular disease [3,9].

In recent years, the incidence of liver failure requiring transplantation has alarmingly increased, and it appears that SLD predisposes to HCC, even without underlying cirrhosis [6]. According to data records of European patients transplanted for end-stage liver disease between January 2002 and December 2016, 4% had SLD, representing an increase from 1%.2% in 2002 to 8%.4% in 2016 [10].

Due to shared pathological characteristics, including deficiencies in systemic inflammatory responses, neurohormonal activity and metabolic systems, patients with SLD cirrhosis frequently exhibit a state of sarcopenia. Sarcopenia is present in 22%-62% of patients with cirrhosis, being more common in those with advanced disease [11].

Sarcopenia is defined by the loss of skeletal muscle mass accompanied by a decrease in muscle strength and physical performance [12-15]. When malnutrition and muscle atrophy progress in these patients, cachexia may appear, which is characterized by systemic tissue depletion with weight loss [16]. In a recent study, 59% of patients with cirrhosis who were on the pre-transplant waiting list were found to have sarcopenia [17]. Moreover, these patients may also present a combined situation of low muscle mass and obesity, a concept known as sarcopenic obesity, which is associated with a worse prognosis and increased mortality in cirrhotic patients [14,15].

These disorders can worsen the clinical condition of patients, deteriorate their quality of life, cause prolonged hospitalizations or readmissions, and potentially worsen the prognosis of the disease. During the last decade, research in this context has focused on better understanding the mechanisms causing sarcopenia in cirrhosis.

It has been shown that the cirrhotic liver's inability to store, synthesize, and mobilize carbohydrates causes patients to rapidly transition to a catabolic state in which proteins and fats are used as sources of energy. This imbalance between protein synthesis and muscle tissue degradation, increased autophagy and proteolytic activity, along with impaired mitochondrial function in cirrhotic patients, contribute to the development of sarcopenia [18,19]. SLD and sarcopenia share common pathophysiological mechanisms, including systemic inflammation, insulin resistance and alterations in the Growth Hormone/Insulin-like Growth Factor-1 (GH/IGF-1) axis. Also, they share nutritional deficits such as vitamin D deficiency, dysregulation of adiponectin and myostatin, hepatic production of catabolic factors and physical deconditioning and inactivity [18].

Given the overlap in the pathophysiology of SLD and sarcopenia, it is difficult to determine whether sarcopenia is a genuine factor in the development of SLD or a complication of it. Skeletal muscle is a tissue that responds to insulin, so its loss and the presence of myosteatosis can lead to a decrease in insulin response and energy expenditure. This, in turn, leads to an increase in hepatic gluconeogenesis and greater absorption of hepatic Free Fatty Acids (FFA). In addition, insulin resistance exacerbates proteolysis and contributes to skeletal muscle loss through mitochondrial dysfunction and reduced muscle protein synthesis [18,19].

Insulin resistance has also been related to myosteatosis and inhibition of GH. Myokines secreted by skeletal muscle include irisin, interleukin-6, myostatin, and adiponectin, which are involved in the regulation of hepatic glucose and fatty acid metabolism. Altered levels of these myokines due to decreased muscle mass have been associated with hepatic fat accumulation [19-21]. The objective of this article is to review the current knowledge about the state of muscle mass, the pathogenesis, diagnosis and treatment of sarcopenia in the event that it exists in metabolic liver disease.

Methodology

Narrative review article of updated literature on metabolic liver disease and sarcopenia. A bibliographic search was carried out in PubMed and Medline databases between 2018 and 2022 with the keywords previously defined by the authors ((pathophysiology(Title/Abstract)) or (prevalence(Title/Abstract)) or (treatment(Title/Abstract))) and ((body mass index(MeSH Terms)) or (agents, weight loss(MeSH Terms)) or (muscle strength(MeSH Terms)) or (atrophic muscular disorder(MeSH Terms)) or (body weight change(MeSH Terms)) or (muscle weakness(MeSH Terms))) and ((liver steatoses(MeSH Terms)) or (steatohepatitis(MeSH Terms)) or (liver fibrosis(MeSH Terms)) or (sarcopenia(MeSH Terms)) or (elastography(MeSH Terms)) or (dietary supplementation(MeSH Terms))). The resulting bibliography was reviewed by the pool of authors, proceeding to select those articles with relevant information for the preparation of the article and the review of key aspects: The assessment of the pathology in terms of prevalence, repercussion, pathophysiology and comorbidities, assessing the spectrum (obese/non-obese patient), diagnosis and treatment (lifestyle changes, nutritional intervention, measurement of muscle mass).

LITERATURE REVIEW

1409 articles that met the defined search criteria were identified. A total of 31 articles were selected for the narrative review based on the selection criteria (articles that answered the questions: What is the pathophysiology/prevalence of loss of muscle mass and function associated with non-alcoholic fatty liver disease, what is the best treatment for the loss of muscle mass and function associated with said disease, and how feasible is the measurement of muscle mass and function in said disease?). The main results are presented below:

Diagnostic methods

Both sarcopenia and cachexia can manifest clinically with weakness, asthenia, frailty, and hyporexia caused by the underlying metabolic dysregulation and impairment of the muscular system.

Since these debilitating disorders have a high impact on the clinical course and prognosis of the primary disease, it is important that they are detected early. Since these debilitating disorders have a high impact on the clinical course and prognosis of the underlying disease, it is important to detect early any type of nutritional deficit in these patients. Any of the available tools can be used (Nutritional Risk Screening 2002 (NRS 2002), Subjective Global Assessment (SGA), Mini Nutritional Assessment (MNA), Malnutrition Universal Screening Tool (MUST), Short Nutritional Assessment Questionnaire (SNAQ)), always taking into account the setting in which they are administered (hospitalized, outpatient or elderly patients) [16] (Table 1).

Table 1: Methods for the diagnosis of nutritional deficiency.

Diagnostic method	Goal
Medical history	Dietary survey, eating habits, Identify history of possible signs of malabsorption, previous gastrointestinal surgeries, taste alterations, anorexia, nausea, vomiting, gastrointestinal rhythm disturbances, dysphagia or history of Broncho aspiration, oral health problems, diabetic gastroparesis, allergies and/or food intolerances, toxic substance consumption, nutritional supplements or usual treatment.
Physical examination	Identifying loss of fat and muscle in specific body regions (such as the orbit, temporal, intercostal regions and in other large muscle groups such as the quadriceps). Presence of edema or ascites. Signs of dehydration. Other signs such as Muehrcke's lines in the nails suggest hypoalbuminemia, alopecia is associated with protein deficiency and scalp scaling with essential fatty acid deficiency.
Anthropometric data	Calculate the BMI, the percentage of unintentional weight loss. Calf circumference, brachial circumference, triceps skinfold, abdominal circumference.
Nutritional screening	Assess nutritional risk using questionnaires: Nutritional Risk Screening 2002 (NRS 2002), Subjective Global Assessment (SGA), Mini Nutritional Assessment (MNA), Malnutrition Universal Screening Tool (MUST), and Short Nutritional Assessment Questionnaire (SNAQ).
Bioelectrical methods	Bioelectrical Impedance Analysis (BIA) provides a detailed description of body composition (water, fat, minerals, and proteins).
Imaging tests	Muscle ultrasound allows for simple, fast and inexpensive measurement of muscle mass, although it is a method that has not yet been validated.
Analytical markers	Several biochemical parameters such as albumin, prealbumin, total proteins, total cholesterol, lymphocytes, IL-1, IL-6, GH/IGF-1 and testosterone can be altered in patients with sarcopenia.

It is worth mentioning the SARC-F questionnaire (simple questionnaire for the diagnosis of sarcopenia risk), which allows evaluating muscle strength through an assessment and scoring system in which patients report their ability in 5 parameters: Strength, walking ability, getting up from a chair, climbing stairs and frequency of falls. For each component, patients are evaluated with 0,1,or 2 points (0 represents no difficulty at all, 1 means some difficulty and 2 means much difficulty or inability). The total score ranges from 0 to 10, and patients who score 4 points or more have sarcopenia [13].

Given that these debilitating disorders have a high impact on the clinical course and prognosis of the primary disease, it is important to detect them early [18,19]. Therefore, until a specific common tool is developed, it is recommended to make the diagnosis using the methods available in each hospital.

Furthermore, possible comorbidities such as type 2 diabetes, dyslipidemia and hypertension should be routinely evaluated, in addition to asking patients about their alcohol consumption patterns. Other causes of liver disease (such as HIV, lipodystrophy, familial hypobetalipoproteinemia and drug-induced disorders) should also be ruled out [22].

It is important to stratify the risk of fibrosis to identify those patients in advanced stages or cirrhosis (transient elastography by Fibro Scan and Magnetic Resonance Elastography (MRE) can be used as alternatives to liver biopsy) [12,14,23]. Several imaging techniques are available to assess body composition and examine tissue depletion.

In Computed Tomography (CT) imaging, the Skeletal Muscle Index (SMI, derived from normalization to the square of total muscle area height) and the Psoas Muscle Index (PMI) can be calculated from images taken at the level of the third lumbar vertebra. Both parameters are used as markers of muscle depletion and can help predict preoperative complications and deaths in cancer patients [12,15]. The cutoff points for both parameters have been investigated in patients with cirrhosis: Low muscle mass was defined as an SMI below 50 cm^2/m^2 in men, and below 39 cm^2/m^2 in women, while a low PMI was defined as a score below 5.1 cm^2/m^2 in men, and below 4.3 cm^2/m^2 in women [14,15].

Bioelectrical Impedance Analysis (BIA), dynamometry and Dual-Energy X-ray Absorptiometry (DEXA) scans are additional objective methods for defining body composition and nutritional status in patients with chronic diseases [14,15]. Biomarkers play an important role in the early detection of tissue depletion. Myostatin, transforming growth factor beta, activin A, as well as proinflammatory cytokines such as TNF, IL-1, or IL-6, are being investigated in this field. However, none of the biomarkers mentioned above has been specifically used in clinical practice so far [16,24].

Therapeutic approach

There is no specific pharmacological treatment regimen for sarcopenia or cachexia at the clinical level. Sarcopenia and SLD have a similar pathophysiology and they could probably benefit from a common therapeutic approach.

The therapeutic goal in these disorders is to increase appetite and food intake, attenuate chronic inflammatory state and improve exercise capacity and quality to limit or slow the progression of sarcopenia and cachexia. Optimizing the quantitative and qualitative aspects of nutrition, ensuring adequate protein intake and covering the energy requirements in an individualized way, along with exercise, are strategies that can be implemented [16,25].

Nutrition: With aging, energy needs decrease and food intake is significantly reduced. This decrease in intake occurs along with changes in appetite, which has been described as "anorexia of aging" [26-28]. This situation has direct implications on muscle mass, strength and physical function, favoring the development

of sarcopenia. Nutrition plays an important role both in the prevention and treatment of sarcopenia [28].

In SLD, the degree of weight loss is proportional to the degree of improvement in liver histology, i.e., at the cellular level, hepatocytes experience a reduction in fibrosis and inflammation. However, weight loss efforts should also be directed at simultaneously preserving muscle mass, for which adequate protein intake and a reduction in fat and fructose intake are recommended to prevent sarcopenia [28].

Compared to other diets, Mediterranean diet appears to show an additional benefit as it tends to be high in MUFA (Monounsaturated Fatty Acids) and ω-3 fatty acids and tends to avoid red meat, processed foods and refined sugars [3]. Additionally, alcohol consumption should be restricted or eliminated. On the other hand, fiber intake positively influences the control of SLD, stimulating a healthy gut microbiota, which reduces the development of inflammation and liver damage. Dietary fiber, especially soluble fiber, has a prebiotic function (FOS (Fructo-Oligo-Saccharide), GOS (Galacto-Oligo-Saccharides)) and promotes the proliferation of bacterial strains that are beneficial for the colonocytes [29].

However, to date, no study has found regression of a more advanced stage of SLD, such as fibrosis, in patients with high fiber or prebiotic supplements intake. More research is needed, but given the evidence, it is reasonable to recommend their consumption in early stages of SLD to prevent disease progression [29]. When oral nutrition is insufficient, oral nutritional supplementation is indicated (Table 2).

Table 2: Specific nutrient supplementation.

Type of nutrient	Benefits
Proteins	Potential to delay muscle mass loss.
β-Hydroxy-β-Methyl-Butyrate (HMB)	Prevention of muscle atrophy.
Vitamin D	Anti-inflammatory role, preservation of muscle mass.
Vitamin E	Possible improvement of oxidative stress markers.
Long-chain polyunsaturated fatty acids	Improvement of muscle strength and functional capacity.

Generally, hypercaloric (1.52 kcal/mL) and, if necessary, hyperproteic supplements are recommended, as they appear to improve the inflammatory status, quality of life, and survival in these patients [17].

Dietary supplementation with amino acids, proteins, vitamin D, and polyunsaturated fatty acids appears to protect against age-related sarcopenia, due to their anti-inflammatory and antioxidant properties. Several studies have shown that branched-chain amino acids increase skeletal muscle protein synthesis, which is a beneficial effect in addressing age-related muscle mass decline [30,31].

There is also interest in β-Hydroxy β-Methyl-Butyrate (HMB), a key metabolite of leucine. Various studies have concluded that supplementation with HMB may be useful in preventing muscle atrophy and have demonstrated an increase in the Fisher index in patients with liver cirrhosis and malnutrition, as well as improvements in liver function scores and nutritional laboratory markers [32,33]. However, more studies are needed to determine its effects in this patient profile.

Physical exercise: In patients with SLD, muscle strength and architecture are altered; therefore, it is important and necessary to initiate a therapeutic exercise-based training from the earliest stages of the disease.

Physical exercise has been studied as a therapy in sarcopenic patients with SLD by treating muscle metabolism through increasing anabolic activity *via* physical training. Aerobic and resistance exercise has also demonstrated beneficial effects on inflammation and as a defense against oxidative stress. The most recommended type of physical exercise is the so-called "multicomponent", based on a physical exercise program with strength and power training, neuromotor exercise (balance, coordination, posture and proprioception) and flexibility (Table 3).

Table 3: Qualitative classification of physical activities.

Aerobic activities	Walking
	Swimming
	Dancing
	Cycling
	Elliptical
	Low impact aerobics
	Water aerobics
Strength exercises	Resistance band exercises
	Self-loading or with a load
	Climbing stairs
	Sit-to-stand
	Carrying things
	Some tai chi exercises
	Yoga
To improve balance or neuromotor fitness	Balance
	Agility
	Coordination
	Gait
	Proprioceptive training
	Multifaceted activities: tai chi and yoga
Flexibility	Take joints through a set of range of motion exercises at the start of each session and perform different sets of stretches at various times throughout the session.

There are many types of training that are aerobic exercises and can be adapted to the preferences, needs, and fitness level of each individual. Some examples of aerobic exercises include: Walking, swimming, dancing, cycling, elliptical, low-impact aerobics and aqua aerobics.

Strength training is the type of training that involves moving the muscles against some type of resistance. The most well-known types of strength exercises are those that can be performed with gym equipment, exercises with elastic bands, bodyweight exercises or exercises with weights, climbing stairs, sitting and standing up from a chair several times, carrying objects, tai chi or yoga, among others.

To work on balance and the neuromotor aspects, exercises such as balance, agility, coordination, gait, or proprioceptive training can be performed.

Finally, flexibility exercises are really beneficial and it is recommended to introduce them before and after performing other types of aerobic and anaerobic exercise. All components of the training will increase their volume and intensity based on individual responses and adaptations. Preferably, the focus will be on working the lower extremities and working throughout the full range of motion, without any pain. In the same session, strength training, cardiorespiratory, balance and agility training can be implemented [11]. In cirrhosis, studies on physical exercise have shown improvements in muscle health, quality of life, fatigue and reductions in the hepatic portal venous pressure gradient, with no reported adverse events [11] (Table 4).

Table 4: Recommendations for physical exercise in cirrhosis.

Type of exercise	Exercise	Intensity	Frequency	Duration
Cardiorespiratory	Prolonged and rhythmic activities (walking, stationary bike, pedals ...)	Light: HR 35%-40%, RPE 3-4. METs: 3 Moderate: HR 50%, RPE 5-6. METs 4-5 Vigorous: HR 60%, RPE 7. METs 6-7	3-5 days/ week	20-30 min/ session 150 min/ week if moderate or 75 min/week if intense
Strength	Free weights or machines or functional exercises	Start below 30% of 1-RM and progress slowly. Rating of Perceived Exertion scale 2-3	2-3 days/ week	At least 1 set of 10-15 repetitions
Flexibility	Stretching of all muscle groups, according to individual limitations	Movements along the entire joint range	3-4 days/ week	10-30 seconds of static stretching of the major muscle groups
Neuromotor	Balance, coordination, posture, agility, and proprioception activities	Not established	2-3 days/ week	20-30 minutes

Note: HR: Heart Ratio; RPE: Rate of Perceived Exertion; METs: Metabolic Equivalent of Tasks

DISCUSSION

Despite the numerous limitations of the existing data, available results reinforce the effectiveness of lifestyle-based programs focusing on nutrition and physical exercise to treat and resolve SLD. Given the high prevalence of sarcopenia in cirrhosis and its impact on long-term outcomes, more research is needed to characterize the mechanisms causing sarcopenia and elucidate the targets of new therapies.

Several factors, such as the dose, type, duration of supplementation, etiology of cirrhosis, amount of protein in the diet, compliance with supplementation and exercise should be the focus of future controlled, randomized clinical trials with sufficient sample size. These studies should investigate both the prevention and treatment of sarcopenia, so that they can generate evidence for this patient population.

Until specific interventions are developed that involve patients with SLD, it may be recommended that, as a clinical approach for this patient population, a screening test for sarcopenia such as the SARC-F test or measurement of handgrip strength using dynamometry are applied. This can help to confirm the presence of sarcopenia in cases where it is suspected, based on the available tests in their healthcare center.

CONCLUSION

The pathogenesis of sarcopenia is multifactorial and results from an imbalance between protein synthesis and degradation. Nutritional, metabolic, and biochemical abnormalities observed in chronic liver disease alter the protein homeostasis of the whole body. Hyperammonemia, increased autophagy, proteasomal activity, reduced protein synthesis and impaired mitochondrial function all play a role in muscle wasting in cirrhosis.

There are many other factors involved in the regulation of muscle mass that influence this process, such as energy status, availability of metabolic substrates (such as branched-chain amino acids), alterations in the endocrine system (such as insulin resistance, circulating insulin levels, IGF-1, corticosteroids and testosterone), cytokines, myostatin and exercise.

In conclusion, a combination of nutritional interventions, physical exercise and pharmacological treatment seems to be necessary to reverse or at least slow down the progression of SLD, since if this disease is left to its natural evolution, a significant percentage of patients may end up developing a malignancy, with the consequent deterioration and impact on quality of life.

CONFLICT OF INTEREST

Juan Bautista Moro Hernandez reports a relationship with Abbott Laboratories S.A. Spain as employee in Medical Department. The rest of the authors declare that they have no known personal relationships that could have appeared to influence the work reported in this paper.

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Author contribution

All the authors have substantially contributed to the conception and design of the manuscript, literature search, drafting, revising critically and final approval of the version to be submitted.

REFERENCES

1. Maurice J, Manousou P. Non-alcoholic fatty liver disease. Clin Med (Lond). 2018;18(3):245- 250.
2. Abeysekera KWM, Fernandes GS, Hammerton G, Portal AJ, Gordon FH, Heron J, et al. Prevalence of steatosis and fibrosis in young adults in the UK: A population-based study. Lancet Gastroenterol Hepatol. 2020;5(3):295-305.
3. Mundi MS, Velapati S, Patel J, Kellogg TA, Abu Dayyeh BK, Hurt RT. Evolution of NAFLD and its management. Nutr Clin Pract. 2020 Feb;35(1):72-84.
4. Powell EE, Wong VW, Rinella M. Non-alcoholic fatty liver disease. Lancet. 2021;397(10290):2212-2224.
5. Long MT, Noureddin M, Lim JK. AGA clinical practice update: Diagnosis and management of non-alcoholic fatty liver disease in lean individuals: Expert review. Gastroenterology. 2022;163(3):764-774.
6. Chrysavgis L, Ztriva E, Protopapas A, Tziomalos K, Cholongitas E. Non-alcoholic fatty liver disease in lean subjects: Prognosis, outcomes and management. World J Gastroenterol. 2020;26(42):6514-6528.
7. Zazai R, Wilms B, Ernst B, Keppler R, Thurnheer M, Schmid SM, et al. Sagittal abdominal diameter does not predict metabolic traits better than waist circumference- related measures of abdominal obesity in obese subjects. Exp Clin Endocrinol Diabetes. 2018;126(10):619-627.
8. Qadri S, Ahlholm N, Lonsmann I, Pellegrini P, Poikola A, Luukkonen PK, et al. Obesity modifies the performance of fibrosis biomarkers in nonalcoholic fatty liver disease. J Clin Endocrinol Metab. 2022;107(5):e2008-e2020.
9. Perdomo CM, Núñez-Córdoba JM, Ezponda A, Mendoza FJ, Ampuero J, Bastarrika G, et al. Cardiometabolic characterization in metabolic dysfunction-associated fatty liver disease. Front Med (Lausanne). 2022;9:1023583.
10. Haldar D, Kern B, Hodson J, Armstrong MJ, Adam R, Berlakovich G, et al. Outcomes of liver transplantation for non-alcoholic steatohepatitis: A European liver transplant registry study. J Hepatol. 2019;71(2):313-322.
11. Tandon P, Ismond KP, Riess K, Duarte-Rojo A, Al-Judaibi B, Dunn MA, et al. Exercise in cirrhosis: Translating evidence and experience to practice. J Hepatol. 2018;69(5):1164-1177.
12. Dent E, Morley JE, Cruz-Jentoft AJ, Arai H, Kritchevsky SB, Guralnik J, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): Screening, diagnosis and management. J Nutr Health Aging. 2018;22(10):1148-1161.
13. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: Revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16-31.
14. Donini LM, Busetto L, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, Batsis JA, et al. Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement. Clin Nutr. 2022;41(4):990-1000.
15. Donini LM, Busetto L`, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, Batsis JA, et al. Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement. Obes Facts. 2022;15(3):321-335.
16. Lena A, Hadzibegovic S, von Haehling S, Springer J, Coats AJ, Anker MS. Sarcopenia and cachexia in chronic diseases: From mechanisms to treatment. Pol Arch Intern Med. 2021;131(12):16135.
17. Younossi ZM, Corey KE, Lim JK. AGA clinical practice update on lifestyle modification using diet and exercise to achieve weight loss in the management of non-alcoholic fatty liver disease: Expert review. Gastroenterology. 2021;160(3):912-918.
18. Li AA, Kim D, Ahmed A. Association of sarcopenia and NAFLD: An overview. Clin Liver Dis (Hoboken). 2020;16(2):73-76.
19. Kim JA, Choi KM. Sarcopenia and fatty liver disease. Hepatol Int.2019;13:674-687.
20. Di Filippo L, de Lorenzo R, Giustina A, Rovere-Querini P, Conte C. Vitamin D in osteosarcopenic obesity. Nutrients. 2022;14(9):1816.
21. Giha HA, Alamin OAO, Sater MS. Diabetic sarcopenia: Metabolic and molecular appraisal. Acta Diabetol. 2022;59(8):989-1000.
22. 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.
23. Marco-Martínez M. Lifelong learning in endocrinology. Saedyn. 2023.
24. Jones RL, Paul L, Steultjens MPM, Smith SL. Biomarkers associated with lower limb muscle function in individuals with sarcopenia: A systematic review. J Cachexia Sarcopenia Muscle. 2022;13(6):2791-2806.
25. Belfort-deAguiar R, Lomonaco R, Cusi K. Approach to the patient with non-alcoholic fatty liver disease. J Clin Endocrinol Metab. 2023;108(2):483-495.
26. Barazzoni R, Jensen GL, Correia MITD, Gonzalez MC, Higashiguchi T, Shi HP, et al. Guidance for assessment of the muscle mass phenotypic criterion for the Global Leadership Initiative on Malnutrition (GLIM) diagnosis of malnutrition. Clin Nutr. 2022;41(6):1425-1433.
27. Malmstrom TK, Miller DK, Simonsick EM, Ferrucci L, Morley JE. SARC-F: A symptom score to predict persons with sarcopenia at risk for poor functional outcomes. J Cachexia Sarcopenia Muscle. 2016;7(1):28-36.
28. Robinson SM, Reginster JY, Rizzoli R, Shaw SC, Kanis JA, Bautmans I, et al. Does nutrition play a role in the prevention and management of sarcopenia?. Clin Nutr. 2018;37(4):1121-32.
29. Pérez-Montes de Oca A, Julián MT, Ramos A, Puig-Domingo M, Alonso N. Microbiota, fiber, and NAFLD: Is there any connection?. Nutrients. 2020;12(10):3100.
30. Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, Newman AB, et al. Dietary protein intake is associated with lean mass change in older, community-dwelling adults: The Health, Aging, and Body Composition (Health ABC) study. Am J Clin Nutr. 2008; 87:150–155.
31. Borack MS, Volpi E. Efficacy and safety of leucine supplementation in the elderly. J Nutr. 2016;146(12):2625S-2629S.
32. Espina S, Sanz-Paris A, Gonzalez-Irazabal Y, Pérez-Matute P, Andrade F, Garcia-Rodriguez B, et al. Randomized clinical trial: Effects of β- Hydroxy-β-Methylbutyrate (HMB)-Enriched vs. HMB-Free oral nutritional supplementation in malnourished cirrhotic patients. Nutrients. 2022;14(11):2344.
33. Espina S, Gonzalez-Irazabal Y, Sanz-Paris A, Lopez-Yus M, Garcia-Sobreviela MP, Moral-Bergos RD, et al. Amino acid profile in malnourished patients with liver cirrhosis and its modification with oral nutritional supplements: Implications on minimal hepatic encephalopathy. Nutrients. 2021;13(11):3764.