Review

Lifestyle Medicine in the Prevention and Treatment of MASLD

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Review

Lifestyle Medicine in the Prevention and Treatment of MASLD

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Abstract: Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease worldwide and affects nearly 30% of the adult population and 10% of the paediatric population. It is estimated that this number will double by 2030. MASLD is one of the leading causes of hepatocellular carcinoma, cirrhosis and liver transplantation, as well as a significant risk factor for cardiovascular disease - heart attack or stroke being the leading cause of death in this group of patients. Due to the ever-increasing number of patients, the long-term asymptomatic course of the disease, serious complications and lack of preventive programmes, as well as insufficient awareness of the disease among patients and doctors themselves, MASLD is a growing interdisciplinary problem and a real challenge for modern medicine. The main cause of MASLD is an inappropriate lifestyle - inadequate nutrition and too little physical activity, which lead to metabolic disorders - overweight and obesity, pre-diabetes and diabetes, hypertension, lipid disorders. Lifestyle changes - appropriate, diet, weight reduction and systematic physical activity - are also the basis for the prevention and treatment of MASLD. Hence, in recent years, so much importance has been attached to lifestyle medicine, to non-pharmacological treatment as prevention of lifestyle diseases. This paper presents methods of non-pharmacological management in the prevention and treatment of MASLD.

Keywords: lifestyle; MASLD; non-pharmacological treatment; diet; physical activity; hepatic steatosis; cardiovascular disease; obesity; diabetes

Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD) is the most common chronic liver disease worldwide, detected most often incidentally. It affects both adults and children, of both sexes, with a female predominance.In developed countries, MASLD may affect more than 30% of the adult population and 10% of the child population. However, this figure may be underestimated due to the long-standing asymptomatic course of the disease and the lack of screening programmes, combined with low awareness of both patients and physicians regarding early detection of MASLD, especially among those at risk - excessive body weight, type 2 diabetes, dyslipidaemia or hypertension [1-3]. When diagnosed late, it can lead to the development of both hepatic and extrahepatic complications. It is one of the leading causes of hepatocellular carcinoma (HCC), cirrhosis and liver transplantation in developed countries - the first cause of cirrhosis and liver

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transplantation in women in the USA, and the second (after alcohol) in men. It is also a significant risk factor for the development of cardiovascular disease, which is the leading cause of death in this patient group (Table 1). Lack of awareness of the risk of developing the disease, the initial absence of clinical signs or uncharacteristic symptoms, means that MASLD is often diagnosed too late at the stage of decompensated cirrhosis or after a first cardiovascular incident (Table 2). It is not uncommon for MASLD to lead to the development of HCC , the incidence of which is independent of the progression of liver fibrosis to cirrhosis, as MASLD risk factors such as type 2 diabetes or obesity are also independent risk factors for the development of HCC. Therefore, the incidence of HCC in patients with MASLD is higher and unfortunately still increasing [4-6]

The main cause of MASLD is an inappropriate lifestyle - poor diet and lack of physical activity - which leads to the development of the metabolic disorders mentioned - overweight and obesity, pre-diabetes and diabetes, hypertension, lipid disorders. These are typical components of the metabolic syndrome, i.e. a set of cardiovascular risk factors that, when present together, further increase this risk, hence extrahepatic complications, i.e. cardiovascular incidents, are a frequent complication.

The diagnosis of the disease is based on the detection of hepatic steatosis by imaging in a patient with cardiometabolic factors and no other detectable cause of hepatic steatosis. The most common imaging modalities used are classic ultrasound or elastography of the liver, e.g. FibroScan, which is used for the early detection of minimal steatosis (when 5 % of hepatocytes are affected, compared to classic ultrasound methods which detect 20-30 % steatosis). For the diagnosis of MASLD, methods based on computed tomography or magnetic resonance imaging are used less frequently due to cost. Classical liver biopsy, on the other hand, is only used for clinically doubtful cases, overlap syndromes or to differentiate with steatohepatitis. The treatment of patients with MASLD should be multidisciplinary and aimed at preventing and treating both hepatic and extrahepatic complications, i.e. reducing cardiovascular risk factors (cardiodiabetic factors) (Table 3). The most important aspect in the prevention and treatment of patients with MASLD is lifestyle change aimed at weight reduction [7-13].

Table 1. Complications of MASLD.

Liver complications	Extrahepatic complications
● *metabolic dysfunction-associated steatohepatitis* (MASH)	● arteriosclerosis
● progression of fibrosis - F0 to F4 - cirrhosis	● cardiovascular diseases
● primary liver cancer	● ischaemic heart disease
● liver failure and need for liver transplantation	● myocardial infarction
	● TIA, ischaemic stroke

Table 2. Clinical manifestations of MASLD.

Clinical symptom	Comment
Asymptomatic course	Most patients up to advanced liver fibrosis
Feelings of chronic fatigue	Regardless of disease severity and transaminase activity
Sensation of discomfort in the right lower abdomen	Regardless of liver enlargement, Not a typical pain, but a feeling of entrapping, squishing
Decompensation of cirrhosis	Stellate hemangiomas can appear on the skin, mainly on the upper chest or face. Palmar erythema may occur. Appearance of lower limb oedema resulting from hypoalbuminaemia and/or ascites and/or yellowing of the skin coverings.

Table 3. Pillars of MASLD treatment.

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Pillar I	Treatment of obesity with target weight reduction - optimally 10% of baseline weight within 6 msc: 1. Lifestyle changes ● diet ● physical activity 2. pharmacotherapy 3. treatment by bariatric surgery
Pillar II	Elimination of cardiometabolic risk factors, which are the main cause of premature mortality in patients with MASLD: 1. Optimal treatment of diabetes 2. Optimal treatment of lipid disorders 3. Optimal treatment of hypertension.
Pillar III	Use in patients with MASH of drugs that have demonstrated in clinical trials the ability to reduce MASH and/or regress liver fibrosis: Pioglitazone, Vitamin E, GLP-1 analogues (semaglutide, liraglutide) GLP-1/GIP analogues (thirzepatide)

In addition, hepatoprotective - hepato-regenerative drugs such as *ursodeoxycholic acid* (UDCA), thymonacin or soy phospholipids are very popular. These drugs should be considered to support the effects of lifestyle changes - diet, weight reduction and physical activity [11-13].

Table 4. effect of weight change on the course of MASLD.

% weight reduction	Clinical effect
Weight reduction of 3%	● Reduction in hepatic steatosis in 35-100% of patients depending on baseline steatosis severity (S1 to S3)
Weight reduction of 5%	● as above, plus a reduction in the severity of ballooning degeneration/inflammation in 41-100% of patients
Weight reduction of 7%	● as above, plus a reduction in the severity of steatohepatitis (MASH) in 64-90% of patients
Weight reduction of 10%	● as above plus regression of initial liver fibrosis (F1,F2) in 49% of patients

The aim is not to lose weight quickly and significantly , but to lose weight in a way that will result in improved health and be sustained over the long term. Optimally, a slow weight loss of 0.5 kg to 1 kg per week is recommended, with a goal of reducing 5-10% of the initial body weight in 3-6 months. The reduced weight should then be maintained for a similar period and, if indicated, weight should be reduced again by 5-10% in the following period.

Dietary Recommendations in MASLD

A healthy diet, combined with regular exercise, is the mainstay of treatment for the vast majority of patients diagnosed with hepatic steatosis - this is in no way surprising, given that the presence and severity of hepatic steatosis are largely determined by excess energy intake, insulin resistance and other factors regulating the supply and distribution of fatty acids, cholesterol or phospholipids [14-16]. A fundamental problem, however, is the inconsistency in official dietary recommendations - while most scientific societies emphasise the importance of reducing excess body weight (usually using a hypocaloric diet with an energy deficit of 500-1000kcal [17-20]), they rightly link the issue of hepatic steatosis to metabolic disorders, primarily obesity. There are discrepancies in specific recommendations - for example, the EASL-EASD-EASO and APASL guidelines recommend the exclusion of processed and high fructose foods, whereas the AASLD and ESPEN guidelines do not [17-20]. Significant differences also apply to the supply of alcoholic beverages: EASL-EASD-EASO

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and AASLD allow moderate alcohol consumption in their recommendations, while the more recent ESPEN and APASL guidelines recommend complete abstinence [17-20]. Although official recommendations are sometimes inconsistent, there are nevertheless many individual reports in the scientific literature on different dietary interventions that may carry limited or global benefits for patients with features of hepatic steatosis; it is worth analysing the most recurrent voices of the scientific community, which we will do later in this section, discussing the Mediterranean, high-protein and ketogenic diets, as well as the intermittent fasting model.

The Mediterranean diet is the traditional dietary approach of the Mediterranean people, characterised by a high proportion of low-processed foods and products: fresh fruits, vegetables, whole grains, nuts, pulses, fish, seafood, fermented dairy products, with a low intake of animal fats and meat - a way of eating that contrasts strongly with the standard Western diet, rich in animal products, including red meat, refined cereals or sweetened beverages [21-27]. Previous scientific reports emphasise the benefits of the Mediterranean diet in patients with metabolic diseases, made possible by its richness in antioxidants, monounsaturated fatty acids, fibre, well-digested animal protein and polyphenols - the interplay of which reduces intrahepatic triglyceride accumulation, influences the expression of genes related to adipogenesis and adipocyte proliferation, sensitises peripheral tissues to insulin (while regulating its secretion) and enhances the inflammatory response associated with adipose tissue activity [23]. Several independent scientific groups have shown that adherence to a Mediterranean diet in patients with previously diagnosed MASLD was associated with less steatosis (with reductions in intrahepatic fat volume reaching up to 39%), as well as a lower likelihood of developing features of hepatitis [19-31]. The group of Marin-Alejandre et al. showed that monounsaturated fatty acids, in particular, which are typical of the Mediterranean diet, may play a key role, improving the lipid profile and control of carbohydrate metabolism, reducing the phenomenon of insulin resistance and having a beneficial effect on blood pressure, with a consequent reduction in intrahepatic fat volume and improvement in the clinical course of NAFLD [28] - these results were de facto confirmation of earlier studies, such as those by Bozetto et al. [31]. Polyunsaturated fatty acids are no less important, especially maintaining an appropriate ratio of n-6 acids to n-3 acids - as it has been previously demonstrated that an appropriate meal composition in this regard (and especially an increased supply of α-linolenic acid relative to n-6 acids) improves peripheral insulin sensitivity and lowers cholesterol and triglyceride concentrations in cases of fructose-dependent insulin resistance burden [32]. Polyunsaturated n-3 fatty acids significantly reduce the activity and expression of the mitochondrial citrate carrier that catalyses the efflux of citrate from the matrix towards the cytosol, which in turn leads to increased activity of acetyl-CoA required for de novo fatty acid and cholesterol biosynthesis [33] - in addition, n-3 fatty acids also up-regulate the expression of genes responsible for peroxisome proliferator-activated receptor alpha (PPARα) and sterol regulatory element-binding protein-1 (SREBP-1), which are responsible for fatty acid oxidation, lipogenesis and glycolysis [34,35]. The anti-inflammatory effect of n-3 fatty acids cannot be underestimated either, related to the effect on suppression of TNFα and IL-6, which are typical cytokines responsible for the development and progression of WASH [36]. There are reports that the Mediterranean diet may be associated with a reduced risk of hepatocellular carcinoma and liver disease-related mortality [37,38]. Although there is a lack of randomised, high-quality studies collectively analysing the Mediterranean diet, the EASL-EASD-EASO, ESPEN and APASL guidelines list it as specifically recommended for patients with MASLD [17,18,19]. However, the Mediterranean diet is not free of drawbacks - one of the main challenges of its use is the potential difficulty of adapting this dietary model to individual patients' needs (especially given financial constraints and the availability of some ingredients, such as fresh fruit, vegetables and fish) [39]. It is also important not to overdo it - the Mediterranean diet, although healthy in principle, can also be hypercaloric, especially with an excessive supply of olive oil or nuts; people with hepatic steatosis should therefore, as always, be aware of the amount of calories consumed.

Protein-rich diets are another type of diet discussed in terms of its potential beneficial effect on hepatic steatosis. The results of studies are inconsistent, on the one hand noting a significantly higher protein intake in patients with MASLD features [40,41], but there are also studies noting such a

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statistically and clinically significant correlation [42,43] - a solution to this controversy may be to look more closely at the quality and source of protein, as Rietman et al. noted that there is an inverse relationship between plant protein intake and MASLD features, while animal protein intake was associated with greater intrahepatic lipid accumulation [44]. Researchers from Taiwan have demonstrated that antioxidant-containing soy protein can improve liver function even at the MASLD stage - this is done by reducing plasma free fatty acid concentrations, decreasing CYP2E1 expression, increasing superoxide dismutase activity, and consequently reducing the action of lipid peroxidation products, including m.malondialdehyde and 4-hydroxy alkenes, among others - the beneficial effect of plant-derived proteins (including soy) on the regulation of the inflammatory response and the activity of the immune system by affecting TNFα concentrations is also not negligible [45]. High consumption of meat, especially processed meat, is associated with impaired diabetes susceptibility and, consequently, increased prevalence of specific features of the metabolic syndrome and its individual components, with a particular focus on obesity and type 2 diabetes and associated features of MASLD [46]. However, with this in mind, the benefits of a high-protein dietary model cannot be overlooked - Xu et al. demonstrated that a 30% protein diet was associated with a 42.6% decrease in intrahepatic fat concentrations, which was linked to beneficial effects on hepatic autophagy and reduced inflammatory response [47]. The EASL-EASD-EASO guidelines include a protein-rich diet as one of the potentially beneficial lifestyle change interventions in MASLD [17]. The ESPEN guidelines state that patients with features of obesity-related disease, hepatic steatosis and comorbidities should follow a hypocaloric diet with an increase in target protein intake (2.0-2.5 g/kg body weight, as recommended by the American Society for Parenteral and Enteral Nutrition for critically ill obese patients [48]), which is expected to contribute to the reduction of fat mass and increase insulin resistance - however, interestingly, this recommendation does not have the full approval of the review board (71% agreement) [19]. Perhaps this is related to concerns about the negative impact of high-protein diets on the development of de novo chronic renal failure, as described by Ko et al.; however, it is worth noting that the concern is mainly with animal protein diets, characterised by high phosphate content [49].

For many years, the scientific community seems to have become increasingly interested in the therapeutic potential of ketogenic diets, mainly characterised by a low carbohydrate and high fat supply. Ketogenic diets may have a beneficial effect on patients with MASLD features by enhancing insulin sensitivity (which happens due to a reduction in the supply of simple carbohydrates, especially fructose, and a secondary reduction in body weight [50, 51]), reducing hepatotoxic oxidative stress with a subsequent increase in mitochondrial efficiency [52,53] as well as the effect on the intestinal microbiota (patients with MASLD and MASH features are characterised by reduced activity of the bacteria Rikenellaceae, Ruminococcaceae, Faecalibacterium, Coprococcus, Anaerosporobacter and Eubacterium, and the ketogenic diet leads to an increase in the abundance of precisely the short-chain fatty acid-producing bacteria beneficial for metabolism [54,55]). The ketogenic diet leads to a state of ketosis in which the body uses ketone bodies rather than glucose as the main energy source - this results in a reduction in insulin and insulin-like growth factor concentrations and an increase in fatty acid oxidation, which in sum modulates the inflammatory response and protects the liver from damage through lipid accumulation [56,57]. Rinaldi et al. on a group of 33 patients following a very low-calorie ketogenic diet demonstrated that it was effective in reducing hepatic steatosis as assessed by elastography (Fibroscan) - patients characterised by a baseline CAP suppression parameter of 266.6±67 dB/m after 8 weeks obtained a decrease in this parameter to a level of 223±64 dB/m, also obtaining an average reduction in BMI of 3 kg/m2 and in body fat mass of 7.5 kg [58]; similar effects with the same dietary model (consumption of 20-50g of carbohydrates per day, 15-30g of fat and protein at 1-1.4g/kg of body weight) were also obtained by De Nucci et al. [59]. The group of Vilar-Gomez et al. showed that following a non-restrictive ketogenic diet (with carbohydrate intake <30g/d, protein of 1.5 g/kg of body weight, and fat to satiety), compared to the standard dietary model proposed by the American Diabetes Association, was characterised in patients with MASLD on a diabetes background by greater success in weight loss, improvement in laboratory parameters (HbA1c, fasting insulinaemia, HOMA-IR index,

 doi:10.20944/preprints202412.1856.v1

aminotransferases, C-reactive protein), and in non-invasive indices of hepatic steatosis and fibrosis [60]. An interesting comparison of hypocaloric diets was made by Crabtree et al. - assessed weight loss and liver fat reduction between study participants on a ketogenic diet with additional ketone supplementation (carbohydrate supply 40 g, protein 99 g, fat 143 g daily), a ketogenic diet with placebo (carbo supply 38 g, protein 100 g, fat 131 g daily) and a high-carbohydrate low-fat diet (with carbohydrate supply 259 g, protein 100 g and fat 51 g per day) - it was found that, although after 6 weeks, the best weight reduction was achieved in patients on the ketogenic diet, at the same time, the strongest reduction in liver fat was seen in patients on the low-fat diet (however, only in absolute terms, with no statistically significant differences noted between groups) [61]. A certain difficulty in the pooled analysis of ketogenic diets is that the dietary models based on this concept are not consistent - the most common differences are in the different proposed percentages or macronutrient weights, as well as the suggested pooled calories. Legitimate concerns regarding the use of a ketogenic diet include the possibility of nutritional deficiencies and an increase in LDL fraction cholesterol (albeit without maintaining the overall negative health atherogenic profile) [62] - to counteract deficiencies, supplementation of water-soluble vitamins (thiamin, riboflavin, niacin, vitamin B6, folic acid, biotin, pantothenic acid in sugar-free formulations) and zinc, selenium, calcium, carnitine and omega-3 fatty acids should be considered [63,64]. The only guidelines that include the low-carbohydrate ketogenic diet as one of the recommended dietary interventions (without going into the details of this dietary model) are those by EASL-EASD-EASO [17].

An interesting concept of dietary intervention that does not strictly focus on the composition of meals, but rather on the timing of their intake, is the intermittent fasting model. In practice, intermittent fasting has been used since the beginning of time, mainly for religious or cultural reasons [65,66]. The potential to stabilise the diurnal rhythm of hormone secretion (specifically insulin and cortisol [67,68]) is considered to be factors promoting the efficacy of intermittent fasting in nutritional therapy for MASLD, regulation of the secretion of adipokines and inflammatory biomarkers derived from visceral adipose tissue (leptin, adiponectin, resistin, IL-6, TNFα [69-70]), effects on the gut microbiota or activation of autophagy with concomitant stimulation of growth hormone secretion [71]. Johari et al. demonstrated a positive effect of applied temporary caloric restriction on ALT levels and hepatic steatosis assessed using magnetic resonance imaging [72] - similar results in their study using liver elastography were obtained by the Australian group Feehan et al. [73]. Dietary models based on time restrictions are characterised by a relatively high degree of acceptability - admittedly, there are known reports of sleep architecture disturbances occurring during the typical Ramadan fasting phase, but at the same time without cognitive and physical impairment in fasting subjects, and even with improvement in mood disturbances if previously present [74]. As with the ketogenic diet, due to the abundance of diverse protocols for this dietary model, it is difficult to generalise the results of the studies to date - despite this, an umbrella review of 11 meta-analyses and 130 RCTs by an international consortium of researchers demonstrated the health benefits of intermittent fasting: weight loss with a reduction in mainly body fat mass, improvement in lipid metabolism parameters, reduction in the severity of insulin resistance and inflammation, and a decrease in blood pressure [75].

As in most cases, the key to appropriate nutritional therapy in hepatic steatosis remains its individualisation and personalisation [76]. In a logistic regression model by Perez-Diaz-del-Campo et al. it was shown that a personalised diet (low-carbohydrate or Mediterranean) to give a reduction in hepatic steatosis must simply be characterised by a decrease in body weight and therefore be primarily hypocaloric [77]. Given the scarcity of high-quality data on restrictive diets, the most sensible choice for the treatment of hepatic steatosis seems to be an individualised hypocaloric diet based on healthy eating patterns: including regular meals eaten at appropriate times, using unprocessed or minimally processed foods, limiting easily digestible simple sugars and saturated fats, yet high in polyphenols and n-3 polyunsaturated fatty acids. The strongest evidence for the efficacy of nutritional treatment seems to be (as described above) the Mediterranean diet, which is additionally relatively easy to convert to individually tailored models according to the patient's experience and preferences [17,18,19,78].

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Recommendations for Physical Activity in MASLD

Patients with MASLD, especially those with obesity, type 2 diabetes, hypertension or a history of cardiovascular incidents, as well as elderly patients, should consult their doctor before deciding on regular physical activity, in addition to regular walking, in order to assess their clinical condition, any contraindications to exercise and to determine the frequency and intensity of exercise. Exercise should be introduced gradually, especially in people who have not been physically active before and at low intensity, thus avoiding overtraining and injury.

Regular physical activity helps to improve fat metabolism and tissue sensitivity to insulin, as well as reducing insulin resistance and fat deposition in the liver [79].

A number of observational studies have shown that exercise reduces the incidence of MASLD. In an Italian cross-sectional study of 191 people, an inverse correlation was found between liver fat content and regular exercise. [80] In a Dutch study of 42,661 people, even lower levels of physical activity than the recommended minimum of 150 minutes per week were shown to have positive effects. The greatest results occur in diabetic and elderly patients. [81] In a cross-sectional study of 139,056 Koreans, spending more than 5 hours in a sedentary position during the day was shown to increase the chances of MASLD being found on ultrasound. [82] Another Korean study found that people who exercised at least three times a week for at least 30 minutes, for more than three months, halved their risk of developing MASLD. [83]

Physical activity can reduce the risk of developing MASLD by acting on multiple factors [6]. Aerobic exercise can reduce visceral adipose tissue and adipocyte size, which reduces the accumulation of free fatty acids in the liver. [84] During exercise, glucose uptake and storage as glycogen by muscle tissue increases. Regular exercise increases the uptake and oxidation of fatty acids by muscle. [85] Physical activity also affects the liver itself through multiple mechanisms - exercise is responsible for reducing oxidative stress, inflammation, the fibrosis process, decreasing de novo lipogenesis and increasing beta-oxidation of fatty acids occurring in the liver. [86] Exercise modulates the gut microbiota, increasing its diversity and changing the ratio of individual bacterial strains in favour of a phenotype less conducive to hepatic steatosis. They also improve the intestinal barrier and bile acid homeostasis. [87]

A number of randomised controlled trials and meta-analyses have been conducted to assess the effect of aerobic exercise on the treatment of MASLD. Exercise-only interventions led to reductions in liver fat ranging from 2% to 50%. [88] In addition, exercise also had a moderate effect on lowering aminotransferase levels. [89] It has been shown that a 1% weight loss corresponds to a 1% decrease in liver fat. [90]

A greater effect of physical activity on the reduction of hepatic steatosis was reported in those with a diagnosis of MASLD and a higher baseline BMI [89,91]. Studies indicate a relationship between fat reduction and total training time. [89] However, the optimal duration and intensity of exercise needed to reduce hepatic steatosis remains uncertain and requires further research.

In a meta-analysis of 17 studies, it was shown that for each week of exercise, liver fat levels decreased by 0.27%. [90] . Keating et al conducted a study on the effects of varying exercise intensity on liver fat. The study was conducted on a group of 48 patients who were divided into four groups. The authors found no differences in visceral or hepatic fat reduction in patients exercising at different intensities and frequencies. [92]

However, in a study involving 169 patients undergoing a 12-week training intervention, a greater reduction in liver fat was observed with high-intensity exercise compared to moderate intensity. The level was measured using the CAP parameter in liver elastography using the Fibroscan® method (32% vs. 23%). [93]

In another meta-analysis of 16 clinical trials involving 706 subjects, it was shown that even physical exercise not accompanied by a change in diet can reduce liver fat. [94]

The effect of resistance exercise, compared to aerobic exercise, on MASLD is less clear, and there is considerable heterogeneity in the findings. Studies suggest that aerobic exercise has a stronger effect on visceral fat reduction and regulation of glucose and lipid metabolism compared to resistance training. [94]

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Nevertheless, despite the lack of direct evidence of a beneficial effect of resistance training on hepatic steatosis, it has led to the maintenance of lean muscle mass during weight loss, improved muscle strength, muscle function and insulin sensitivity, which argues for its addition to aerobic training in people with MASLD. [95,96]

As Wu et al. showed in their pooled analysis, the combination of diet and exercise results in a weight loss 1.1kg greater than diet alone [97]. Analyses of fatty liver biopsy results, on the other hand, showed that the combination of a hypocaloric diet and the recommendation to walk 200 minutes per week was associated with significantly significant clinical benefits in terms of steatosis, fibrosis and liver function [98]. Engaging in physical activity alone, even if not associated with dietary management and weight loss, is effective in reducing intrahepatic and peripheral triglyceride concentrations [99,100].

However, it is important that exercise becomes a regular part of patients' behaviour (the effects do not last longer than 12 months after cessation of regular exercise) and that it is not too strenuous (as this does not increase the effectiveness in reducing hepatosteatosis) [101-103]. Official guidelines for the management of MASLD are inconsistent, and the most precise guidance can be found in the EASL-EASD-EASO guidelines - they suggest that patients with MASLD should undertake moderate-intensity aerobic activity for 150-200 minutes per week (in 3-5 sessions) and at the same time exploit the benefits of resistance training.

Regular aerobic exercise such as brisk walking, Nordic-walking etc. has a beneficial effect on the remission of hepatic steatosis mainly due to the regulation of fatty acid oxidation (using adiponectin and AMP kinase), leptin, intrahepatic SREBP-1c levels and the action of antioxidant enzymes [104,105].

Resistance exercise, on the other hand, has been associated with improved health in patients, particularly those with carbohydrate metabolism disorders - although data on the effect of this type of exercise on hepatic fat accumulation are inconsistent, due to its beneficial effects on strength and endurance capacity (and therefore facilitation of aerobic exercise progression), this type of training should be considered beneficial for patients with MASLD [106].

In patients with MASLD, it is also worth paying attention to daily non-exercise physical activity, or what is known as NEAT stands for Non-Exercise Activity Thermogenesis, which is the energy spent on daily activities that are not formal training or exercise.

NEAT encompasses all movements and activities during the day, such as:

- Walking (e.g. to work, shopping, walking the dog, walking while on the phone).
- Standing up and sitting down.
- Housework (cleaning, cooking, laundry, washing up, gardening).
- Involuntary movements such as toe tapping, fidgeting or moving the legs while sitting.
- Occupational work that requires physical activity (e.g. standing, walking around the office).

People who are more active in their daily activities have been shown to burn more calories, which can support weight maintenance or reduction. Differences in NEAT can be as much as a few hundred calories per day between people with different lifestyles, and on a weekly , monthly or yearly basis make a significant difference in weight loss.

NEAT is particularly important for people who do not have time for regular training, as daily small activities can significantly increase their total energy expenditure [107-110].

Various mobile apps, fitness bands and classic pedometers are interesting options for controlling quantitative exercise. The recommended number of steps per day for patients with obesity and MASLD is 10 000 steps. However, in the beginning, for those starting regular physical activity, this can be 4 000- 5 000 steps per day, which should be gradually increased. On the other hand, the number of steps in seniors should be adjusted individually - mandated between 6,000 and 8,000 steps per day or as many as the senior's health condition allows using the principle that every step counts. It is worthwhile using the aforementioned apps to enable notifications reminding of the need to move during the day [111-114].

 doi:10.20944/preprints202412.1856.v1

Physical activity recommendations should be aimed at all patients with MASLD. When implementing physical activity, it is important to remember to tailor training on an individual basis, taking into account physical capacity, co-morbidity and other potential factors hindering the initiation of regular physical activity, adherence to recommendations and patient cooperation. Factors cited in the literature include insufficient patient education about the benefits of physical activity and exercise technique itself, fatigue, lack of energy, pain, fear of falling and pain , as well as decreased motivation and willpower in those with anxiety and depressive disorders, which are often observed in patients with MASLD. In this group of patients, regular group exercises, bringing together patients with obesity and MASLD, which have a positive effect on motivation and maintaining the willpower of patients, and sports and rehabilitation holidays combined with nutritional education, therefore seem ideal. Any physical activity in patients with MASLD is extremely important, ranging from leisurely walks, cycling, jogging, Nordic-walking, swimming in the pool or tennis to team games such as volleyball, basketball or resistance exercises, gym workouts. General recommendations recommend 150-300 min/week of moderate-intensity physical activity (3-6 MET) or 75-150 min/week of high-intensity (>6 MET). [115-119].

Summary

Steatohepatic disease associated with metabolic dysfunction is now a real challenge for modern medicine, as are other lifestyle-dependent diseases dependent on excessive body weight. It is the most common liver disease in the world and its prevalence is increasing year on year in both adults and children, which is very worrying. This disease has led to a change in the epidemiology of causes of cirrhosis and causes of liver transplantation in developed countries in recent years, where MASLD is beginning to dominate. This is mainly related to the growing epidemic of obesity in all age groups, associated with poor eating patterns and lack of regular physical activity.

The main treatment for patients with MASLD is lifestyle change, targeting dietary treatment and increased exercise to translate into weight loss and improved cardiometabolic parameters. On the one hand, this is the simplest, easiest and cheapest recommendation with a proven impact on the course of MASLD, but it is also the most difficult to implement and, at the same time, to maintain in the long term by the patient, which usually ends in repeated effects - yo-yo (recurrence of obesity), further adversely affecting the course of hepatic steatosis and associated diseases.

Therefore, it seems necessary to educate the public from an early age about lifestyle medicine as a long-term prevention of MASLD, obesity and cardiovascular disease. Paying attention Continuous encouragement of physical exercise and adherence to a healthy diet.

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