

METABOLIC ASSOCIATED FATTY LIVER DISEASE AND EXERCISE

PROFESSIONAL

WHAT IS METABOLIC ASSOCIATED FATTY LIVER DISEASE (MAFLD)?

Metabolic associated fatty liver disease (MAFLD), formally known as non-alcoholic fatty liver disease (NAFLD) is a chronic liver disease that encompasses a range of conditions linked to an excess accumulation of fat within the liver. MAFLD is the most common liver disease worldwide affecting 20-30% of adults, however many people are unaware that they have the condition. In its simplest form (hepatic steatosis, defined as approximately > 5.0 % liver fat), MAFLD is strongly linked with abnormal blood lipids, hyperglycaemia and type 2 diabetes, hyperinsulinaemia and hypertension, and is often referred to as the 'hepatic manifestation' of the metabolic syndrome.

Approximately 5-20% of patients with MAFLD progress to steatohepatitis, which presents as hepatic steatosis with liver injury (including hepatocyte ballooning, inflammatory changes and variable degrees of hepatic fibrosis). Steatohepatitis is strongly linked with both liver-related and cardiovascular disease morbidity and mortality and can further progress to liver cirrhosis and hepatocellular carcinoma. Given its increasing prevalence, steatohepatitis is expected to become the leading cause for liver transplantation within the next five to ten years.

HOW IS METABOLIC ASSOCIATED FATTY LIVER DISEASE TREATED?

With no approved pharmacological agents for long-term treatment, lifestyle intervention is the first-line management strategy for MAFLD. The greatest benefits on the liver occur with weight loss, which is usually achieved via diet and exercise therapy. A body mass reduction of at least 7-10 % can significantly reduce liver fat, improve liver injury, and may reverse steatohepatitis. Modest reductions in liver fat and improvements in metabolic health can also be achieved with exercise and dietary modifications in the absence of weight loss.



WHY IS EXERCISE IMPORTANT FOR METABOLIC ASSOCIATED FATTY LIVER DISEASE?

Exercise has both hepatic and other extra-hepatic health benefits for people with MAFLD. Regular moderate- to vigorous-intensity aerobic exercise can reduce liver fat by 2-10 % and improve blood lipid profiles, insulin sensitivity, blood glucose control and hypertension. Regular aerobic exercise plays a key role in weight management and also reduces visceral adipose tissue. These changes may directly impact the liver by reducing inflammation and the delivery of free fatty acids to the liver. While the evidence for resistance training is less clear, it may also reduce liver fat and improve liver enzymes. There is currently no evidence to suggest that exercise directly improves the histological features of steatohepatitis, although engaging in vigorous exercise is associated with a reduced likelihood of having steatohepatitis or advanced fibrosis. Until further evidence is available, exercise for the management of steatohepatitis should be prescribed as per Table 1 in conjunction with dietary intervention and pharmacological management of co-morbidities, with the primary goal being weight loss.

Exercise has other well documented benefits for people with MAFLD such as:

- Improving cardiorespiratory fitness
- Improving vascular function
- Improving body composition
- Assisting in weight management
- Improving mental health
- Improving quality of life

Diet-induced weight loss may lead to loss of lean muscle tissue in addition to fat tissue. Therefore regular exercise, and in particular resistance training, plays an important role in promoting maintenance of lean muscle mass during diet-induced weight loss.

IMPORTANT CONSIDERATIONS FOR METABOLIC ASSOCIATED FATTY LIVER DISEASE AND EXERCISE?

All individuals with MAFLD should be screened by an appropriately qualified health professional (e.g. Accredited Exercise Physiologist or Physiotherapist) prior to initiating a new exercise program, or significantly altering or changing the approach to a current exercise program. As MAFLD is a condition associated with obesity and metabolic dysfunction, exercise should be prescribed as appropriate for other primary diagnoses (e.g. type 2 diabetes, chronic kidney disease, cardiovascular disease) with cognisance of co-morbidities (e.g. hypertension, hyperglycaemia, dyslipidaemia, osteoarthritis). If an individual with MAFLD is also being managed by other health professionals such as a cardiologist or an endocrinologist, it is important to communicate the exercise prescription plan with them.

Individuals with steatohepatitis may exhibit exercise intolerance due to diastolic cardiac dysfunction and thus perceived exertion may exceed apparent heart-rate measured relative intensity. In these individuals, initial exercise prescription may need to be of low relative intensity (i.e. 45-55 % HRmax). As low cardiorespiratory fitness has been shown to be associated with MAFLD, improving cardiorespiratory fitness should be a goal of exercise programming. Aerobic interval training may be a useful option to increase exercise capacity.

Identified barriers to the adoption of exercise in people with MAFLD are a lack of self-confidence in ability to exercise and a fear of falling. In people with MAFLD with no or low exercise experience, early exercise intervention should focus on improving exercise-related self-efficacy and utilising exercises that support balance (e.g. using stationary bikes or machine-based resistance exercises). Mastery of resistance training technique should be attained before progressing resistance training intensity.

Exercise should be prescribed with consideration of safety and co-morbidities, but also according to individual exercise preferences and alongside the implementation of strategies to support individuals in making sustainable lifestyle changes. Strategies may include frequent contact and assessment from an appropriately qualified health care professional, goal setting and self-monitoring.



WHAT TYPE OF EXERCISE IS BEST?

Individuals should target 150-300 minutes per week of moderate to vigorous intensity aerobic exercise per week (see Table 1). Smaller benefits can likely be achieved with lower doses of aerobic exercise, however it is recommended that patients exercise on at least three days per week. While the evidence for direct hepatic benefit is less compelling, resistance training may have benefit in some individuals with MAFLD. Two to three resistance training sessions could be undertaken in addition to regular aerobic exercise. As high sitting time has been shown to be associated with an increased prevalence of MAFLD, strategies to reduce sedentary time may also be considered, however the benefits of reducing sedentary time alone in MAFLD are unknown, and emphasis should be placed on adopting and adhering to regular aerobic exercise.

Mode	Frequency	Intensity	Duration	Hepatic benefits	Other health benefits
Aerobic training (examples: walking, jogging, cycling, swimming)	3-7 days per week	Moderate intensity: 55-69 % HRmax [#] Rating of perceived exertion [^] (RPE/10) 3-4 Or Vigorous intensity: 70-89 % HRmax RPE 5-6 Or A combination of moderate and vigorous exercise intensity	150-300 minutes Start at 5-10 minutes and increase gradually to 30-60 minutes per session. Or 75-150 minutes Start at 5-10 minutes and increase gradually to 20-30 minutes per session. Or Aiming for 150-300 total minutes per week Total minutes = minutes of moderate + (2 x minutes of vigorous)	<ul style="list-style-type: none"> • Reduced liver fat • May improve liver aminotransferases • Decreased activity of hepatic lipase • Reduced visceral adipose tissue • May improve inflammation 	<ul style="list-style-type: none"> • Improved cardiorespiratory fitness • Improved glycaemic control • Improved hypertension • Improved blood lipid profile • improved mental health • Improved quality of life
Resistance Training (examples: machine weights, circuit training, resistance bands, body weight exercise)	2-3 non-consecutive days per week, <i>in addition</i> to aerobic exercise prescription	Moderate to vigorous: 70-84 % 1 rep maximum (1-RM)* 8-12 exercises* 2-4 sets 8-10 repetitions 1-2 minutes rest between sets	30-60 mins	<ul style="list-style-type: none"> • May reduce liver fat • May improve liver aminotransferases 	<ul style="list-style-type: none"> • Improved glycaemic control • Improved muscle mass • Improved muscle function

Table 1. Recommended Exercise Targets for Patients with MAFLD

[#]HRmax, maximal heart rate: this is your age-predicted maximal heart rate and is calculated as (220 - age); [^]RPE, rating of perceived exertion: a subjective rating out of 10 describing 'how hard you feel you are working' considering all physiological systems- cardiorespiratory and musculoskeletal. *1 repetition maximum: the maximal weight that you can lift only once with good technique. 70-84% 1-RM equates to a weight that you can lift at least 8 times, but no more than 10 times before fatigue, in one set. *examples of exercises that can be tailored to the individual: squats, calf raises, lunges, chest press, seated row, shoulder press, biceps curl, triceps extension, prone hold.

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If you have any concerns about the safety of your patient in commencing an exercise program, please consider referral to a Sport and Exercise Physician.

REFERENCES AND FURTHER INFORMATION

1. Johnson NA, Keating SE, and George J. Exercise and the liver: implications for therapy in fatty liver disorders. *Seminars in Liver Disease*, 2012; 32: 1-15
2. Romeo-Gomez M, Zelber-Sagi S, Trenell M. Treatment of NAFLD with diet, physical activity and exercise. *Journal of Hepatology*, 2017; 67:829-846

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