Physical Activity and Nonalcoholic Fatty Liver Disease: A Roundtable Statement from the American College of Sports Medicine

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ABSTRACT

STINE, J. G., M. T. LONG, K. E. COREY, R. E. SALLIS, A. M. ALLEN, M. J. ARMSTRONG, D. E. CONROY, D. J. CUTHBERTSON, A. DUARTE-ROJO, K. HALLSWORTH, I. J. HICKMAN, M. R. KAPPUS, S. E. KEATING, C. J. A. PUGH, Y. ROTMAN, T. L. SIMON, E. VILAR-GOMEZ, V. W.-S. WONG, and K. H. SCHMITZ . Physical Activity and Nonalcoholic Fatty Liver Disease: A Roundtable Statement from the American College of Sports Medicine. *Med. Sci. Sports Exerc.*, Vol. 55, No. 9, pp. 1717–1726, 2023. Although physical activity (PA) is crucial in the prevention and clinical management of nonalcoholic fatty liver disease, most individuals with this chronic disease are inactive and do not achieve recommended amounts of PA. There is a robust and consistent body of evidence highlighting the benefit of participating in regular PA, including a reduction in liver fat and improvement in body composition, cardiorespiratory fitness, vascular biology, and health-related quality of life. Importantly, the benefits of regular PA can be seen without clinically significant weight loss. At least 150 min of moderate or 75 min of vigorous intensity PA are recommended weekly for all patients with nonalcoholic fatty liver disease, including those with

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compensated cirrhosis. If a formal exercise training program is prescribed, aerobic exercise with the addition of resistance training is preferred. In this roundtable document, the benefits of PA are discussed, along with recommendations for 1) PA assessment and screening; 2) how best to advise, counsel, and prescribe regular PA; and 3) when to refer to an exercise specialist. **Key Words:** EXERCISE, STEATOHEPATITIS, STEATOSIS, LIFESTYLE MODIFICATION, PREVENTION

Nonalcoholic fatty liver disease (NAFLD) has become a widespread pandemic driven by the increasing prevalence and incidence of obesity. Conservative estimates suggest that 25% to 30% of the global population has NAFLD (1,2). In the United States, almost 100 million adults have NAFLD, 25 million of whom have the progressive type called nonalcoholic steatohepatitis (NASH) (3,4). In the absence of a regulatory agency-approved drug therapy or cure, disease progression to cirrhosis or primary liver cancer with hepatocellular carcinoma (HCC) is not uncommon and may necessitate life-saving liver transplantation. In fact, NASH-cirrhosis continues to grow as a leading reason for liver transplantation (5,6). Although regular physical activity (PA) has many well-established benefits and may prevent or delay NAFLD and its complications, most individuals with NAFLD are inactive and fail to achieve recommended amounts of PA (7–15). In this roundtable document, the benefits of PA are discussed, along with recommendations for 1) PA assessment and screening; 2) how best to advise, counsel, and prescribe regular PA; and 3) when to refer a patient with NAFLD to an exercise specialist.

Diagnosis, classification, and etiology of NAFLD. Currently, the American Association for the Study of Liver Diseases requires the following to diagnose NAFLD: 1) at least 5% hepatic steatosis in the absence of an alternative cause of steatosis (e.g., steatogenic medication use, starvation, monogenic disorders) and 2) the absence of significant alcohol consumption, defined as <20 g·d^{-1} for women and <30 g·d^{-1} for men (16). Nonalcoholic fatty liver disease comprises two histological entities—nonalcoholic fatty liver (NAFL) and NASH. Nonalcoholic steatohepatitis, which can occur with or without liver fibrosis, is the progressive type of disease, which may lead to cirrhosis or HCC. Although NAFLD remains a complex disease process, it is generally agreed that a "multiple hit" pathogenesis, where environmental factors act on a genetically predisposed individual, is required to develop NAFLD and progress to NASH (17). Nonalcoholic fatty liver disease occurs frequently in individuals with other metabolic conditions, such as dyslipidemia, metabolic syndrome, obesity, polycystic ovary syndrome and/or type 2 diabetes.

Treatment goals in NAFLD. The primary goal of treatment in people with NAFLD/NASH is to prevent mortality and major adverse liver outcomes. It is generally accepted that reversing, arresting, or preventing liver fibrosis will lead to decreased risk for these clinical outcomes and that a reduction in hepatic steatosis may be beneficial as well. Patients with NAFLD can decrease their liver fat by enacting a lifestyle intervention with Mediterranean-informed dietary change and increased PA. When coupled with clinically significant body weight loss of 7% or greater, histologic improvement with liver fibrosis reversal can be expected (18). As lifestyle intervention is often viewed as a vehicle for clinically significant body weight loss, dietary change and PA remain crucial in the prevention and clinical management of NAFLD. Because most patients with NAFLD will not die from a major adverse liver outcome but rather from extrahepatic cancers or a cardiovascular disease (CVD) event (19), therapeutic approaches that also decrease oncologic and CVD risk are ideal. Importantly, regular PA may also play a role in these extrahepatic treatment goals. In addition, although there is no current regulatory agency-approved drug therapy for NASH, novel treatments seem possible in the near future. Regardless of when a drug therapy is approved for NASH, it should augment lifestyle intervention rather than replace it.

METHODOLOGY

To develop a consensus regarding PA and NAFLD, we carried out a Delphi study with a multidisciplinary international panel of 19 academic experts from four countries and 18 academic institutions (20). The core group of five members developed the initial consensus statements following individual and group systematic reviews. An iterative process was then undertaken with three rounds of review. The first round (R1) was survey-based, followed by an online consensus meeting [American College of Sports Medicine (ACSM) International Multidisciplinary Roundtable on PA and NAFLD] (20) and discussion of each statement and the corresponding levels of evidence (Table 1) for the second round (R2) and a final survey round (R3) of the consensus statements and recommendation. We achieved response rates of 89% in the R1, 100% in R2, and 94% in R3. A super majority (75%) was used for final agreement and inclusion of each statement in this position statement. No consensus could be achieved about the relationship between PA and change in liver fibrosis. The resulting consensus statements and recommendations (Table 2) can serve as a strong guidance for routine clinical management in patients with NAFLD with regard to PA.

Role of PA in NAFLD pathogenesis. Physical activity and NAFLD are intricately linked. There is a robust and consistent body of epidemiological evidence demonstrating regular

TABLE 1. Levels of evidence.

Levels	Type of Evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow CIs)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual cohort study (including low quality RCT)
2C	"Outcomes" research Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
2B	Individual case-control study
4	Case series Poor quality cohort or case-control study
5	Expert opinion without explicit critical appraisal or based on physiology bench research or "first principles"

TABLE 2. Consensus evidence statements and recommendations.

Role of PA in NAFLD pathogenesis:

1. Regular PA prevents the development of NAFLD (LOE 2B, individual cohort).
2. Emerging evidence suggests individuals who are less physically active may be at increased risk for disease progression to NASH with liver fibrosis and/or cirrhosis (LOE 2B, individual cohort).
3. Individuals who are less physically active have greater risk of primary liver cancer (e.g., HCC) and other extrahepatic cancers commonly associated with NAFLD (e.g., breast, colorectal, esophageal, gastric, pancreatic, prostate and kidney) (LOE 2B, individual cohort).
4. PA offers promise to reverse NAFLD pathogenesis by impacting multiple mechanistic pathways simultaneously and possibly synergistically (LOE 2B, individual cohort studies including low-quality RCT).

Assessing and screening patients with NAFLD for PA:

5. All patients with NAFLD should be screened for PA during routine health care visits with primary care and specialist (e.g., hepatologist) health care providers (LOE 2B, cohort/low-quality RCT).
6. Tools that provide standardized measures of PA (e.g., ACSM physical activity vital sign) should be administered regularly at routine health care visits (LOE 5, expert opinion).
7. Barriers to PA should be assessed systematically. While no one optimal tool has been identified, the SBIRT framework or NAFLD-specific questionnaires may be considered (LOE 5, expert opinion).

Advising and counseling patients with NAFLD about the benefits of PA:

8. All patients with NAFLD, regardless of disease stage, should be counseled on the benefits of PA by their primary care and specialist (e.g., hepatologist) health care providers (LOE 5, expert opinion).
9. Patient-centered language should be used at all counseling sessions. Stigmatizing language about body weight and body image should be avoided (LOE 5, expert opinion).
10. Behavioral approaches such as motivational interviewing may be beneficial in helping patients with NAFLD become more physically active (LOE 5, expert opinion).
11. Print or web-based educational materials specific to patients with NAFLD, including those from the ACSM Exercise is Medicine initiative, should be provided to all patients with NAFLD to reinforce in-person counseling by health care providers (LOE 5, expert opinion).
12. Established benefits of PA in patients with NAFLD include:
    a. Loss of liver fat on imaging (LOE 1A systematic review with homogeneity of RCTs).
    b. Improvement in histologic NASH activity (LOE 2B, low-quality RCT).
    c. Reversal of endothelial dysfunction (LOE 2B, low-quality RCT).
    d. Change in body composition (loss of adipose tissue and gain of lean muscle mass) (LOE 2B, low-quality RCT).
    e. Gain in physical fitness (LOE 1A, systematic review with homogeneity of RCTs).
    f. Improvement in HRQOL across multiple domains of health (LOE 2B, low-quality RCT).
13. Most benefits of regular PA in patients with NAFLD are independent of clinically significant weight loss (LOE 1B, individual RCT with narrow confidence intervals).
14. Emerging evidence suggests that sustained PA may improve liver histology (NASH activity and liver fibrosis) independent of significant weight loss; however, at this time, it remains accepted that weight loss may lead to the greatest impact on liver histology (LOE 1A, systematic review with homogeneity of RCTs).
15. In individuals with NAFLD who are overweight or obese, 7%–10% weight loss may improve liver histology (LOE 1A systematic review with homogeneity of RCTs).
16. Modest weight loss between 3% and 5% may lead to the same benefits in lean individuals as seen for patients who are overweight or obese (LOE 1A, systematic review with homogeneity of RCTs).

Referring a patient with NAFLD to an exercise specialist:

17. Referral to an exercise specialist should be considered for all patients with NAFLD to support the clinician in designing and implementing an exercise training program to allow patients with NAFLD to become more physically active (LOE 5, expert opinion).
18. For patients not meeting recommended activity amounts or intensities, referral to an exercise specialist is strongly recommended for individual exercise prescription feedback and development (LOE 5, expert opinion).
19. Routine use of exercise specialist databases, including those maintained by the ACSM, may assist the clinician in finding the most appropriate exercise professional for each individual patient (LOE 5, expert opinion).
20. Before starting a moderate-to-vigorous exercise training program, patients with NAFLD who are inactive are encouraged to seek medical clearance. For those who are actively engaged in a moderate exercise training program, medical clearance is recommended if seeking to begin a vigorous exercise training program (LOE 1A, systematic review with homogeneity of RCTs).
21. In patients with signs or symptoms suggestive of cardiovascular, metabolic and/or renal disease, starting with low-intensity exercise and progressing in intensity as physiologic acclimation occurs may be considered (LOE 5, expert opinion).

Continued next page

TABLE 2. *(Continued)*

22. An exercise specialist with additional training or expertise in metabolic disease and obesity is preferred and may offer the ability to expertly address physical conditions unique to patients with NAFLD that may prevent certain types of activity (e.g., osteoarthritis, sarcopenia, frailty, and deconditioning) (LOE 5, expert opinion).

PA recommendations in patients with NAFLD:

23. At least 150 min·wk^{-1} of moderate intensity PA or 75 min·wk^{-1} of vigorous PA are recommended each week for all adult patients with NAFLD (LOE 1B, individual RCT with small CI).
24. A graded, "staircase" approach is encouraged for patients with NAFLD to progress and achieve moderate-vigorous intensity activity (LOE 1B, individual RCT with small CI).
25. If a formal exercise training program is to be prescribed, aerobic exercise with the addition of resistance training is the preferred type of exercise (LOE 5, expert opinion).
26. In select patients, HIIT can be considered as an alternative to traditional aerobic exercise and resistance training. Inclusion of low-impact exercises may lessen the risk of injury with HIIT (LOE 2B, low-quality clinical trial).
27. Supervised and unsupervised PA appear to be equally safe and feasible, although efficacy data directly comparing the two are lacking (LOE 5, expert opinion).
28. An individualized approach where components of ACSM's FITT exercise principles (e.g., frequency, intensity, time, and type) are varied to achieve recommended amounts of weekly PA may help improve adherence (LOE 5, expert opinion).
29. Emerging evidence suggests that telehealth, including mobile health applications, may be considered as a safe, feasible, and effective way to increase PA in patients with NAFLD (LOE 2B, low-quality trial).
30. Patients with NAFLD and advanced liver disease, including those with cirrhosis, may safely perform regular PA at amounts similar to what is recommended for all patients with NAFLD (LOE 1B, individual RCT with small CI).

*No consensus was achieved about PA and improvement in liver fibrosis stage.

PA reduces the risk of NAFLD, especially if guideline-based amounts of activity are achieved (7–13,21). Over time, consistently performing regular moderate-to-vigorous PA (MVPA) can lead to lower mortality overall and from CVD (8), even if performed in short, continuous bouts of at least 10 min in length (21–23). Patients with NAFLD spend more time in sedentary behavior (15,24,25). For those individuals who are more sedentary, the risk of liver fibrosis and disease progression to cirrhosis may be greater (10). Physical activity is also closely related to oncologic risk. Multiple systematic reviews and meta-analyses have shown at the population level both hepatic and extrahepatic malignancy risk to be less in individuals who perform regular MVPA or leisure-time activity, including primary cancers, which are more commonly found in patients with NAFLD, including as breast, colorectal, and pancreatic (14,26,27).

Although the mechanisms underpinning the complex interplay between PA and NAFLD pathogenesis are not yet fully elucidated, regular PA impacts multiple pathways simultaneously (28–30), including uncoupling protein-1, peroxisome proliferator-activated receptor gamma, adipocytokines, branched chain amino acids, which feedback to reduce insulin resistance, and AMP-activated protein kinase (29,31–42). Regular PA may also influence gene expression (43,44) and reverse gut–liver–axis dysfunction (28,45,46).

Evidence statements:

1. Regular physical activity prevents the development of NAFLD (LOE 2B, individual cohort).
2. Emerging evidence suggests individuals who are less physically active may be at increased risk for disease progression to NASH with liver fibrosis and/or cirrhosis (LOE 2B, individual cohort).

3. Individuals who are less physically active have greater risk of primary liver cancer (e.g., hepatocellular carcinoma) and other extrahepatic cancers commonly associated with NAFLD (e.g., breast, colorectal, esophageal, gastric, pancreatic, prostate and kidney) (LOE 2B, individual cohort).
4. Physical activity offers promise to reverse NAFLD pathogenesis by impacting multiple mechanistic pathways simultaneously and possibly synergistically (LOE 2B, individual cohort studies including low-quality RCT).

Assessment and screening patients with NAFLD for PA. Routine health care visits offer opportunities for all clinicians to screen patients with NAFLD for PA. Although several validated tools exist in research and clinical practice (47–49), the two-question Physical Activity Vital Sign (50–52) is most easily performed and can readily be incorporated into electronic health records. At the population level, implementation of the Physical Activity Vital Sign has been reported to lead to significant loss of body weight in individuals with or at risk for metabolic disease (53).

Because most individuals with NAFLD do not achieve recommended amounts of weekly PA, screening for barriers preventing routine PA can be helpful and may identify areas to intervene. This intervention should follow an individualized approach, including addressing common self-reported barriers, such as cost, energy, fear of injury, motivation, time, skill or social support (15,54). Although no one optimal tool has been identified, the screening, brief intervention, and referral to a treatment framework (SBIRT) may be considered (55) and used as a scaffolding to design a personalized exercise prescription. Nonalcoholic fatty liver disease–specific questionnaires do exist as well for the busy clinician; however, their efficacy remains unknown (15).

Evidence statements:

5. All patients with NAFLD should be screened for physical activity during routine health care visits with primary care and specialist (e.g., hepatologist) health care providers (LOE 2B, cohort/low-quality RCT).
6. Tools that provide standardized measures of physical activity (e.g., ACSM Physical Activity Vital Sign) should be administered regularly at routine health care visits (LOE 5, expert opinion).
7. Barriers to physical activity should be assessed systematically. While no one optimal tool has been identified, the Screening, Brief Intervention and Referral to Treatment (SBIRT) framework or NAFLD-specific questionnaires may be considered (LOE 5, expert opinion).

Advising and counseling patients with NAFLD about PA. Because regular PA is important across all stages of NAFLD, all patients with NAFLD should be counseled about the benefits of PA. When approaching this conversation, it is important for the clinician to understand factors that determine whether a person engages in or avoids a certain behavior. Unfortunately, behavioral medicine is a field that is largely ignored across NAFLD research and recommendations in this area are adapted from non-NAFLD populations with metabolic disease. Nevertheless, the importance of multidisciplinary teams, use of patient-centered language, and avoidance of stigmatizing words about body weight and body image have all been successful (56,57). Using these tools may help encourage NAFLD patients to choose help seeking behavior more often.

Motivational interviewing is perhaps the most widely studied behavioral change technique in patients with NAFLD. A feasible approach can empower patients with NAFLD to make health-related decisions (58), within the context of a short clinic visit and may also lead to a reduction in body weight through dietary change and increased PA (59). Other techniques, which have been studied in patients with NAFLD and may also lead to greater amounts of PA completion, include cognitive behavioral therapy (60) and social-cognitive therapy (61,62).

Another tool available to the busy clinician comes from widely available print and web-based educational materials, which can be provided to reinforce the knowledge delivered as a part of an in-person conversation. When elected, these education materials, including that available from the ACSM Exercise is Medicine initiative, may lead to success in promoting health behavior change in patients with NAFLD (63), and should be provided to all patients with NAFLD.

Evidence statements:

8. All patients with NAFLD, regardless of disease stage, should be counseled on the benefits of physical activity by their primary care and specialist (e.g., hepatologist) health care providers (LOE 5, expert opinion).
9. Patient-centered language should be used at all counseling sessions. Stigmatizing language about body weight and body image should be avoided (LOE 5, expert opinion).
10. Behavioral approaches such as motivational interviewing may be beneficial in helping patients with NAFLD become more physically active (LOE 5, expert opinion).
11. Print or web-based educational materials specific to patients with NAFLD, including those from the ACSM Exercise is Medicine initiative, should be provided to all patients with NAFLD to reinforce in-person counseling by health care providers (LOE 5, expert opinion).

Benefits of PA in patients with NAFLD. There are many well-established benefits of regular PA and, in particular, exercise training in patients with NAFLD and NASH, including loss of liver fat on imaging, improvement in NASH activity on histology, reversal of endothelial dysfunction, change in body composition, gain in physical fitness, and improvement in health-related quality of life (HRQOL). Importantly, many of these benefits appear independent of clinically significant body weight loss (45,64). Whether weight loss is required for liver fibrosis improvement with exercise training remains unclear; however, in general, it is accepted that at least 7% body weight loss is required to lead to improvement in liver fibrosis across all treatment interventions (18,65,66).

The most widely studied and established benefit of exercise training in patients with NAFLD is improvement in liver fat measured by magnetic resonance imaging (MRI) scan (35,67–81). This benefit appears to be independent of significant body weight loss and is greatest for aerobic exercise training. Other modalities of exercise, which have also been shown to reduce liver fat, include resistance training, high-intensity interval training (HIIT), and combined aerobic and resistance training. A recent systematic review and meta-analysis (64) suggests that exercise training achieves rates of clinically significant reduction in MRI-measured liver fat at the threshold, which may be a surrogate for histologic improvement in both NASH activity and liver fibrosis at thresholds adapted from NASH drug trials (82,83). This is important because to date, there is inconsistent evidence that exercise training independently improves liver fibrosis when liver histology is directly examined, despite multiple studies showing histologic NASH activity can be improved, especially in the presence of significant body weight loss (84–87).

Cardiovascular disease is a leading cause of death in patients with NAFLD (19). Fortunately, exercise training has been shown to improve biomarkers of CVD, including reversal of endothelial dysfunction (88) and reduction in serum plasminogen activator inhibitor 1 concentration (45). Exercise training also improves body composition favorably, by reducing adipose tissue volume and possibly increasing lean body mass. Both visceral adipose tissue and subcutaneous adipose tissue have been shown to be reduced by aerobic exercise training (32,45,89–93). The evidence supporting improvement in lean body mass is less consistent, where a statistically significant improvement in lean body mass has not been demonstrated, perhaps owing to short study durations (45,94–98).

Exercise training consistently improves cardiorespiratory fitness. There is a robust body of evidence demonstrating that peak oxygen uptake ($\dot{V}O_{2peak}$), which is universally poor in patients with NAFLD (24,99) and related to liver fibrosis stage (24,100,101), can be improved with regular exercise training (68,80,94). This is consistent across multiple exercise types, including both moderate-intensity aerobic exercise and HIIT protocols (45,68,77,80,94). Health-related quality of life, which is also poor in patients with NAFLD (102,103), may also be improved with aerobic exercise based on a recent single-center RCT (45).

Evidence statements:

12. Established benefits of physical activity in patients with NAFLD include:
    a. Loss of liver fat on imaging (LOE 1A systematic review with homogeneity of RCTs.
    b. Improvement in histologic NASH activity (LOE 2B, low-quality RCT).
    c. Reversal of endothelial dysfunction (LOE 2B, low-quality RCT).
    d. Change in body composition (loss of adipose tissue and gain of lean muscle mass) (LOE 2B, low-quality RCT).
    e. Gain in physical fitness (LOE 1A systematic review with homogeneity of RCTs).
    f. Improvement in health-related quality of life across multiple domains of health (LOE 2B, low-quality RCT).
13. Most benefits of regular physical activity in patients with NAFLD are independent of clinically significant weight loss (LOE 1B, individual RCT with narrow confidence intervals).
14. Emerging evidence suggests that sustained physical activity may improve liver histology (NASH activity and liver fibrosis) independent of significant weight loss, however, at this time it remains accepted that weight loss may lead to the greatest impact on liver histology (LOE 1A Systematic Review with Homogeneity of RCTs).
15. In individuals with NAFLD who are overweight or obese, 7%–10% weight loss may improve liver histology (LOE 1A Systematic Review with Homogeneity of RCTs).
16. Modest weight loss between 3% and 5% may lead to the same benefits in lean individuals as seen for patients who are overweight or obese (LOE 1A Systematic Review with Homogeneity of RCTs).

Referring a patient with NAFLD to an exercise specialist. Because physicians are not routinely trained in exercise prescription during medical education and may not feel comfortable delivering this information (104), the exercise specialist remains a crucial member of the multidisciplinary NAFLD treatment team and may be found across various exercise society databases. Exercise specialists are encouraged to assess a patient's understanding of NAFLD and how lifestyle impacts this common disease and also to establish goals for treatment. Exercise specialists have an additional role in assessing: 1) current and historical PA level; 2) physical fitness in the context of cardiometabolic risk factors and other pertinent medical comorbidities and; 3) barriers and facilitators to PA completion.

Published ACSM guidelines exist to help the exercise specialist determine when medical referral should be sought prior to initiating an exercise training program (105). Because many patients with NAFLD are inactive and have a history of either CVD or metabolic disease, medical guidance from a treating physician may be necessary prior to beginning an exercise program, especially if a moderate-intensity program is to be prescribed. For individuals who are actively engaged in a moderate-intensity training program already, medical clearance is recommended before progressing to a vigorous-intensity program (105). Progressive exercise, starting with low-intensity activities, should also be considered in individuals with NAFLD who have signs or symptoms suggestive of CVD, metabolic and/or renal disease. No physician clearance is required for low intensity activity, which is performed at <50% $\dot{V}O_{2peak}$ (e.g., slowly walking).

Evidence statements:

17. Referral to an exercise specialist should be considered for all patients with NAFLD to support the clinician in

designing and implementing an exercise training program to allow patients with NAFLD to become more physically active (LOE 5, Expert opinion).

18. For patients not meeting recommended activity amounts or intensities, referral to an exercise specialist is strongly recommended for individual exercise prescription feedback and development (LOE 5, Expert opinion).
19. Routine use of exercise specialist databases, including those maintained by the ACSM, may assist the clinician in finding the most appropriate exercise professional for each individual patient (LOE 5, Expert opinion).
20. Prior to starting a moderate to vigorous exercise training program, patients with NAFLD who are inactive, are encouraged to seek medical clearance. For those who are actively engaged in a moderate exercise training program, medical clearance is recommended if seeking to begin a vigorous exercise training program (LOE 1A, Systematic Review with Homogeneity of RCTs).
21. In patients with signs or symptoms suggestive of cardiovascular, metabolic and/or renal disease, starting with low-intensity exercise and progressing in intensity as physiologic acclimation occurs may be considered (LOE 5, Expert opinion).
22. An exercise specialist with additional training or expertise in metabolic disease and obesity is preferred and may offer the ability to expertly address physical conditions unique to patients with NAFLD that may prevent certain types of activity (e.g., osteoarthritis, sarcopenia, frailty and deconditioning) (LOE 5, Expert opinion)

PA recommendations in patients with NAFLD. Exercise training remains a key component in the clinical management of patients with NAFLD. To date, there is a clear and consistent body of evidence supporting this statement despite the heterogeneity across the individual clinical trials, which vary widely in each of the ACSM FITT principles of exercise prescription. Because exercise frequency (3–7 $d \cdot wk^{-1}$), intensity (low, moderate, moderate-vigorous, and vigorous), time (20–60 min), and type (aerobic, resistance, aerobic and resistance combined, HIIT, Pilates, yoga) are variable in the published literature (35,67,77,106–109), no single optimal exercise prescription has been defined for patients with NAFLD. However, it has been suggested that the combination of aerobic and resistance training is likely more effective than either independently (106), although this remains controversial and in need of further validation.

What appears to be more important than each individual FITT component is the total dose of exercise delivered. Exercise dose is routinely reported in metabolic equivalent of task (MET) minutes and is calculated by intensity (METs) by time and aggregated each week. An exercise dose of 750 MET-$min \cdot wk^{-1}$, which is the equivalent of 150 $min \cdot wk^{-1}$ of moderate-intensity activity or 75 $min \cdot wk^{-1}$ of vigorous intensity activity, appears sufficient to improve clinical outcomes in patients with NASH (64). In addition, although the majority of the published literature uses direct, in-person supervision of exercise, emerging evidence suggests that remote monitoring with telehealth or unsupervised mobile health-delivered lifestyle intervention programs may be equally feasible, safe, acceptable, and possibly as efficacious as traditional, supervised in-person exercise training (110–114).

Patients with advanced liver disease, including those with cirrhosis, represent a unique patient population that has traditionally been viewed independently of patients with earlier-stage disease. Several exercise intervention trials challenge this historical perspective and show that exercise training is feasible, safe, and highly efficacious in patients with cirrhosis, including those whose primary etiology of liver disease is NASH (115–118). Collectively, these studies have shown that regular exercise training decreases portal hypertension (115), and may improve physical performance, frailty and HRQOL (116,117). It is important to recognize that these studies did not include patients with decompensated cirrhosis and therefore no recommendation can be made in this patient population (20,119).

Evidence statements:

23. At least 150 $min \cdot wk^{-1}$ of moderate intensity physical activity or 75 $min \cdot wk^{-1}$ of vigorous physical activity are recommended each week for all adult patients with NAFLD (LOE 1B, individual RCT with small CI).
24. A graded, "staircase" approach is encouraged for patients with NAFLD to progress and achieve moderate-vigorous intensity activity. (LOE 1B- Individual RCT with small CI).
25. If a formal exercise training program is to be prescribed, aerobic exercise with the addition of resistance training is the preferred type of exercise (LOE 5, Expert opinion).
26. In select patients, supervised high-intensity interval training (HIIT) can be considered as an alternative to traditional aerobic exercise and resistance training. Inclusion of low-impact exercises may lessen the risk of injury with HIIT (LOE 2B, Low-quality clinical trial).
27. Supervised and unsupervised physical activity appear to be equally safe and feasible, although efficacy data directly comparing the two are lacking (LOE 5, Expert opinion)
28. An individualized approach where components of ACSM's FITT exercise principles (e.g., frequency, intensity, time and type) are varied in order to achieve recommended amounts of weekly physical activity may help improve adherence (LOE 5, Expert opinion)
29. Emerging evidence suggests that telehealth, including mobile health applications, may be considered as a safe, feasible and effective way to increase physical activity in patients with NAFLD (LOE 2B, Low quality trial)
30. Patients with NAFLD and advanced liver disease, including those with compensated cirrhosis, may safely perform regular physical activity at amounts similar to what is recommended for all patients with NAFLD (LOE1B, individual RCT with small CI).

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