

Telemonitoring-Supported Exercise Training in Employees With Metabolic Syndrome Improves Liver Inflammation and Fibrosis

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INTRODUCTION: Metabolic syndrome (MetS) is a major health problem worldwide and the main risk factor for metabolic-associated fatty liver disease (MAFLD). Established treatment options are lifestyle interventions facilitating dietary change and increased physical activity. Here, we tested the effect of a telemonitoring-supported intervention on liver parameter of inflammation and fibrosis in individuals with MetS.

METHODS: This was a prospective, randomized, parallel-group, and assessor-blind study performed in workers of the main Volkswagen factory (Wolfsburg, Germany). Volunteers with diagnosed MetS were randomly assigned (1:1) to a 6-month lifestyle intervention focusing on supervised, activity-tracker-guided exercise or to a waiting-list control group. This secondary analysis assessed the effect of the intervention on liver enzymes and MAFLD-related parameters.

RESULTS: We screened 543 individuals between October 10, 2017, and February 27, 2018, of whom 314 were randomly assigned to the intervention group (n = 160) or control group (n = 154). Liver transaminases, alkaline phosphatase, and gamma-glutamyl transferase significantly decreased after 6 months in the intervention group compared with the CG. Furthermore, an aspartate aminotransferase-to-platelet ratio index score as a marker for liver fibrosis significantly decreased in the intervention group. These improvements were associated with changes in obesity and exercise capacity.

DISCUSSION: A 6-month lifestyle intervention based on exercise training with individualized telemonitoring-based supervision led to improvements of liver inflammation and fibrosis in employees with MetS. Therefore, this intervention shows therapeutic potential for individuals at high risk of MAFLD (ClinicalTrials.gov Identifier: NCT03293264).

SUPPLEMENTARY MATERIAL accompanies this paper at <http://links.lww.com/CTG/A639>

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INTRODUCTION

Metabolic syndrome (MetS) is a major health problem worldwide, affecting nearly 25% of the population (1) with inactive lifestyle and overeating as the main risk factors. Insulin resistance is a key factor in the pathogenesis of MetS because it leads to an increase of visceral fat and fat accumulation in other organs, such as the liver (2,3). MetS is associated with various diseases. Importantly, it is the major risk factor for the development of

metabolic-associated fatty liver disease (MAFLD) (4,5), which is defined by the presence of liver steatosis plus 2 of the 3 following risk factors: overweight, diabetes mellitus, and evidence of metabolic dysregulation (6). About 40%–60% of patient with MetS are suffering from MAFLD (7). In addition, about 15% of patients with MAFLD develop metabolic-associated steatohepatitis, which could lead to severe fibrosis and progression to end-stage liver disease and hepatocellular carcinoma (8).

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Therefore, patients with MetS should be monitored for hepatic abnormalities. Patients with elevated liver enzymes and further risk factors for MAFLD should receive liver etiology screening because MAFLD is the most common cause for incidentally detected elevated transaminases (9).

Treatment options for MAFLD are rare but urgently needed. Therapeutic lifestyle changes including weight loss and increased physical activity might have a greater impact on improvement of MetS than pharmacological options (10). The recommendations of the Diabetes Prevention Program included dietary intervention and 150 minutes of physical activity per week, besides pharmacologic options. Previous studies also showed promising results of aerobic and resistance exercise on hepatic fat content and insulin resistance (11).

However, long-term compliance to physical activity and lifestyle modifications are hard to achieve in daily practice. Furthermore, the widespread prevalence of MetS and MAFLD requires technology-assisted interventions to treat the large target group and to strengthen effectiveness of physical activity in the long term. In a randomized controlled trial in employees with MetS, we previously observed that a 6-month lifestyle intervention focusing on exercise training with individualized telemonitoring-based supervision reduced the severity of MetS. In this secondary analysis, we tested whether this intervention could also improve liver parameters and therefore decrease risk of MAFLD.

MATERIALS AND METHODS

Study design and participants

This study is a secondary analysis of a recently published trial reporting the primary outcome MetS severity after exercise training (12). This was a prospective, randomized, and single-blind (assessor blind) trial conducted as a collaborative project between Volkswagen AG and Hannover Medical School (ClinicalTrials.gov Identifier: NCT03293264). Details on participant recruitment and exclusion criteria are given in the online supplement (see Text, Supplementary Digital Content 1, <http://links.lww.com/CTG/A639>).

Volunteers diagnosed with MetS were randomized 1:1 to a 6-month exercise group (EG) or a waiting-control group (CG) using a computer-based list of random numbers generated by an external collaborator. Variable block length was used to avoid selection bias because of predictability. Study nurses and physicians screening volunteers and assessing the primary outcome at baseline and after 6 months were blinded for the randomization sequence (Figure 1).

Anthropometric and cardiometabolic assessments. After a general medical examination by a physician (including electrocardiogram, case history, and physical examination), body weight, waist circumference, and height were recorded. Blood pressure, fat mass, and exercise capacity are detailed in the supplementary data (see Text, Supplementary Digital Content 1, <http://links.lww.com/CTG/A639>).

Serum measurements. Blood samples were analyzed in the certified clinical chemistry laboratory of the occupational healthcare center (Volkswagen AG, Wolfsburg, Germany). Transaminase measurements and calculation of the aspartate aminotransferase-to-platelet ratio index (APRI) score and the Fibrosis-4 score are

detailed in the supplementary data (see Text, Supplementary Digital Content 1, <http://links.lww.com/CTG/A639>).

Questionnaires. We distributed questionnaires for the estimation of anxiety severity and depression severity. Scores for the anxiety and depression subscale range from 0 to 21, with higher score indicating more severe anxiety or depression (13), health-related quality of life (short-form 36) (14), and daily physical activity (Freiburger Physical Activity Questionnaire and work ability index) (15). Questionnaire details are available in the supplementary data (see Text, Supplementary Digital Content 1, <http://links.lww.com/CTG/A639>).

Study intervention

The study intervention is described in detail in the online supplement (see Text, Supplementary Digital Content 1, <http://links.lww.com/CTG/A639>) and elsewhere (12). In brief, participants performing the 6-month exercise intervention received a personal counseling with recommendations aiming to perform 150 minutes of moderate-intense physical activity per week.

The EG was equipped with an activity monitor (Forerunner 35, Garmin, Garching, Germany) and asked to wear the monitor throughout the intervention period. Furthermore, participants completed a 7-day food diary which was analyzed and reviewed by dietitians for macronutrient and micronutrient content using professional nutrition analysis software (DGE-PC professional Version 5.1.0.048, DGE; Germany).

Statistical analysis

All authors had access to the study data and reviewed and approved the final manuscript. The primary outcome of our study was the change in the MetS severity after a 6-month exercise intervention compared with controls. Based on an earlier study using a similar intervention (16), a sample size of 264 participants was calculated to achieve a significant between-group difference for the primary outcome with 90% power and significance level of 0.05 (MedCalc Statistical Software version 17.6, Ostend, Belgium). With an anticipated dropout rate of 18%, we calculated a final sample size of 312 subjects for inclusion in the study. For the analysis of the primary and all secondary outcomes, an analysis of covariance model was used with the change in the parameter of interest (6 months and baseline) as the response variable. Explanatory variables were sex, the respective parameter at baseline, and study group (exercise vs control). Normality distribution was tested using the Kolmogorov-Smirnov test. Analysis was performed according to the intention-to-treat principle for all outcomes, including all randomized subjects. Missing values were replaced by the baseline observation carried-forward method. For descriptive analysis, absolute frequencies were calculated for categorical variables and mean and SD for continuous variables. To test for within-group differences from baseline to end of the intervention, a 2-sided Student *t* test for paired samples was used. Univariate associations between parameters were tested using the Pearson correlation coefficient. Stepwise backward multivariate linear regression was used to estimate predictors of changes in liver enzymes with the 6-month intervention.

The study was performed in accordance with the Declaration of Helsinki and current guidelines of good clinical practice. The institutional review board of Hannover Medical School approved

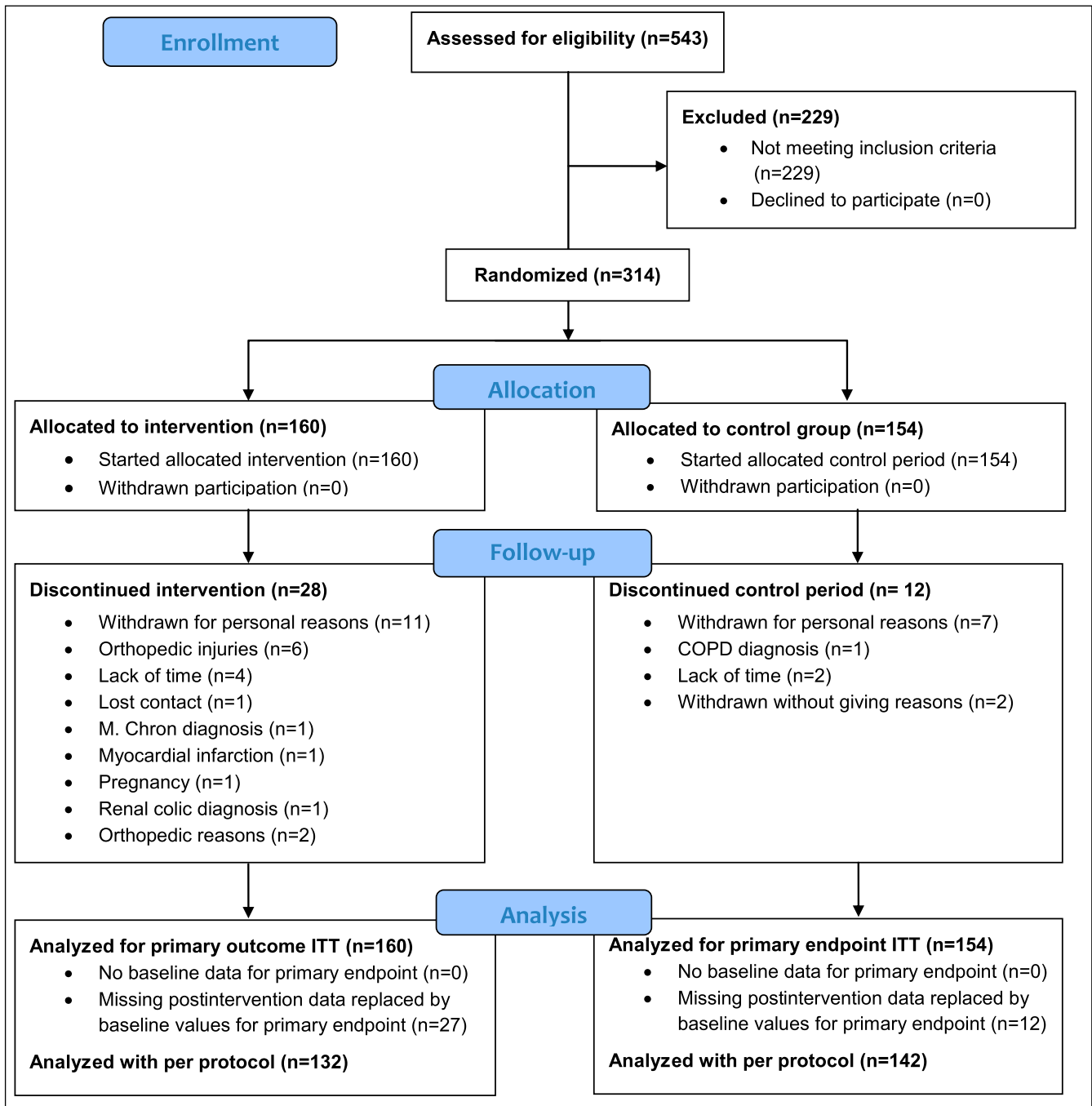


Figure 1. Participant flow chart.

the study (No. 7531), and written informed consent was obtained before inclusion of study participants.

RESULTS

Of 314 randomized subjects, 274 (87%) completed the intervention, with 28 (17.5%) subjects in the EG and 12 (7.8%) in the CG dropped out during the 6-month period. For more details on reasons for dropouts in both study groups, see Figure 1. Transaminases could not be determined for 10 subjects in the EG and 9 in the CG because of blood sampling or laboratory shortcomings. Subjects in the EG and CG did not differ for sex

distribution, age, body composition, daily physical activity, and exercise capacity at baseline (Table 1).

Compliance to physical activity, exercise training characteristics, and exercise capacity

Questionnaire-estimated exercise activities increased more for subjects in the EG during the 6-month intervention (EG before: 6.5 ± 13.7 ; after: 15.9 ± 20.1 metabolic equivalent of task hr/wk; CG before: 6.4 ± 9.0 , after: 10.5 ± 15.6 metabolic equivalent of task hr/wk; $P < 0.01$ between groups). As assessed by the activity monitor worn by the EG subjects, compliance to the scheduled

Table 1. Subject characteristics at baseline

	Intervention group	Control group	P value
Subjects (women/men)	160 (24/136)	154 (21/133)	0.74
Age (yr)	48.3 ± 7.9	47.8 ± 8.5	0.62
Body weight (kg)	107.6 ± 18.3	106.1 ± 20.3	0.43
Body mass index (kg/m ²)	33.6 ± 5.3	33.0 ± 5.4	0.33
Waist circumference (cm)	115.6 ± 12.1	114.7 ± 12.7	0.52
HbA1c (%)	5.7 ± 1.0	5.6 ± 0.9	0.30
Total cholesterol (mg/dL)	215 ± 46	214 ± 46	0.84
LDL cholesterol (mg/dL)	138 ± 39	137 ± 40	0.89
Depression severity (points)	5.3 ± 3.2	5.0 ± 3.3	0.46
Anxiety severity (points)	4.8 ± 2.6	4.6 ± 3.1	0.68
Mental component score of SF-36 (points)	49.2 ± 9.4	49.9 ± 9.7	0.79
Physical activity/exercise testing			
Total physical activity (MET-hr/wk)	25.9 ± 23.8	21.8 ± 16.5	0.47
Exercise activity (MET-hr/wk)	6.4 ± 13.7	6.5 ± 9.0	0.80
Exercise capacity (peak watt)	174 ± 36	176 ± 37	0.91
Medication			
Antihypertensive drugs (n)	124	151	0.11
Antidiabetic drugs (n)	39	29	0.23
Lipid-lowering drugs (n)	19	31	0.09
Thyroid drugs (n)	14	17	0.59
Anticoagulant drugs (n)	11	9	0.66
Others (n)	35	33	0.81
Differences between groups were analyzed with the Student <i>t</i> test for unpaired samples or the χ^2 test; data are mean ± SD. LDL, low density lipoprotein; MET, metabolic equivalent of task; SF-36, short-form 36 questionnaire of health-related quality of life.			

target of 150 minutes of physical activities per week was 147 ± 46 min/wk. The average heart rate for manually started physical activities during the intervention was 117 ± 11 beats/min ($72.4\% \pm 9.8\%$ of HR_{max}) meeting the targeted heart rate range between 65% and 75% relative to measured maximum heart rate. Average steps during the intervention were $9,612 \pm 2,498$ steps/d. The maximum power output during incremental exercise testing increased for the EG (before: 1.66 ± 0.38 , after: 1.89 ± 0.46 -W/kg body weight [BW], $P < 0.01$) and CG (before: 1.69 ± 0.40 , after: 1.77 ± 0.44 -W/kg BW; $P < 0.01$) with a significant difference between groups of 0.16-W/kg BW (95% confidence interval: 0.10–0.21; $P < 0.01$).

Nutritional intake

Energy intake, macronutrient intake, and alcohol consumption were similar between groups at baseline. The EG reduced intake of total energy, fat, and carbohydrates, with no difference for changes between study groups over time (Table 2).

Blood parameters and renal function

At baseline, participants showed normal leukocyte and platelet count, hemoglobin, and hs-CRP values as well as creatinine and urea levels, with no difference between study groups over time (see Supplementary Table S1, Supplementary Digital Content 1, <http://links.lww.com/CTG/A639>).

Liver enzymes

Both groups showed slightly elevated alanine aminotransferase (ALT) levels at baseline (EG: 47.0 U/L; CG: 47.8 IU/L). In detail, 113 patients had elevated ALT levels at baseline (EG: 50; CG: 63) according to the laboratory reference levels for upper limits of normal. For aspartate aminotransferase (AST), 75 patients had levels above normal at baseline (EG: 34; CG: 41).

After 6 months of the physical activity intervention, ALT and AST levels significantly decreased in the EG compared with the CG (Figure 2a). Alkaline phosphatase and gamma-glutamyl transferases (gGT) also significantly decreased in the EG but not in the CG, with significant differences between groups over time (Figure 2b).

In a second step, we analyzed all patients with elevated ALT levels at baseline and their changes over time ($n = 113$) according to local laboratory reference values. In the EG, 62 patients with elevated ALT at baseline could achieve normalization of ALT levels after 6 months of a physical intervention compared with 34 patients in the CG (Figure 3). We further evaluated the cohort again according to the American Association for the Study of Liver Diseases recommended upper limits of normal for ALT for a clearer assessment between patients with high risk of liver damage (17,18). Of these, 200 patients had increased ALT levels at baseline (EG: 94 patients; CG: 106 patients). After a 6-month intervention, 31 patients (33%) could achieve normalization of ALT levels in the EG compared with only 15 patients (14%) in the CG ($P = 0.002$) (Figure 3).

Fibrosis scores

The Fibrosis-4 score was within the normal range in both groups (EG: 1.03 ± 0.29 to 1.09 ± 0.35 , $P < 0.01$; CG: 0.95 ± 0.32 to 1.00 ± 0.38 , $P < 0.05$) with no significant changes during 6 months between groups ($P = 0.49$).

The APRI score could be calculated in 254 patients of 274 patients, who completed the intervention. At baseline, we could exclude advanced fibrosis in 222 patients in both groups (EG: 101 patients, APRI mean = 0.35 ± 0.10 ; CG: 115 patients, APRI mean = 0.36 ± 0.10). However, 32 patients had APRI scores between 0.5 and 1.5 (EG: 17 patients, APRI: 0.72 ± 0.22 ; CG: 15 patients, APRI: 0.69 ± 0.09) (19) (Figure 4). After 6 months of the physical activity intervention, the APRI score was significantly reduced in the EG after 6 months but not in the CG, with a significant difference between groups over time (Figure 4). In an additional exploratory analysis, the APRI score was significantly reduced in these patients with previously elevated APRI scores (0.5–1.5) but not in those with an APRI score from 0 to 0.5 (no fibrosis) (Figure 4).

In the EG, changes in body mass index (BMI) correlated with changes in ALT ($r = 0.37$, $P < 0.001$) and AST ($r = 0.24$; $P < 0.01$). Furthermore, improvement of exercise capacity correlated with improvement of transaminases (AST: $r = -0.23$, $P < 0.05$; ALT: $r = -0.31$, $P < 0.001$). When stratified in tertiles of changes in BMI and changes in exercise capacity, those with highest improvements for BMI and exercise capacity showed significantly

Table 2. Change in dietary intake after a 6-month intervention

	Exercise group		Control group		Between-group difference	
	Baseline	6 mo	Baseline	6 mo	Mean (95% confidence interval)	P value
Energy intake (kcal/d)	2,358 ± 1,167	2,138 ± 1,166*	2,170 ± 697	2,092 ± 721	97 (−53 to 249)	0.21
Fat intake (g/d)	101 ± 57	91 ± 58*	97 ± 36	90 ± 38	6.1 (−1.7 to 13.9)	0.12
Carbohydrate intake (g/d)	228 ± 119	205 ± 113*	207 ± 74	197 ± 72*	7.8 (−6.7 to 22.2)	0.29
Protein intake (g/d)	109 ± 53	105 ± 55	101 ± 36	100 ± 38	2.0 (−8.3 to 12.2)	0.57
Alcohol intake (g/d)	10.7 ± 13.4	8.8 ± 10.2*	13.0 ± 11.3	11.3 ± 13.1	1.2 (−0.8 to 3.1)	0.24

*P < 0.05 different between baseline and 6 months, differences between groups over time as analyzed with an analysis of covariance model adjusted for sex and the respective baseline value, and data are mean ± SD except for the between-group difference over time (95% confidence interval).

greater improvements in ALT compared with participants in the lowest tertile (Figure 5).

In a multivariate linear regression analysis including age, sex, changes in exercise capacity, changes in total energy intake, and changes in BMI as independent variables, only changes in BMI predicted ALT ($\beta = 0.33, P > 0.001$) and AST changes ($\beta = 0.26, P > 0.01$) during the 6-month intervention.

DISCUSSION

Change of lifestyle and physical activity are already established therapy options for MetS and MAFLD (20). However, this study investigates the impact of a physical activity–focused lifestyle intervention by using telemonitoring-supported systems, a new strategy that allows supervising a large number of individuals independent of residence or workplace. A major strength of this study is the proof of clinical effectiveness of telemonitoring-supported systems on parameters of liver inflammation and fibrosis in a very large population of individuals with high risk of MAFLD.

In our study including employees with MetS, participants showed slightly elevated liver enzymes at baseline. As MAFLD is the most common cause for incidentally detected elevated transaminases (9,17), the liver enzyme profiles in this high-risk group might point to existing liver steatosis. The prevalence of MAFLD ranges between 40% for patients with MetS and up to 98% for patient with severe obesity (21). Furthermore, a large prospective German study could show a strong association between elevated liver enzymes and hepatic steatosis in the general population (22). Although liver enzymes are not above normal in all patients suffering from MAFLD, elevated liver enzymes are associated with a clinically significant risk of developing end-stage liver disease (23).

After the 6-month lifestyle intervention focusing on exercise training, we observed significant reduction of transaminases. In addition to a reduction of absolute ALT values, we observed a greater number of normalization of ALT in patients with previous elevated ALT after the intervention, even in accordance to the American Association for the Study of Liver Diseases recommendation for upper limits of normal. In line with this finding, we previously showed that this intervention reduced the severity of MetS (12), an important risk factor for MAFLD.

A principal limitation of the study is the lack of further surrogate parameters for liver damage and liver fibrosis, such as elastography or histology, as transaminases could show a spontaneous fluctuation (24). However, previous pharmacological studies in patient with biopsy-proven nonalcoholic steatohepatitis (NASH)

demonstrated that increased ALT levels are associated with increased histological disease activity and normalization of ALT levels correlates with histological improvement of NASH (25,26). Furthermore, a study with 12 months of lifestyle interventions in patients with histological-proven NASH showed that normalization of ALT has independently predicted improvement of fibrosis (27). Therefore, the improvement of ALT in our study might be

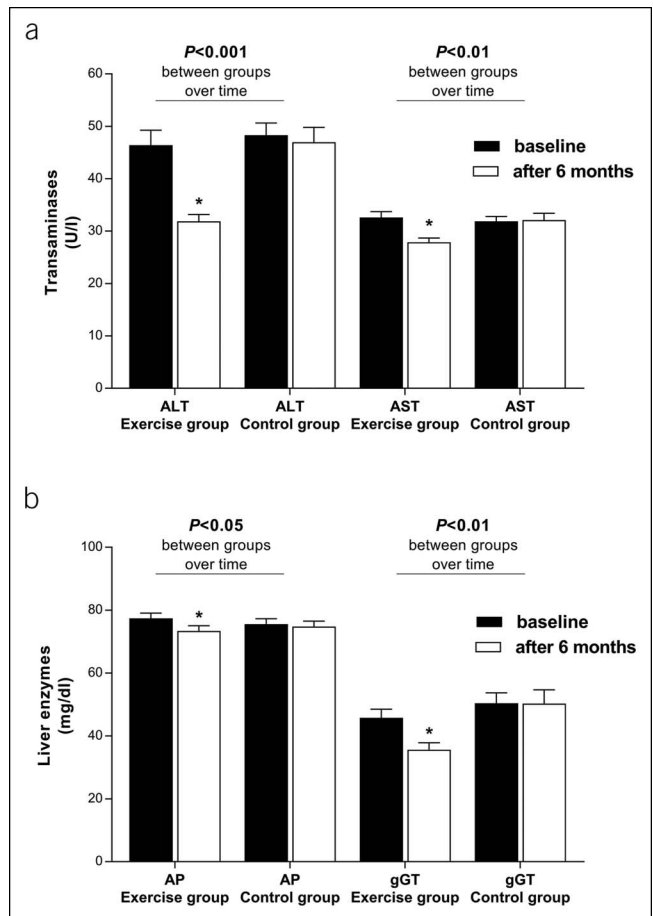


Figure 2. (a) Liver transaminases and (b) liver enzymes before and after the intervention. *Significant within groups from before to after the intervention. Data are mean ± SEM. ALT, alanine aminotransferase; AP, alkaline phosphatase; AST = aspartate aminotransferase; gGT = gamma-glutamyl transferases.

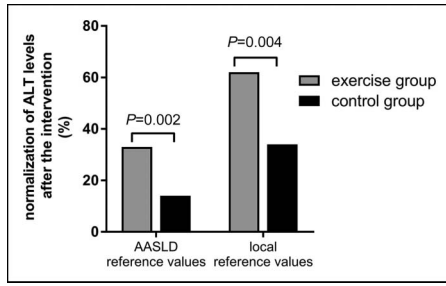


Figure 3. Percentage of patients with elevated ALT levels at baseline, who could achieve normalization of ALT levels at the end of treatment according to the local reference values (female: 34 IU/L; male: 45 IU/L) and in accordance to the AASLD recommendation (female: 19 IU/L; male: 30 IU/L). Data are mean \pm SEM. AASLD, American Association for the Study of Liver Diseases; ALT, alanine aminotransferase.

also correlated with significant improvement of liver damage. We could also show a significant impact on gGT and alkaline phosphatase after the intervention. Increased gGT is discussed as a predictor for liver-related mortality (28) and is correlated with advanced fibrosis (29). Therefore, the decrease of gamma-GT shown in this study might be an important factor for prognostic evaluation of the long-term outcome after a lifestyle intervention.

In our study population, only a small group was suspicious for fibrosis based on the results of the APRI score. Besides reduction of transaminases, the physical activity and lifestyle intervention significantly decreased the APRI score in these patients. As liver fibrosis is the most important survival predictor in patients with NASH (30), this result is important and in line with a previous study which showed improvement of surrogate parameter of liver fibrosis after an exercise intervention (31). Noninvasive parameters of liver fibrosis such as blood-based biomarkers are well established and helpful alternatives to identify patients as high risk of liver damage and fibrosis in daily routine (32). Nevertheless, further surrogate parameter for liver fibrosis such as elastography would have been helpful to analyze the effect on liver fibrosis in more detail. Furthermore, a longer treatment period might be needed to demonstrate stronger and sustained effects on liver fibrosis. Therefore, further studies with a more detailed investigation of liver damage and liver fibrosis are needed to confirm our results.

Reasons for the good lifestyle-induced response on liver parameters may include the provision of an activity monitor to have information on performed activities and the opportunity to

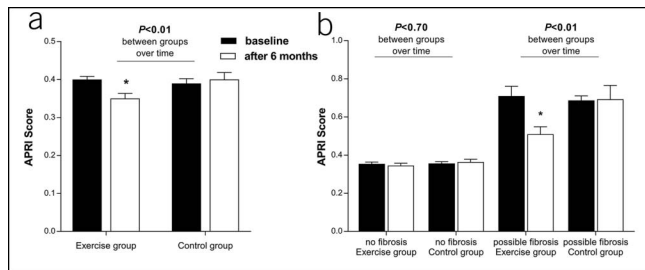


Figure 4. (a) The calculated APRI score before and after the intervention. (b) Subgroup of patients without fibrosis (APRI score < 0.5) and with possible fibrosis (APRI score: $> 0.5 < 1.5$) before and after the intervention. *Significant within groups from before to after the intervention. Data are mean \pm SEM. APRI, aspartate aminotransferase-to-platelet ratio index.

receive individualized feedback on the training process and content by a qualified exercise scientist. A further factor could be the use of a custom-built app informing about healthy nutrition, stress management, and appropriate sports activities. Weight loss and lifestyle modification both improve liver function and therefore are primary therapies for the management of MAFLD (20). Given the high acceptance of recommended activity and technologies, with a dropout rate commensurate to that commonly observed in exercise programs, the intervention appears feasible for real-life application for the studied population. In this context, the transfer from activity data to a central database facilitates the monitoring of a large number of individuals, regardless of their residence or workplace. However, implementation of strategies to achieve long-term adherence to avoid relapse and weight regain is needed because relapse of weight gain and unhealthy lifestyle are common problems (33).

Accordingly, improvements of liver enzymes in our participants were associated with changes in adiposity. Yet, the observed associations were also evident for changes in exercise capacity which likely link adiposity as well as exercise-induced response rates to improvements of liver transaminases.

Improvement of transaminases by exercise and weight loss might be explained by various factors. Basically, excessive accumulation of free fatty acids in the liver could lead to increased oxidative stress and stress at the endoplasmic reticulum, triggering the activation of proinflammatory processes (34) which might lead to progressive liver disease. In this context, physical exercise favorably modifies serum lipids and enhances insulin sensitivity (35,36), resulting in an increased ability to suppress lipolysis in adipose tissue with insulin, presumably leading to decreased free fatty acid delivery to the liver (37). Aerobic training also augments the capacity for fatty acid uptake, β -oxidation, insulin sensitivity, and triglyceride storage within skeletal muscle, potentially serving to partition fatty acids away from the liver (38). These adaptations could trigger the physical activity-

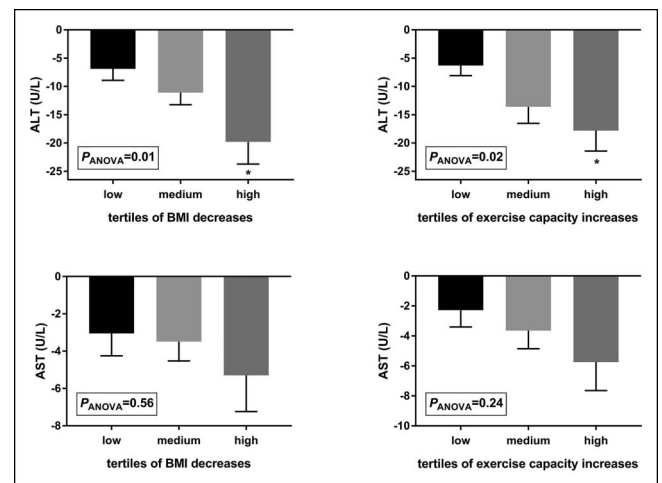


Figure 5. Change in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) according to change in exercise capacity or change in body mass index (BMI). The framed P values are given for differences across tertiles as analyzed with a 1-way ANOVA. *Different to low tertile with $P < 0.01$ as analyzed with Bonferroni *post hoc* tests. Data are mean \pm SEM.

induced decrease in intrahepatic fat with parallel improvements in liver enzymes as observed in our participants.

Furthermore, change of dietary intake regarding the quantity and quality of macronutrition and micronutrition is also an important treatment option for nonalcoholic fatty liver disease (20,39). However, we could not show significant changes between study groups for total energy intake or macronutrient intake. Therefore, the independent contribution of dietary changes and physical activity changes on liver transaminases and nonalcoholic fatty liver disease severity warrants further investigations.

Besides absence of confirmed liver disease and histological diagnosis of MAFLD, exclusion of other liver diseases such as viral infection might be another limitation of the study. Yet, the observed reduction of liver enzymes is encouraging for further investigations to confirm the role of mobile health interventions in the treatment of MetS and its associated diseases such as MAFLD.

In conclusion, we show that a 6-month telemonitoring-guided lifestyle intervention improved markers of liver inflammation and liver fibrosis. We observed that the activity duration and intensity as well as applied telemonitoring systems were well accepted, with attrition rates in line with those commonly observed for exercise programs. As MetS and MAFLD also carry a large economic burden with rising prevalence, a telemonitoring-guided intervention might also be a cost-effective approach to support treatment of both diseases independent of residence or workplace.

CONFLICTS OF INTEREST

Guarantor of the article: Uwe Tegtbur.

Specific author contributions: Sven Haufe and Katharina Luise Hupa-Breier contributed equally to this work. Study concept and design: U.T., D.H.-K., M.S., C.T., D.H.-K., and A.H. Administrative support: U.T., L.N., and D.L. Performed experiment: P.B., H.T.B., S.R., T.S., A.K., J.E., M.K., A.A.H., and R.E. Analysis and interpretation of data: S.H., K.L.H.-B., and H.W. Statistical analysis: S.H. and D.B. Manuscript writing: S.H. and K.L.H.-B. Obtained funding: U.T. and A.H. All authors approved the final version of the manuscript.

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Potential competing interests: H.W. received lecture fees from Falk Pharma, Gore, Merz, and Norgine and acts as a principal investigator for Falk Pharma. He received grants from Merz and Norgine. K.H.-B. received lecture fees from Falk Pharma and Gilead. These activities do not relate to the current manuscript which was performed without any support from the above mentioned companies. All other authors declare no conflicts of interest.

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Study Highlights

WHAT IS KNOWN

- ✓ Metabolic syndrome and its associated metabolic-associated fatty liver disease are major health problems.
- ✓ Changes of lifestyle are established treatment options, but hard to achieve in clinical care.

WHAT IS NEW HERE

- ✓ Telemonitoring-based lifestyle interventions improve transaminases and parameters of liver fibrosis.
- ✓ Improvements were associated with changes in obesity and exercise capacity.

TRANSLATIONAL IMPACT

- ✓ Telemonitoring-guided lifestyle intervention is a therapeutic tool for metabolic-associated fatty liver disease.

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