ORIGINAL ARTICLE

Effects of Therapeutic Lifestyle Program on Ultrasound-diagnosed Nonalcoholic Fatty Liver Disease

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Background: To investigate the effects of varied therapeutic lifestyle programs on patients with ultrasound-diagnosed nonalcoholic fatty liver disease (NAFLD).

Methods: A prospective, case-controlled study was conducted. A total of 54 subjects with NAFLD were subdivided into 3 groups: (1) diet plus exercise group (DPE group, $n=16$); (2) exercise group (E group, $n=23$); and (3) control group (C group, $n=15$). The DPE group received a low-calorie balanced diet and regular high-intensity stationary bicycle exercise program for 10 weeks, while the E group received the same exercise protocol as the DPE group but without any changes in diet. Anthropometric indices, biochemical data, physical fitness data and liver ultrasound findings were recorded. A generalized estimating equation method was used to determine the differences among groups.

Results: Compared with the C group, the DPE group demonstrated significant improvements in anthropometric indices, total cholesterol, insulin sensitivity, liver biochemistry, ultrasound finding and physical fitness, while the E group showed significant improvements in anthropometric indices, insulin sensitivity status, ultrasound finding and physical fitness but not liver biochemistry. Compared with the E group, the DPE group showed greater reduction in anthropometric indices (body mass index, body weight, abdominal circumference, hip circumference), total cholesterol, alanine aminotransferase, and γ-glutamyltransferase.

Conclusion: Our data suggest that both 10-week diet-plus-exercise and exercise-only therapeutic lifestyle programs are effective for improving anthropometric indices, insulin sensitivity, ultrasound findings and physical fitness in ultrasound-diagnosed NAFLD patients. However, the range of improvement in patients on the diet-plus-exercise program is more obvious than that in patients on the exercise-only program. Moreover, the diet-plus-exercise program resulted in significant improvement in liver biochemistry, but the exercise-only program did not. In summary, diet plus exercise is more efficacious than exercise alone in the lifestyle modification treatment of NAFLD. [*J Chin Med Assoc* 2008;71(11):551–558]

Key Words: lifestyle program, nonalcoholic fatty liver disease, spinning exercise

Introduction

The prevalence of obesity and obesity-related disease has increased dramatically in recent years, which puts a large population at risk of developing nonalcoholic fatty liver disease (NAFLD).[1] NAFLD is closely associated with metabolic disorder, even in the non-obese, non-diabetic population.[2] NAFLD exists as a spectrum of liver disease with characteristics of liver fat accumulation.[3] It may progress to nonalcoholic steatohepatitis (NASH), liver cirrhosis and even liver failure. In the United States and developed countries, it is the most common liver disease, with the prevalence of NAFLD and NASH being around 20% and 2–3%, respectively. The incidence of NAFLD increases to 57–74% in obese persons.[1,4–6] In a study by Adams et al, 37% of patients with NAFLD progressed to fibrosis, 34% remained the same and 29% regressed.[7] NAFLD is now considered to be the most common cause of abnormal liver function and presumed liver injury in Taiwan, exceeding even viral hepatitis B.[8]

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Treatment of NAFLD includes weight reduction and exercise, insulin-sensitizing drugs, antioxidants, lipid-lowering drugs and other hepatoprotective agents.[9] Previous studies have shown body weight loss by diet control and/or exercise-improved insulin resistance, alanine aminotransferase (ALT)/aspartate aminotransferase (AST) level, and hepatic steatosis in NAFLD.[10–16] Exercise intervention in those reports included regular walking, jogging, stationary biking, stepping, and aerobic exercise. Diet control was done with a suggested daily calorie intake of 25 kcal/ideal body weight (IBW), or by decreasing daily calorie intake by 500 kcal or 20%. However, most previous studies were conducted in Western countries, where people consume more fat than people in Asia. To date, no study has investigated the effects of varied therapeutic lifestyle modification programs on Taiwanese with NAFLD. The purpose of the present study was to compare the effects of varied therapeutic lifestyle modification programs on patients with NAFLD in Taiwan. For our subjects, we chose stationary bicycling as an appropriate intervention to achieve exercise effect while having a low likelihood of causing sport-related injury. Considering the differences in baseline, we selected 25 kcal/IBW daily calorie intake for diet control.

Methods

Subjects

Subjects were recruited from the Department of Internal Medicine and the Women's Weight Reduction Clinic in the Department of Obstetrics and Gynecology, Taiwan Adventist Hospital, between April 2006 and December 2007. Subjects who had any 3 of the following features were included in the study: (1) central obesity—an abdominal circumference (AC) ≥ 90 cm for men, ≥ 80 cm for women, or body mass index (BMI) > 25 kg/m^2; (2) total cholesterol level ≥ 200 mg/dL or triglyceride level ≥ 150 mg/dL; (3) high-density lipoprotein cholesterol (HDL-C) level < 40 mg/dL for men, < 50 mg/dL for women; (4) blood pressure ≥ 130/≥ 85 mmHg (or under treatment for hypertension).

Patients were excluded if they had a history of alcohol abuse or chronic intake (> 1 drink/week confirmed by self-reported questionnaire), diabetes, hepatitis B or C, hypothyroidism, anemia or hyperlipidemia. Subjects who could not participate in an aerobic exercise program due to high risk of adverse events were also excluded.

The study was approved by the Institutional Review Board of Taiwan Adventist Hospital, and all subjects provided written informed consent.

Subjects were divided into 3 groups: (1) diet-plus-exercise group (DPE group, $n = 16$); (2) exercise group (E group, $n = 23$); and (3) control group (C group, $n = 25$). An ultrasound examination of the liver was performed at baseline and at 10 weeks. At baseline and at 5 weeks and 10 weeks, 3 further measurements were taken: blood samples, anthropometric indices, and a physical fitness test. Subjects in the DPE group received guidance on a low-calorie balanced diet with a suggested daily calorie intake of 25 kcal/IBW; the range in daily calorie intake was 1,200–1,500 kcal. DPE subjects also participated in a high-intensity stationary bicycle exercise program at a frequency of 1 hour twice a week for 10 weeks. In addition, they were asked to record a diet diary and were monitored by a dietician. Subjects in the E group received the same 10-week exercise program as the DPE group but without any change in diet. All subjects performed the exercise under a professional instructor.

Liver ultrasound

Liver ultrasound was performed by an expert gastroenterologist and graded on a scale of 0 to 3 (0 = none, 1 = mild, 2 = moderate, 3 = severe) at baseline and at study end. Mild was recognized by slight increase in liver echogenicity and relative preservation of echoes from the walls of the portal vein.[17] Moderate was recognized by moderate loss of echoes from the walls of the portal vein, particularly from the peripheral branches, and moderate diffuse abnormally bright echoes. Severe was recognized by a greater reduction in beam penetration, loss of echoes from most of the portal vein wall, and extensive abnormally bright echoes.[18,19]

Blood samples

Blood samples were obtained after an overnight fasting period of at least 8 hours. Levels of fasting glucose, triglycerides, HDL-C, low-density lipoprotein cholesterol, uric acid, AST, ALT and γ-glutamyltransferase (γ-GT) were measured using commercial kits on an automated analyzer (Synchron CX9; Beckman Coulter Co., Fullerton, CA, USA). Fasting insulin levels were also determined using commercial kits on an automated analyzer (Access Immunoassay System; Beckman Coulter Co.). A homeostasis model assessment (HOMA) was used to evaluate insulin resistance using fasting insulin and fasting glucose levels as described by Matthews et al.[20] Insulin resistance was defined as HOMA ≥ 3.0.[21] Abnormal liver function was defined as a serum level of AST ≥ 40 IU/L (reference, 10–40 IU/L) and/or a serum level of ALT ≥ 45 IU/L (reference, 6–45 IU/L).

Anthropometric indices

The anthropometric indices included BMI, AC, hip circumference (HC), and abdomen-to-hip ratio (AHR).

Physical fitness test

The physical fitness examination included cardiovascular endurance, flexibility, muscular endurance and resting heart rate performed in the exercise center of Taiwan Adventist Hospital. Cardiovascular endurance was measured using the 3-minute step-test. The sit-and-reach test was used to measure flexibility, and the 1-minute sit-up test was used to test measure muscular endurance.

Statistical analysis

Results were expressed in terms of mean ± standard deviation. The multi-measurement design of the study allowed for analysis of adjusted comparisons of differences among the 3 groups using generalized estimating equations (GEE).[22] In addition, the ordinal scale of the liver ultrasound results (0, 1, 2 and 3 implying none, mild, moderate and severe, respectively) enabled comparisons to be performed by using ordinal regression,[23] controlling for the same covariates as in the GEE models. All statistical analyses were performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA), and a p value < 0.05 was considered statistically significant.

Results

A total of 54 subjects with NAFLD were recruited, including 15 in the C group, 23 in the E group, and 16 in the DPE group. There was no subject who dropped out. Subjects in the DPE group cooperated with the low-calorie balanced diet very well, and all subjects adhered to the 10-week exercise program. Table 1 lists the basic characteristics of the subjects at

Table 1. Baseline characteristics of the study subjects*

	Control group ($n=15$)	Exercise group ($n=23$)	Diet + exercise group ($n=16$)	$p^{\dagger}$
Sex				0.60
Male	8	16	10	
Female	7	7	6	
Age (yr)	37.7 ± 6.6	36.0 ± 6.9	40.1 ± 6.2	0.16
Anthropometric indices				
Body mass index (kg/m^2)	29.3 ± 3.7	30.7 ± 4.3	30.2 ± 3.7	0.55
Body weight (kg)	84.2 ± 15.2	85.3 ± 12.1	83.3 ± 10.9	0.91
Abdominal circumference (cm)	98.4 ± 11.4	100.3 ± 10.9	97.4 ± 8.6	0.69
Hip circumference (cm)	107.7 ± 7.9	107.9 ± 6.7	108.1 ± 6.6	0.98
Abdomen-to-hip ratio	0.91 ± 0.06	0.93 ± 0.05	0.90 ± 0.05	0.35
Biochemical profile				
Total cholesterol (mg/dL)	229.0 ± 23.7	224.1 ± 34.0	215.7 ± 23.9	0.42
Triglycerides (mg/dL)	162.6 ± 93.3	192.0 ± 100.4	165.9 ± 68.9	0.57
HDL-C (mg/dL)	42.7 ± 7.5	41.7 ± 9.4	41.8 ± 8.7	0.94
LDL-C (mg/dL)	154.0 ± 29.2	144.0 ± 32.8	140.7 ± 25.9	0.44
Fasting plasma glucose (mg/dL)	97.7 ± 8.3	93.9 ± 8.1	107.2 ± 18.7	0.01†
Fasting plasma insulin (μU/mL)	12.8 ± 8.6	10.5 ± 5.0	9.0 ± 4.7	0.24
HOMA-IR index	3.1 ± 2.2	2.5 ± 1.2	2.4 ± 1.3	0.41
AST (IU/L)	30.7 ± 14.7	34.5 ± 13.0	36.6 ± 18.8	0.56
ALT (IU/L)	47.3 ± 30.1	54.0 ± 29.4	63.4 ± 49.2	0.47
γ-GT (IU/L)	34.0 ± 26.2	42.4 ± 32.7	40.1 ± 23.3	0.67
Severity of fatty liver on ultrasound	1.8 ± 0.7	1.8 ± 0.7	1.4 ± 0.5	0.16
Physical fitness				
Cardiovascular endurance	50.5 ± 8.2	49.4 ± 6.1	48.4 ± 3.7	0.66
Flexibility (cm)	17.8 ± 11.5	16.5 ± 9.6	17.1 ± 12.3	0.94
Muscular endurance (number/min)	18.8 ± 7.5	23.1 ± 8.0	17.6 ± 9.6	0.12
Resting heart rate (per min)	78.1 ± 9.8	82.9 ± 12.5	75.3 ± 15.1	0.19

**Data presented as n (for categorical variables) or mean ± standard deviation (for continuous variables); †χ^2 test for categorical data and F test for continuous data; ‡$p < 0.05$.*

the start of the study. No significant intergroup differences were noted, with the exception of fasting plasma glucose level. Table 2 shows the unadjusted estimates of the effects. Compared with baseline, mean body weight and AC were slightly, but not significantly, decreased in the E and DPE groups. Reductions in the levels of total cholesterol, ALT and γ-GT were significant only in the DPE group. Table 3 shows the adjusted estimates using the GEE model. The DPE group showed significant reductions in anthropometric indices and demonstrated significant improvements in the serum level of total cholesterol, insulin sensitivity, liver biochemistry, severity of fatty liver, physical fitness and diastolic blood pressure. Subjects in the E group had significant improvements in some anthropometric indices, insulin sensitivity, severity of fatty liver, cardiovascular endurance and diastolic blood pressure, whereas liver biochemistry was not significantly changed. Compared with the E group, the DPE group showed significantly greater reduction in anthropometric indices (BMI, body weight, AC, HC), total cholesterol, HDL-C, ALT, and γ-GT. The ultrasound score for the severity of fatty liver for the 3 groups at baseline and at study end are shown in Table 4. There were no significant differences among the 3 groups at the baseline ultrasound examination. However, a statistically significant difference was seen at study end (10 weeks).

Discussion

The present study demonstrated the effects of 10-week therapeutic lifestyle programs—diet plus exercise versus exercise only—on anthropometric indices, serum cholesterol, liver biochemistry, insulin sensitivity and severity of fatty liver on ultrasound in patients with ultrasound-diagnosed NAFLD. With regard to anthropometric indices, our study results are in line with those of previous studies;[12–16] we observed that exercise alone and diet plus exercise significantly decreased BMI and AC. We also found that DPE group patients had significant reduction in body weight. Ueno et al[12] and Thomas et al[15] reported similar findings: after 3 and 6 months of diet and exercise intervention, subjects with fatty liver had significant weight loss.

This study showed that even short-term lifestyle change with diet and exercise can markedly improve liver biochemistry with the benefit of significant weight loss. Our results are compatible with those of previous studies.[19,20,21] A recent study by Suzuki et al showed that a reduction of 5% or more of original weight by diet control and regular exercise for 3 months was associated with improvement in total cholesterol and ALT levels.[13] Sreenivasa Baba et al reported that calorie restriction and regular aerobic exercise for 30 minutes a day for 3 months resulted in normalization of liver biochemistry (ALT, AST) in patients with nonalcoholic steatohepatitis.[24] Our data revealed that diet plus exercise, but not exercise alone, decreased total cholesterol by 11%, AST by 21%, ALT by 23%, and γ-GT by 37%. According to previous reports, body weight loss is correlated with reductions in AST and ALT levels. Body weight loss > 5% is associated with significant improvement in liver biochemistry,[13] and Palmer and Schaffner reported that even a 1% reduction in body weight can improve ALT by 8.1%.[16] Although the exercise program in this study resulted in significant reduction in BMI and AC, the change in liver biochemistry was not statistically significant. A possible explanation is that the exercise program was less strenuous or shorter in duration than those in previous studies; body weight did not change significantly to alter liver biochemistry.

Significant improvement in severity of intrahepatic fat accumulation on ultrasound score was observed in both the DPE and E groups. This finding is consistent with those reported by others.[25,26] Perseghin et al showed that a higher level of habitual physical activity is associated with lower intrahepatic fat content.[25] Tamura et al demonstrated that calorie restriction for 2 weeks with or without exercise caused a 27% reduction in intrahepatic fat despite a minimal change in body fat in type 2 diabetic patients.[26]

Significant improvement in fasting insulin levels as well as HOMA-IR index were noted in both the DPE and E groups in the present study. These findings are compatible with those of previous reports.[27–29] Exercise training had an independent effect on insulin concentrations and resulted in lower insulin concentration after a glucose challenge test.[27,28] However, exercise might not result in a significant change in glucose concentrations.[29] The role of exercise in improving insulin sensitivity remains controversial. A high-fat diet results in decreased muscle insulin sensitivity. Exercise training may reverse the impairment, resulting in improved insulin-stimulated glucose transport and increasing the rates of fatty acid oxidation in skeletal muscle.[30] In the present study, we found that when compared with the C group, although better cardiovascular and muscular endurance were noted in the DPE group, insulin resistance improvement was less than that in the E group. The reason for this paradoxical finding is unknown. Possible explanations include population bias due to a relatively small population

Table 2. Unadjusted estimates of effects in the 3 groups during the study period*

	Control group ($n=15$)			Exercise group ($n=23$)			Diet + exercise group ($n=16$)		
	Baseline	5 wk	10 wk	Baseline	5 wk	10 wk	Baseline	5 wk	10 wk
Anthropometric indices									
Body mass index (kg/m^2)	29.25 ± 3.68	29.15 ± 3.72	29.23 ± 3.86	30.68 ± 4.28	30.19 ± 4.23	30.16 ± 4.21	30.19 ± 3.72	28.92 ± 3.83	28.31 ± 3.90
Body weight (kg)	84.19 ± 15.22	83.87 ± 14.98	84.08 ± 15.25	85.31 ± 15.67	83.98 ± 15.64	83.90 ± 15.72	83.25 ± 10.96	79.70 ± 10.66	78.05 ± 10.59
Abdominal circumference (cm)	98.37 ± 11.44	99.00 ± 11.25	99.46 ± 11.17	100.26 ± 10.94	97.83 ± 11.18	97.09 ± 10.56	97.41 ± 8.62	92.91 ± 8.59	91.41 ± 8.34
Hip circumference (cm)	107.67 ± 7.88	107.07 ± 7.43	107.23 ± 7.87	107.93 ± 6.72	106.54 ± 7.16	106.76 ± 6.84	108.06 ± 6.56	105.63 ± 6.33	104.63 ± 6.43
Abdomen-to-hip ratio	0.91 ± 0.06	0.92 ± 0.06	0.93 ± 0.06	0.93 ± 0.05	0.92 ± 0.06	0.91 ± 0.05	0.90 ± 0.05	0.88 ± 0.05	0.87 ± 0.05
Biochemical profile									
Total cholesterol (mg/dL)	229.13 ± 23.71	225.47 ± 35.72	226.33 ± 28.54	224.13 ± 34.01	217.26 ± 35.93	214.91 ± 35.98	215.75 ± 23.98	195.50 ± 27.13†	190.94 ± 27.68†
Triglycerides (mg/dL)	162.60 ± 93.30	169.1 ± 114.9	151.7 ± 100.7	192.0 ± 110.4	155.6 ± 59.0	183.1 ± 89.6	165.9 ± 68.9	129.0 ± 81.8	130.4 ± 99.1
HDL-C (mg/dL)	42.65 ± 7.51	41.29 ± 6.89	41.36 ± 6.47	41.71 ± 9.36	38.58 ± 6.87	40.25 ± 8.89	41.83 ± 8.66	37.74 ± 9.44	40.19 ± 9.18
LDL-C (mg/dL)	153.96 ± 29.22	150.4 ± 42	154.64 ± 33.53	144.02 ± 32.83	147.56 ± 31.59	138.05 ± 33.74	140.74 ± 25.85	131.96 ± 25.94	124.66 ± 25.13
Fasting plasma glucose (mg/dL)	97.67 ± 8.33	102.27 ± 8.49	97.87 ± 6.64	93.91 ± 8.13	96.96 ± 8.39	98.48 ± 15.83	107.25 ± 18.72	101.94 ± 14.59	101.19 ± 16.18
Fasting plasma insulin (μU/mL)	12.79 ± 8.62	13.80 ± 9.05	10.46 ± 7.41	10.51 ± 4.97	7.14 ± 3.77	8.99 ± 7.75	9.04 ± 4.65	8.77 ± 8.50	8.59 ± 4.97
HOMA-IR index	3.05 ± 2.04	3.58 ± 2.29	2.57 ± 1.97	2.46 ± 1.19	1.73 ± 0.99	2.27 ± 2.16	2.40 ± 1.31	2.24 ± 2.19	2.21 ± 1.48
AST (IU/L)	30.67 ± 14.74	29.73 ± 10.85	35.00 ± 23.62	34.48 ± 12.96	29.87 ± 9.40	30.43 ± 10.89	36.56 ± 18.80	31.00 ± 10.98	25.56 ± 6.54
ALT (IU/L)	47.27 ± 30.13	43.60 ± 27.82	44.27 ± 22.45	54.04 ± 29.41	45.65 ± 22.00	44.78 ± 23.78	63.4 ± 49.20	46.56 ± 33.44	34.00 ± 18.84†
γ-GT (IU/L)	34.01 ± 26.19	34.67 ± 27.75	33.20 ± 27.49	42.39 ± 32.70	44.26 ± 35.96	40.30 ± 31.94	40.06 ± 23.28	28.13 ± 15.74†	23.00 ± 13.20†
Severity of fatty liver on ultrasound‡	1.80 ± 0.68	–	1.53 ± 0.74†	1.83 ± 0.71	–	1.22 ± 0.67†	1.44 ± 0.51	–	1.00 ± 0.37†
Physical fitness									
Cardiovascular endurance	50.46 ± 8.16	53.49 ± 9.75	55.84 ± 7.32	49.42 ± 6.12	57.66 ± 6.68†	57.50 ± 11.16†	48.36 ± 3.68	54.99 ± 7.06†	58.40 ± 7.99†
Flexibility (cm)	17.79 ± 11.46	19.00 ± 13.02	22.15 ± 12.74	16.52 ± 9.64	20.83 ± 8.29	21.29 ± 8.67	17.06 ± 12.33	23.81 ± 10.97	25.31 ± 8.75
Muscular endurance (number/min)	18.80 ± 7.47	20.47 ± 8.87	22.79 ± 8.85	23.14 ± 7.96	25.05 ± 6.91	23.10 ± 10.57	17.57 ± 9.65	21.47 ± 10.31	20.19 ± 10.93
Resting heart rate (per min)	78.07 ± 9.76	77.93 ± 10.50	78.36 ± 10.16	82.87 ± 12.53	79.48 ± 12.21	82.27 ± 13.70	75.33 ± 15.12	79.06 ± 11.10	79.38 ± 11.44

**Data presented as mean ± standard deviation and all 5- and 10-week values were compared with baseline values using 1-way ANOVA; †$p < 0.05$; ‡although data also displayed as mean ± standard deviation, data were analyzed using χ^2 test with Fisher's exact test.*

Table 3. Adjusted estimates of the effects of exercise only and diet plus exercise compared with control

Variables	Effects*		
	Exercise group	Diet + exercise group	Diet + exercise group (compared with exercise only)
Anthropometric indices			
Body mass index (kg/m^2)	–0.35†	–1.62§	–1.31§
Body weight (kg)	–0.76	–4.43§	–3.84§
Abdominal circumference (cm)	–3.58§	–6.39§	–2.91§
Hip circumference (cm)	–0.72	–2.45§	–1.77§
Abdomen-to-hip ratio	–0.03§	–0.04§	–0.14
Biochemical profile			
Total cholesterol (mg/dL)	–5.15	–24.32§	–18.27§
Triglycerides (mg/dL)	–7.06	–36.31	–24.52
HDL-C (mg/dL)	–0.60	–2.61	–2.45†
LDL-C (mg/dL)	–2.31	–16.24	–13.13
Fasting plasma glucose (mg/dL)	–1.02	–4.46	–0.17
Fasting plasma insulin (μU/mL)	–5.11†	–3.22†	1.29
HOMA-IR index	–1.33†	–0.97†	0.21
AST (IU/L)	–4.15	–7.92†	–3.25
ALT (IU/L)	–3.27	–15.40†	–10.39†
γ-GT (IU/L)	0.08	–15.17§	–15.41§
Severity of fatty liver on ultrasound†	–2.19†	–2.85†	–0.93
Physical fitness			
Cardiovascular endurance	3.95†	4.55†	0.19
Flexibility (cm)	1.41	4.10†	2.42
Muscular endurance (number/min)	–1.68	1.28	1.96
Systolic blood pressure (mmHg)	–2.33	–2.19	1.05
Diastolic blood pressure (mmHg)	–4.08†	–6.13†	–1.65
Resting heart rate (per min)	3.21	2.94	0.05

**Effect values were estimated using the generalized estimating equation method, and all effect values were adjusted for age, sex and the baseline measurements of body mass index, fasting sugar and each variable; †data were ordinal, so the effect values were estimated using the ordinal regression method and adjusted for age, sex and the baseline measurements of body mass index, fasting sugar and severity of fatty liver on ultrasound; ‡$p < 0.05$; §$p < 0.01$.*

Table 4. Severity of fatty liver on ultrasound score in the 3 groups during the study period

Time	Liver ultrasound score	Control group	Exercise group	Diet + exercise group	Total	χ^2 test	
						Value	Exact significant value (2-sided)
Initial	1 (mild)	5	8	9	22	4.101	0.402
	2 (moderate)	8	11	7	26		
	3 (severe)	2	4	0	6		
	Total	15	23	16	54		
10 wk	0 (none)	0	3	1	4	10.265*	0.050
	1 (mild)	9	12	14	35		
	2 (moderate)	4	8	1	13		
	3 (severe)	2	0	0	2		
	Total	15	23	16	54		

**$p < 0.05$.*

and most subjects having a HOMA index <3.0. HOMA index is an indirect quantitative method and more suitable for large sample size. Might it or other reasons have caused the insoluble difference? Further investigation is needed to answer the question. Additionally, when we compared the effects of exercise-only and diet plus exercise, there was no significant difference in fasting insulin levels and HOMA-IR index

between the 2 groups. This suggests that exercise might play a key role in the improvement of insulin sensitivity, and diet control might not provide significant additional effects.

Limitations of the present study included the small sample size and lack of histologic proof of NAFLD. In spite of these limitations, this study confirms the beneficial effect of therapeutic lifestyle programs for Asian patients with NAFLD.

Our data suggest that 10-week diet-plus-exercise and exercise-only therapeutic lifestyle programs are both effective for improving anthropometric indices, insulin sensitivity, ultrasound findings and physical fitness in ultrasound-diagnosed NAFLD patients. The improvement range from the diet-plus-exercise program was more obvious than that of the exercise-only program. Moreover, the diet-plus-exercise program appeared to offer significant improvement in liver biochemistry, but the exercise-only program did not.

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