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Original Research

Association between Cardiorespiratory Fitness, Muscle Strength, and Non-Alcoholic Fatty Liver Disease in Middle-Aged Men

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Abstract

Background: Nonalcoholic fatty liver disease (NAFLD) occurs when more than 5% of fat accumulates in the liver parenchyma without excess alcohol consumption. The objective of this study is to investigated the association between cardiorespiratory fitness (CRF), muscle strength (MS), and NAFLD. **Methods**: The subjects of this study were 1325 males aged 40–50 who had visited the National Fitness Center located in the Republic of Korea from 2017 to 2019. Abdominal ultrasonography testing was used for NAFLD diagnosis. For CRF, an MS test was used to measure maximal oxygen intake and grip strength. CRF and MS were classified into 3 quartiles (high, middle, low-level). In addition, both the CRF level and MS level were classified into 9 quadrants. **Results**: With confounding factors (age, body mass index, exercise, smoking) controlled, there was no relative risk of NAFLD between middle and high levels of CRF (95% CI, 0.92–2.17). However, the relative risk of NAFLD in the case of low-level CRF was 1.63-fold (95% CI, 1.03–2.60, $p < 0.05$) higher than that in the case of high-level CRF. Meanwhile, there was no significant difference between middle-level MS (95% CI, 0.68–1.65) and high-level MS (95% CI, 0.84–1.99) in terms of NAFLD relative risk. The NAFLD relative risk in the case of low-level CRF/MS was 2.27-fold (95% CI, 0.94–1.99, $p < 0.05$) higher than that of high-level CRF/MS. **Conclusions**: The low CRF and MS group had a higher risk of NAFLD compared with the high CRF and MS group. Maintenance of high CRF and MS may be beneficial in preventing NAFLD.

Keywords: middle-aged men; nonalcoholic fatty liver disease; cardiorespiratory fitness; muscle strength

1. Introduction

Nonalcoholic fatty liver disease (NAFLD) occurs when more than 5% of fat accumulates in the liver parenchyma without excessive alcohol as determined in a diagnostic test or biopsy [1]. NAFLD develops into simple fatty liver, steatohepatitis, hepatocirrhosis, etc. Also, the mortality rate of cardiovascular disease is high [2–4]. Although the prevalence rate of NAFLD has been reported differently depending on the criteria of diagnosis, it is generally estimated to be 22 to 29% globally [5]. According to previous studies, the pathogenesis of NAFLD results from fat accumulation in the liver causing obesity, type-2 diabetes, lipid metabolism disorder, and insulin resistance [6–8]. In particular, insulin resistance is known to play a key role in NAFLD pathogenesis [9–11]. Previous studies have reported that this is because insulin resistance causes beta oxidation of free fatty acid to be reduced, leading to fat deposit in liver tissues [12].

Recent epidemiological studies have shown that both the prevalence rate of NAFLD and the fat content in liver were high when physical activity, which is a risk factor of cardiovascular disease, is insufficient or no exercise is practiced [13–15]. As well as playing a role in reducing adipogenesis in the liver tissue and stimulating fatty acid oxidization, exercise also enhances the insulin sensitivity of muscles [16,17]. Thus, exercise is an effective and valid method for NAFLD prevention and nonpharmacologic intervention. In particular, it has been demonstrated that cardiorespiratory fitness (CRF) and muscle strength (MS) enhancement through exercise reduce insulin resistance, which affects NAFLD outbreaks [18–20]. Many previous studies have shown that low-level CRF is related to NAFLD outbreaks [21–23]. Furthermore, a recent study of Kang *et al*. [24] suggests that as grip strength, which is a muscle strength (MS) index, decreases, the NAFLD occurrence risk increases as much as 1.6-fold. As such, low-level CRF and MS can affect NAFLD occurrence risks.

Other previous studies also clarified the association between NAFLD and CRF or MS, both of which are regarded as important in health enhancement as independent risk factors of cardiovascular disease and NAFLD. However, there has been little research on the relationship between both these two factors and NAFLD. Therefore, the objective of this study is to investigate the association between CRF, MS level, and NAFLD in middle-aged men.

2. Methods

2.1 Participants

This study was conducted among 1325 individuals (NAFLD group: 339; control group: 986) with alcohol consumption less than 40 g per week among men in their 40s to 50s who visited a health examination department of a National Fitness Center in Seoul, Republic of Korea, and participated in a health survey, blood test, abdominal ultrasonography test, exercise test, and hand grip test from January 2017 to December 2019. In this study, the determination of NAFLD was based on abdominal ultrasonography test results. Individuals meeting any of the following conditions were excluded: ① values of aspartate aminotransferase (AST) and (alanine aminotransferase (ALT) 3 times higher than the normal upper limit, ② a history of chronic liver disease and thyroid disease, ③ HBeAg positive or C-type infection antibody positive in immune serum tests, ④ liver fibrosis or liver cancer in an abdominal ultrasonography test, and ⑤ taking medication affecting liver function.

2.2 Health Survey

Every subject was given a self-administered questionnaire to survey present and past medical history, drug use history, drinking, smoking, and exercise. The current drinking status and drinking times per week (unit: drinking cup) were surveyed. For smoking, subjects were classified into current smokers and non-smokers. Those who had not smoked for at least 6 months were classified as non-smokers. Subjects who practiced physical activity or exercise at least 150 minutes per week were indicated.

2.3 Physical Measurement Test

While the subjects were wearing a gown for health examination, their height and weight were measured by means of an automatic measuring device (X-Scan II, Jawon medical, Korea). Body mass index (BMI) was determined as weight (kg)/height (m^2).

2.4 Blood Pressure and Blood Test

For blood pressure testing, subjects were induced to rest for at least 10 minutes, and then systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured at the left brachial artery at the same height of the heart by means of an automatic blood pressure measuring device (FT500R, Korea). If the blood pressure was not in the normal range, the subject was induced to rest for 10 minutes, and then the blood pressure was measured again.

The blood test was implemented by means of an automatic biochemical analyzer (Hitachi 7600-110, Hitachi Co., Tokyo, Japan) after gastric emptying for at least 10 hours. Measurement items included total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG), aspartate aminotransferase (AST), alanine aminotransaminase (ATL), and gamma glutamyl transferase (γ-GTP).

2.5 Abdominal Ultrasonography Test

An abdominal ultrasonography test was conducted to collect images by means of a 3.5 MHz probe. The abdominal ultrasonography test was implemented by a radiologist. If the liver echo increased in comparison with the right renal cortex, the subject was diagnosed with fatty liver [25].

2.6 Cardiorespiratory Fitness (CRF) Test

An exercise test was conducted to measure maximum oxygen intake (VO_2max), which is a CRF index. The exercise test was conducted by means of a treadmill (Medtrack ST 55; Quinton Instrument, Boston, MA, USA) and the modified Balke protocol. The modified Balke protocol was to start exercise at 0 degree and then increase the gradient gradually as much as 2.5% per minute with the speed fixed to 85 m/min.

The following items were measured at every 15 seconds by means of a breathing gas analyzer (Q4500, Quinton, Bothell, WA, USA) and an automatic heart rate monitor (Model 412, USA): oxygen intake, heart rate, and respiratory exchange ratio. For the criteria of determination in the exercise test, because there was little change in the oxygen intake of the subject even if there was a symptom such as difficult breathing and fatigue while the exercise intensity increased, the exercise was considered to have been completed when the exercise perception degree was at least 17, the heart rate reached 90% of the target heart rate (220-age), and the respiratory exchange ratio was at least 1.15.

2.7 Muscle Strength (MS) Test

In the MS test, grip strength was measured. The grip strength of both hands was measured by means of a digital hand dynamometer (Digital grip strength dynamometer, TKK 5401, Japan), twice for each hand, and the maximum values out of the measurements were used.

2.8 Data Analysis

For continuous variables of each measurement item, M (mean) and SD (standard error) are indicated. Categorical variables are presented with frequency and percentage. In this study, CRF and MS were classified into 3 quartiles (33.3%, 66.6%). A value of 33.3% or less was indicated as "low-level fitness". A value exceeding 33.3% and less than 66.6% was indicated as "middle-level fitness". A value exceeding 66.6% was indicated as "high-level fitness". In addition, considering both CRF and MS, subjects were classified into the following 9 groups: ① high-level CRF and high-level MS (Q1), ② high-level CRF and middle-level MS (Q2), ③ high-level CRF and low-level MS (Q3), ④ middle-level CRF and high-level MS (Q4), ⑤ middle-level CRF and middle-level MS (Q5), ⑥ middle-level CRF and low-level MS (Q6), ⑦ low-level CRF and high-level MS (Q7), ⑧ low-level CRF and middle-level MS (Q8), and ⑨ low-level CRF and low-level MS (Q9).

Table 1. Clinical characteristics in NAFLD and Non-NAFLD.

	NALD (n = 339)	Non-NALD (n = 986)	*p*-value
Age (years)	49.91 ± 5.43	49.41 ± 5.51	0.150
Height (cm)	168.72 ± 5.26	169.76 ± 5.58	<0.003
Weight (kg)	70.31 ± 9.56	70.02 ± 8.94	0.609
BMI (kg/m^2)	24.69 ± 3.10	24.28 ± 2.72	<0.029
Exercise status (%)	258 (76.3)	820 (83.2)	0.058
Smoking status (%)	99 (29.2)	240 (27.2)	0.473
SBP (mmHg)	123.93 ± 15.68	121.80 ± 15.18	<0.030
DBP (mmHg)	77.76 ± 11.01	75.93 ± 10.70	<0.008
T-Chol (mg/dL)	184.31 ± 36.27	181.24 ± 33.06	0.170
TG (mg/dL)	132.32 ± 68.02	128.66 ± 65.74	0.381
LDL-C (mg/dL)	107.96 ± 32.90	105.74 ± 30.73	0.278
HDL-C (mg/dL)	49.89 ± 11.63	49.76 ± 10.79	0.586
FBG (mg/dL)	87.66 ± 14.10	88.05 ± 13.28	0.651
AST (IU/L)	23.65 ± 10.79	22.88 ± 8.80	0.190
ALT (IU/L)	30.93 ± 20.08	29.29 ± 17.68	0.181
γ-GTP (IU/L)	31.50 ± 22.06	29.15 ± 17.88	0.077
VO_2max	37.69 ± 7.17	39.37 ± 7.02	<0.001
Grip strength	43.78 ± 7.12	44.76 ± 6.95	<0.026

Data shown as Mean ± SD or n (%).

NALD, non-alcoholic liver disease; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; T-Chol, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; FBG, fasting blood glucose; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma glutamyl transpeptidase; VO_2max, maximal oxygen uptake; *p*-value, *t*-test or chi-square test, comparison between NAFL and Non-NAFL group.

An student's *t*-test was conducted to compare measurements between the NAFLD group and the control group. In order to clarify the difference among variables depending on the CRF and MS levels, one-way ANCOVA (Analysis of Covariance) was implemented with the following covariates: age, BMI, exercise, and smoking. The odds ratio was also calculated in a way of logistics regression analysis in order to investigated the relation of NAFLD depending on the CRF and MS levels. All statistical analysis was performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA), and the significance level was set at $p < 0.05$.

3. Results

3.1 Comparison of General Characteristics between NAFLD Group and Control Group

In this study, the NAFLD group included 339 individuals and the control group included 986 individuals. There was a statistically significant difference between the NAFLD group and the control group in BMI ($p < 0.05$), SBP ($p < 0.05$), DBP ($p < 0.001$), CRF ($p < 0.01$), and MS ($p < 0.05$). On the other hand, there was no significant difference in TC, LDL-C, HDL-C, FBG, AST, ALT, and γ-GTP (Table 1).

3.2 Difference in General Characteristics Depending on Cardiorespiratory Fitness Level

There was a statistically significant difference depending on the CRF level in BMI ($p < 0.01$), SBP ($p < 0.01$), DBP ($p < 0.01$), TC ($p < 0.05$), TG ($p < 0.01$), FBG ($p < 0.01$), AST ($p < 0.01$), ALT ($p < 0.01$), and γ-GTP ($p < 0.01$). On the other hand, there was no significant difference in TC, LDL-C, HDL-C, FBG, AST, ALT, and γ-GTP (Table 2).

3.3 Difference in General Characteristics Depending Muscle Strength Level

There was a statistically significant difference depending on the MS level in BMI ($p < 0.01$) and HDL-C ($p < 0.05$). On the other hand, there was no significant difference in SBP, DBP, TC, TG, LDL-C, FBG, AST, ALT, and γ-GTP (Table 2).

3.4 Difference in General Characteristics Depending on Cardiorespiratory Fitness and Muscle Strength Levels

There was a statistically significant difference depending on the CRF and MS levels in BMI ($p < 0.001$), SBP ($p < 0.001$), DBP ($p < 0.001$), TG ($p < 0.001$), FBG ($p < 0.05$), ALT ($p < 0.001$), and γ-GTP ($p < 0.001$). On the other hand, there was no significant difference in TC, LDL-C, HDL-C, and AST (Table 3).

Table 2. Clinical characteristics in accordance with cardiorespiratory fitness level and muscle strength level.

	VO_2max (mL/kg/min)				Grip strength (kg)			
	Low	middle	high	*p*-value	low	Middle	High	*p*-value
	(n = 439)	(n = 448)	(n = 438)		(n = 442)	(n = 442)	(n = 441)	
	31.49 ± 3.60	38.67 ± 1.67	46.69 ± 4.54		36.94 ± 3.94	44.61 ± 1.54	51.99 ± 4.00	
Age (years)	51.10 ± 5.40	49.36 ± 5.42	48.16 ± 5.28	<0.001	50.28 ± 5.62	49.76 ± 5.57	48.58 ± 5.16	<0.001
Height (cm)	169.60 ± 5.55	169.61 ± 5.59	169.26 ± 5.42	0.554	167.41± 5.40	169.51 ± 5.27	171.56 ± 5.09	<0.001
Weight (kg)	72.45 ± 9.91	70.31 ± 8.67	67.52 ± 7.95	<0.001	67.12 ± 8.29	69.58 ± 8.74	73.59 ± 9.06	<0.001
BMI (kg/m^2)	25.16 ± 3.02	24.43 ± 2.73	23.56 ± 2.47	<0.001	23.94 ± 2.71	24.21 ± 2.77	25.00 ± 2.88	<0.001
Exercise status (%)	333 (75.9)	376 (83.9)	365 (83.4)	<0.001	364 (82.3)	365 (82.6)	349 (79.2)	0.571
Smoking status (%)	160 (36.4)	119 (26.6)	88 (20.1)	<0.001	120 (27.1)	110 (24.9)	137 (31.1)	0.116
SBP (mmHg)	125.19 ± 16.48	121.59 ± 14.65	120.26 ± 14.41	<0.001	122.04 ± 16.08	122.33 ± 14.86	122.66 ± 15.05	0.837
DBP (mmHg)	78.37 ± 10.84	76.04 ± 10.67	74.79 ± 10.62	<0.001	76.07 ± 11.13	76.34 ± 10.67	76.79 ± 10.63	0.610
T-Chol (mg/dL)	184.43 ± 5.06	182.89 ±2.73	178.73 ± 33.79	<0.036	182.46 ± 33.62	180.77 ± 33.29	182.84 ± 34.88	0.627
TG (mg/dL)	147.38 ± 68.47	128.38 ±65.97	113.02 ± 59.84	<0.001	124.48 ± 61.28	130.33 ± 68.23	133.99 ± 68.99	0.099
LDL-C (mg/dL)	105.53 ± 31.99	107.72 ± 30.78	105.65 ± 31.17	0.505	106.65 ± 30.56	105.76 ± 30.06	106.51 ± 33.27	0.903
HDL-C (mg/dL)	49.42 ± 11.53	49.49 ± 10.62	50.47 ± 10.85	0.287	50.92 ± 10.17	48.94 ± 11.26	49.53 ± 11.48	<0.023
FBG (mg/dL)	89.63 ± 14.82	87.52 ± 12.36	86.71 ± 13.06	<0.004	87.43 ± 13.42	87.95 ± 12.86	88.47 ± 14.18	0.515
AST (IU/L)	24.22 ± 10.68	22.49 ± 8.33	22.53 ± 8.80	<0.007	22.90 ± 10.42	22.95 ± 8.30	23.38 ± 9.21	0.695
ALT (IU/L)	32.82 ± 21.66	29.69 ± 17.51	26.61 ± 14.65	0.001	29.18 ± 19.85	29.51 ± 17.08	30.44 ± 17.96	0.573
γ-GTP (IU/L)	32.65 ± 20.81	29.85 ± 18.25	26.74 ± 17.55	<0.001	29.56 ± 20.41	29.59 ± 17.06	30.11 ± 19.57	0.892

Data shown as Mean ± SD or n (%).

VO_2max, maximal oxygen uptake; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; T-Chol, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; FBG, fasting blood glucose; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma glutamyl transpeptidase; *p*-value, one-way ANCOVA test or chi-square test.

3.5 Relative Risks of NAFLD Depending on Cardiorespiratory Fitness Level

The relative risk of NAFLD of the low-level CRF group was 1.74 times (95% CI, 1.27–2.37. $p < 0.01$) higher than that of the high-level CRF group. With confounding factors (age, BMI, exercise, smoking) as well, the relative risk of NAFLD of the low-level CRF group was 1.63-fold (95% CI, 1.03–2.60, $p < 0.05$) higher than that of the high-level CRF group. However, there was no relative risk of NAFLD between middle and high levels of CRF (95% CI, 0.92–2.17) (Table 4).

3.6 Relative Risks of NAFLD Depending on Muscle Strength Level

The relative risk of NAFLD of the low-level MS group was 1.54-fold (95% CI, 1.14–2.10, $p < 0.01$) higher than that of the high-level MS group. However, with confounding factors (age, BMI, exercise, smoking) controlled, there was no significant difference in the relative risk between the low-level MS (95% CI, 0.68–1.65) and the high-level MS groups (95% CI, 0.84–1.99) (Table 4).

3.7 Relative Risks of NAFLD Depending on Cardiorespiratory Fitness and Muscle Strength Level

For the relative risk of NAFLD depending on the CRF and MS levels and with the high-level CRF/high-level MS group (Q1) as a basis, the relative risks of the middle-level CRF/low-level MS group (Q6), the low-level CRF/middle-level MS group (Q8), and the low-level CRF/low-level MS (Q9) group were 2.06-fold (95% CI, 1.30–3.54, $p < 0.01$), 2.22-fold (95% CI, 1.31–3.76, $p < 0.01$), and 2.48-fold (95% CI, 1.50–4.11, $p < 0.01$) higher respectively. In addition, with confounding factors (age, BMI, exercise, smoking) controlled and the relative risk of NAFLD of the high-level CRF/high-level MS group (Q1) as the basis, there was only higher relative risk 2.27-fold (95% CI, 0.94–1.99, $p < 0.05$) for the low-level CRF/low-level MS group (Q9) (Table 4).

4. Discussion

This study was conducted to investigate the association between CRF-MS and NAFLD. The results showed that the levels of CRF and MS in the NAFLD group were lower than those in the control group. There was a significant difference depending on the CRF and MS levels for BMI, SBP, DBP, TG, FBG, ALT, and γ-GTP. Also, when the CRF-MS level was low, the relative occurrence risk of NAFLD was higher than when the CRF-MS level was high.

NAFLD is a disease in which fat accumulates in the liver, as with alcoholic fatty liver, without excess alcohol consumption, virus infection, or other liver diseases. While the cause of NAFLD is not certain, obesity and insulin resistance are two highly influential factors [26,27]. It is also

Table 3. Clinical characteristics in accordance with cardiovascular fitness and muscle strength levels (Q1–Q9).

CRF & MS	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	*p*-value
	High & high	High & middle	High & low	Middle & high	Middle & middle	Middle & low	Low & high	Low & middle	Low & low	
	(n = 169)	(n = 129)	(n = 140)	(n = 150)	(n = 168)	(n = 130)	(n = 122)	(n = 145)	(n = 172)	
Age (years)	47.31 ± 4.89	48.57 ± 5.29	48.81 ± 5.62	48.66 ± 5.29	49.58 ± 5.63	49.90 ± 5.25	50.25 ± 4.92	51.04 ± 5.51	51.75 ± 5.57	<0.001
Height (cm)	171.28 ± 5.08	168.84 ± 4.75	167.20 ± 5.56	171.33 ± 5.29	170.02 ± 5.44	167.10 ± 5.27	172.23 ± 4.84	169.51 ± 5.49	167.81 ± 5.37	<0.001
Weight (kg)	65.90 ± 7.38	65.06 ± 7.43	74.01 ± 9.08	69.82 ± 7.89	66.67 ± 7.44	76.96 ± 9.60	72.57 ± 9.61	69.14 ± 9.11	70.09 ± 9.10	<0.001
BMI (kg/m^2)	24.14 ± 2.50	23.11 ± 2.31	23.27 ± 2.44	25.20 ± 2.78	24.17 ± 2.63	23.89 ± 2.61	25.96 ± 3.16	25.23 ± 2.94	24.53 ± 2.86	<0.001
Exercise status (%)	136 (80.2)	111 (86.2)	118 (84.3)	119 (79.4)	146 (87.1)	110 (84.3)	94 (76.9)	103 (70.7)	136 (79.0)	0.289
Smoking status (%)	34 (20.1)	23 (17.8)	31 (22.1)	47 (31.3)	38 (22.6)	34 (26.2)	56 (45.9)	49 (33.8)	55 (32.0)	<0.001
SBP (mmHg)	120.60 ± 15.24	119.71 ± 14.20	120.34 ± 13.63	121.93 ± 14.24	120.88 ± 13.31	122.12 ± 16.69	126.39 ± 15.20	126.34 ± 16.33	123.36 ± 17.37	<0.001
DBP (mmHg)	74.82 ± 11.02	74.71 ± 9.69	76.42 ± 10.01	75.28 ± 9.84	76.60 ± 12.34	79.95 ± 10.02	78.93 ± 10.87	76.77 ± 11.22	76.40 ± 10.81	<0.001
T-Chol (mg/dL)	180.29 ± 34.83	178.12 ± 34.51	177.39 ± 31.95	182.12 ± 34.13	181.57 ± 32.63	185.48 ± 31.27	187.26 ± 35.72	182.20 ± 33.04	184.31 ± 36.27	0.227
TG (mg/dL)	116.76 ± 72.75	106.36 ± 49.36	133.62 ± 70.55	124.68 ± 64.45	127.11 ± 62.46	159.80 ± 74.69	148.97 ± 64.67	137.23 ± 65.74	129.60 ± 66.32	<0.001
LDL-C (mg/dL)	104.51 ± 31.50	104.98 ± 29.08	106.28 ± 32.97	108.08 ± 29.16	108.90 ± 30.37	106.03 ± 34.67	104.19 ± 29.81	106.31 ± 31.93	106.31 ± 31.30	0.942
HDL-C (mg/dL)	50.08 ± 11.49	50.26 ± 10.76	51.14 ± 10.16	49.11 ± 10.85	48.55 ± 10.97	51.15 ± 9.76	49.27 ± 12.25	48.21 ± 11.99	50.55 ± 10.53	0.189
FBG (mg/dL)	87.07 ± 13.28	86.24 ± 11.46	86.71 ± 14.21	89.47 ± 15.58	86.83 ± 8.87	86.15 ± 11.84	89.20 ± 13.51	90.77 ± 16.92	88.98 ± 13.81	<0.023
AST (IU/L)	21.67 ± 7.06	22.51 ± 10.04	22.78 ± 8.58	22.47 ± 7.66	22.19 ± 8.91	24.38 ± 10.32	24.64 ± 9.70	23.74 ± 11.71	23.08 ± 9.35	0.117
ALT (IU/L)	27.31 ± 14.95	25.42 ± 12.69	26.86 ± 15.96	31.18 ± 17.00	29.37 ± 16.46	28.39 ± 19.32	33.86 ± 21.93	33.31 ± 20.17	31.66 ± 22.73	<0.001
γ-GTP (IU/L)	28.04 ± 19.47	24.68 ± 14.26	31.40 ± 20.00	28.49 ± 16.27	29.83 ± 18.54	32.20 ± 20.34	32.25 ± 15.40	33.32 ± 24.82	29.75 ± 19.05	<0.001

Data shown as Mean ± SD or n (%).

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; T-Chol, total cholesterol; TG, triglycerides; LDL-C, low density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; FBG, fasting blood glucose; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, gamma glutamyl transpeptidase; *p*-value, one-way ANCOVA test or chi-square test.

Table 4. Odds ratio of NAFLD in accordance with cardiovascular fitness and muscle strength level.

	Nonalcoholic fatty liver disease					
	Unadjusted OR	(95% CI)	p-value	Adjusted OR	(95% CI)	p-value
Cardiovascular fitness (CRF)						
High	1.00			1.00		
Middle	1.35	0.98–1.86	0.059	1.40	0.92–2.17	0.128
Low	1.74	1.27–2.37	<0.001	1.63	1.03–2.60	<0.043
Muscle strength (MS)						
High	1.00			1.00		
Middle	1.20	0.87–1.63	0.274	1.06	0.68–1.65	0.808
Low	1.54	1.14–2.10	<0.005	1.30	0.84–1.99	0.247
CRF & MS						
High & high	1.00			1.00		
High & middle	1.17	0.65–2.10	0.599	1.07	0.50–2.26	0.866
High & low	1.43	0.82–2.49	0.207	1.41	0.69–2.88	0.343
Middle & high	1.57	0.92–2.70	0.100	1.88	0.89–3.98	0.095
Middle & middle	1.31	0.76–2.24	0.327	1.48	0.72–3.03	0.289
Middle & low	2.06	1.20–3.54	<0.009	1.52	0.72–3.21	0.274
Low & high	1.38	0.77–2.46	0.274	1.32	0.58–3.04	0.508
Low & middle	2.22	1.31–3.76	<0.003	1.79	0.83–3.89	0.140
Low & low	2.48	1.50–4.11	<0.001	2.27	1.12–4.61	<0.024

OR, Odds ratio.

Adjusted for age, body mass index, exercise, smoking.

reported that there is a positive effect from CRF and MS [28]. In this study, CRF and MS were classified into 3 quartiles. Then the subjects were classified into 9 quadrants by considering both the CRF level and MS level. After controlling for confounding factors (age, BMI, exercise, smoking), the results of this study showed that the relative risk of NAFLD in the case of a low CRF level was 1.63-fold higher than that of a high CRF level. This result corresponds to the findings of many previous studies that show that when the level of CRF is low, the risk of NAFLD is high accordingly [21,22]. Meanwhile, there was no significant difference in the relative risk of NAFLD in relation to the level of MS, although there was an increase. This result is different from the finding of previous studies that the risk of NAFLD was relatively high as the grip strength level decreased [24,29,30]. When individual fitness factors of middle-aged men were examined in this study, it was shown that CRF was more influential on the risk of NAFLD than that of MS.

In addition, an examination in this study of the relative risk of NAFLD in consideration of both CRF and MS showed that the relative risk of low CRF/MS was 2.27-fold higher than that of high CRF/MS. This result corresponds to the finding of Hao *et al*. [28] where, among adult men, the risk of NAFLD decreased as VO_2max (>30 mL/kg^{-1} min^{-1}) and MS levels increased. This result indicates that a decrease of CRF and MS, both of which are regarded as being important in adult health and fitness, increases the risk of NAFLD. Therefore, in order to reduce the risk of NAFLD, it is important to maintain both CRF and MS at high levels. However, further study is necessary in order to clarify the direct causal relations between the relative risk of CRF-MS levels and NAFLD.

The mechanism of how low CRF and MS levels increase NAFLD outbreaks has yet to be clarified. Insulin resistance is known to play a key role in NAFLD pathogenesis [9–11]. Many studies report that aerobic exercise is effective for CRF and increases the insulin sensitivity of fat tissues and beta oxidation of free fatty acid, thereby reducing the accumulation of neutral fat in the liver [31,32]. In addition, it is known that resistance exercise is effective for MS and improves insulin sensitivity [33]. In order to prevent NAFLD, therefore, it is important to increase the levels of both CRF and MS, which promote the physiological reactions of insulin.

This study has limitations in that the subjects are only middle-aged men who visited a medical center for health examination, and the number of subjects is too small for the results to be applied generally. Also this study did not consider factors such as hypertension, diabetes, dyslipidemia, metabolic syndrome, and insulin resistance, which are cardiovascular risk factors that may affect NAFLD. In addition, NAFLD diagnosis may involve classification errors because measurement was practiced by ultrasonography testing, not by a biopsy. However, despite such limitations this study is of significance in that it examines the association between NAFLD and the two factors of CRF and MS among middle-aged men.

5. Conclusions

This study investigated the association between the two factors of CRF-MS and NAFLD in middle-aged men. From the results, it was verified that the risk of NAFLD is higher when the CRF-MS level is low than when it is high. Thus, it was shown that, in middle-aged men, there is a close association between NAFLD and the two factors regarded as important for their health, namely CRF and MS levels. Therefore, CRF and MS enhancement through aerobic and resistance exercise is important in NAFLD prevention.

Author Contributions

SJK conceived the study design. SJK, KJK, STP and GCH managed the data and performed statistical analyses. SJK drafted the initial manuscript, and STP, KJK, GCH revised the manuscript. All authors approved the final manuscript.

Ethics Approval and Consent to Participate

This study was conducted in compliance with the ethical principles of the Declaration of Helsinki. Before data collection, the study was approved by the ethics review committee (Institutional Review Board of Changwon National University: 7001066-202002-HR-005).

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Conflict of Interest

The authors declare no conflict of interest.

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