Associations of Cardiorespiratory Fitness with Estimated Remnant Cholesterol and Non-High-Density Lipoprotein Cholesterol in Healthy Men

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Abstract

Remnant cholesterol (RC) and non-high-density lipoprotein cholesterol (non-HDL-C) may contribute to the residual risk for atherosclerotic cardiovascular disease (ASCVD). High cardiorespiratory fitness (CRF) is associated with favorable traditional lipid profiles, but its relationship with RC and non-HDL-C remains unclear. We analyzed cross-sectional data on 4,613 healthy men (mean age 49 years). CRF was measured using peak oxygen uptake during incremental exercise testing and categorized into quartiles. RC was estimated as total cholesterol (TC) minus HDL-C and low-density lipoprotein-cholesterol (LDL-C), and elevated RC defined as ≥38 mg/dL (90 percentile). Non-HDL-C was calculated as TC minus HDL-C and high non-HLD-C was defined as ≥190 mg/dL. CRF was inversely associated with RC (β=-0.31, 95% CI=-0.39 to -0.24) and non-HDL-C (β=-0.34, 95% CI=-0.57 to -0.11) after adjustment for several risk factors. Each MET increment in CRF was associated with a lower odds of having elevated RC (odds ratio [OR] 0.85, 95% confidence interval [95% CI] 0.77 to 0.93) and non-HDL-C (OR 0.93, 95% CI 0.85 to 1.00) in multivariable analysis. Compared with the bottom quartile, the top quartile of CRF had significantly lower odds of elevated RC (OR 0.63, 95% CI 0.45 to 0.88) and non-HDL-C (OR 0.68, 95% CI 0.51 to 0.91). In conclusion, higher CRF was independently associated with lower levels of RC and non-HDL-C and lower odds of the prevalence of elevated RC and non-HDL-C in healthy men.

Keywords: *cardiorespiratory fitness; remnant cholesterol; non-high-density lipoprotein cholesterol*

Despite positive modulation of traditional lipid profiles including achieving optimal low-density lipoprotein cholesterol (LDL-C) levels, a residual risk for atherosclerotic cardiovascular disease (ASCVD) remains. This may in part be due to remnant cholesterol (RC), which is the cholesterol content of the triglyceride (TG)-rich lipoproteins and comprises very low-density lipoproteins (VLDL) and intermediate-density lipoproteins with chylomicron remnants.[1,2] In addition, non-HDL-C, which is the TG-rich lipoprotein related to highly atherogenic lipoprotein, is a better risk predictor for ASCVD than LDL-C.[3] Importantly, both elevated RC and non-HDL-C are associated with increased risk of CVD outcomes independently of LDL-C and other traditional lipid parameters[4] and considerably improve CVD risk prediction beyond these risk factors.[5] High cardiorespiratory fitness (CRF) is strongly associated with a lower risk of ASCVD[6,7] and well documented to be associated with favorable traditional lipid and lipoprotein profiles,[8-10] but its relationship with RC and non-HDL-C is less certain.[11,12] We tested the hypothesis that higher CRF would have a beneficial effect on RC and non-HLD-C independently of established risk factors.

Methods

Among a sample of 5,616 men who participated in a routine medical screening program in 2009 at Samsung Medical Center (Seoul, South Korea), we analyzed data of 4,613 healthy men (mean age 49±7 years) who were free of known cardiovascular disease, hypertension or diabetes, and had undergone maximal exercise testing with blood-based biomarkers assessment. Written informed consent was obtained from all participants before undergoing health screening, and the study was approved by the Samsung Medical Center Institutional Review Board.

Smoking status was obtained by self-reported questionnaire. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Systolic blood pressure (SBP)

and diastolic blood pressure (DBP) were measured in the sitting position using an automated blood pressure monitor (Dinamap PRO 100; GE Healthcare, Milwaukee, Wisconsin).

Blood samples were collected following a 12-h overnight fast. Blood biomarkers (TC, LDL-C, HDL-C, and TG), were analyzed by enzymatic colorimetric and liquid selective detergent methods, using a Hitachi 7600 analyzer (Hitachi Co., Tokyo, Japan) in the Clinical Medicine Laboratory of the Samsung Medical Center. High-sensitivity C-reactive protein (CRP) was measured using a CRP (II) Latax X2 turbidimetric method (Hitachi Co., Tokyo, Japan). Fasting glucose levels were determined using the Hexokinase, UV method (Hitachi-7600, Tokyo, Japan). Fasting insulin concentrations were measured with an immunoradiometric assay (TFB, Tokyo, Japan). Serum uric acid levels were assessed by the enzymatic colorimetric method using a clinical chemistry auto analyzer (Aeroset, Abbot Lab, Abbott Park, IL, USA). The homeostatic model assessment for insulin resistance (HOMA-IR) was calculated using the following formula: fasting glucose [mg/dL] × fasting insulin [μU/L] / 405 for insulin resistance. Inter- and intra-assay coefficients of variation were <5% for all blood-based biomarkers. Detailed measurements of these blood biomarkers have been described elsewhere.[13]

RC was estimated as TC minus HDL-C minus LDL-C, and elevated RC defined as ≥38 mg/dL (90 percentile). Non-HDL-C was calculated as TC minus HDL-C, and high levels defined as ≥190 mg/dL based on lipid and atherosclerosis guidelines.[14]

CRF was directly measured by peak oxygen uptake (VO_{2peak}) during cardiopulmonary treadmill exercise testing using the Bruce protocol (Jaeger Oxycon Delta, Erich Jaeger, Hoechberg, Germany). VO_{2peak} using gas analysis was defined as the highest or peak attained oxygen consumption, expressed as mL/kg/min, recorded during the test (Jaeger Oxycon Delta, Eric Jaeger, Hoechberq, Germany). VO_{2peak} was also expressed in metabolic equivalents

(METs) (1 MET is defined as the amount of oxygen consumed while sitting at rest and corresponds to an oxygen uptake of 3.5 mL/kg/min).

Data was expressed as mean (standard deviation) or median (interquartile range) for continuous variables based on their distributions and as counts (%) for categorical variables. Baseline characteristics were summarized for the overall population and by quartiles of CRF. Analysis of variance was used to compare between group means for continuous variables and chi-square test was used to compare categorical variables across the quartiles of CRF. Pearson's correlations and multiple linear regression analyses were used to determine independent relationships of CRF with RC and non-HDL-C. Multivariable logistic regression was used to estimate odds ratios (OR) with 95% confidence interval (CI) for the associations of CRF with elevated RC (defined as ≥38 mg/dL) and elevated non-HLD-C (defined as ≥190 mg/dL). The analyses were adjusted for age, BMI, SBP, smoking, uric acid, HOMA-IR, and CRP. CRF was modelled as continuous (per 1 MET increase) and categorical variables (quartiles). All analyses were conducted using SPSS (IBM Corp., SPSS Version 26.0, Armonk, NY, USA), and alpha was set at $P<0.05$.

Results

Table 1 presents the baseline characteristics of study participants overall and according to CRF quartiles. Men in the highest quartile of CRF had significantly lower TC, LDL-C, TG, non-HDL-C, RC, but higher HDL-C than men in the lowest quartile of CRF (all, $p <0.01$).

CRF was significantly inversely correlated with RC ($r = -0.19$, $p <0.001$) and non-HDL-C ($r = -0.11$, $p <0.001$) (Figure 1). In multivariable linear regression models CRF was inversely associated with RC (β=-0.31, 95% CI=-0.39 to -0.24) and non-HDL-C (β=-0.34, 95% CI=-0.57 to -0.11) (Table 2).

Comparing the top versus the bottom quartile of CRF, the multivariable-adjusted ORs (95% CIs) for having abnormal HDL-C (≤40 mg/dL) and TG (≥150 mg/dL) were 0.51 (0.41 to 0.64) and 0.54 (0.44 to 0.67), respectively; the associations were not significant for abnormal TC (0.97, 0.81 to 1.17) and LDL-C (0.93, 0.77 to 1.12) (Table 3).

Each MET increment in CRF was associated with a lower odds of having elevated RC (OR 0.85, 95% CI 0.77 to 0.93) (Table 4). Compared with the bottom quartile, the top quartile of CRF had significantly lower odds of elevated RC (OR 0.63, 95% CI 0.45 to 0.88) and non-HDL-C (OR 0.68, 95% CI 0.51 to 0.91).

In addition, each MET increment in CRF was associated with a lower odds of having elevated RC (OR 0.83, 95% CI 0.75 to 0.92) in men with LDL ≥100 mg/dL. Comparing the top versus bottom quartile of CRF, the OR was 0.58 (95% CI 0.41 to 0.83). The association between CRF and elevated RC was not significant in men with LDL-C <100 mg/dL (Supplementary Table 1).

Discussion

Higher levels of CRF are strongly associated with a lower risk of ASCVD, and favorable traditional lipid profiles have been suggested as the potential mechanisms underlying the cardioprotective effects of high CRF. RC and non-HLD-C are strong risk markers for ASCVD and may contribute to the residual risk for ASCVD[4,5]; however, whether CRF has a favorable effect on RC and non-HLD-C is not very clear. We found that higher levels of CRF were associated with a lower odds of the prevalence of abnormal HDL-C (≤40 mg/dL) and TG (≥150 mg/dL), but not TC and LDL-C. These results are consistent with previous studies that reported a beneficial effect of CRF on the prevalence of traditional dyslipidemia.[8-10] We tested the hypothesis that the association between CRF and RC would persist in the presence of optimal levels of LDL-C.[1] However, our results showed that higher CRF levels were

independently associated with a lower odds of the prevalence of elevated RC in men with LDL-C ≥100 mg/dL, but the association was not significant in men with LDL-C <100 mg/dL. Given the relatively small sample for men with LDL-C <100 mg/dL, the analysis may be underpowered and hence, needs careful interpretation. Large-scale cohorts are warranted to confirm or refute these results.

Several studies have suggested an association between CRF and atherogenic lipoprotein particles. In the HUNT3 fitness study, lower levels of CRF were associated with higher VLDL particles and increased TG content in the small-sized and dense HDL and LDL particles in healthy individuals.[15] In addition, high CRF was associated with a less lipoprotein profiles in women and healthy children.[16,17] However, the relationship between CRF and RC has not been previously reported. The novel finding of the present study is that CRF levels were inversely correlated with RC levels and higher CRF levels were associated with a lower odds of the prevalence of elevated RC, independent of established risk factors in apparently healthy men. To our knowledge, this is the first study to report this relationship between CRF and RC in healthy men. The lower risk of ASCVD in individuals with higher levels of CRF may partly be due to the favorable effects of CRF on RC levels in addition to levels of traditional lipid parameters. However, future studies are needed to confirm these results in participants with different racial or ethnic origins and women and to clarify the longitudinal associations of CRF with RC.

The association between CRF and non-HDL-C as an atherogenic lipoprotein has not been well studied; a few studies conducted in health Japanese and Caucasian have reported inverse associations between CRF and elevated non-HDL-C.[11,12] Our study results showed that CRF was inversely correlated with non-HDL-C and high CRF was associated with a lower odds of the prevalence of elevated non-HDL-C values, independently of established risk factors.

Our results are consistent with these previous studies that reported an inverse relationship between CRF and non-HDL-C, and add to the accumulating literature on the relationship between CRF and non-HDL-C in healthy men.

The role of abnormal lipid profiles (dyslipidemia) has been implicated in the pathogenesis of ASCVD. Pharmacological interventions with statin therapy are well known to substantially lower LDL-C levels, which reduce the risk for the ASCVD.[18,19] However, it appears abnormal levels of traditional lipid parameters are often absent in a proportion of individuals who develop ASCVD. It appears there might be a residual risk that is not attributable to LDL-C or other established risk factors. Several reports have suggested that RC and non-HDL-C may be superior to LDL-C and other traditional lipid parameters as risk indicators and predictors for ASCVD.[3-5] Decreasing levels of RC and non-HDL-C may be additional strategies to further reduce the risk of ASCVD, but this would need to be demonstrated in definitive trials.

Aside from pharmacological interventions, lifestyle changes can be used to effectively modulate hypertriglyceridemia.[20,21] Although it is well documented that physical activity can favorably impact on levels of traditional lipid parameters,[22] a few studies have suggested that aerobic exercise can reduce levels of RC[23] and non-HDL-C.[24,25] Our findings of inverse associations of CRF with RC and non-HDL-C and the fact that CRF is largely influenced by aerobic exercise, suggests that regular aerobic exercise can favorably impact on levels of RC and non-HDL-C. Future studies are needed to clarify whether higher CRF is more closely associated with remnant cholesterol levels than levels of conventional lipid parameters.

The mechanisms underlying the association between higher CRF and lower odds of elevated RC and non-HDL-C are unclear, but several possible mechanistic pathways may be involved. Individuals with high CRF, reflective of regular exercise training or physically

activity,[7] have increased expression of lipoprotein lipase, the enzyme which degrades TG into free fatty acids and responsible for hydrolyzed chylomicrons and VLDL (TG-rich lipoprotein particles). In addition, several risk factors such as obesity, inflammation, and insulin resistance, that potentially contribute to an increase in levels of RC and non-HDL-C[2,26,27] were lower in individuals with high CRF levels,[27] which may contribute to the observed associations. A previous study suggested that the inverse association between CRF and LDL-C could be largely attributed to obesity.[28] However, it is noteworthy in our study that the associations of higher CRF with lower RC and non-HDL-C persisted after adjusting for BMI, insulin resistance, and inflammation, which suggests that other factors may be involved. Our study was not designed to investigate underlying mechanistic pathways, hence mechanistic studies are warranted.

We acknowledge several methodological limitations to our study. Due to the cross-sectional design, the temporal associations between CRF and lipid parameters could not be evaluated. Our study population included only Korean men, which limits the generalizability of our findings to women and other racial/ethnic populations. Future studies are needed to clarify the potential role of sex and racial differences and should prospectively evaluate these associations. We did not have information on dietary data and lipid-lowering medications, which are potential confounders. Strengths of the study are the novelty, the large sample size, and the direct assessment of VO_{2peak} using expired gas analysis, which provides a gold standard measure of CRF.[28]

In conclusion, higher CRF was independently associated with lower levels of RC and non-HDL-C and lower odds of the prevalence of elevated RC and non-HDL-C in healthy men. Large-scale prospective cohort studies are warranted to confirm or refute these findings.

Disclosures

The authors have no conflicts of interest to declare.

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Figure Legend

Figure 1. Scatter plot for the correlation between cardiorespiratory fitness and remnant cholesterol (r = -0.19, p <0.001) (Panel A) and non-high-density lipoprotein cholesterol (r = -0.11, p <0.001) (Panel B). Abbreviations: non-high-density lipoprotein cholesterol (non-HDL-C), peak oxygen uptake (VO_{2peak}), remnant cholesterol (RC).

Table 1. Characteristics of study participants overall and according to quartiles of cardiorespiratory fitness.

Variables	Total (n=4613)	Q 1 (n=1176)	Q 2 (n=1152)	Q 3 (n=1143)	Q 4 (n=1142)	*P* value
Age (years)	49.1 ± 7.4	52.3 ± 7.3	49.6 ± 7.0	48.1 ± 6.6	46.2 ± 7.1	<0.001
BMI (kg/m^2)	24.3 ± 2.5	24.8 ± 2.9	24.6 ± 2.4	24.2 ± 2.4	23.7 ± 2.4	<0.001
Current smoker	902 (19.6 %)	253 (21.5 %)	230 (20.0 %)	237 (20.7 %)	182 (15.9 %)	0.002
SBP (mmHg)	116.0 ± 11.5	116.0 ± 11.9	116.0 ± 11.5	115.4 ± 11.4	116.4 ± 11.1	0.184
DBP (mmHg)	74.8 ± 8.3	75.1 ± 8.3	74.9 ± 8.4	74.7 ± 8.4	74.6 ± 8.0	0.435
TC (mg/dL)	200.6 ± 33.4	202.6 ± 35.4	202.1 ± 33.2	200.4 ± 32.4	197.0 ± 32.0	0.001
HDL-C (mg/dL)	49.4 ± 12.0	47.0 ± 11.1	48.5 ± 11.6	50.1 ± 11.8	52.4 ± 13.3	<0.001
LDL-C (mg/dL)	128.2 ± 29.3	129.9 ± 31.1	129.7±29.2	127.9 ± 28.6	124.9 ± 28.4	<0.001
TG (mg/dL)	140.0 ± 72.3	152.7 ± 73.8	147.3 ± 74.4	136.6 ± 71.2	123.3 ± 65.9	<0.001
Non-HDL-C (mg/dL)	151.2 ± 33.6	155.6 ± 35.7	153.7 ± 32.9	150.4 ± 32.7	144.9 ± 31.9	<0.001
RC (mg/dL)	23.0 ± 11.5	25.4 ± 11.8	23.9 ± 11.5	22.5 ± 11.1	20.0 ± 10.8	<0.001
Glucose (mg/dL)	94.2 ± 9.9	94.6 ± 9.9	94.5 ± 10.2	93.9 ± 9.9	93.4 ± 9.7	0.015

Insulin (mg/dL)	8.0 ± 4.1	8.9 ± 4.7	8.3 ± 4.1	7.8 ± 3.9	6.9 ± 3.3	<0.001
HOMA-IR	1.9 ± 1.1	2.1 ± 1.2	1.9 ± 1.1	1.8 ± 1.0	1.6 ± 0.8	<0.001
Uric acid (mg/dL)	5.9 ± 1.1	6.0 ± 1.2	5.9 ± 1.1	5.8 ± 1.2	5.7 ± 1.1	0.001
hsCRP (mg/L)	0.06 (0.03-0.12)	0.07 (0.04-0.14)	0.06 (0.03-0.12)	0.06 (0.03-0.11)	0.05 (0.03-0.08)	<0.001
$VO_{2\ peak}$ (mL/kg/min)	33.2 ± 4.6	27.6 ± 2.2	31.7 ± 0.8	34.5 ± 0.9	39.1 ± 2.6	<0.001

Data are expressed as mean ± standard deviation, n (% of group), or median (interquartile range).

Abbreviations: Body mass index (BMI), , diastolic blood pressure (DBP), high-density lipoprotein cholesterol (HDL-C), high-sensitivity C-reactive protein (hsCRP), homeostasis model assessment for insulin resistance (HOMA-IR), low-density lipoprotein cholesterol (LDL-C), peak oxygen uptake (VO_{2peak}), quartile (Q), triglycerides (TG), total cholesterol (TC), remnant cholesterol (RC), systolic blood pressure (SBP).

Table 2. Multiple linear regression analysis with remnant cholesterol and non-high-density lipoprotein cholesterol as dependent variables and selected factors as independent variables.

	RC			non-HDL-C		
	β Coefficient	95% CI	p-value	β Coefficient	95% CI	p-value
VO_{2peak}	-.31	-0.39 to -0.24	<0.001	-.34	-0.57 to -0.11	0.004
Age	-.09	-0.13 to -0.04	<0.001	.09	-0.05 to 0.23	0.207
Body mass index	.58	0.44 to 0.72	<0.001	2.08	1.66 to 2.50	<0.001
Systolic blood pressure	.001	-0.03 to 0.03	0.925	.02	-0.07 to 0.10	0.706
C-reactive protein	2.01	1.16 to 2.85	<0.001	1.53	-1.05 to 4.11	0.245
Smoking status (yes/no)	4.48	3.69 to 5.28	<0.001	5.38	2.96 to 7.80	<0.001
HOMA-IR	1.82	1.49 to 2.14	<0.001	.3.37	2.38 to 4.36	<0.001
Uric acid	1.25	0.98 to 1.53	<0.001	3.98	3.13 to 4.83	<0.001

Abbreviations: confidence interval (CI), homeostasis model assessment for insulin resistance (HOMA-IR), non-high-density lipoprotein cholesterol (non-HDL-C), peak oxygen uptake ($VO_{2\ peak}$), remnant cholesterol (RC).

Table 3. Multivariable adjusted odd ratios for the associations of cardiorespiratory fitness with the prevalence of traditional dyslipidemia.

Variables	n	Prevalence, n (%)	Adjusted OR (95% CI)
TC (≥200 mg/dl)			
Per 1-MET increase	4613	2205	0.99 (0.95-1.05)
Q1 (<30.1 ml/kg/min)	1176	584 (49.7)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	1152	567 (49.2)	1.03 (0.87-1.23)
Q3 (33.1-36.0 ml/kg/min)	1143	544 (47.6)	1.02 (0.86-1.21)
Q4 (≥36.1 ml/kg/min)	1142	510 (44.7)	0.97 (0.81-1.17)
HDL-C (≤40 mg/dl)			
Per 1-MET increase	4613	1064	0.81 (0.76-0.86)
Q1 (<30.1 ml/kg/min)	1176	351 (29.8)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	1152	296 (25.7)	0.88 (0.72-1.07)
Q3 (33.1-36.0 ml/kg/min)	1143	248 (21.7)	0.73 (0.59-0.89)
Q4 (≥36.1 ml/kg/min)	1142	169 (14.8)	0.51 (0.41-0.64)

LDL-C (≥130 mg/dl)			
Per 1-MET increase	4613	2081	0.98 (0.93-1.03)
Q1 (<30.1 ml/kg/min)	1176	563 (47.9)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	1152	545 (47.3)	1.02 (0.86-1.21)
Q3 (33.1-36.0 ml/kg/min)	1143	504 (44.1)	0.96 (0.81-1.15)
Q4 (≥36.1 ml/kg/min)	1142	469 (41.1)	0.93 (0.77-1.12)
TG (≥150 mg/dl)			
Per 1-MET increase	4613	1616	0.80 (0.76-0.85)
Q1 (<30.1 ml/kg/min)	1176	502 (42.7)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	1152	453 (39.3)	0.89 (0.74-1.07)
Q3 (33.1-36.0 ml/kg/min)	1143	379 (33.2)	0.71 (0.58-0.85)
Q4 (≥36.1 ml/kg/min)	1142	282 (24.7)	0.54 (0.44-0.67)

Adjusted for age, body mass index, systolic blood pressure, smoking, uric acid, HOMA-IR, and C-reactive protein.

Abbreviations: confidence interval (CI), high-density lipoprotein cholesterol (HDL-C), homeostatic model assessment for insulin resistance (HOMA-IR), low-density lipoprotein cholesterol (LDL-C), metabolic equivalent (MET), odds ratio (OR), quartile (Q), total cholesterol (TC), triglycerides (TG).

Table 4. Multivariable adjusted odd ratios for the associations of cardiorespiratory fitness with the prevalence of elevated remnant cholesterol and non-high-density lipoprotein cholesterol.

Variables	n	Prevalence, n (%)	Adjusted model OR (95% CI)
RC (≥38 mg/dl)			
Per 1-MET increase	4613	424	0.85 (0.77-0.93)
Q1 (<30.1 ml/kg/min)	1176	149 (12.7)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	1152	121 (10.5)	0.90 (0.68-1.19)
Q3 (33.1-36.0 ml/kg/min)	1143	84 (7.3)	0.65 (0.49-0.88)
Q4 (≥36.1 ml/kg/min)	1142	70 (6.1)	0.63 (0.45-0.88)
Non-HDL-C (≥190 mg/dl)			
Per 1-MET increase	4613	572	0.93 (0.85-1.00)
Q1 (<30.1 ml/kg/min)	1176	184 (15.6)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	1152	143 (12.4)	0.79 (0.62-1.02)
Q3 (33.1-36.0 ml/kg/min)	1143	142 (12.4)	0.88 (0.69-1.11)

Q4 (≥36.1 ml/kg/min)	1142	103 (9.0)	0.68 (0.51-0.91)

Adjusted for age, body mass index, systolic blood pressure, smoking, uric acid, HOMA-IR, and C-reactive protein.

Abbreviations: confidence interval (CI), homeostatic model assessment for insulin resistance (HOMA-IR), metabolic equivalent (MET), non-high-density lipoprotein cholesterol (non-HDL-C), odds ratio (OR), quartile (Q), remnant cholesterol (RC).

Supplementary Table 1. Multivariable adjusted odd ratios for the associations of cardiorespiratory fitness with the prevalence of elevated remnant cholesterol in men with low-density lipoprotein cholesterol <100 versus low-density lipoprotein cholesterol ≥100 mg/dl.

Variables	n	Prevalence, n (%)	Adjusted model OR (95% CI)
RC (≥38 mg/dl), LDL (<100 mg/dl)			
Per 1-MET increase	773	43	0.97 (0.74-1.26)
Q1 (<30.1 ml/kg/min)	184	11 (6.0)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	178	15 (8.4)	1.77 (0.75-4.20)
Q3 (33.1-36.0 ml/kg/min)	195	8 (4.1)	0.92 (0.34-2.53)
Q4 (≥36.1 ml/kg/min)	216	9 (4.2)	1.21 (0.43-3.43)
RC (≥38 mg/dl), LDL (≥100 mg/dl)			
Per 1-MET increase	3840	381	0.83 (0.75-0.92)
Q1 (<30.1 ml/kg/min)	992	138 (13.9)	1 (reference)
Q2 (30.2-33.0 ml/kg/min)	974	106 (10.9)	0.82 (0.61-1.10)
Q3 (33.1-36.0 ml/kg/min)	948	76 (8.0)	0.62 (0.45-0.85)

Q4 (≥36.1 ml/kg/min)	926	61 (6.6)	0.58 (0.41-0.83)

Adjusted for age, body mass index, systolic blood pressure, smoking, uric acid, HOMA-IR, and C-reactive protein.

Abbreviations: confidence interval (CI), homeostatic model assessment of insulin resistance (HOMA-IR), low-density lipoprotein cholesterol (LDL-C), metabolic equivalents (MET), odds ratio (OR), quartile (Q), remnant cholesterol (RC).

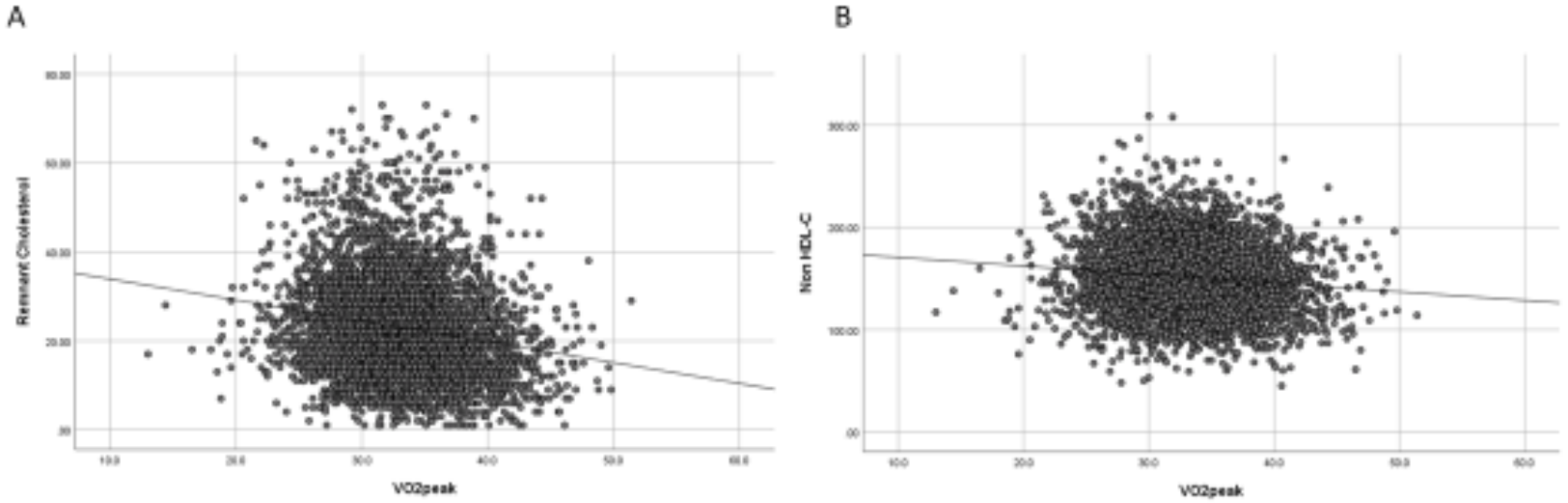

Figure 1. Scatter plot for the correlation between cardiorespiratory fitness and remnant cholesterol (r = -0.19, p <0.001) (Panel A) and non-high-density lipoprotein cholesterol (r = -0.11, p <0.001) (Panel B). Abbreviations: non-high-density lipoprotein cholesterol (non-HDL-C), peak oxygen uptake (VO_{2peak}), remnant cholesterol (RC).