

Effect of Physical Activity Type on Serum Remnant Cholesterol Level in Korean Adults: A Nationwide Population-Based Study

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Keywords

Serum remnant cholesterol · Physical activity · Dyslipidemia · Cardiovascular disease · Korean adults

Abstract

Introduction: Remnant cholesterol (RC) is an important contributor to cardiovascular disease development. We aimed to investigate the effect of physical activity (PA) type on serum RC levels in Korean adults. **Methods:** We used data from the 2016–2021 Korea National Health and Nutrition Examination Survey, and included 32,877 adults. Serum RC was calculated by subtracting the low-density lipoprotein cholesterol and high-density lipoprotein cholesterol levels from the total cholesterol level. Hyper-remnant cholesterolemia was defined as a serum RC level of ≥ 30 mg/dL. PA was classified into aerobic, resistance, and walking exercises, which involved practicing 150 min of moderate, 75 min of high-intensity PA, or a combination of the 2, per week; doing resistance exercise more than 2 days per week; walking more than 150 min per week, respectively. Multivariate logistic regression analysis was performed to examine the association between serum RC and PA type. **Results:** Among those aged < 65 years, the odds ratio (OR) of hyper-remnant cholesterolemia was 1.23 times higher in the group that did not perform resistance exercise than in the group that performed more than 2 resistance exercises per week (95%

confidence interval [CI] 1.12–1.36, $p < 0.0001$). Among those aged ≥ 65 years, the OR of hyper-remnant cholesterolemia was 1.31 times higher in the group that did not practice walking exercise than in the group that walked for more than 150 min per week (95% CI: 1.11–1.55, $p < 0.01$). **Conclusion:** This study revealed that resistance exercise in those aged < 65 years and walking exercise in those aged ≥ 65 years were significantly associated with low RC levels in Korean adults.

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Introduction

The social and medical burden of cardiovascular diseases (CVDs) and other metabolism-related diseases is rapidly increasing worldwide [1]. In particular, CVD remains the leading cause of death worldwide despite significant progress in prevention and treatment [2], and a report on the global burden of CVD showed that nearly 197 million people had CVD in 2019 [3]. Low-density lipoprotein cholesterol (LDL-C) is used for primary lipid analysis in the screening, diagnosis, and management of primary and secondary prevention of CVD [4]. Although the link between LDL-C concentration and CVD is concrete and intensive LDL-C-lowering therapy is adopted in high-risk CVD populations, residual risks for CVD still exist [4].

In recent years, robust evidence has implicated remnant cholesterol (RC) as an important contributor to atherosclerosis, CVD development, and residual risk of CVD [1]. Moreover, in a pooled cohort of individuals without CVD, elevated RC levels were found to be related to atherosclerotic CVD, independent of the traditional risk factors, namely, LDL-C and apolipoprotein B levels [5], and several reports have suggested that RC and non-high-density lipoprotein cholesterol (HDL-C) may be better CVD risk indicators and predictors than LDL-C and other traditional lipid parameters [6, 7]. Furthermore, as a new indicator of atherosclerosis, RC is considered a priority treatment target for individuals at a high risk of CVD [2]. RC is a group of highly atherogenic lipids that includes several lipoproteins such as intermediate-density lipoprotein cholesterol, very-low-density lipoprotein cholesterol, and chylomicron remnants, which are triglyceride (TG)-rich lipoproteins (TGRLs) that are the direct precursors of atherogenic small dense LDL with a highly atherogenic effect [7]. It has emerged as a crucial residual risk factor for CVD [8], and the American Heart Association lists it as an emerging atherogenic risk factor [9].

Many studies have shown that physical activity (PA) lowers traditionally known cholesterol levels, including LDL-C, in relation to CVD risk; however, there are no studies on the relationship between RC levels and PA. Therefore, we hypothesized that RC and PA are associated, and this association would vary depending on the type of PA. In our study, we used nationwide population-based data to investigate the association between RC and the types of PA and provide new ideas for the early prevention of CVD risk.

Methods

Study Population

This cross-sectional study used data from the 2016–2021 Korea National Health and Nutrition Examination Survey (KNHANES). The KNHANES is a nationwide survey of the general health and nutritional status of all civilian, non-institutionalized Koreans conducted by the Korean Ministry of Health and Welfare and the Division of Health and Nutrition Research, and Analysis of the Korean Centers for Disease Control and Prevention. Among 46,828 participants from the 2016–2021 KNHANES, 37,708 were aged ≥ 20 years; after excluding those without a lipid profile or PA data, the number of eligible participants was 32,877 (Fig. 1).

All participants provided written informed consent before participating in the study, and the KNHANES was conducted following the ethical approval of the Institutional Review Board of the Korea Centers for Disease Control and Prevention (KNHANES was exempt from an ethics review, based on the bioethics and safety act from 2016 to 2017, No. 2018-01-03-P-A in 2018, 2018-01-03-C-A in 2019, 2018-01-03-2C-A in 2020, and 2018-01-03-3C-A in 2021).

Data Collection

Trained staff interviewed the participants using standardized health questionnaires that collected demographic and clinical information including medical history, smoking status, PA, and anthropometric data. PA was classified into aerobic exercise (AE), resistance exercise (RE), and walking exercise (WE). AE was defined as practicing 150 min of moderate or 75 min of high-intensity PA, or an equivalent time of a combination of the 2 per week; RE was assessed by the number of days of RE per week; and WE involved more than 150 min of walking per week. Current smoking was defined as smoking more than 5 packs (100 cigarettes) in a lifetime and currently smoking regularly; high-risk alcohol intake was defined as drinking 2 or more times a week, with an average number of ≥ 7 drinks for men and ≥ 5 drinks for women each time. Subjective perception of health was defined as the state of health that one usually perceived. Depression was defined using the Patient Health Questionnaire-9, a depression screening tool, with a total score of ≥ 10 indicating depression. Medical history, including hypertension, diabetes mellitus, stroke, myocardial infarction or angina, osteoarthritis or rheumatoid arthritis, thyroid disease, renal disease, and cancer (stomach, liver, colon, breast, cervix, lung, thyroid, or others) was defined as a diagnosis by a physician, and dyslipidemia was defined as taking lipid-lowering medications. The intake of energy and nutrients was evaluated using the 24-h recall method.

Obesity was defined as a body mass index ≥ 25 kg/m², calculated by dividing weight (kg) by the square of height (m²). Hypertriglyceridemia was defined as a serum TG level ≥ 150 mg/dL, and hyper-LDL cholesterolemia as a serum LDL-C level ≥ 130 mg/dL [10]. Non-HDL-C was calculated by subtracting the HDL-C level from the serum total cholesterol (TC) level, and hyper-non-HDL cholesterolemia was defined as serum non-HDL-C ≥ 160 mg/dL [11]. Serum RC was calculated by subtracting the LDL-C and HDL-C levels from the serum TC level, and hyper-remnant cholesterolemia was defined as serum

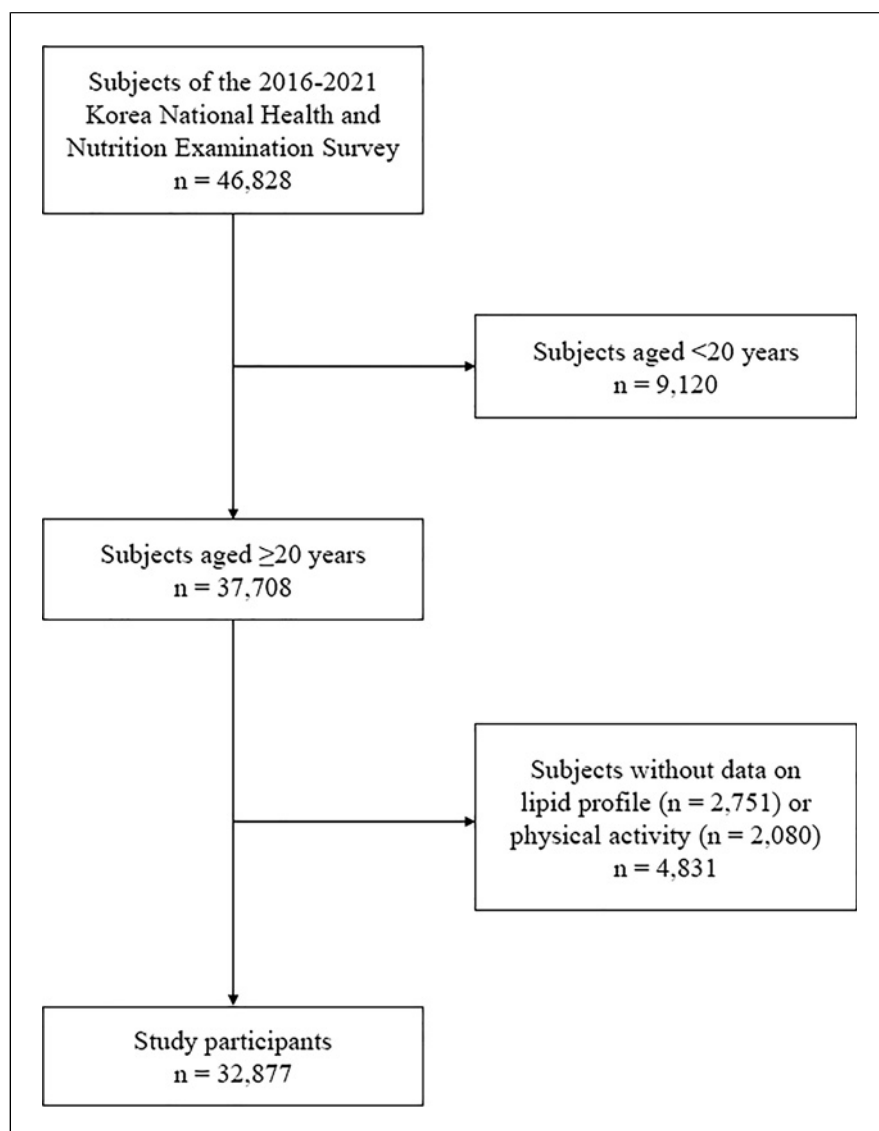


Fig. 1. Flow chart of participant inclusion in the study.

RC ≥ 30 mg/dL [12]. Serum TC, TG, HDL-C, and LDL-C levels were measured using an automatic analyzer (Hitachi 7600; Hitachi, Tokyo, Japan).

Statistical Analysis

The KNHANES uses a stratified, multistage, clustered probability sampling method to select a representative sample of the non-institutionalized civilian Korean population. Therefore, the statistical analyses in this study were conducted by adopting stratification, clustering, and weight variables.

The participants' characteristics were stratified based on their age and hyper-remnant cholesterolemia, and were reported as means and standard errors for con-

tinuous variables and as weighted percentages and standard errors for categorical variables. They were compared using independent *t* tests for continuous variables and chi-square tests for categorical variables. Multivariate logistic regression analysis was performed to examine the association between hyper-remnant cholesterolemia and the PA type. Odds ratios (ORs) and 95% confidence intervals (CIs) were determined.

Especially, CVD increases progressively with age and has a high prevalence in older adults ≥ 65 years of age [13]. In addition, the PA participation rate among older adults is reduced due to various limitations [14]. Therefore, we investigated the presence of hyper-remnant cholesterolemia, an important risk factor of CVD, according to PA

type in older adults and non-older adults based on the age of 65.

We adjusted for multiple variables that showed significant associations in univariate analysis and those with clinical relevance. Model 1 was adjusted for age and sex; Model 2 was adjusted for income level, education status, occupation, marital status, AE, RE, WE, current smoking status, high-risk alcohol intake, obesity, and energy and nutrient consumption (total energy, carbohydrate, protein, fat, cholesterol, fiber, and sugar) in addition to age and sex; Model 3 was adjusted for a subjective perception of health, depression, serum LDL-C level, diagnosis of hypertension, diabetes mellitus, stroke, myocardial infarction or angina, osteoarthritis or rheumatoid arthritis, thyroid disease, renal disease, cancer (stomach, liver, colon, breast, cervix, lung, thyroid, or other), and dyslipidemia, in addition to the variables of Model 2.

All variables included in the logistic regression analysis were examined for multicollinearity, and only variables with a variance inflation factor of <5 were used. All statistical analyses were performed using the SAS statistical software version 9.3 (SAS Institute Inc. Cary, NC, USA). The level of statistical significance was set at two-tailed p values of <0.05 .

Results

Demographic Characteristics of the Participants

In total, 32,877 participants were included in this study (Fig. 1). Table 1 shows the demographic characteristics of the participants. The group with individuals aged <65 years included 24,360 (84.36%) participants and that with individuals aged ≥ 65 years included 8,517 (16.64%) participants. The mean age was 47.60 ± 0.17 years, and there were 18,349 (50.01%) women. The groups engaging in AE and WE comprised 14,027 (45.58%) and 16,571 (51.08%) participants, respectively, and the group not engaging in RE was the largest group at 24,778 (73.16%) participants. The mean serum TC, LDL-C, HDL-C, and RC levels among all participants were 192.80 ± 0.27 mg/dL, 115.94 ± 0.24 mg/dL, 51.72 ± 0.10 mg/dL, and 25.14 ± 0.13 mg/dL, respectively. The group with hyper-remnant cholesterolemia was 8,918 (27.51%).

Association between High RC Level and the Type of PA

Table 2 shows the ORs and 95% CIs for hyper-remnant cholesterolemia according to type of PA in 32,877 Korean adults. The model was adjusted for age,

sex, income level, educational status, occupation, marital status, AE, RE, WE, current smoking status, high-risk alcohol intake, obesity, energy and nutrient consumption (total energy, carbohydrate, protein, fat, cholesterol, fiber, and sugar), subjective perception of health, depression, serum LDL-C level, and diagnosis of hypertension, diabetes mellitus, stroke, myocardial infarction or angina, osteoarthritis or rheumatoid arthritis, thyroid disease, renal disease, cancer (stomach, liver, colon, breast, cervix, lung, thyroid, or other), and dyslipidemia. In the group of individuals aged <65 years, the OR of hyper-remnant cholesterolemia was 1.23 times higher in the group that did not perform RE than in the group that performed RE more than 2 times per week (95% CI: 1.12–1.36, $p < 0.0001$, for Model 3). In the group of individuals aged ≥ 65 years, the OR of hyper-remnant cholesterolemia was 1.31 times higher in the group that did not practice WE than in the group that practiced more than 150 min WE per week (95% CI: 1.11–1.55, $p < 0.01$, for Model 3).

Discussion

This cross-sectional study based on data from 2016 to 2021 KNHANES showed that the OR of hyper-remnant cholesterolemia was higher in the group of participants aged <65 years not engaging in RE and the group of participants aged ≥ 65 years not engaging in WE compared to the groups practicing regular RE and WE, respectively. To the best of our knowledge, this is the first study to investigate the association between serum RC levels and PA type in adults.

In 2021, the European Society of Cardiology guidelines recommended lifestyle interventions, including increased PA, as fundamental for controlling elevated TG-rich lipoproteins, including RC levels [15]. In addition, the Italian Federation of Cardiology reported on the effects of PA on reducing LDL-C, total cholesterol, non-HDL-C, TGs, apolipoprotein B, and lipoprotein (a), which are risk factors for CVD [16]. PA is a well-established non-pharmacological strategy for the management of lipid metabolism, reducing plasma TG and small dense LDL concentrations, and increasing HDL-C [17, 18]. Although the mechanism of PA-induced changes in lipid levels is unclear, PA may increase blood lipid consumption, thereby decreasing lipid levels (e.g., enhancing the ability of skeletal muscles to utilize lipids, as opposed to glycogen) [19]. In addition, several other studies have revealed the mechanisms by which PA alters lipid profiles. Increased

Table 1. Demographic characteristics of Korean adults from the KNHANES 2016 to 2021 according to age and high RC levels

Variables	Age <65 years (n = 24,360)			Age ≥65 years (n = 8,517)		
	non-hyper-remnant cholesterolemia (n = 17,758)	hyper-remnant cholesterolemia ^a (n = 6,602)	p value	non-hyper-remnant cholesterolemia (n = 6,201)	hyper-remnant cholesterolemia (n = 2,316)	p value
Age, years	41.55±0.13	45.37±0.18	<0.001	72.75±0.09	72.31±0.13	0.003
Female sex, %	55.76 (0.38)	30.42 (0.59)	<0.001	56.92 (0.66)	54.19 (1.10)	0.044
Income			<0.001			0.438
Q ₁ lowest	8.16 (0.35)	9.88 (0.47)		44.07 (0.98)	42.99 (1.39)	
Q ₂ lower-middle	22.06 (0.52)	22.94 (0.66)		27.92 (0.78)	28.23 (1.17)	
Q ₃ upper-middle	32.17 (0.55)	31.71 (0.73)		16.58 (0.68)	18.16 (1.03)	
Q ₄ highest	37.60 (0.75)	35.47 (0.89)		11.43 (0.66)	10.61 (0.85)	
Education			<0.001			0.198
Below middle school graduation	10.52 (0.32)	14.60 (0.52)		69.38 (0.86)	71.15 (1.22)	
Above high school graduation	89.48 (0.32)	85.40 (0.52)		30.62 (0.86)	28.85 (1.22)	
Occupation			<0.001			0.416
Non-manual worker	33.49 (0.49)	33.61 (0.76)		3.93 (0.31)	3.93 (0.46)	
Service or sales worker	15.68 (0.35)	15.09 (0.51)		5.69 (0.36)	4.64 (0.54)	
Manual worker	20.13 (0.44)	25.82 (0.64)		25.74 (0.77)	26.62 (1.20)	
Unemployed ^b	30.71 (0.43)	25.48 (0.63)		64.63 (0.79)	64.81 (1.22)	
Married, %	63.41 (0.58)	71.26 (0.73)	<0.001	66.50 (0.86)	67.40 (1.16)	0.513
Current smoking ^c , %	18.27 (0.39)	33.92 (0.71)	<0.001	8.42 (0.40)	12.40 (0.88)	<0.001
High-risk alcohol intake ^d , %	11.37 (0.29)	23.30 (0.61)	<0.001	4.23 (0.32)	6.38 (0.60)	0.002
AE, %			<0.001			0.176
None	27.71 (0.44)	32.45 (0.73)		43.45 (0.84)	45.98 (1.27)	
Adequate	49.63 (0.48)	45.08 (0.74)		32.08 (0.77)	30.24 (1.10)	
RE, %			<0.001			0.200
None	71.01 (0.41)	74.25 (0.61)		78.92 (0.65)	80.96 (0.98)	
≥2 days per week	24.49 (0.40)	21.39 (0.59)		19.90 (0.64)	18.06 (0.96)	
WE, %			<0.001			<0.001
None	14.85 (0.34)	17.53 (0.57)		22.75 (0.73)	27.49 (1.12)	
More than 150 min per week	52.17 (0.51)	48.71 (0.75)		51.96 (0.86)	46.17 (1.24)	
Obesity ^e , %	23.97 (0.47)	45.67 (0.87)	<0.001	28.64 (0.74)	36.31 (1.25)	<0.001
Subjective perception of health, %			<0.001			0.801
Very good or good	34.66 (0.63)	27.97 (0.88)		23.48 (0.92)	22.08 (1.42)	
Average	51.55 (0.48)	54.33 (0.71)		48.12 (0.75)	48.60 (1.18)	
Poor or very poor	13.79 (0.41)	17.70 (0.70)		28.40 (1.01)	29.32 (1.59)	
Depression ^f	2.35 (0.16)	2.49 (0.22)	0.569	2.62 (0.24)	3.31 (0.41)	0.110
Diagnosis by a physician						
Hypertension	10.78 (0.27)	19.00 (0.54)	<0.001	54.36 (0.77)	58.53 (1.17)	0.003
Diabetes mellitus	4.13 (0.17)	8.24 (0.38)	<0.001	21.20 (0.59)	26.20 (1.03)	<0.001
Stroke	0.78 (0.07)	1.28 (0.16)	0.002	5.81 (0.34)	6.63 (0.62)	0.225

Table 1 (continued)

Variables	Age <65 years (n = 24,360)			Age ≥65 years (n = 8,517)		
	non-hyper-remnant cholesterolemia (n = 17,758)	hyper-remnant cholesterolemia ^a (n = 6,602)	p value	non-hyper-remnant cholesterolemia (n = 6,201)	hyper-remnant cholesterolemia (n = 2,316)	p value
Myocardial infarction or angina	0.94 (0.08)	1.25 (0.15)	0.055	8.15 (0.39)	8.62 (0.66)	0.541
Osteoarthritis or rheumatoid arthritis	5.32 (0.18)	5.08 (0.28)	0.463	31.88 (0.67)	32.59 (1.12)	0.589
Thyroid disease	3.72 (0.15)	2.87 (0.22)	0.003	4.72 (0.31)	4.33 (0.51)	0.521
Renal disease	0.56 (0.07)	0.48 (0.10)	0.516	1.25 (0.17)	0.89 (0.23)	0.234
Cancer ^g	3.28 (0.14)	2.91 (0.23)	0.178	10.15 (0.45)	8.69 (0.66)	0.080
Dyslipidemia (on medication)	7.78 (0.23)	10.38 (0.41)	<0.001	30.11 (0.70)	27.45 (1.08)	0.034
<i>Intake of energy and nutrients per day</i>						
Total energy, kcal	1,993.75±10.02	2149.48±16.07	<0.001	1,616.74±11.83	1,604.68±16.80	0.514
Protein, g	74.96±0.46	78.64±0.72	<0.001	56.11±0.53	53.74±0.68	0.003
Carbohydrate, g	283.80±1.33	298.07±2.08	<0.001	271.47±1.83	272.97±3.10	0.642
Fat, g	51.54±0.41	51.14±0.63	0.571	29.74±0.43	27.13±0.51	<0.001
Cholesterol, mg	271.89±2.35	274.47±3.92	0.549	159.61±2.90	140.05±3.88	<0.001
Fiber, g	25.02±0.15	26.08±0.23	<0.001	26.73±0.29	25.26±0.41	<0.001
Sugar, g	63.93±0.47	61.01±0.74	<0.001	50.71±0.68	48.01±1.03	0.015
<i>Lipid profile</i>						
Serum total cholesterol, mg/dL	189.10±0.33	210.09±0.55	<0.001	177.80±0.58	194.45±1.02	<0.001
Serum HDL-C, mg/dL	55.27±0.12	44.55±0.15	<0.001	51.00±0.18	42.81±0.26	<0.001
Serum LDL-C, mg/dL	116.29±0.30	120.52±0.51	<0.001	107.62±0.53	110.24±0.93	0.012
Serum non-HDL-C ^h , mg/dL	133.84±0.31	165.54±0.53	<0.001	126.80±0.54	151.63±0.95	<0.001
Serum TG, mg/dL	89.96±0.33	260.42±2.73	<0.001	96.83±0.48	218.56±2.37	<0.001
Serum RC ⁱ , mg/dL	17.55±0.05	45.02±0.34	<0.001	19.18±0.09	41.40±0.37	<0.001
Hypo-HDL cholesterolemia ^j , %	7.98 (0.24)	33.63 (0.69)	<0.001	15.32 (0.52)	41.18 (1.26)	<0.001
Hyper-LDL cholesterolemia ^k , %	31.57 (0.42)	38.34 (0.68)	<0.001	25.35 (0.65)	28.64 (1.13)	0.007
Hyper-non-HDL cholesterolemia ^l , %	20.90 (0.36)	54.64 (0.70)	<0.001	17.99 (0.58)	40.32 (1.23)	<0.001
Hypertriglyceridemia ^m , %	2.27 (0.14)	99.99 (0.01)	<0.001	1.14 (0.15)	100.00 (0.00)	<0.001

HDL-C, high-density lipoprotein cholesterol; KNHANES, Korea National Health and Nutrition Examination Survey; LDL-C, low-density lipoprotein cholesterol; RC, remnant cholesterol. Data were obtained from the 2016–2021 Korean National Health and Nutrition Examination Survey. *p* values were calculated using an independent *t* test or chi-square test. Continuous variables are expressed as means and standard errors, whereas categorical variables are expressed as weighted percentages and standard errors. ^aHyper-remnant cholesterolemia is defined as serum RC ≥30 mg/dL. ^bIncluding homemakers and students. ^cDefined as smoking more than 5 packs (100 cigarettes) in a lifetime and currently smoking. ^dDefined as 2 or more times a week, average number per time (≥7 drinks for men and ≥5 drinks for women). ^eDefined as a body mass index ≥25 kg/m². ^fDefined as Patient Health Questionnaire-9 (a depression screening tool) score with a total score of ≥10. ^gDefined as stomach, liver, colon, breast, cervix, lung, thyroid, or other cancer. ^hNon-HDL-C was calculated by subtracting the HDL-C level from the serum total cholesterol level. ⁱSerum RC was calculated by subtracting the LDL-C and HDL-C levels from the serum total cholesterol level. ^jHypo-HDL cholesterolemia was defined as a serum HDL-C level <40 mg/dL. ^kHyper-LDL cholesterolemia is defined as serum LDL-C ≥130 mg/dL. ^lHyper-non-HDL cholesterolemia is defined as serum non-HDL-C ≥160 mg/dL. ^mHypertriglyceridemia is defined as serum TG ≥150 mg/dL.

ATP-binding cassette transporter A-1 gene expression in macrophages strongly favors reverse cholesterol transport, plasma HDL-C formation, and protection against atherosclerosis [20] resulting from the upregulation of the liver X receptor, a transcription factor of the nuclear receptor superfamily that plays a key role in liver cholesterol metabolism [21]. Moreover, other studies have reported that the effects of the PA are probably mediated by modifications in the activities of enzymes such as lecithin cholesterol acyltransferase (the enzyme responsible for ester transfer to HDL-C) [21], lipoprotein lipase [22], and hepatic TG lipase implicated in the synthesis, transport, and catabolism of lipoproteins [23]. Another proposed mechanism is through adenosine monophosphate-activated protein kinase, which is a classical target of PA in many tissues, including the arterial wall, acting as a sensor of energy levels [24]. Recent studies suggest that adenosine monophosphate-activated protein kinase plays an important role in mediating the effects of PA on arterial wall lipid homeostasis and atherogenesis [25]. Previous studies have investigated differences in the mechanisms affecting lipid profiles depending on the type of PA. Increased volume of RE is usually accompanied by increased caloric expenditure and improved body composition (e.g., increased lean mass and decreased subcutaneous and visceral fat mass) [26], and a study speculated that the reduction in TC resulted from the exchange of cholesterol ester from tissues and lipoproteins to HDL-C [26]. In addition, RE stimulates the secretion of IL-6, an anti-inflammatory cytokine, which is the key intermediary agent for lipid degradation and release involved in lipid metabolism [27]; IL-6 can also improve motor unit activation and increase the secretion of lipolytic hormones [28]. WE may improve insulin sensitivity according to a previous study [29]. As insulin resistance increases with age [30], WE is an efficient strategy to reduce RC in older adults. In a recent review, the formation of walking groups was found to be efficacious in increasing PA, particularly in older adults [31], which is consistent with the results of our study. Although the association between AE and RC was not significant in our study, previous study has shown that AE is effective in increasing HDL-C and decreasing TC, LDL-C, and TG levels [32]. A possible mechanistic pathway is that AE increases reverse cholesterol transport, which causes more cholesterol to be transported to the liver, contributing to the prevention of atherosclerosis [18]. Further studies investigating the underlying mechanistic pathways are required to confirm the association between AE and RC.

In our study, the PAs associated with low RC levels in those aged under 65 years and over 65 years were RE and WE, respectively. However, there has been no research on the type of PA that has a significant effect on RC depending on age. Nevertheless, RE is reported to protect against endothelial ischemia-reperfusion injury and reduce the risk of developing cardiometabolic disease in young adults [33]; growth hormone, insulin-like growth factor-1, sex hormones or modifying plasma cytokine (reduced IL-6 and increased IL-10) levels, which decrease with aging, may be related to this association in young adults [34]. For older adults, WE presumably not only maintains healthy body composition but also causes positive changes in muscle contractility, which slows sarcopenia, thereby preventing the worsening of insulin resistance and leads to a decrease in RC [35]; WE may also reduce RC levels through anti-inflammatory effects [36]. Moreover, because older individuals have lower muscle strength and a tendency for greater baseline oxidative stress than young individuals, the effect of RE on RC may not be significant [37], as also observed in our study. Based on the results of our study, we hope to suggest a volume (amount), intensity, and frequency of PA that can maintain optimal RC and prevent CVD.

Limitations

This study has some limitations. First, it was a cross-sectional study. Therefore, a causal relationship could not be established. Further prospective longitudinal studies with larger sample sizes are required to establish precise interrelationships. Second, we did not directly measure the RC levels but instead calculated them. However, the estimated RC is reported to correlate well with the direct measurement and can be easily applied in clinical practice [38], and no significant difference is observed between the directly calculated and measured RC levels [39]. In addition, one study reported that the calculated RC showed a strong correlation with an increased risk of major adverse cardiovascular events [40]. Therefore, the calculation of RC as an alternative method is more convenient and easier to implement in clinical diagnosis and therapy, with significantly reduced time and economic costs [2]. Third, since PA type was based on self-reports, these findings may be subject to recall bias. However, KNHANES survey interviews are conducted by well-trained staff to obtain consistent and reliable answers [41], and self-reports are common in population-based studies [42]. Furthermore, the reliability of the data and the representativeness of the entire Korean population are

Table 2. Unadjusted and adjusted ORs (95% CI) of hyper-remnant cholesterolemia^a according to the type of PA in Korean adults from the KNHANES 2016–2021

Multivariable model	Model 1		Model 2		Model 3	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Age <65 years						
AE						
Practiced 150 min of moderate, 75 min of high-intensity PA, or an equivalent time of a combination of the 2 per week	Reference		Reference		Reference	
Did not practice 150 min of moderate, 75 min of high-intensity PA, or an equivalent time of a combination of the 2 per week	1.13 (1.03–1.24)	0.008	1.11 (0.997–1.23)	0.058	1.10 (0.99–1.22)	0.088
No PA related to work, leisure, or moving	1.21 (1.11–1.31)	<0.0001	1.10 (0.99–1.22)	0.085	1.08 (0.98–1.20)	0.139
RE						
≥2 days per week	Reference		Reference		Reference	
1 day per week	1.22 (1.02–1.47)	0.034	1.13 (0.92–1.40)	0.243	1.11 (0.90–1.37)	0.332
None	1.44 (1.33–1.57)	<0.0001	1.27 (1.15–1.40)	<0.0001	1.23 (1.12–1.36)	<0.0001
WE						
More than 150 min per week	Reference		Reference		Reference	
Less than 150 min per week	1.09 (1.01–1.18)	0.123	1.03 (0.94–1.13)	0.547	1.02 (0.93–1.12)	0.724
None	1.08 (0.98–1.19)	0.021	0.95 (0.84–1.08)	0.417	0.94 (0.83–1.07)	0.354
Age ≥65 years						
AE						
Practiced 150 min of moderate, 75 min of high-intensity PA, or an equivalent time of a combination of the 2 per week	Reference		Reference		Reference	
Did not practice 150 min of moderate, 75 min of high-intensity PA, or an equivalent time of a combination of the 2 per week	1.08 (0.93–1.26)	0.314	0.98 (0.83–1.16)	0.845	0.99 (0.83–1.17)	0.879
No PA related to work, leisure, or moving	1.19 (1.04–1.35)	0.009	0.99 (0.86–1.16)	0.941	0.99 (0.85–1.15)	0.910
RE						
≥2 days per week	Reference		Reference		Reference	
1 day per week	0.91 (0.52–1.58)	0.014	0.76 (0.41–1.43)	0.395	0.76 (0.41–1.41)	0.382
None	1.21 (1.04–1.42)	0.431	1.04 (0.88–1.123)	0.653	1.03 (0.87–1.22)	0.736
WE						
More than 150 min per week	Reference		Reference		Reference	
Less than 150 min per week	1.12 (1.05–1.37)	0.009	1.11 (0.96–1.30)	0.166	1.10 (0.95–1.29)	0.212
None	1.45 (1.27–1.67)	<0.0001	1.33 (1.13–1.57)	<0.0001	1.31 (1.11–1.55)	0.002

CI, confidence interval; KNHANES, Korean National Health and Nutrition Examination Survey; OR, odds ratio; RC, remnant cholesterol. Data were obtained from the 2016–2021 Korean National Health and Nutrition Examination Survey. ^aHyper-remnant cholesterolemia is defined as serum RC ≥30 mg/dL. Model 1 was adjusted for age and sex. Model 2 was adjusted for income level, education status, occupation, marital status, AE, RE, WE, current smoking, high-risk alcohol intake, obesity, and energy and nutrition consumption (total energy, carbohydrates, protein, fat, cholesterol, fiber, and sugar) in addition to the variables of Model 1. Model 3 was adjusted for subjective perception of health, depression, serum low-density cholesterol level, diagnosis of hypertension, diabetes mellitus, stroke, myocardial infarction or angina, osteoarthritis or rheumatoid arthritis, thyroid disease, renal disease, cancer (stomach, liver, colon, breast, cervix, lung, thyroid, or other), and dyslipidemia on medication, in addition to the variables of Model 2.

guaranteed, considering that the KNHANES comprises the largest source of open data in Korea and is conducted by the government.

Strengths

Nevertheless, our study has several strengths. First, we used data from the KNHANES, which has a homogenous ethnicity and large, contemporary population data with protocolled data collection using validated questionnaires and assessments. Therefore, the current study provides valuable information regarding the role of PA in RC in predicting CVD. Second, although we did not include any type of pharmacological intervention other than lipid-lowering agents that could affect lipid and lipoprotein levels (e.g., oral contraceptives and estrogen replacement therapy) [30], our study models were fully adjusted for important potential confounders such as dietary intake and lipid-lowering agents. Therefore, this association may be considered robust.

Clinical Implications

Through our study, PA can be proposed as a novel therapeutic strategy to lower RC and is expected to serve as a basis for the development of clinical indications and appropriate recommendations in an easily accessible, economically useful, and convenient manner. In addition, based on the results that different types of PA by age group were associated with low RC levels, PA could be a promising intervention as an adjunct or alternative to other healthcare measures or as a proactive health-promoting activity [43]. In particular, WE is meaningful for older adults because it is effective and safe, with good adherence, and wide-ranging health benefits [43]. In addition, this positive evidence may benefit more patients at CVD risk worldwide in the future [2] and will be of great help in health monitoring, disease prevention, and treatment decision-making in clinical practice.

Conclusion

This quantitative cross-sectional analysis of data from the 2016–2021 KNHANES revealed that RE in those aged <65 years and WE in those aged ≥65 years were significantly associated with low RC levels. These findings indicate that the type of PA can lower RC according to age group and may help prevent future CVD onset and progression. The most recent national cholesterol education report on the detection, evaluation, and treatment

of high blood cholesterol in adults includes recommendations for increased PA to improve lipid and lipoprotein levels [44]; PA is a cost-effective, non-pharmacological intervention that is available to the vast majority of the general public. Future studies need to validate definitive trials regarding the different results of the association between RC and the type of PA according to age group. Moreover, investigation of the underlying mechanistic pathways is required to confirm the association between AE and RC.

Statement of Ethics

The KNHANES was conducted following the ethical approval of the Institutional Review Board of the Korea Centers for Disease Control and Prevention (KNHANES was exempt from an ethics review, based on the bioethics and safety act from 2016 to 2017, No. 2018-01-03-P-A in 2018, 2018-01-03-C-A in 2019, 2018-01-03-2C-A in 2020, and 2018-01-03-3C-A in 2021). All participants provided written informed consent before participating in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Conceptualization, data curation, methodology, and writing – review and editing: H.J.L. and J.-H.K. Formal analysis, project administration, software, supervision, and validation: J.-H.K. Visualization, resources, investigation, and writing – original draft: H.J.L. All authors have read and approved the final version of the manuscript.

Data Availability Statement

Data were obtained from the 2016–2021 Korea National Health and Nutrition Examination Survey (KNHANES). The KNHANES is a nationwide population-based survey that is being conducted by the Korean Ministry of Health and Welfare and the Division of Chronic Disease Surveillance of the Korean Centers for Disease Control and Prevention. All data underlying the findings are fully available without restriction. All data files are available from the KNHANES database (<https://knhanes.cdc.go.kr/knhanes/index.do>).

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