

Effects of a moderate exercise session on postprandial lipoproteins, apolipoproteins and lipoprotein remnants in middle-aged men

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Abstract

Prior moderate exercise reduces postprandial triglyceride concentrations. Its effects on the concentrations, compositions and potential atherogenicity of lipoprotein subfractions were investigated in the present study. Twenty normoglycaemic middle-aged men each underwent two fat tolerance tests (blood taken fasting and for 8 h after a meal containing 80 g fat and 70 g carbohydrate). On the afternoon before one test, subjects performed a 90-min treadmill walk (exercise); no exercise was performed before the control test. Prior exercise significantly reduced postprandial concentrations of chylomicrons (Sf >400) by 28.6% (absolute reduction 14.6 mg dl⁻¹), of large VLDL₁ (Sf 60–400) by 34.4% (39.7 mg dl⁻¹) and of small VLDL₂ (Sf 20–60) by 23.0% (9.6 mg dl⁻¹). Over 95% of VLDL₁ and VLDL₂ comprised apolipoprotein (apo) B100-containing particles. Exercise also reduced postprandial remnant-like lipoprotein cholesterol (by 35%) and triglyceride concentrations (by 29%). Postprandial apo CIII/apo B and apo E/apo B ratios in VLDL₁ were lower following exercise. Postprandial cholesteryl ester/triglyceride ratios were lower in VLDL₁ and VLDL₂ and higher in HDL₂ following exercise. These data suggest that the effect of prior moderate exercise on VLDL₁ is quantitatively greater than its effect on chylomicrons and that, in addition to reducing lipoprotein concentrations, exercise induces compositional changes to lipoprotein species which are likely to influence their metabolism and atherogenicity.

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Keywords: Exercise; Postprandial; Triglyceride; Cholesteryl ester; Apolipoprotein; VLDL; Remnant-like lipoprotein

1. Introduction

A large number of studies have demonstrated that a session of moderate exercise can reduce subsequent postprandial lipaemia by ~15–25% [1]. However, relatively little is known about the qualitative nature of the changes to postprandial lipoprotein subclasses elicited by prior exercise. Such data are important as they can provide clues to the potential mechanisms responsible for the exercise-induced reduction in postprandial triglyceride (TG) concentrations and because they provide insights into exercise-induced

changes to the potential atherogenicity of lipoprotein species.

Previous studies have shown that TG decreases in the very low density lipoprotein (VLDL, Sf 20–400) density range account for a much greater proportion of the reduction in postprandial TG concentrations following a moderate intensity exercise session than decreases in chylomicron (Sf >400) TG [2,3]. While this VLDL–TG reduction could conceivably be the consequence of reduced hepatic VLDL production and/or increased clearance of VLDL–TG, a growing body of indirect evidence suggests that the former option may play an important role. Firstly, chylomicrons compete much more effectively than VLDL for clearance by lipoprotein lipase (LPL), such that the presence of chylomicrons [4]

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or chylomicron-like particles [5] in the circulation almost completely abolishes VLDL clearance. Thus, any effect of exercise on TG clearance might be expected to induce quantitatively greater reductions in chylomicrons than VLDL. Furthermore, recent studies have shown that, despite significantly reducing postprandial triglyceride (TG) concentrations, 90 min of prior moderate exercise does not increase clearance of chylomicron-like particles [6] or significantly increase post-heparin plasma [7] or skeletal muscle [8] LPL activity. This contrasts with findings from studies of prolonged (≥ 3 h) exercise or periods of exercise training where increased clearance of chylomicron-like particles [9,10] and increased LPL activity in post-heparin plasma [10,11] or skeletal muscle [12,13] is clearly seen.

However, there are a number of important limitations to the existing data on moderate exercise and postprandial VLDL. Firstly, there is accumulating evidence from kinetic studies that VLDL are metabolically heterogeneous, with both the production and catabolism of large TG-rich VLDL₁ (Sf 60–400) and smaller cholesterol-rich VLDL₂ (Sf 20–60) being regulated independently of each other [14,15], emphasising the need for these subclasses to be considered separately in studies of human metabolism. In addition, as the VLDL density range contains intestinally – as well as hepatically – derived particles in the postprandial state, it is possible that exercise-induced VLDL–TG reductions are due, at least in part, to TG decreases in small chylomicrons and/or chylomicron remnants rather than decreases in the concentration of true hepatically derived VLDL particles.

Furthermore, the effects of prior moderate exercise on postprandial lipoprotein compositions are not well understood and this could potentially influence both the metabolism and atherogenicity of lipoprotein species. It has previously been observed that there is a postprandial reduction in the number of apolipoprotein (apo) CII molecules per VLDL₁ particle, accompanied by an increase in the number of apo E and a transient rise in the number of apo CIII per VLDL₁ particle [16]. As apo CII is a co-factor for LPL [17] whereas apos CIII [18] and E [19] inhibit LPL action, these changes act to inhibit LPL-mediated clearance of these particles in the postprandial state. Prior moderate exercise has been shown to reduce postprandial apo E concentrations in a ‘triglyceride-rich’ lipoprotein fraction, but as this fraction contains chylomicrons, as well as VLDL, and as apo B concentrations (i.e. the number of particles) in this fraction were also reduced [20], it is not currently clear whether prior exercise induces changes to the apolipoprotein composition of VLDL (such as a decrease in the number of E apo molecules per particle) which would enhance their potential for degradation by LPL. In addition, through its effects in reducing VLDL concentrations – the acceptor particles for cholesteryl ester transfer protein (CETP)-mediated neutral lipid exchange – prior exercise could reduce cholesteryl ester (CE) enrichment of VLDL and increase CE enrichment of HDL, a potentially atheroprotective effect [21,22].

The aim of this study was therefore to determine the effects of a session of prior moderate exercise on the concentrations and compositions of lipoprotein subfractions in the postprandial state.

2. Methods

2.1. Subjects

Twenty men participated in this study; their characteristics are shown in Table 1. All were apparently healthy normotensive, normoglycemic non-smokers who displayed no symptoms of coronary artery disease during a clinical exercise stress test. None was taking any drugs thought to affect lipid or carbohydrate metabolism. One subject possessed the E2/E2 apo E phenotype, 2 possessed the E3/E2 phenotype, 10 possessed the E3/E3 phenotype and 6 possessed the E4/E3 phenotype. It was not possible to determine the apo E phenotype of one subject. We have previously found that apo E phenotype does not significantly influence the reduction in postprandial TG concentrations seen following moderate exercise [23]. The study was conducted with the approval of North Glasgow University Hospitals NHS Trust Ethics Committee and subjects gave written informed consent prior to participation.

2.2. Study design

Each subject participated in two oral fat tolerance tests in a randomized, cross-over design with an interval of 7–14 days and different pre-conditions, i.e. exercise and control. In one trial, subjects walked on a treadmill for 90 min at an intensity of $\sim 50\%$ of maximal oxygen uptake ($\dot{V}O_2$ max) on the day prior to the oral fat tolerance test (exercise trial). In the other trial subjects performed no exercise on the day preceding the oral fat tolerance test (control trial).

Subjects weighed and recorded their dietary intake and abstained from alcohol for the 2 days prior to the first oral fat tolerance test and replicated this prior to the second fat tolerance test. In addition, subjects were instructed to perform

Table 1
Subject characteristics

	Mean \pm S.D.
Age (years)	47.2 \pm 9.2
Body mass index (kg m ⁻²)	27.3 \pm 5.7
Waist circumference (cm)	94.7 \pm 14.3
Hip circumference (cm)	103.1 \pm 9.8
Fasting triglyceride (mmol l ⁻¹)	1.31 \pm 0.64
Fasting total cholesterol (mmol l ⁻¹)	4.98 \pm 0.80
Fasting LDL-cholesterol (mmol l ⁻¹)	3.30 \pm 0.62
Fasting HDL-cholesterol (mmol l ⁻¹)	1.14 \pm 0.31
Fasting plasma glucose (mmol l ⁻¹)	5.32 \pm 0.60
Fasting plasma insulin (μ U ml ⁻¹)	5.99 \pm 3.64
Maximal oxygen uptake ^a (ml kg ⁻¹ min ⁻¹)	42.2 \pm 6.5

^a Estimated from a four-stage submaximal incremental treadmill test [24].

no exercise, other than the treadmill walk in the exercise trial, during the 3 days preceding each oral fat tolerance test.

2.3. Treadmill walk

A preliminary sub-maximal incremental treadmill test was performed at least 1 week prior to the first oral fat tolerance test to estimate $\dot{V}O_2$ max and determine the speed and gradient required to elicit 50% $\dot{V}O_2$ max [24]. The 90-min walk in the exercise trial was performed on the afternoon prior to the oral fat tolerance test and completed ~16–18 h prior to ingestion of the test meal. Oxygen uptake and carbon dioxide production were measured using an online gas analysis system (CPX/D BreezeEx v3.0, MedGraphics Cardiorespiratory Diagnostic Systems, St. Paul, MN, USA), heart rate was measured by short range telemetry (Polar Electroky, Kempele, Finland) and ratings of perceived exertion [25] were obtained at 15-min intervals during the walk.

2.4. Oral fat tolerance tests

On the morning of the oral fat tolerance tests subjects reported to the laboratory after a 12-h fast. A venous cannula was placed in an antecubital vein and, after an interval of 10 min, a baseline blood sample was withdrawn. Subjects then consumed a high-fat test meal comprising whipping cream, fruit, cereal, nuts and chocolate which provided 80 g fat, 70 g carbohydrate, 12 g protein and 4.3 MJ (1028 kcal) energy. Further blood samples were obtained at 2-h intervals for 8-h postprandially. Subjects rested throughout this day and consumed only water. This was provided ad libitum during the first fat tolerance test and the volume and pattern of water intake was replicated during the second test.

2.5. Analytical procedures

Blood samples were collected into potassium EDTA tubes and placed on ice. Plasma was separated within 15 min of collection and stored at 4°C until lipoprotein analyses (commenced within 48 h of collection). Chylomicrons (Sf >400), VLDL₁ (Sf 60–400), VLDL₂ (Sf 20–60) were isolated from EDTA plasma by a cumulative gradient ultracentrifugation technique which has been previously described [26]. LDL (d 1.019–1.063 g ml⁻¹), HDL₂ (1.063–1.125 g ml⁻¹) and HDL₃ (1.125–1.21 g ml⁻¹) were isolated from EDTA plasma by sequential flotation ultracentrifugation as described previously [27]. Each lipoprotein fraction sample was assayed for cholesterol, free cholesterol, triglyceride and phospholipid by enzymatic colorimetric methods using commercially available kits (Roche Diagnostics GmbH, Mannheim, Germany and Wako Chemicals USA, Inc., VA, USA) on an automated Clinical Chemistry analyzer (Models 704 and 717, Hitachi Ltd.,

Tokyo, Japan). Protein was determined using a modified Lowry Assay [28]. Cholesteryl ester concentration was determined by multiplying the difference between total cholesterol and free cholesterol concentrations (in mg dl⁻¹) by 1.68 to account for the difference in mass between cholesterol and cholesteryl ester. Lipoprotein concentration was calculated by summing the concentrations of these components in mg dl⁻¹ (i.e. TG, free cholesterol, cholesteryl ester, phospholipid and protein). Concentrations of apo B, CII, CIII and E were determined in the chylomicron, VLDL₁ and VLDL₂ fractions using commercially available immunoturbidimetric kits (Wako Chemicals USA, Inc.) on an automated Clinical Chemistry analyzer (Models 704 and 717, Hitachi Ltd.). Apo B48 and B100 concentrations in the chylomicron, VLDL₁ and VLDL₂ fractions were determined by SDS-PAGE as previously described [26]. The cholesterol and triglyceride in remnant-like lipoprotein particles (RLP-C, RLP-TG) were measured using a diagnostic reagent kit from Japan Immunoresearch Laboratories (JIMRO), Takasaki, Japan [29]. LDL subfraction distribution was determined in the fasted state using the method of Griffin et al. [30], with LDL I, LDL II and LDL III characterized by densities of 1.025–1.034, 1.034–1.044 and 1.044–1.060 g ml⁻¹, respectively. Plasma glucose and was determined by enzymatic colorimetric methods using a commercially available kit (Roche Diagnostics GmbH). Insulin was determined using a commercially available enzyme-linked immunoassay (ELISA) with <0.01% cross-reactivity with pro-insulin (Mercodia AB, Uppsala, Sweden).

2.6. Calculations and statistics

Energy expenditure during the 90-min treadmill walk was calculated using indirect calorimetry assuming no protein oxidation [31]. Time-averaged postprandial concentrations, defined as the trapezium rule-derived area under the plasma concentration versus time curve, divided by the duration of postprandial observation period (8 h), were used as summary measures of the postprandial responses. Postprandial rises in concentration were defined as the time-averaged postprandial concentration minus the fasting concentration (i.e. the incremental area under the concentration versus time curve, divided by 8 h). The number of apo CII, apo CIII and apo E molecules per particle in the VLDL₁ and VLDL₂ fractions were calculated by dividing the apolipoprotein concentrations in mmol l⁻¹ by the apo B concentration in mmol l⁻¹. For these calculations, it was assumed that all apo B was apo B100 as these lipoprotein fractions contained <5% apo B48-containing particles. The homeostasis model assessment (HOMA) was used as a validated surrogate measure of insulin resistance [32].

Statistical analyses were performed using Statistica (Version 6.0, StatSoft Inc., Tulsa) and Minitab (Version 13.1, Minitab Inc., State College). Where necessary, data were logarithmically transformed prior to statistical analysis.

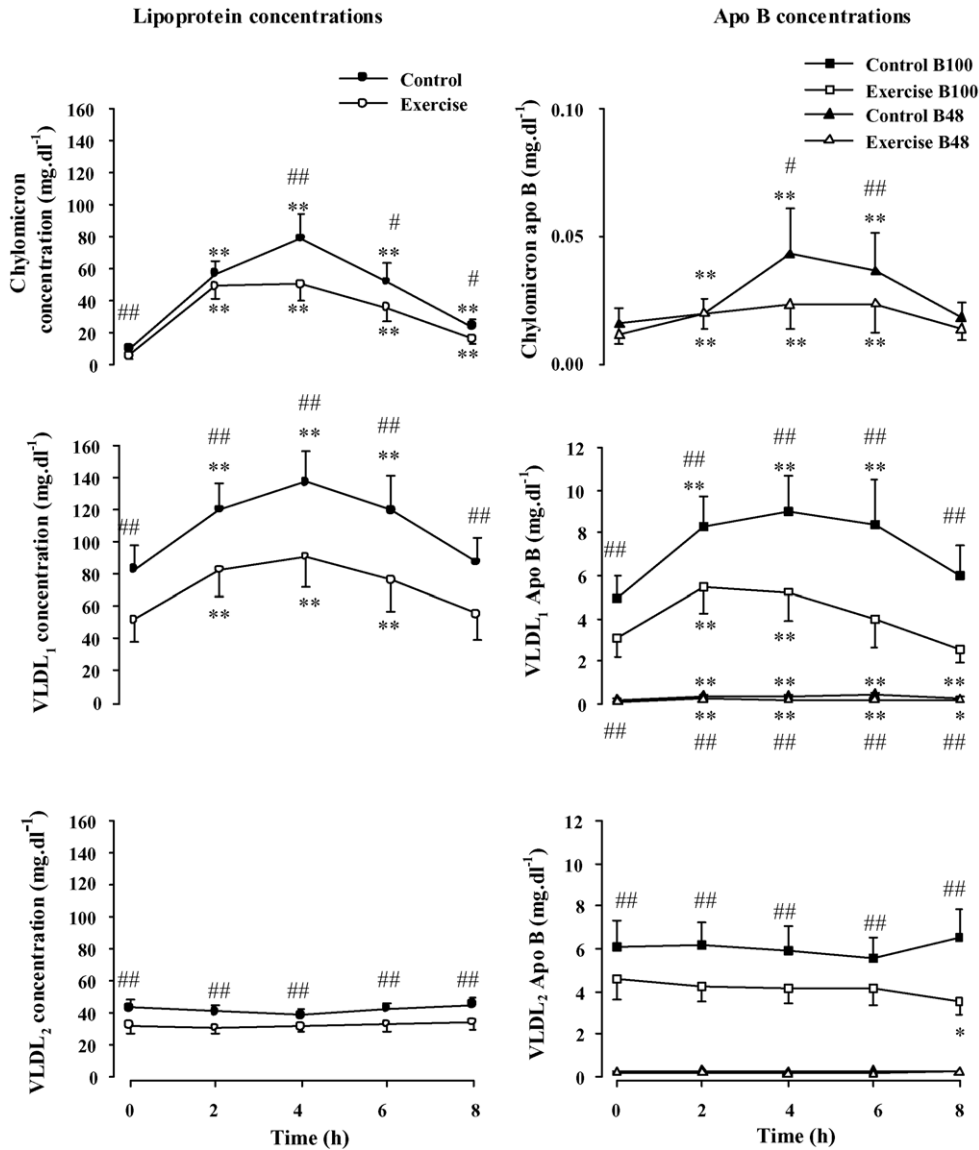


Fig. 1. Postprandial lipoprotein (left panels) and apo B48 and B100 concentrations (right panels) in the Control and Exercise trials in the chylomicron (Sf >400) (top panels), VLDL₁ (Sf 60–400) (middle panels) and VLDL₂ (Sf 20–60) (bottom panels) lipoprotein fractions. Statistics performed on logarithmically transformed data. *Different from fasting value in the same trial, $p < 0.05$ (** $p < 0.01$). #Difference between Control and Exercise trials, $p < 0.05$ (## $p < 0.01$).

Table 2

Postprandial concentrations and postprandial rises in concentration for TG-rich lipoprotein fractions calculated as the area under the total or incremental concentration vs. time curve divided by the duration of the postprandial observation period (8 h).

	Lipoprotein concentration (mg dl ⁻¹)		Apo B100 (mg dl ⁻¹)		Apo B48 (mg dl ⁻¹)	
	Control	Exercise	Control	Exercise	Control	Exercise
Chylomicrons (Sf >400)						
Postprandial concentration	51.1 ± 8.6	36.5 ± 6.4**	–	–	0.029 ± 0.010	0.020 ± 0.007*
VLDL₁ (Sf 60–400)						
Postprandial concentration	115.4 ± 17.8	75.7 ± 16.4**	8.17 ± 1.57	4.50 ± 1.18**	0.35 ± 0.09	0.19 ± 0.05**
Postprandial rise in concentration	32.2 ± 4.6	24.0 ± 3.5*	2.95 ± 0.75	1.40 ± 0.35*	0.14 ± 0.03	0.06 ± 0.01**
VLDL₂ (Sf 20–60)						
Postprandial concentration	41.8 ± 3.7	32.3 ± 3.9**	5.95 ± 1.08	4.11 ± 0.67**	0.24 ± 0.04	0.18 ± 0.03**
Postprandial rise in concentration	-1.5 ± 1.9	-0.3 ± 1.6	-0.19 ± 0.41	-0.45 ± 0.38	0.01 ± 0.01	-0.01 ± 0.02

Data are mean ± S.E.M. Statistics performed on logarithmically transformed data.

* Different from control trial $p < 0.05$.

** Different from control trial $p < 0.01$.

Comparisons of fasting values and summary postprandial responses were made using paired *t*-tests and changes over the postprandial period were assessed by two-way ANOVA (trial × time) with repeated measures on both factors. Post hoc Fisher LSD tests were used to identify exactly where any differences lay. Significance was accepted at the $p < 0.05$ level and data are presented as mean ± S.E.M. unless otherwise stated.

3. Results

3.1. Treadmill walk

Subjects walked at a speed of $5.9 \pm 0.1 \text{ km h}^{-1}$, up a gradient of $4.0 \pm 0.4\%$ and all completed the 90-min walk without undue difficulty, rating their level of exertion as 12.3 ± 0.4 (between ‘fairly light’ and ‘somewhat hard’) on the Borg

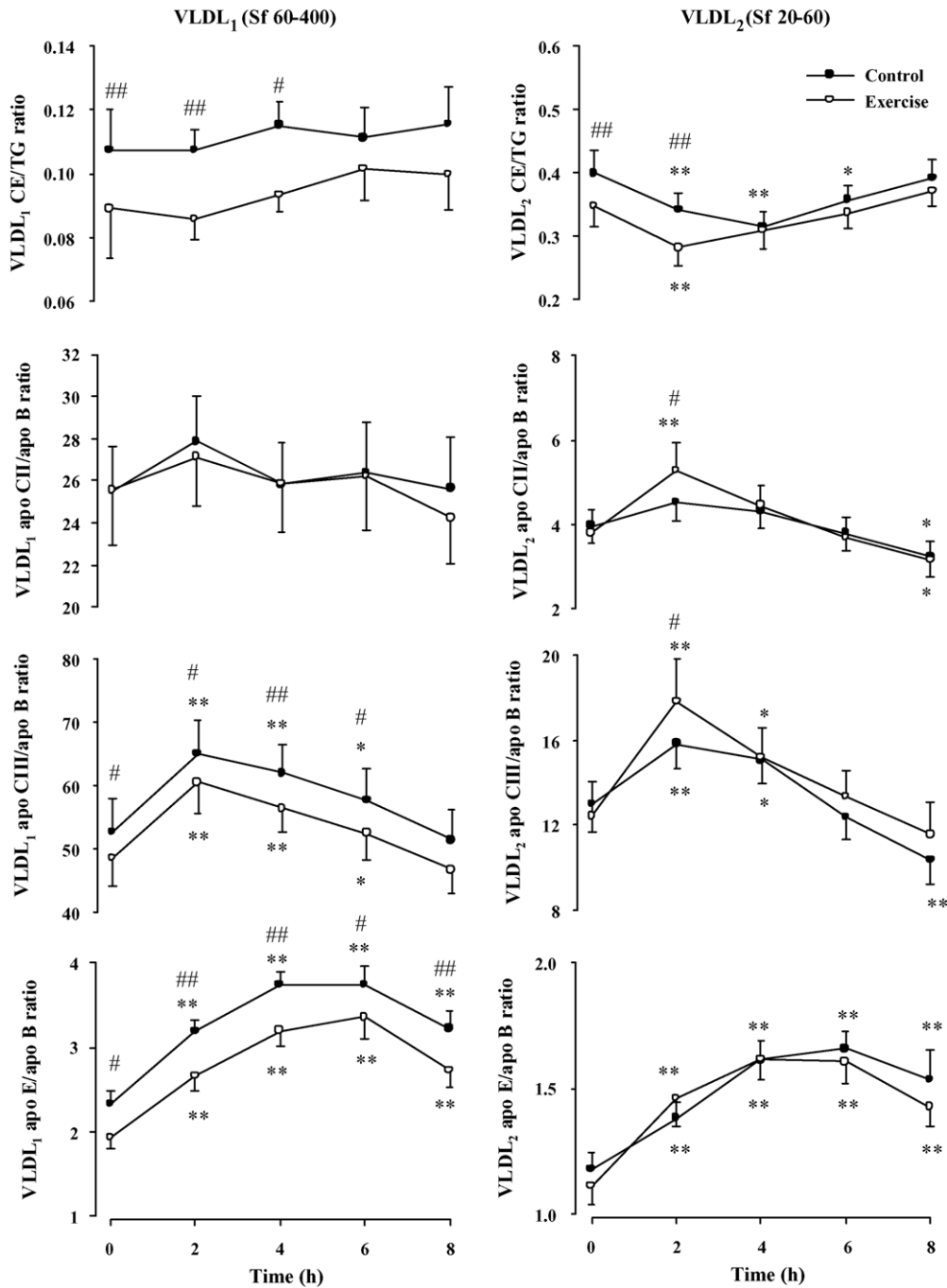


Fig. 2. Ratios describing the postprandial compositional characteristics of VLDL₁ and VLDL₂. CE/TG ratios (top panels), apo CII/apo B ratios (2nd top panels), apo CIII/apo B ratios (2nd bottom panels) and apo E/apo B ratios (bottom panels) in the VLDL₁ (Sf 60–400) (left panels) and VLDL₂ (Sf 20–60) (right panels) lipoprotein fractions in the Control and Exercise trials. * Different from fasting value in the same trial, $p < 0.05$ (** $p < 0.01$). # Difference between Control and Exercise trials, $p < 0.05$ (## $p < 0.01$).

scale of 6–20 [25]. Mean $\dot{V}O_2$ was 21.3 ± 0.6 ml kg^{-1} min^{-1} ($50.9 \pm 0.7\%$ $\dot{V}O_2$ max), mean heart rate was 123 ± 2 $beat\ min^{-1}$ and gross energy expenditure for the walk was 3.32 ± 0.15 MJ (796 ± 36 kcal).

3.2. Lipid and lipoprotein concentrations

Postprandial chylomicron, VLDL₁ and VLDL₂ lipoprotein and apo B48 and B100 concentrations are shown in Fig. 1, with summary measures of these responses presented in Table 2. Exercise significantly reduced postprandial concentrations of chylomicrons, VLDL₁ and VLDL₂, but the reduction in both absolute and percentage terms was greater in the VLDL₁ fraction (39.7 mg dl^{-1} (34.4%) reduction in time-averaged postprandial concentration) than in either the chylomicron (14.6 mg dl^{-1} , 28.6%) or VLDL₂ (9.6 mg dl^{-1} , 23.0%) fractions. Exercise also significantly reduced the postprandial rise in VLDL₁ concentration and VLDL₁ concentrations returned to baseline by 8-h postprandially in the Exercise, but not Control, condition. We found no detectable apo B100 in the chylomicron fraction; apo B48 concentrations in this fraction were significantly reduced by exercise. Exercise significantly reduced both apo B100 and apo B48 concentrations, and their respective rises in concentration, in the VLDL₁ fraction. However, apo B100 accounted for >95% of all apo B in this lipoprotein fraction. Exercise also reduced apo B100 and apo B48 concentrations in the VLDL₂ fraction; again apo B100 accounted for >95% of apo B in this fraction.

Exercise also induced changes to the composition of VLDL₁ and VLDL₂ lipoproteins (Fig. 2). The time-averaged postprandial CE/TG ratio in the VLDL₁ fraction – reflecting the neutral lipid composition of the lipoprotein core – was significantly lower in the Exercise trial than the Control trial (Control: 0.11 ± 0.01 , Exercise: 0.09 ± 0.01 , $p < 0.01$). There was a borderline-significant difference between trials in the time-averaged postprandial CE/TG ratio in the VLDL₂ fraction (Control: 0.36 ± 0.02 , Exercise 0.32 ± 0.02 , $p = 0.05$), but observation of Fig. 2 indicates that this was entirely due to significantly lower CE/TG ratios in the Exercise trial than the Control trial at the 0 and 2 h time points. The CE/TG ratio in the VLDL₂ fraction also declined significantly after meal ingestion in both trials, before returning to baseline at the late postprandial time points. The apo CII/apo B ratio (i.e. the number of CII molecules per lipoprotein particle) in the VLDL₁ fraction was unchanged postprandially and did not differ between the Control and Exercise trials, but there was a transient postprandial increase at the 2 h time point in the apo CII/apo B ratio in the VLDL₂ fraction in the Exercise trial. The apo CII/apo B ratio in the VLDL₂ fraction decreased significantly below baseline at the 8 h postprandial time point in both trials. Apo CIII/apo B ratios and apo E/apo B ratios increased postprandially in both the VLDL₁ and VLDL₂ fractions, with the apo CIII/apo B ratios peaking 2 h after meal ingestion and the apo E/apo B ratio peaking later at 6-h postprandially in both fractions. Apo CIII/apo B

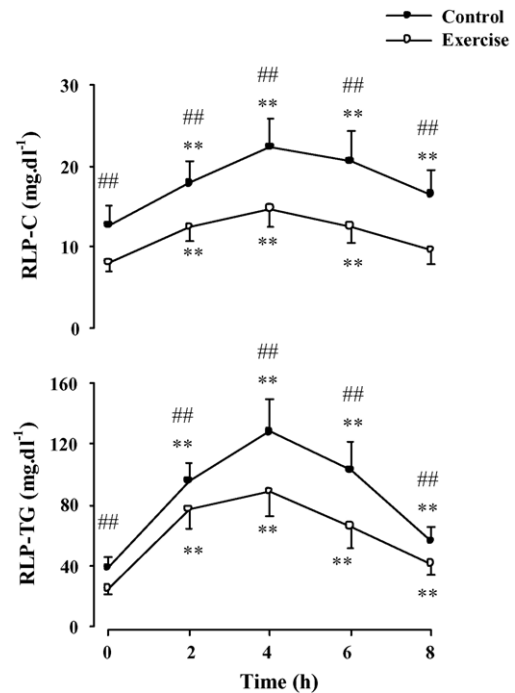


Fig. 3. Postprandial RLP-C (top panel) and RLP-TG (bottom panel) concentrations in the Control and Exercise trials. *Different from fasting value in the same trial, $p < 0.05$ (** $p < 0.01$). #Difference between Control and Exercise trials, $p < 0.05$ (## $p < 0.01$).

ratios in the VLDL₁ fraction were significantly lower in the Exercise trial than the Control trial at the 0, 2, 4 and 6 h time points; apo E/apo B ratios in this fraction were significantly lower in the Exercise trial at all observed time points.

Fig. 3 shows RLP-TG and RLP-C concentrations. Concentrations of both significantly rose after meal ingestion in both Control and Exercise trials. The time-averaged RLP-C concentration was 35% lower in the Exercise trial than the Control trial (Control: 19.0 ± 3.1 mg dl^{-1} , Exercise 12.3 ± 1.8 mg dl^{-1} , $p < 0.01$) and postprandial rise in RLP-C concentration tended to be lower in the Exercise trial (Control: 6.3 ± 1.2 mg dl^{-1} , Exercise 4.2 ± 0.9 mg dl^{-1} , $p = 0.06$). The time-averaged postprandial RLP-TG concentration was 29% lower (Control: 94.3 ± 14.1 mg dl^{-1} , Exercise: 66.9 ± 11.5 mg dl^{-1} , $p < 0.01$) and the postprandial rise in RLP TG concentration was 24% lower (Control: 55.8 ± 8.7 mg dl^{-1} , Exercise: 42.0 ± 7.9 mg dl^{-1} , $p < 0.01$) in the Exercise trial than the Control trial.

Fig. 4 shows LDL, HDL₂ and HDL₃ concentrations and CE/TG ratios. There were no significant differences in concentrations of LDL or either HDL fraction between the two trials, but in both trials HDL₂ concentrations increased during the postprandial period with concentrations significantly higher at 8 h postprandially than at baseline. There was also a significant postprandial change in the composition of the neutral lipid core of HDL₂ particles; in both the Control and Exercise the CE/TG ratio was significantly lower during postprandial time points than in the fasted states. Exercise

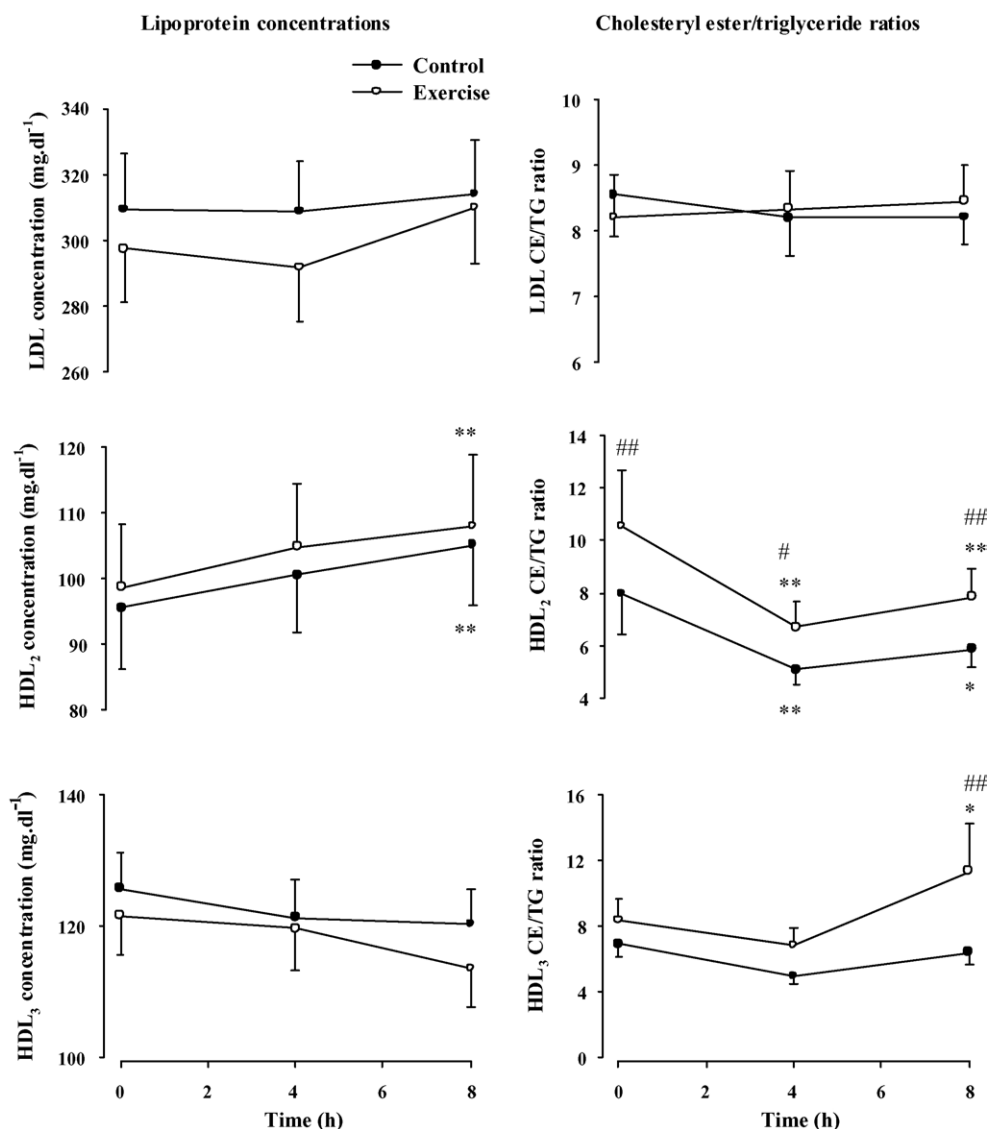


Fig. 4. Postprandial lipoprotein concentrations (left panels) and CE/TG ratios (right panels) in the LDL (top panels), HDL₂ (middle panels) and HDL₃ (bottom panels) lipoprotein fractions in the Control and Exercise trials. *Different from fasting value in the same trial, $p < 0.05$ (** $p < 0.01$). #Difference between Control and Exercise trials, $p < 0.05$ (## $p < 0.01$).

also influenced the HDL₂ CE/TG ratio; this was significantly higher in the Exercise trial than the Control trial at all measured time points. The CE/TG ratio in HDL₃ was also significantly higher in the Exercise trial than the Control trial at the 8-h postprandial time point.

The LDL subfraction distribution did not differ significantly between the Control and Exercise trials (LDL I concentration—Control: 55.3 ± 9.5 mg dl⁻¹, Exercise: 57.8 ± 8.2 mg dl⁻¹, NS; LDL II concentration—Control: 168.3 ± 15.6 mg dl⁻¹, Exercise: 157.7 ± 15.3 mg dl⁻¹, NS; LDL III concentration—Control: 85.7 ± 16.6 mg dl⁻¹, Exercise: 81.2 ± 16.4 mg dl⁻¹, NS).

There was no significant effect of exercise on HOMA-estimated insulin resistance (Control: 1.48 ± 0.23 , Exercise: 1.42 ± 0.25).

4. Discussion

This study makes a number of contributions to our understanding of exercise-induced changes to postprandial lipoprotein metabolism. Firstly, the results confirm and expand on earlier observations that changes in the VLDL lipoprotein fraction following a moderate intensity exercise session are of a greater magnitude than the changes in chylomicrons [2,3]. The present data indicate that large VLDL₁ are the dominant lipoprotein class influenced by prior moderate exercise, with exercise-induced lipoprotein concentration reductions in this fraction being greater than reductions in the chylomicron and VLDL₂ fractions in both absolute and percentage terms. Furthermore, as apo B100-containing lipoproteins accounted for >95% of the lipoprotein number in the VLDL₁ (and VLDL₂)

fraction, it is clear that the exercise-induced reduction in VLDL₁ concentration was predominantly due to decreases in the concentration of hepatically derived lipoproteins. This contrasts with the effects of long-term vigorous exercise training on postprandial lipoprotein metabolism, where much larger changes in chylomicron concentrations are observed [33].

The lower VLDL₁ concentrations following exercise could be due to increased clearance and/or reduced hepatic production of these lipoproteins. A recent study investigating the effects of a long-term moderate exercise program on VLDL kinetics in patients with type 2 diabetes confirms that this level of exercise can have a major effect on hepatic VLDL synthesis rates [34], but the effects of a single exercise session on VLDL synthesis and clearance rates are not clear and require further investigation. The present finding that the exercise-induced reduction in VLDL₁ concentration was greater than the reduction in chylomicron concentration in both absolute and percentage terms, would be consistent with reduced VLDL synthesis playing a major role in the reduction in VLDL concentration: chylomicrons are the preferred substrate for LPL [4,5] so an exercise-induced increase in TG clearance might be expected to induce a quantitatively greater reduction in chylomicron than VLDL concentrations. In addition, previous reports have shown no clear effect of prior moderate exercise on clearance of chylomicron-like particles [6,9] or on LPL activity in post-heparin plasma [7] or skeletal muscle [8], arguing against a clear role for increased LPL activity in mediating the reduction in postprandial lipaemia induced by moderate exercise. However, present data raise the possibility that exercise-induced alterations to the apolipoprotein composition of VLDL₁ may also play a role. In agreement with earlier reports, we observed postprandial increases in the number of apo CIII and apo E molecules per VLDL₁ lipoprotein particle [16,35]. These apolipoproteins are acquired by VLDL from circulating HDL and, as apo CIII [18] and apo E [19] both act to inhibit lipolysis by LPL, it has been suggested that these compositional changes might contribute to the impaired postprandial lipolysis of VLDL [16]. However, we also observed that there were fewer apo CIII and apo E molecules per VLDL₁ lipoprotein particle in the Exercise trial than the Control trial. This could conceivably have increased the potential of post-exercise VLDL₁ as an LPL substrate raising the possibility that LPL-mediated lipolysis of VLDL₁ might be increased by prior moderate exercise, irrespective of any clear changes in chylomicron clearance or in *ex vivo* measurements of LPL activity assessed using a standard substrate.

The reduced apo CIII enrichment of VLDL₁ following exercise may also have an antiatherogenic effect. Clinical trial data indicates that the apo CIII level in apo B containing lipoproteins (largely reflecting VLDL apo CIII) is an independent predictor of coronary angiographic progression [36] and risk of recurrent coronary events [37]. Furthermore, as apo CIII has been shown to stimulate CETP activity [17], the reduced VLDL apo CIII levels following exercise may contribute to the inhibition of this potentially atherogenic

lipid exchange [38]. Consistent with reduced CETP action, prior exercise had a marked effect on the core neutral lipid composition VLDL and HDL, reducing the CE/TG ratio in both VLDL₁ and VLDL₂ and reciprocally increasing the CE/TG ratio in HDL (largely in the HDL₂ subfraction). However, this is likely to be a consequence of the reduced VLDL concentration in the Exercise trial resulting in fewer TG-rich acceptor particles for CE from HDL [39] in addition to any specific effect of reduced apo CIII. The exercise-induced reduction in VLDL CE-enrichment may reduce the atherogenicity of VLDL (particularly, of smaller VLDL₂), over and above the effects of lowering VLDL concentrations; the extent of CE enrichment in small (Sf 20–60) VLDL has been shown to correlate significantly with severity of coronary artery disease in young myocardial infarction patients [21]. Furthermore, the reduced TG-enrichment of HDL₂ following exercise reduces the potential for hepatic lipase-mediated lipolysis of HDL₂ and helps maintain HDL particle stability, thereby reducing HDL particle catabolism and helping to preserve circulating concentrations of this atheroprotective lipoprotein subfraction [22].

Remnant lipoproteins have been identified as a particularly atherogenic subclass of TG-rich lipoproteins. Concentrations of RLP-C predict carotid artery intima-media thickness, independently of plasma TG and LDL cholesterol concentration [40] and are a strong determinant of endothelial dysfunction both the fasted and postprandial states [41]. In the present study prior moderate exercise reduced postprandial RLP-C and RLP-TG concentrations by 35 and 29%, respectively. This magnitude of reduction, evident after a single exercise session, is comparable to that observed following statin treatment [42] and suggests that moderate exercise could be a viable treatment option in patients with elevated RLP levels. Furthermore, we recently reported that vascular vasodilator function in both the fasted and postprandial states was improved by a prior session of moderate exercise [43]; we hypothesise that exercise-induced reductions in RLP-C and RLP-TG concentrations may have contributed to this effect [41].

In conclusion, this report has provided a detailed characterisation of the effects of a moderate intensity exercise session on postprandial lipoprotein metabolism. In particular, exercise induced substantial reductions in concentrations of VLDL₁ (to a greater extent than in chylomicrons) and of RLP-C and RLP-TG. Furthermore, as well as reducing TG-rich lipoprotein concentrations, exercise influenced the composition of VLDL and HDL particles; this is likely to exert an additional influence on the metabolism and atherogenicity of these lipoprotein species.

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