Favorable and Prolonged Changes in Blood Lipid Profile after Muscle-Damaging Exercise

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[1]Institute of Human Performance and Rehabilitation, Center for Research and Technology – Thessaly, Trikala, GREECE; [2]Department of Physical Education and Sport Science, University of Thessaly, Trikala, GREECE; [3]Department of Physical Education and Sport Science, Democritus University of Thrace, Komotini, GREECE; and [4]School of Sport, Performing Arts and Leisure, Wolverhampton University, Walshall, UNITED KINGDOM

ABSTRACT

NIKOLAIDIS, M. G., V. PASCHALIS, G. GIAKAS, I. G. FATOUROS, G. SAKELLARIOU, A. A. THEODOROU, Y. KOUTEDAKIS, and A. JAMURTAS. Favorable and Prolonged Changes in Blood Lipid Profile after Muscle-Damaging Exercise. *Med. Sci. Sports Exerc.*, Vol. 40, No. 8, pp. 1483–1489, 2008. **Purpose:** To examine the effect of repeated muscle-damaging exercise on the time-course changes in blood lipid and lipoprotein profile and compare them with changes in indices of muscle function and damage. **Methods:** Twelve women underwent an isokinetic exercise session consisting of 75 eccentric knee flexions, which was repeated after 3 wk. Triacylglycerols (TG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDLC) in plasma were measured before, immediately, 1, 2, 3, 4, and 7 d after muscle-damaging exercise. Low-density lipoprotein cholesterol (LDLC) and TC/HDLC were also calculated. **Results:** The largest changes in TG and lipoproteins appeared 3 d after exercise, returning toward baseline thereafter. The magnitudes of these changes at 3 d compared with rest were −18% and −8% for TG, −14% and −10% for TC, 8% and 7% for HDLC, −25% and −18% for LDLC, and −20% and −15% for TC/HDLC after sessions 1 and 2, respectively. In addition, the incremental or decremental area under the curve for the TG and lipoproteins measured after the first session was higher than that after the second session—except for HDLC concentration. **Conclusion:** These findings reveal that lipid and lipoprotein profile was favorably affected by both sessions of muscle-damaging exercise but relatively less so after a repeated session of muscle-damaging exercise. **Key Words:** ATHEROSCLEROSIS, FREE RADICALS, LIPIDS, OXIDATIVE STRESS, REACTIVE OXYGEN SPECIES, SKELETAL MUSCLE

BASIC SCIENCES

Changes in the concentration of blood lipids have been observed after a single exercise session (28). Reductions in triacylglycerols (TG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDLC) and increases in high-density lipoprotein cholesterol (HDLC) concentration have been reported after a single aerobic exercise session. Consequently, these changes may play a role in the improvement of blood lipid profile observed in trained individuals (28). The favorable influence of aerobic exercise on circulating lipids and lipoproteins is thought to be one of the reasons by which habitual exercise reduces cardiovascular disease risk (9).

Although numerous human studies have investigated the effects of aerobic non–muscle-damaging exercise on blood lipid profile (14,18,28), to our knowledge, only two studies addressed partially the effects of acute eccentric muscle-damaging exercise (26,27). In our opinion, the most interesting finding reported by these two studies is that TC (the only lipid or lipoprotein measured) concentration decreased by 10–15% 1 to 4 d after an acute eccentric exercise session (26,27). This finding cannot be easily explained by the common notion that changes in lipid and lipoprotein profile are related to total energy expenditure of the exercise session (28) because the oxygen cost of producing eccentric muscular forces is much lower than equal amounts of force produced concentrically (1,4). Specifically, it has been suggested that the oxygen requirement of submaximal eccentric cycling is only 1/6 to 1/7 of that of concentric cycling at the same workload (4). Therefore, possibly the extensive muscle damage (23) and/or concomitant oxidative stress (20) induced by eccentric muscle-damaging exercise may be related to the reported decreases in TC.

In addition to "pure" eccentric exercise, some studies used partially eccentric exercise by using acute resistance exercise—which comprises eccentric muscle actions in the

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negative phase—and measured blood lipid and lipoprotein levels (15,17,29). These studies reported divergent results including increased HDLC immediately after exercise and no changes in TG, TC, and LDLC (15), increased HDLC 1 h after exercise and no changes in TG, TC, and LDLC (17), and increased HDLC and decreased TG 24 h after exercise and no changes in TC (29). These discrepancies may be due to the differences in subjects (trained vs untrained), type of protocol (differences in duration and intensity), and blood sampling time points. It is noteworthy that only Wallace et al. (29) collected blood samples after the first 24 h after exercise, and none of them monitored muscle damage.

Based on the above, the primary purpose of the present study was to examine the effects of muscle-damaging exercise on the time-course changes in blood lipid and lipoprotein profile and compare them with changes in indices of muscle function and damage to explore potential relationships among these phenomena. It is well known that unaccustomed exercise, particularly eccentric exercise, results in muscle damage (19). In the days after eccentric exercise, extensive disruption of the ultrastructure of skeletal muscle occurs, muscle proteins [e.g., creatine kinase (CK)] are released into the blood, and delayed onset of muscle soreness (DOMS) appears (19). These indices of muscle damage are substantially reduced when the same muscle-damaging exercise is performed several weeks later, indicating a rapid adaptation of skeletal muscle to eccentric actions (5). This phenomenon has been called the repeated bout effect (19). Therefore, secondarily, we sought to determine whether a session of eccentric exercise could influence the response of blood TG and lipoproteins after a second session of eccentric exercise performed approximately 3 wk later. We hypothesized that eccentric exercise would change the blood lipid and lipoprotein profile that will be sustainable for days after exercise, and these changes will be attenuated after a second exercise session.

METHODS

Subjects. This study is part of a larger research project on the effect of muscle-damaging exercise on muscle physiology and blood biochemistry (21). Twelve healthy females (age = 23 ± 2 yr, height = 165 ± 2 cm, mass = 54 ± 3 kg, and body fat = 24.9 ± 2.0%) participated in this study. The subjects participated in low-intensity leisure activities (such as jogging, swimming, and dancing) two to three times per week for less than 3 $h \cdot wk^{-1}$ and had no experience with eccentric exercise training for at least 6 months before the study. In addition, they were not taking any medication, oral contraceptives, or dietary supplements during the study period and 1 month before the initiation of the experiment. They were instructed to abstain from strenuous exercise for 7 d before and during data collection. All volunteers were eumenorrheic (reporting their menstrual cycle as lasting 24–30 d). The eccentric exercise trial fell within the luteal phase of the menstrual cycle (2–6 d after ovulation) in an attempt to avoid any variance in estrogen levels between the first and the second exercise session. The luteal phase of the subjects was identified through completion of a self-reported history of their menstrual cycle. Finally, all volunteers were asked not to modify their usual way of life (including physical activity) in any respect during the study period. A written informed consent to participate in the study was provided by all participants after the volunteers were informed of all risks, discomforts, and benefits involved in the study. The procedures were in accordance with the 1975 Declaration of Helsinki, and approval was received from the institutional review board.

Design. Volunteers performed two isokinetic eccentric exercise sessions, separated by 24–30 d, depending on the duration of their menstrual cycle. The exercise protocols were undertaken by all participants in their dominant leg (hamstrings), whereas the contralateral leg was served as control. Biochemical markers and muscle damage indices were determined before, immediately, 1, 2, 3, 4, and 7 d after exercise. CK activity was determined at the same time points except for immediately after exercise. These measurements were assessed after both eccentric exercise sessions. All measurements and blood samplings were performed between 9 and 11 a.m. after an overnight fast and abstaining from alcohol and caffeine for 24 h. Each subject was familiarized at least 5 d before the experimental procedures. This familiarization procedure involved 8–10 isokinetic eccentric actions at very low intensity not capable to induce muscle damage, assessment of range of motion (ROM), and DOMS.

Anthropometric measurements. During their first visit, body mass was measured to the nearest 0.5 kg (Beam Balance 710; Seca, Birmingham, UK) with subjects wearing their underclothes and barefooted. Standing height was measured to the nearest 0.5 cm (Stadiometer 208; Seca, Birmingham, UK). Percentage body fat was calculated from seven skinfold measures (average of two measurements of each site) using a Harpenden caliper (John Bull, London, UK). The Siri skinfold equation was used to calculate body fat.

Isokinetic exercise protocol. The isokinetic dynamometer Cybex Norm (Ronkonkoma, NY) was calibrated weekly according to the manufacturer's instructions. Subjects laid prone on the isokinetic dynamometer, and their position was recorded for the follow-up measurements. Their lateral femoral condyle was aligned to the axis of rotation of the dynamometer, while the ankle cuff was attached proximally to the lateral malleolus. Each subject's functional ROM was set electronically between 0° (full knee extension) and 90° of knee flexion to prevent hyperextension and hyperflexion. Gravitational corrections were made to account for the effect of limb weight on torque measurements. Feedback of the eccentric exercise intensity and duration was automatically provided by the dynamometer.

In each of the two eccentric exercise sessions, volunteers had to accomplish five sets of 15 eccentric maximal voluntary contractions at an angular velocity of $60°\cdot s^{-1}$ in the prone position. A 2-min rest interval was incorporated between sets. Before each exercise session, subjects performed a warm-up consisting of 8-min cycling on a Monark cycle ergometer (Vansbro, Sweden) at 70 rpm and 50 W followed by 5 min of ordinary stretching exercises of the major muscle groups of the lower limbs.

Muscle damage indices. The isokinetic dynamometer was also used for the measurement of isometric knee flexors peak torque at 90° knee flexion. The best of the three maximal voluntary contractions was recorded. To ensure that the subjects provided their maximal effort, we repeated the measurements if the difference between the lower and the higher torque value exceeded 10%. There was a 1-min rest between isometric efforts. The test–retest reliability of isometric peak torque measurement was 0.98.

The assessment of ROM was performed manually. The investigator extended the calf at a very low angular velocity from full knee flexion to the position where the subject felt any discomfort. The angle was recorded to indicate the end of the pain-free ROM. The test–retest reliability of ROM measurement was 0.96.

Each subject assessed DOMS by palpation of the muscle belly in the distal region of the hamstrings in a seated position with the muscles relaxed. The assessment of soreness of the exercised lower limb was also performed during walking. Perceived soreness for both conditions was rated on a scale ranging from 1 (normal) to 10 (very, very sore). The test–retest reliability of DOMS by palpation and by walking measurement was 0.94 and 0.92, respectively.

Dietary analysis. To control the effect of previous diet on the outcome measures of the study and establish that after both exercise sessions, the participants had similar levels of macronutrient and micronutrient intake, they were asked to record their diet for 3 d preceding the first exercise session and repeat this diet before the second exercise session. A written set of guidelines for monitoring dietary consumption and a record sheet for recording food intake was provided to each subject. Diet records were analyzed using the nutritional analysis system Science Fit Diet 200A (Sciencefit, Athens, Greece).

Assays. Subjects provided venous blood samples in the sitting position from a forearm vein. After clotting, serum was prepared by centrifugation at 1500*g* for 10 min and was stored in multiple aliquots at −30°C and thawed only once before analysis. TG and TC were assayed by enzymic spectrophotometric methods by reagent kits from Zafiropoulos (Athens, Greece). HDLC was determined the same as TC after precipitation of very low density and low-density lipoproteins with a reagent from Zafiropoulos. CK was assayed using a kit from Spinreact (Sant Esteve, Spain). These biochemical parameters were determined in duplicate with simultaneous use of a control serum from Roche (Mannheim, Germany). Each parameter was assayed on a single day to eliminate interassay variability. Intra-assay coefficients of variation for CK, TG, TC, and HDLC were 3.9%, 2.4%, 2.1%, and 2.3%, respectively. LDLC was calculated according to the following equation: LDLC = TC − HDLC − (TG / 5) (12). TC/HDLC (considered an atherogenic index) was also calculated.

For hematology, an aliquot of each blood sample was mixed with ethylenediaminetetraacetic acid solution to prevent clotting. Hematocrit was measured by microcentrifugation, and hemoglobin was measured using a kit from Spinreact (Santa Coloma, Spain). Postexercise plasma volume changes were computed on the basis of hematocrit and hemoglobin as previously described (7).

Calculations and statistical analysis. The incremental or decremental area under the curve (AUC) over the 7-d protocol was calculated for all parameters using the trapezoidal rule and by subtracting the area attributable to the baseline concentration. The distribution of all dependent variables was examined by Shapiro–Wilk test and was found not to differ significantly from normal, except for CK values. Two-way ANOVA

TABLE 1. Muscle damage indices after sessions 1 and 2 of eccentric exercise (mean ± SD).

	Pre	Post	1 d	2 d	3 d	4 d	7 d
Torque (N·m)							
Session 1	39 ± 8	22 ± 7*	24 ± 8*	26 ± 10*	29 ± 9*	28 ± 7*	39 ± 5
Session 2	36 ± 7	28 ± 8*	30 ± 9*	32 ± 9#	34 ± 8#	35 ± 7	35 ± 4
DOMS palpation (0–10)							
Session 1	1 ± 0	1.5 ± 0.7*	4.1 ± 1.9*	6.1 ± 1.9*	5.1 ± 3.1*	2.7 ± 1.8*	1.5 ± 1.1
Session 2	1 ± 0	1.3 ± 0.5	2.3 ± 1.9*	2.8 ± 2.4*#	2.0 ± 1.6*#	1.7 ± 0.9	1.2 ± 0.7
DOMS walk (0–10)							
Session 1	1 ± 0	3.0 ± 1.1*	4.5 ± 2.2*	6.5 ± 2.8*	6.2 ± 3.0*	3.5 ± 2.8*	1.5 ± 1.7
Session 2	1 ± 0	1.7 ± 1.2*	2.7 ± 1.9*	2.5 ± 2.5*#	2.5 ± 1.7*#	1.6 ± 0.8	1.2 ± 0.7
ROM (°)							
Session 1	128 ± 5	121 ± 9*	114 ± 14*	98 ± 19*	103 ± 27*	119 ± 10	131 ± 8
Session 2	130 ± 6	127 ± 7	120 ± 7*#	118 ± 14*#	127 ± 7#	129 ± 7	129 ± 5
CK ($U\cdot L^{-1}$)							
Session 1	82 ± 84	90 ± 91	162 ± 166	306 ± 308	1290 ± 1117*	1730 ± 1792*	560 ± 308
Session 2	68 ± 74	72 ± 81	115 ± 137	207 ± 221	330 ± 396#	540 ± 518*#	199 ± 224

* Significantly different compared with preexercise values in the same session ($P < 0.05$).
\# Significant difference between sessions 1 and 2 in the same parameter and in the same time point ($P < 0.05$).

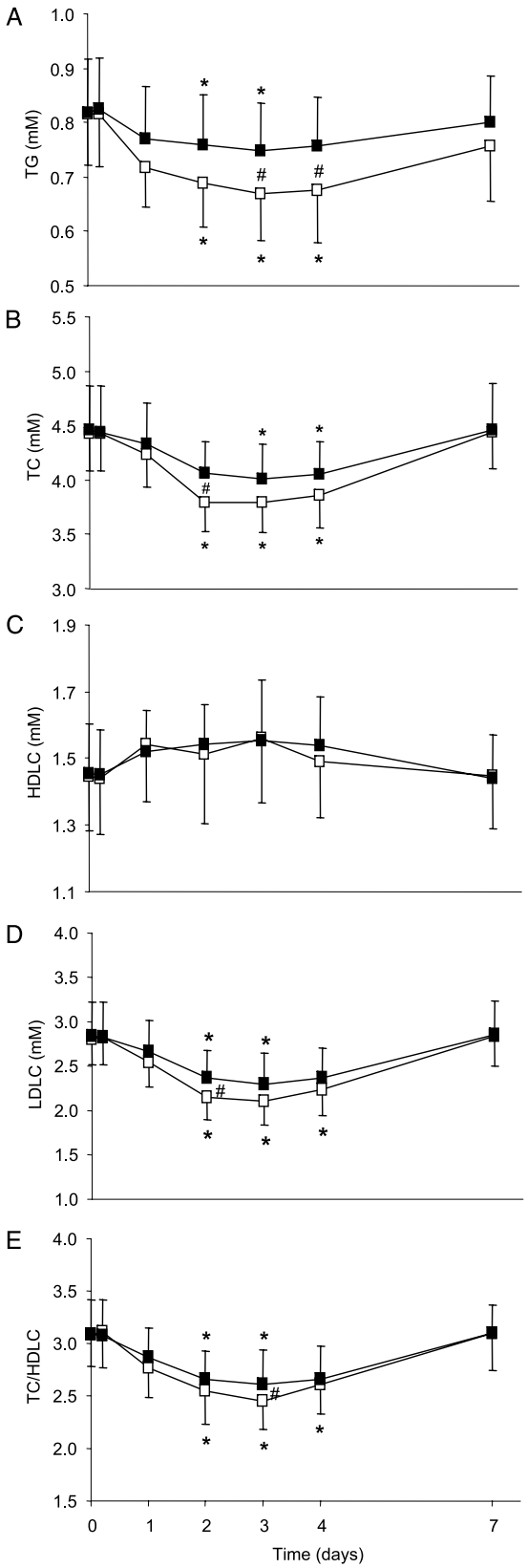

FIGURE 1—TG (A), TC (B), HDLC (C), and LDLC (D) concentrations and TC/HDLC (E) ratio after session 1 (*open rectangles*) and session 2 (*close rectangles*) (mean ± SD). * Significantly different from the preexercise value in the same session ($P < 0.05$). # Significantly different between sessions 1 and 2 at the same time point ($P < 0.05$).

(session × time) with repeated measurements on both factors were used to analyze isometric peak torque, DOMS, ROM, and all lipids and lipoproteins. CK activity was analyzed nonparametrically by Friedman's test. If a significant interaction was obtained, pairwise comparisons were performed through simple contrasts and simple main-effects analysis. Differences between the first and the second sessions with respect to incremental or decremental AUC were examined by Student's paired *t*-test. Correlation between the postexercise changes in the indices of muscle damage, lipid, and lipoproteins was performed by Pearson's product moment correlation. The test–retest reliability of the functional muscle damage indices was determined by performing the intraclass reliability test. The level of significance was set at 0.05. The SPSS version 13.0 was used for all analyses (SPSS, Inc, Chicago, IL, USA).

RESULTS

There were no significant differences in daily energy, macronutrient, and micronutrient intakes between the first and the second exercise sessions (21). There were no significant changes in plasma volume between any postexercise time point and the baseline values after both sessions; therefore, no adjustment to the measured concentrations was made.

Muscle damage indices. The effect of eccentric exercise on indices of muscle damage has already been reported (21) and is reproduced in Table 1. In brief, the main effects of bout and time and their interaction were significant concerning isometric peak torque. Compared with baseline values, isometric torque was significantly declined up to 4 d after the first bout and returned to baseline values at 7 d. After the second bout, the decline in isometric torque was significant only up to 1 d after exercise and did not differ significantly from the resting value thereafter. Concerning ROM, the main effects of bout and time and their interaction were significant. ROM values, compared with rest, were decreased up to 3 d after the first bout and returned to baseline values at 7 d. After the second bout, the decrease in ROM was up to 2 d after exercise and did not differ significantly from the resting value thereafter. The interaction of protocol and time and both main effects were significant concerning DOMS after palpation and after walking. Compared with baseline values, DOMS after palpation and after walking was increased up to 4 d after the first bout and returned to preexercise values at 7 d. After the second bout, the increase in both types of DOMS was, on average, lower and lasted for only up to 3 d after exercise. The main effects of bout and time and their interaction were significant concerning serum CK activity. Compared with resting activity, CK was increased at 3 and 4 d after the first exercise bout, although after the second bout, the increase in CK was, on average, lower and significant only at 4 d after exercise.

Lipid profile. The main effects of session and time and their interaction were significant concerning TG (Fig. 1A),

TABLE 2. Incremental or decremental AUC per day in lipid and lipoproteins after sessions 1 and 2 of eccentric exercise (mean ± SD).*

	Incremental or Decremental AUC per day	
	Session 1	Session 2
TG (mmol·L^{-1})	−0.106 ± 0.017	−0.047 ± 0.009
TC (mmol·L^{-1})	−0.366 ± 0.064	−0.255 ± 0.042
HDLC (mmol·L^{-1})	0.052 ± 0.010	0.055 ± 0.008
LDLC (mmol·L^{-1})	−0.397 ± 0.073	−0.301 ± 0.064
TC/HDLC	−0.343 ± 0.079	−0.277 ± 0.066

* Values between sessions 1 and 2 in all parameters, except for HDLC, are significantly different ($P < 0.05$).

TC (Fig. 1B), LDLC (Fig. 1D), and TC/HDLC (Fig. 1E). In contrast, regarding HDLC, only the main effect of time was significant (Fig. 1C). Eccentric exercise affected the concentration of all lipid and lipoproteins at several time points after both exercise sessions. Specifically, the magnitudes of these changes at 3 d compared with rest were −18% and −8% for TG, −14% and −10% for TC, 8% and 7% for HDLC, −25% and −18% for LDLC, and −20% and −15% for TC/HDLC after sessions 1 and 2, respectively. Incremental or decremental AUC of lipid and lipoproteins are presented in the Table 2.

Correlation among indices of muscle damage and lipid profile. Pearson's test revealed many significant correlations for almost any combination between postexercise changes in muscle damage and lipids or lipoproteins (Table 3). However, no strong significant correlation coefficients (>0.70) were evident between postexercise changes in any of the variables examined (range = 0.09–0.61, median value = 0.34 for all postexercise time points). No single muscle damage index proved optimal for assessing the extent of lipid or lipoprotein changes.

DISCUSSION

To our knowledge, this is the first investigation examining the effects of eccentric exercise on the lipid and lipoprotein profile of blood in humans. For this purpose, several functional and biochemical indices to study the effect of repeated bout of muscle-damaging exercise on lipid metabolism of females were used, and six postexercise measurements were performed up to 7 d after both exercise sessions. The 7 d proved to be a good end time point, because all lipid and lipoproteins had already returned to preexercise values by this time point. The present results revealed that eccentric exercise uniformly (i.e., in a similar pattern through time) modified the levels of the lipids and lipoproteins indicating favorable and prolonged changes in the blood peaking at 2 to 4 d after exercise and returning toward baseline afterward. As predicted by the repeated bout effect phenomenon, the indirect indices of muscle damage changed dramatically after session 1 but much less after session 2. Accordingly, the magnitudes of the responses of circulating lipids and lipoproteins (except for HDLC) were higher after the first session of exercise compared with those induced by the same session performed approximately 4 wk later.

In this study, our interest laid not only in the way TG and lipoproteins changed with time but also in the total response of these molecules. To obtain this information, incremental or decremental AUC was calculated. This summary measure provides a more honest indication of the magnitude of change of these molecules through the whole observation period. In addition, from a biologic perspective, this summary measurement provides a fairly good picture of the adaptations that occurred in the human organism during the study period. It is conceivable that the impact of the modifications observed in the lipid and lipoprotein profile on human health depends on both the magnitude and duration of these modifications.

Muscle function and damage after muscle-damaging exercise. Five indirect indices of muscle function and damage were used in the present study. Maximal isometric torque and ROM are considered the

TABLE 3. Correlation coefficients between the postexercise changes after session 1 of muscle damage and lipid/lipoproteins.

		Change at Day 1				Change at Day 2				Change at Day 3				Change at Day 4			
		Torque	DOMS	ROM	CK	Torque	DOMS	ROM	CK	Torque	DOMS	ROM	CK	Torque	DOMS	ROM	CK
Change at day 1	TG	0.28*	NS	NS	NS	0.32*	−0.28*	NS	NS	0.52*	NS	NS	NS	NS	NS	NS	−0.49*
	TC	NS	−0.61*	NS	NS	0.32*	NS	0.33*	NS	NS	NS	0.39*	NS	0.44*	NS	NS	NS
	HDLC	NS	NS	NS	NS	NS	NS	NS	NS	NS	0.22*	NS	NS	NS	NS	NS	NS
	LDLC	NS	NS	NS	NS	NS	−0.30*	NS	−0.27*	NS	−0.49*	NS	−0.21*	NS	−0.41*	0.33*	NS
	TC/HDLC	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Change at day 2	TG	0.29*	NS	NS	−0.49*	NS	NS	0.09*	NS	NS	NS	NS	NS	NS	NS	NS	−0.26*
	TC	NS	−0.33*	0.29*	NS	0.37*	NS	0.27*	NS	0.41*	NS	NS	NS	0.49*	NS	NS	NS
	HDLC	NS	NS	NS	0.27*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	LDLC	NS	NS	NS	NS	NS	NS	NS	NS	0.39*	NS	NS	−0.26*	NS	NS	NS	NS
	TC/HDLC	NS	NS	NS	−0.44*	NS	NS	NS	−0.42*	NS	−0.45*	0.29*	NS	NS	−0.31*	0.29*	NS
Change at day 3	TG	NS	NS	NS	NS	NS	NS	NS	NS	NS	−0.32*	NS	NS	NS	NS	NS	NS
	TC	NS	NS	NS	NS	0.33*	NS	NS	NS	0.31*	NS	NS	NS	0.30*	NS	NS	−0.33*
	HDLC	NS	NS	NS	NS	NS	0.33*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
	LDLC	NS	−0.13*	NS	NS	NS	NS	0.28*	NS	NS	NS	NS	NS	NS	NS	NS	NS
	TC/HDLC	0.28*	NS	NS	NS	NS	NS	NS	−0.38*	0.36*	NS	0.18*	−0.24*	NS	NS	0.27*	NS
Change at day 4	TG	NS	NS	0.25*	−0.47*	NS	NS	NS	−0.44*	NS	NS	NS	NS	NS	−0.49*	NS	NS
	TC	NS	NS	NS	NS	0.28*	−0.31*	0.27*	NS	0.39*	NS	NS	NS	NS	NS	NS	NS
	HDLC	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	0.13*	NS	NS	NS
	LDLC	NS	−0.24*	NS	−0.21*	NS	NS	NS	NS	NS	NS	0.47*	NS	NS	NS	NS	NS
	TC/HDLC	0.26*	NS	0.24*	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS

* Significant at $P < 0.05$.

best tools for quantifying muscle damage in the absence of histologic verification in humans (30). The peak change in ROM and DOMS of both types after sessions 1 and 2 appeared at 2 d after exercise. On the other hand, the largest alterations in isometric torque appeared immediately after exercise, whereas CK activity peaked at 4 d after exercise. Although all muscle damage indices were affected significantly after both eccentric exercise sessions, the changes after session 2 were much less compared with those produced after session 1. Therefore, as expected, exercise-induced muscle damage was largely attenuated after the second session of eccentric exercise, confirming the repeated bout effect phenomenon (19).

Potential mechanisms underlying the favorable changes in lipid profile after muscle-damaging exercise. TG concentration remained diminished 4 d after the first exercise session and 3 d after the second exercise session. Serum TG concentration may have been reduced because of the increased activity of lipoprotein lipase (LPL) that acts on lipoprotein particles passing through the capillaries, releasing free fatty acids that may be taken up by skeletal muscle and either esterified in phospholipids and intramuscular TG or oxidized in the mitochondria. Increased LPL activity may be related to the increased demand of the working muscle for fatty acids as energy-yielding substrate and to the replenishment of muscle phospholipid and TG stores with fatty acids for the regeneration of damaged muscle fibers (16,22,25). Indeed, replenishment of phospholipids with fatty acids may be the major reason for the decreased TG levels of serum because the muscle damage induced by eccentric exercise may have hydrolyzed phospholipid fatty acids from the damaged membranes. This, in turn, may have increased the free fatty acid pool inside the muscle and therefore have increased β-oxidation during the muscle-regeneration period. Finally, the decreased levels of serum TG after muscle-damaging exercise may also have appeared to be due to the higher levels of resting energy expenditure that is sustainable for days after eccentric exercise (8), when there is increased need for adenosine triphosphate mainly for the regeneration of damaged and/or for the formation of new muscle fibers from satellite cells.

In the present investigation, it was found that HDLC increased after both eccentric exercise sessions and remained altered compared with baseline values until 3 d after exercise. The movement of the rise in HDLC after exercise was similar to the drop in TG in terms of culmination and disappearance. The link between these opposite changes might be explained by the increased LPL activity that augments the degradation of TG from VLDL and causes the lipoprotein particles to shrink. This, in turn, creates a surplus of shell lipids that are mainly transferred to HDLC (10). One of the most interesting points was that HDLC responded favorably after both bouts. This finding indicates that the lesser muscle damage produced after bout 2 compared with bout 1 did not impair the effect of eccentric exercise on HDLC levels. Taking into account that the correlation coefficients produced among muscle damage indices and HDLC were lower compared with the other lipoproteins and TG, it seems that the degree of muscle damage after eccentric exercise plays a minor role to HDLC concentration. Finally, a probable reason for the similar changes noted after both bouts may be a similar increase in LPL activity after both sessions, leading to a surplus of shell lipids that are mainly transferred to HDLC, ultimately increasing its concentration.

Because cholesterol may constitute approximately 13% of muscle membranes (13) and the signs of healing have been observed in human subjects as early as 36 h after eccentric exercise (11), it can be suggested that the reduction in serum TC and LDLC during the day when muscle regeneration culminates (i.e., 2 to 4 d after exercise) owes to the outflow of cholesterol from plasma in muscle-promoting synthesis of new cell membranes. Therefore, the depressed TC and LDLC values found after the second session may be, at least in part, due to the less muscle damage because less cholesterol molecules would be needed for the repair process that takes place in the damaged muscle cells.

Although the mechanisms of the favorable changes in lipid profile that appeared after muscle-damaging exercise can only be speculated, another mechanism might be a connection of exercise-induced oxidative stress and lipid profile. In a recent study from our group (21), we identified that after the same exercise regimen, which was performed by the same subjects, oxidative stress increased in the blood in a similar time course to that of lipid profile. Therefore, this muscle-damaging exercise has the potential to oxidize lipids and lipoproteins. It has been suggested that oxidatively modified lipoproteins may be cleared more rapidly from the blood than nonmodified lipoproteins (3). This probably occurs because oxidized lipoproteins have been suggested to be ligands for several peroxisomal proliferator activator receptors (6,24), which might up-regulate the expression of LDLC receptor (2).

It is worth mentioning that the present study was not able to isolate the effect of muscle damage on lipids and lipoproteins. Therefore, this work evaluated the effects of muscle-damaging resistance exercise on lipids and lipoproteins. The only way to establish a definite answer on whether muscle damage on its own constitutes the main cause for the observed modifications in lipoprotein profile is by comparing the lipoprotein responses after a damaging and a less-damaging resistance exercise protocol (e.g., eccentric-only vs concentric-only exercise). In addition, given the fact that low-significant correlation coefficients appeared between postexercise changes in muscle damage indices and TG and lipoproteins examined, it is evident that muscle damage is just one of the underlying causes for the observed effects.

CONCLUSION

To the best of our knowledge, this is the first study that investigated the effects of a "pure" muscle-damaging

exercise protocol on blood lipid profile. Participation in activities inducing physiological muscle damage, such as stair descending and downhill walking or running, should be considered in the future as a tool to improve blood lipid profile. Certainly, further studies are needed to verify and extend the present findings and to investigate the effects of chronic muscle-damaging exercise on blood lipid profile.

The results of the present study do not constitute endorsement by ACSM.

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