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Role of exercise intensities in oxidized low-density lipoprotein-mediated redox status of monocyte in men

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Wang, Jong-Shyan, Tan Lee, and Shu-Er Chow. Role of exercise intensities in oxidized low-density lipoprotein-mediated redox status of monocyte in men. *J Appl Physiol* 101: 740–744, 2006. First published May 25, 2006; doi:10.1152/japplphysiol.00144.2006.—Exercise significantly influences the progression of atherosclerosis. Oxidized LDL (ox-LDL), as a stimulator of oxidative stress, facilitates monocyte-related atherogenesis. This study investigates how exercise intensity impacts ox-LDL-mediated redox status of monocytes. Twenty-five sedentary healthy men exercised mildly, moderately, and heavily (i.e., 40, 60, and 80% maximal oxygen consumption, respectively) on a bicycle ergometer. Reactive oxygen species (ROS) production, cytosolic and mitochondrial superoxide dismutase (c-SOD and m-SOD, respectively) activities, and total and reduced-form γ-glutamylcysteinyl glycine (t-GSH and r-GSH, respectively) contents in monocytes mediated by ox-LDL were measured. This experiment obtained the following findings: *1*) ox-LDL increased monocyte ROS production and was accompanied by decreased c-SOD and m-SOD activities, as well as t-GSH and r-GSH contents, whereas treating monocytes with diphenyleneiodonium (DPI) (a NADPH oxidase inhibitor) or rotenone/2-thenoyltrifluoroacetone (TTFA) (mitochondrial complex I/II inhibitors) hindered ox-LDL-induced monocyte ROS production; *2*) production of ROS and reduction of m-SOD activity and r-GSH content in monocyte by ox-LDL were enhanced by heavy exercise and depressed by mild and moderate exercise; and *3*) heavy exercise augmented the inhibition of ox-LDL-induced monocyte ROS production by DPI and rotenone/TTFA, whereas these DPI- and rotenone/TTFA-mediated monocyte ROS productions were unchanged in response to mild and moderate exercise. We conclude that heavy exercise increases ox-LDL-induced monocyte ROS production, possibly by decreasing m-SOD activity and r-GSH content in monocytes. However, mild and moderate exercise likely protects individuals against suppression of anti-oxidative capacity of monocyte by ox-LDL.

physical activity; reactive oxygen species; SOD, GSH

ALTHOUGH REGULAR MODERATE-INTENSITY EXERCISE decreases the risk of cardiovascular disease (10, 20), episodes of vigorous exertion transiently increase the occurrence of sudden cardiac arrest (1, 18). Atherosclerosis, a chronic inflammatory disease of the vessel wall, is characterized by archetypical chronic inflammatory cell infiltration of monocytes (5, 6, 11). Experimental evidence indicates that reactive oxygen species (ROS) derived from infiltrated monocytes contribute to oxidative stress at inflammatory sites, thereby promoting oxidation of low-density lipoprotein (LDL) (3). Moreover, oxidized LDL (ox-LDL) has been identified as a potent chemoattractant and oxidative stressor of atherogenesis, typically causing endothelium dysfunction and facilitating monocyte emigration into the subendothelial space (11). Therefore, elucidating the regulation of ox-LDL-induced ROS production in monocytes can lead to a novel therapeutic intervention for prevention of atherosclerosis.

Physical exercise modulates inflammatory reactions in leukocytes, according to reactions based on the exercise type/intensity/duration (16). Previous studies (7, 21) indicated that strenuous exercise generates an imbalance between ROS and antioxidant defense, resulting in an oxidative stressful environment in the body. Conversely, regular moderate-intensity exercise hinders LDL oxidation by enhancing antioxidant release or production (24). Whether physical exercise influences oxidant production and antioxidative capacity of monocyte mediated by ox-LDL remains unclear. We hypothesize that exercise impacts ox-LDL-mediated redox status of monocytes, with reactions determined by exercise intensity.

This study clarifies how exercise intensity affects ox-LDL-mediated ROS production and antioxidative capacity in monocytes. Furthermore, activating membrane-associated NADPH oxidase (2) and changing the coupling of the mitochondrial respiratory chain (15) are the critical pathways in monocyte ROS-mediated atherogenesis noted in previous studies. Therefore, this study also determined whether exercise affects ox-LDL-induced monocyte ROS production through altering the signal transductions in these pathways.

METHODS

Subjects. The Ethics Committee of Chang Gung Memorial Hospital reviewed and approved the protocol for this study. Procedures corresponded to institutional guidelines. All subjects provided informed, written consent. Twenty-five healthy sedentary men were enrolled in this study. Subject characteristics (expressed as means ± SE) were as follows: age, 23.7 ± 0.4 yr; height, 171.5 ± 1.1 cm; and body weight, 67.3 ± 1.4 kg (Table 1). No subject had engaged in regular physical activity for at least 1 yr before study start. All subjects were infection free or cardiovascular risk free and abstained from all medication and vitamins at least for 2 wk before the study. Subjects fasted for at least 8 h before study participation and were instructed to refrain from exercise for at least 24 h before blood sampling. All subjects arrived at the test center at 9:00 AM to eliminate possible diurnal influence.

Exercise and blood collection protocol. The subjects came to the laboratory on 4 different days to receive four distinct exercise protocols on a bicycle ergometer (Lode, Corival 400) (Table 1). The first protocol comprised 2 min of unloaded pedaling, after which workload was increased incrementally by 20–30 W every 3 min until subjects

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Table 1. *Anthropometric characteristics and exercise performance in all subjects*

	Max	LIE	MIE	HIE
Anthropometric characteristics				
Age, yr	23.7±0.4			
Height, cm	171.5±1.1	171.5±1.1	171.5±1.1	171.5±1.1
Weight, kg	67.3±1.4	67.5±1.6	67.4±1.5	67.5±1.2
BMI, kg/m^2	22.9±0.4	22.9±0.5	22.9±0.4	67.5±1.2
Exercise performance				
Workload, W	196±3	79±4	118±3	161±4
HR, beats/min	193±4	121±3	146±4	168±5
$\dot{V}_E$, 1/min	106.8±4.4	32.5±3.4	55.2±4.5	78.4±5.2
$\dot{V}_{O_2}$, ml·min^{-1}·kg^{-1}	35.9±1.4	14.5±1.4	21.6±1.8	28.9±1.6
$\dot{V}_{CO_2}$, ml·min^{-1}·kg^{-1}	45.5±1.7	12.4±1.2	21.7±1.9	32.4±1.3
RER	1.26±0.04	0.85±0.02	1.01±0.05	1.12±0.4

Values are means ± SE. Max, maximal exercise test; LIE, light-intensity exercise; MIE, moderate-intensity exercise; HIE, heavy-intensity exercise; BMI, body mass index; HR, heart rate; $\dot{V}_E$, minute ventilation; $\dot{V}_{O_2}$, oxygen consumption; $\dot{V}_{CO_2}$, CO_2 uptake; RER, respiratory exchange ratio.

were exhausted. Heart rate, minute ventilation, oxygen consumption, and carbon dioxide production were measured during the exercise with an automated system (PowerLab/8M; AD Instruments). This exercise test determined each subject's maximal oxygen consumption ($\dot{V}_{O_2\,max}$) (25). The $\dot{V}_{O_2\,max}$ was defined as the following four criteria: *1*) the increase of oxygen consumption was <2 ml·kg^{-1}·min^{-1} in the last 2 min of exercise; *2*) heart rate arrived at its predicted maximum; *3*) the respiratory exchange ratio exceeded 1.20; and *4*) venous lactate concentration after the termination of exercise exceeded 8 mM. The value of subjects' $\dot{V}_{O_2\,max}$ was 35.9 ± 1.4 ml·kg^{-1}·min^{-1} (mean ± SE). In the second, third, and fourth exercise protocols, subjects performed at ~40% (mild), 60% (moderate), and 80% (heavy) of predetermined $\dot{V}_{O_2\,max}$ for 40 min (Table 1). According to the values of heart rate and oxygen consumption during exercise, the workload of bicycle ergometer was adjusted in real time to confirm that the subjects truly exercised at the prescribed exercise intensities. The second to fourth exercise protocols were randomized in a counterbalanced order. Each test was separated by 2 wk to ensure complete recovery between trials. If a subject was ill or had a fever, the test was postponed until the subject was symptom free and medication free for least 2 wk. At rest and immediately after mild, moderate, or heavy exercise, blood samples, collected from a forearm vein, were used to measure hematological parameters and monocyte function. Blood cell counts were analyzed using a Sysmex KX-21 cell counter.

ox-LDL preparation in human. ox-LDL was prepared from fresh human plasma, as described previously (26). Thiobarbituric acid reactive substances was estimated colorimetrically by using malondialdehyde as a standard; starting LDL was 0.06 nmol of malondialdehyde/mg protein, and ox-LDL was 13.80 nmol of malondialdehyde/mg protein.

Monocyte separation. Thirty milliliters of blood sample at rest and immediately after exercise was transferred into polypropylene tubes containing sodium citrate. Peripheral blood monocytes were isolated by Dynabead M-450 CD14 (Dynal ASA) using an immunomagnetic selection technique, as described previously (19). Monocytes were resuspended in Hanks' solution with 2 mM $CaCl_2$, pH 7.4, and adjusted to 2×10^5 cells/ml. Analysis of monocyte function was completed within 2 h following cell purification.

Monocyte ROS production. Monocytes (2×10^5 cells/ml) were incubated in 495 μl of Hanks' solution, pH 7.4, with 5 μl of dihydroethidium working solution (final concentration, 5 μM) (Sigma) in a polypropylene test tube for 20 min at 37°C. Following incubation, monocytes were washed and respuspended in Hank's solution, pH 7.4 (2×10^5 cells/ml) (Sigma). For certain experiments, various pharmacological reagents, such as 1, 5, and 10 μM diphenylene iodonium (DPI; a compound that binds to and inhibits flavin-containing oxidase) (Sigma), 10, 100, and 1,000 μM staurosporin A (an inhibitor for protein kinase C) (Sigma), and 1, 5, and 10 μM glibeclamide (a selective blocker of mitochondrial K_{ATP} channel) (Sigma), as well as 10 μM rotenone (Sigma), 2-thenoyltrifluoroacetone (TTFA; Sigma), and antimycin A (Sigma) (i.e., mitochondrial complex I, II, and III inhibitors, respectively) were added to the monocyte suspension, which was then warmed to 37°C for 10 min. Following incubation, these reagent-treated monocytes were washed and immediately added to a polypropylene test tube with and without ox-LDL (final concentration, 10 μg/ml) for 30 min at 37°C. The fluorescence obtained from 5,000 events that represented the monocyte, was determined using a flow cytometer, as described previously (23).

Monocyte SOD activities and GSH contents. The monocyte suspensions (2×10^5 cells/ml) were incubated in the absence or presence of ox-LDL (final concentration, 10 μg/ml) for 30 min at 37°C. Then a mitrochondria/cytosol fractionation kit (Biovision) was applied to separate mitochodria from cytosols of monocytes. In brief, the monocyte suspensions (2×10^5 cells/ml) were incubated with cytosol extraction buffer mix (Biovision) at 4°C for 10 min and then centrifuged at 700 *g* for 10 min at 4°C. The suspension was recentrifuged at 10,000 *g* for 30 min at 4°C, and then the supernatant was collected cytosolic fraction. The pellet was resuspended with mitochondrial extraction buffer mix (Biovision), vortexed for 10 s, and saved as the mitochondrial fraction. Cytosolic and mitochondrial superoxide dismutase (c-SOD and m-SOD, respectively) activities in monocytes were calculated with a commercial SOD assay kit (Cayman). This SOD assay kit utilizes a tetrazolium salt for detecting superoxide radicals produced by xanthine oxidase and hypoxanthine. One unit of SOD is defined as the amount of enzyme needed to exhibit 50% dismutation of the superoxide radical. Additionally, total and reduced-form γ-glutamylcysteinly glycine (t-GSH and r-GSH, respectively) contents in monocytes were measured with commercial GSH colorimeter detection kit (BioVision). This assay was based on the glutathione recycling system by 5,5-dithio-(2-nitrobenzoic acid) (DTNB) and glutathione reductase. DTNB and GSH reacted to generate 2-nitro-5-thiobenzoic acid and GSSG. Therefore, concentration of GSH was determined by measuring absorbance of 2-nitro-5-thiobenzoic acid at 412 nm. GSH was regenerated from GSSG by glutathione reductase and reacted with DTNB again to produce more 2-nitro-5-thiobenzoic acid. Thus total GSH concentration was obtained from this recycling system. This kit also specifically detected the reduced form of GSH by omitting the glutathione reductase from the reaction mixture.

Statistics. Data are expressed as means ± SE. The StatView IV statistical software package was employed for data analysis. Monocyte counts, ROS production, SOD activity, and GSH content at rest and immediately after mild, moderate, and heavy exercise were compared using repeated-measure ANOVA and Tukey's multiple range test. Statistical significance was set at $P < 0.05$.

RESULTS

Leukocyte counts. Heavy exercise significantly elevated levels of total leukocyte counts, including neutrophils, eosinphils, basophils, lymphocytes, and monocytes of its subgroups (data not shown) ($P < 0.05$). Although moderate exercise modestly increased neutrophil and lymphocyte counts ($P < 0.05$), no significant changes occurred for eosinphil, basophil, and monocyte counts. Additionally, no significant changes occurred for all leukocyte subgroups immediately after mild exercise (data not shown).

Monocyte ROS production. ox-LDL induced a significant increase in ROS production of monocytes (Table 2). Heavy

Table 2. *Effects of exercise intensities on ROS production in monocytes*

	LIE	MIE	HIE
Basal MFI			
R	15.8±3.1	18.7±3.8	17.0±3.6
E	14.5±3.9	16.9±4.5	20.3±4.5
ox-LDL treatment MFI			
R	55±7.2*	54.5±6.5*	51.2±6.5*
E	50±5.5*	48.1±5.2*	83.5±8.7*†‡§

Values are means ± SE. R, at rest; E, immediately after exercise; MFI, mean fluorescence intensity; ox-LDL, oxidated LDL; ROS, reactive oxygen species. *$P < 0.05$, basal vs. ox-LDL. †$P < 0.05$, LIE vs. HIE. ‡$P < 0.05$, MIE vs. HIE. §$P < 0.05$, R vs. E.

exercise further enhanced monocyte ROS production by ox-LDL compared with that for moderate and mild exercise ($P < 0.05$) (Table 2). Although enhancement of ox-LDL was suppressed by rotenone (30.5 ± 4.2%), TTFA (42.5 ± 5.6%), and rotenone plus TTFA (62.5 ± 3.5%), it remained unaltered in response to antimycin A (Fig. 1). Furthermore, incubation of monocytes in the presence of DPI, glibeclamide, or staurosporin A also caused a marked concentration-dependent suppression of ox-LDL-promoted ROS production of monocytes ($P < 0.05$) (Fig. 1). Inhibition of ox-LDL-induced monocyte ROS production by DPI and rotenone plus TTFA was enhanced by heavy exercise ($P < 0.05$) (Fig. 2) and was unchanged by moderate and mild exercise (Fig. 2).

Monocyte SOD activity and GSH content. ox-LDL suppressed c-SOD and m-SOD activities ($P < 0.05$) (Table 3) as well as r-GSH and t-GSH contents and r-GSH-to-t-GSH ratio ($P < 0.05$; Table 4) in monocytes. Heavy exercise reduced basal and ox-LDL-treated c-SOD and m-SOD activities, r-GSH and t-GSH contents, and r-GSH-to-t-GSH ratio in monocytes ($P < 0.05$) (Tables 3 and 4). Conversely, moderate and mild exercise did not yield these changes in basal c-SOD and m-SOD activities, t-GSH and r-GSH contents, and r-GSH-to-t-GSH ratio in monocytes, whereas the two exercise regimes

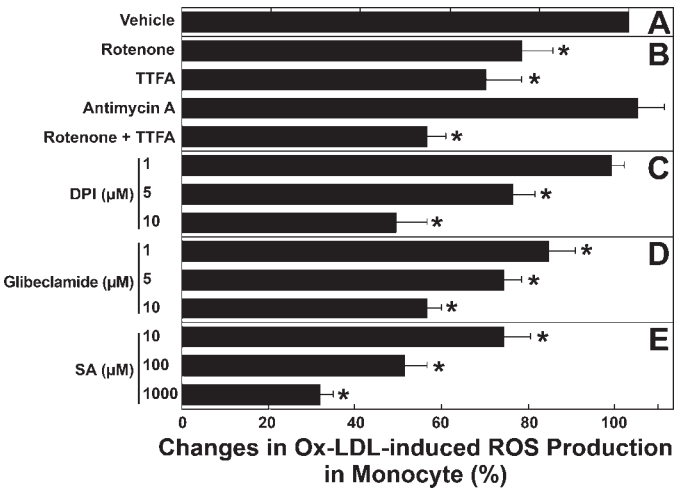

Fig. 1. Effects of vehicle (Hanks' solution; *A*), mitochondrial complex I (rotenone), II (TTFA), and III (antimycin A) inhibitors (*B*), NADPH oxidase inhibitor (DPI; *C*), mitochondrial K_{ATP} channel blockor (glibeclamide; *D*), and protein kinase C inhibitor (SA; *E*) on oxidated LDL (ox-LDL)-induced reactive oxygen species (ROS) production of monocyte. *$P < 0.05$, vehicle vs. various pharmacological reagents.

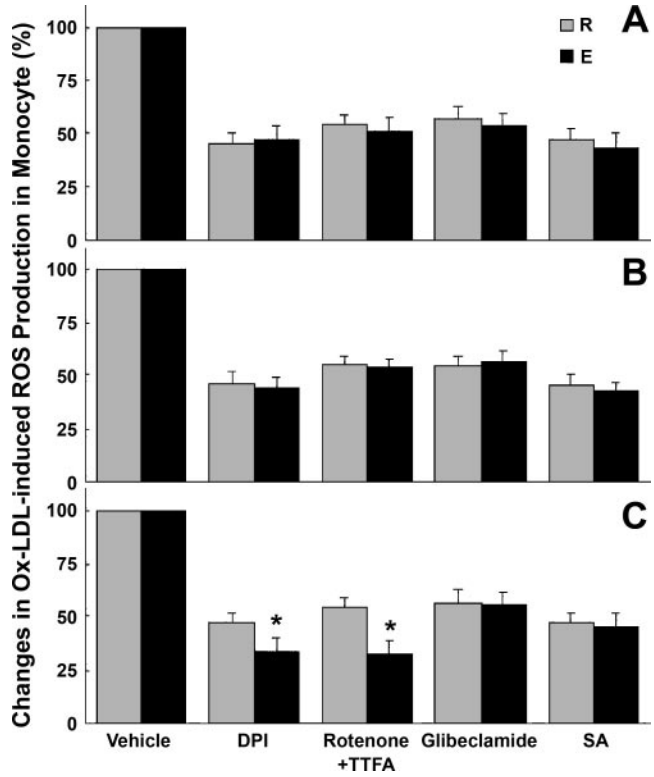

Fig. 2. Effects of mild (*A*), moderate (*B*), and heavy exercise (*C*) on inhibitions of ox-LDL-induced monocyte ROS production by 10 μM rotenone/TTFA, 10 μM DPI, 10 μM glibeclamide, and 1,000 μM SA. R, at rest; E, immediately after exercise. *$P < 0.05$, R vs. E.

prevented monocytes from diminishing c-SOD and m-SOD activity and t-GSH and r-GSH content by ox-LDL treatment (Tables 3 and 4). Additionally, no significant change was observed in plasma SOD activity, t-GSH and r-GSH content, and r-GSH-to-t-GSH ratio after mild, moderate, and heavy exercise (Tables 3 and 4).

DISCUSSION

This study is the first to clearly demonstrate that exercise intensity is an important factor impacting ox-LDL-mediated

Table 3. *Effects of exercise intensities on SOD activities in plasma and monocytes*

	LIE	MIE	HIE
	Plasma, U/ml		
R	6.12±0.18	6.27±0.24	6.34±0.15
E	5.30±0.42	6.14±0.29	6.20±0.38
	Monocyte, U/10^6 cells		
Cytosol			
R, basal	11.33±0.50	11.02±0.48	11.98±0.50
R, ox-LDL	8.99±0.56*	8.56±0.38*	8.31±0.54*
E, basal	10.91±0.96	12.70±0.68	10.77±1.16
E, ox-LDL	9.88±1.27	11.16±0.93	7.65±0.88*†‡
Mitochondria			
R, basal	5.30±0.40	5.35±0.43	5.29±0.35
R, ox-LDL	3.69±0.41*	3.65±0.35*	3.71±0.44*
E, basal	4.92±0.63	4.79±0.47	2.80±0.31†‡§
E, ox-LDL	3.98±0.76	3.94±0.62	2.02±0.20*†‡§

Values are means ± SE. SOD, superoxide dismutase. *$P < 0.05$, basal vs. ox-LDL. †$P < 0.05$, LIE vs. HIE. ‡$P < 0.05$, MIE vs. HIE. §$P < 0.05$, R vs. E.

Table 4. *Effects of exercise intensities on GSH contents in plasma and monocytes*

	LIE	MIE	HIE
	Plasma		
Total, ng/ml			
R	40.4±3.2	39.8±6.9	46.6±4.8
E	46.3±2.7	49.6±6.8	54.3±4.2
Reduced form, ng/ml			
R	1.15±0.16	1.29±0.10	1.16±0.11
E	1.26±0.11	1.33±0.10	1.30±0.18
Reduced-to-total ratio			
R	0.028±0.002	0.032±0.02	0.025±0.003
E	0.027±0.002	0.027±0.03	0.024±0.002
	Monocyte		
Total, ng/10^6 cells			
R, basal	16.6±0.8	16.8±1.1	16.9±0.9
R, ox-LDL	14.1±0.5*	14.0±0.4*	14.2±0.5*
E, basal	16.9±1.1	16.6±1.5	15.8±1.0
E, ox-LDL	15.2±0.9	15.6±1.4	12.1±0.8*
Reduced form, ng/10^6 cells			
R, basal	2.56±0.20	2.53±0.18	2.57±0.09
R, ox-LDL	1.94±0.16*	1.93±0.15*	1.92±0.20*
E, basal	2.54±0.23	2.89±0.25	1.83±0.10†‡§
E, ox-LDL	2.47±0.20	2.35±0.21	1.38±0.12*†‡§
Reduced-to-total ratio			
R, basal	0.154±0.010	0.151±0.011	0.152±0.012
R, ox-LDL	0.137±0.007*	0.137±0.010*	0.135±0.009*
E, basal	0.150±0.012	0.174±0.011	0.116±0.010†‡§
E, ox-LDL	0.163±0.008	0.151±0.012	0.114±0.009*†‡

Values are means ± SE. *$P < 0.05$, basal vs. ox-LDL. †$P < 0.05$, LIE vs. HIE. ‡$P < 0.05$, MIE vs. HIE. §$P < 0.05$, R vs. E.

redox status in monocytes. *1*) Heavy exercise enhances suppression of m-SOD activity and r-GSH content by ox-LDL, whereas both mild and moderate exercise reduce the effects of ox-LDL on m-SOD and r-GSH. *2*) Although heavy exercise increases ox-LDL-induced ROS production from NADPH oxidase and mitochondria in monocyte, both moderate and mild exercise did not influence ox-LDL-induced monocyte ROS production.

Regulation of ROS production in monocytes contributes to the atherosclerotic process (2, 15). Increased ROS level by changed coupling of mitochondrial electron transport chain or activated mitochondrial K_{ATP} channel participate in abnormal vascular responses and subsequent progression of atherosclerosis (9, 12, 13). Additionally, leukocyte-derived ROS was also elevated by the enhancement of NADPH oxidase activity under vascular inflammatory conditions (29). Production of ROS induced by chemoattractants promoted expression of adhesion molecules (e.g., Mac-1) and strengthened adhesion by leukocytes, whereas suppression of ROS production by NADPH oxidase through interfering with PKC-dependent signals limited leukocyte adhesion to endothelium (29). Experimental results in this study showed that ox-LDL increased monocyte-derived ROS. However, treating monocytes with DPI, staurosporin A, rotenone/TTFA, or glibeclamide hindered ROS production induced by ox-LDL. Therefore, ox-LDL enhanced monocyte ROS production, likely by activating membrane-associated NADPH oxidase and changing the coupling of the mitochondrial respiratory chain. Heavy exercise further enhanced monocyte-derived ROS by ox-LDL and also increased the inhibition of ox-LDL-induced monocyte ROS production by DPI and rotenone/TTFA, suggesting that heavy exercise can increase ox-LDL-induced ROS production from both NADPH oxidase and mitochondria of monocytes. However, moderate and mild exercise did not influence the degree of monocyte-derived ROS enhanced by ox-LDL; the NADPH oxidase- and mitochondria-mediated ROS production of monocytes remained unchanged in response to moderate and mild exercise.

Numerous scavenging systems limit cellular ROS levels in leukocyte; i.e., superoxide is dismutated by a family of SODs (such as MnSOD in mitochodria and Cu/ZnSOD in cytoplasm) to H_2O_2, and then H_2O_2 is scavenged into water by glutathione peroxidase in the presence of r-GSH (8). ox-LDL suppresses antioxidative capacity in monocytes by decreasing c-SOD and m-SOD activities and r-GSH and t-GSH contents as well as r-GSH-to-t-GSH ratio in this study. Furthermore, heavy exercise decreased basal and ox-LDL-treated c-SOD and m-SOD activities, r-GSH and t-GSH contents, and r-GSH-to-t-GSH ratio in monocyte. Therefore, heavy exercise decreased levels or activities of these antioxidants in monocytes, possibly predisposing monocytes toward the pro-oxidative status, thereby enhancing ox-LDL-induced ROS production from cytoplasm and mitochondria of monocytes. Although moderate and mild exercise did not change basal c-SOD and m-SOD activities, t-GSH and r-GSH contents, and r-GSH-to-t-GSH ratio in monocytes, diminished SOD and GSH bioavailability by ox-LDL was retarded by the two exercise regimes. Therefore, increased antioxidative capacity of monocytes after mild- and moderate-intensity exercise lowers monocyte activation induced by oxidative stress, which, in turn, typically inhibits monocyte-related atherogenesis.

The amount of oxidative stress induced by physical exercise is determined by the level of free-radical generation and the defensive capacity of antioxidants (8). A previous study demonstrated that mitochondrial lipid peroxidation in skeletal muscle was enhanced after strenuous exercise, accompanied by a loss of protein thiol content (14). A recent investigation by the authors of this study also demonstrated that heavy exercise reduced lymphocyte GSH content and mitochondrial transmembrane potential (27). Their experimental findings were similar with some of the results obtained by this study that evaluated redox status of monocytes. Declining leukocyte GSH level following heavy exercise potentially may result in an accelerated cell efflux or a lowered rate of uptake of precursors and subsequent resynthesis (4, 22). A previous study showed that oxidative stress enhanced glutathione efflux of leukocytes through activating the plasma membrane enzyme γ-glutamyl transpeptidase (4). When moncocytes are treated with ox-LDL, accelerated monocyte GSH depletion by heavy exercise leads to reduced antioxidative capacity of monocytes, subsequently promoting monocyte ROS production induced by ox-LDL. Conversely, a recent work displayed that moderate exercise elevated GSH content and decreased lipid peroxidation in lymphocytes, suppressing H_2O_2-induced oxidative damage of lymphocytes (27). Additionally, regular moderate exercise also suppresses ox-LDL-promoted platelet activation by enhancing nitric oxide release (as an antioxidant) of platelets (26). Moreover, this study also identified an inhibitive effect on diminished SOD activity and GSH content by ox-LDL following mild and moderate exercise. Therefore, mild- to moderate-intensity exercise can plausibly be considered safe and effective for minimizing atherosclerotic risk by promoting antioxi-

dative capacity in monocytes or other atherogenetic-related cells such as platelets and lymphocytes.

In conclusion, ox-LDL-mediated redox status in monocytes is affected by acute exercise in an intensity-dependent manner (i.e., heavy exercise promotes ox-LDL-induced monocyte ROS production, likely by reducing m-SOD activity and r-GSH content in monocytes), whereas mild and moderate exercise attenuate suppression of monocyte antioxidative capacity by ox-LDL. These experimental findings can assist in determining suitable exercise regimes to prevent early atherosclerotic events and further hinder cardiovascular disease progression.

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