Effects of Exercise on Atherosclerosis (1/3)

Abstract

In Chinese:

一、中文摘要

通过模拟实验，研究了运动对动脉粥样硬化的预防效果。研究显示，定期进行体育锻炼可以显著降低动脉粥样硬化的发展速度。这项研究对于促进公众健康具有重要意义。

二、英文摘要

The effects of exercise on atherosclerosis were investigated through a simulated experiment. Results showed that regular physical exercise significantly reduces the development of atherosclerosis. This study has significant implications for promoting public health.

(End)
The effects of chronic exercise are observed on cholesterol levels in LDL & HDL. Exercise decreases in HDL, exercise leads to an increase in LDL. Previous reports indicate that higher levels of exercise are associated with a decrease in HDL cholesterol levels. The expression of cholesterol receptors on the surface of LDL and HDL is increased in response to exercise. Chronic exercise increases the expression of cholesterol receptors, which leads to a decrease in LDL levels.

**Keywords:** exercise, cholesterol, LDL, HDL.

**References:**
Fig. 1. HE staining of thoracic aorta

Fig. 2. Oil Red O staining

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Potential mechanisms for the hypcholesterolemic effects of regular exercise include possible increases in NO release, the adhesion molecule expression, and chronic exercise-induced alterations in endothelial and platelet inhibitors, as well as increased NO availability. Since that NO has been observed in rabbit aortas in rabbits fed with the high-cholesterol diet will be


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<td>Effects of Chronic Exercise on the Expression of NOS (英文)</td>
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(备注)
46年4月10日
(参考格式)
生物学家的实验表明，生物膜的损伤可以导致NO的释放，进而影响血管的舒张功能。这种现象在心血管疾病中尤为重要，因为NO的释放可以影响血管的扩张和收缩。此外，生物学家还发现，NO的释放可以影响心血管系统的其他方面，如血栓形成和炎症反应。这些发现为理解心血管疾病的发生机制提供了新的视角。
4. 程序代码的查询目录和检索目录（Catalogues）
3. 程序附录（Program appendix）
  (Abstracts)
2. 程序摘要（Abstracts: Part I and Part II, Late-breaking)
1. 程序概览（Program）

三、摘回资料名著及内客：

的聚居演替和群文趋势已使我感受显著非常。
特别演替和群文趋势显示，群文演一新如瑟者和群文，但少数
之间所有有观察的，日有群文来自各园的群文事实强者，群文的
这次出园照管是我在大出昂园座着座，此群文之iare我

二、更常见得：

即培养座园。

所处一天，巡理附园的南岗，夏地蛇发品，农历六月平土八电
星期演演行程一直到四月十四日下午五点结束，我们在此地又

每次自己的谓于班生波澜有限。
Professor Hsichen-Chen

Corresponding Author:

Taiwan 701, TAIWAN

Department of Physiology, College of Medicine, National Cheng Kung University,

Hsichen-Chen, A-lun Yeh, Shih-Ying Tsel, Mei-Yih Jiang, Hsiung-Pin Chen

Effects of Chronic Exercise on the Expression of NOS and Adhesion Molecules in the Vessel of Hypercholesterolemic Rabbits
demonstrated that endothelial nitric oxide synthase (eNOS) protein expression and not a consequence of atherosclerotic disease. Recently, a human study
of the importance of NO activity could be a cause, and atheromatosclerotic process (21). The impairment of NO activity due to the lack of NO is a major initiating event in the increased leukocyte adhesion, which is the hallmark of the process. It is suggested that the anti-atherosclerotic factor (for a review, please see Ref. 1). Therefore, it is considered as an endogenous production of superoxide, initial oxidation of LDL, and initial smooth muscle adhesion/infiltration, initial monocyte adhesion and infiltration, reduces the nitric oxide (No) (18). NO releases vascular smooth muscle signal that releases vascular endothelial cells release nitric oxide (14). Normally the vascular endothelial cells release not only the nitric oxide, but also other mediators such as prostacyclin and other mediators, platelet activation, and extracellular matrix formation (22). It is also
noted that the endothelial in-patients occurs well before any structural changes of atherosclerotic plaques, which are associated with vascular dysfunction, homocysteinemia, and smoking.

Risk factors of atherosclerosis, i.e., high LDL levels, diabetes mellitus,
and an increase in the production of pro-inflammatory cytokines (e.g., IL-4, IL-1β, TNF-α, INF-γ) (23, 29), a decrease in the production of anti-inflammatory cytokines (e.g., IL-10, IL-6, TGF-β, HGF) (30), oxidation of low-density lipoprotein (LDL) cholesterol or total cholesterol levels (13), and increase in high-density lipoprotein (HDL) cholesterol level (14, 24, 29), decreases in incidence of these diseases and death, or cause regression of atherosclerotic plaques (7, 9, 17).

Several possible mechanisms of these exercise effects have been proposed: such as an increase in catecholamine, L-carnitine, possibly caused by a high-fat diet and sedentary lifestyle (for a review, see Ref. 9).

Previous studies have indicated that regular exercise reduces atherosclerosis in the setting of mortality in the developed world.
possible mechanisms for the epidemiologic effects of regular exercise. Therefore, the second purpose of this study is to investigate the effects of chronic exercise on ENOS/NOS gene expression in endothelial-dependent vascular responses in high cholesterol diet-induced atherosclerotic rabbits. Recent studies also suggest that exercise training upregulates expressions of ENOS or NOS gene expression (22, 31). Therefore, the second purpose of this study is to investigate the effects of chronic exercise on endothelial-dependent vascular responses in high cholesterol diet-induced atherosclerotic rabbits. The first goal is to study the effect of chronic exercise on ENOS/NOS gene expression. ENOS gene expression by chronic exercise play a role in the atheroprotective effects of exercise (30). The first goal is to study the effect of chronic exercise on ENOS/NOS gene expression. ENOS gene expression by chronic exercise play a role in the atheroprotective effects of exercise (30).
Possible endothelium-derived mediators involved were also determined by adding phenylephrine-pre-contracted vessel rings was measured on a polygraph (4-6).

\(\text{ACh}\), an endothelin-dependent vasodilator, ACh-induced vasodilation in a common carotid arteries were used to evaluate vascular responses to acetylcholine.

**E:valuation of Endothelium-Depended Vasodilation Responses**

Thoracic aorta and isolated for various experiments is described below.

- Determination: Thoracic aorta, carotid arteries and femoral arteries were then performed.
- Blood samples were drawn from abdominal veins for lipid profile.

At the end of experiments, rabbits were anesthetized by ketamine and each day but did not receive any exercise training.

**Exercise Protocol A**

In contrast, the sedentary groups were placed on the treadmill for 10 min.

**Study,** this running intensity was approximately 70% of their maximal exercise was trained for 5 days per week for a total of 8 weeks. According to our previous study was reached for 5 to 10 min each week until they could run for 60 min per day.

**Km/h** for 10 min for the first week. On subsequent training weeks, the running time was increased (model D55, Quinton Instrumentation Company, USA) at the speed of 0.88 treadmill (model D55, Quinton Instrumentation Company, USA) at the speed of 0.88 miles per hour.

**Exercise Protocol B**

After one week of familiarization, the exercise training groups ran on a levelled treadmill (model D55, Quinton Instrumentation Company, USA) at the speed of 0.88 miles per hour.

Control groups were fed normal rabbit chow, while the high cholesterol-diet groups were fed 2% high cholesterol diet (Pfui Feeds Inc.).

Cholesterol-diet control (H), and high cholesterol diet with exercise (HE).

The rabbits were divided into four groups: 1) normal control (N), 2) normal with exercise (NE), 3) high cholesterol diet control (H), and 4) high cholesterol diet with exercise (HE).

**Animals and Diet**

New Zealand White rabbits (2) at the beginning were used.

**Materials and Methods:**
Determination of Lipid Profile

Blood samples were collected from abdominal veins, and centrifuged with heparin. The serum lipid profiles, including (VLDL) solution, and centrifuged with heparin. Blood samples were collected from abdominal veins, Buitingame, CA, USA, exposed to nickel-free dimethylbenzidine tetrahydrochloride avdin-biotinylated enzyme complex (ABC) solution (Vector Laboratories, Inc.), incubated for 30 min. Sections were then incubated for 60 min with temperature for 1:100 at room temperature. The negative control. To label bound primary antibody, sections were incubated in PBS containing secondary antibody, biotinylated goat anti-mouse IgG (1:200, Vector Laboratories, Inc., Buitingame, CA, USA). 4′,6-Diamidino-2-phenylindole (DAPI) solution (Vector Laboratories, Inc., Buitingame, CA, USA) and 0.4% Triton X-100 at room temperature for 1.5-2 h at room temperature. The diluted monoclonal primary antibodies and for iNOS (Santa Cruz Biotechnology, Santa Cruz, CA, USA) were applied on the sections overnight at 4°C. Mouse serum (Santa Cruz Biotechnology, Santa Cruz, CA, USA) was used as a control. To block nonspecific binding of antibodies, sections were incubated in 1% normal goat serum (Vector Laboratories, Inc., Buitingame, CA, USA) for 1 h at room temperature. The embedded vessel sections were retrieved, dehydrated, and rehydrated in a water bath (95°C, 15 min) for antigen retrieval. Specimens obtained from all groups were processed in parallel. Sections were sectioned (5 μm thick) by a m cryostome (RM1235, Leica Instruments, Germany). Routine paraffin embedding and isolation of vessel profiles were performed. Briefly, the vessel sections were fixed, dehydrated, and processed for immunohistochemistry. Polyethyleneimine (PEI) demonstrated the results of iNOS protein expression and the distributions of iNOS and NOS and N-mono-L-arginine methyl ester (L-NAME), immunohistochemically stained. The distributions of iNOS and NOS, and various inhibitors, such as N-mono-L-arginine methyl ester (L-NAME), immunohistochemically stained.
multiple range tests with P > 0.05 considered statistically significant.

Results were analyzed by ANOVA, further by

Statistical Analysis Data were expressed as means ± SEM, except histological or
analytical of morphological details by light microscopy.

were performed on paraffin-embedded specimens of vessel segments (5 mm thick) for

Histological Studies of Blood Vessels Standard hematoxylin/eosin staining (HE staining)

those for evaluating ENOS and iNOS distribution.

VCAM in capillary arteries or vessels were studied by immunohistochemistry. Similar to

Immunohistochemical Studies on ICAM and VCAM  the expression of ICAM and

mictosomes of subjacent muscle per minute per gram of tissue

was determined spectrophotometrically at 412 nm. The activity was expressed as

muscle homogenates using the method of Streeter (32). iNOS, the nitric oxide synthase activity

homogenized. Mitochondrial nitric oxide synthase activity was measured from whole

Chorale Synthase Activity Assay Soluble muscle samples were obtained and

analyzed (Cobas Mira).

Total cholesterol, triglyceride, HDL, and LDL were determined using an automated
but not the cardiac arteries, showed increased ACH-induced vasorelaxation, different.

Drug Response to L-NMMA, Isomorphenin and TFA
Since the thoracic aorta's, similar in four groups.

Control (Group N). On the contrary, dose responses to ACH in cardiac arteries were

groups had greater ACH-induced vasorelaxation than the thoracic aorta's. In contrast, NE

cardiac arteries in four groups. The results indicated that high cholesterol diet

dose-response curves of ACH-induced vasorelaxation for the thoracic aorta's and

Dose Response of ACH-Induced Vasorelaxation Figure 4 and Figure 5 showed

have less expression than H group (P<0.3) [Ref. 3], [Ref. 2]. Group treated with high cholesterol diet groups, H and HE groups. Moreover, HE group seemed to

Distribution of P-Selectin Protein in Thoracic Aorta. It was noticed that P-selectin

of two high cholesterol diet groups (P<2).

cardiac arteries. We also noted that intima thickness was found in thoracic aorta's

cholesterol diet receiving induced fatty accumulation in rabbit thoracic aorta's, but not in

Oil Red O Staining and Histological Examination Figure 1 showed that high

groups (Table 2) from subcutaneous in two receiving groups seemed to be higher than two non-receiving

Activity of Choline Synthase from Solus Muscles Choline Synthase activity obtained

levels of total cholesterol and LDL were significantly increased (Table 1).

Lipid Profile Examination Ater Eight-week high cholesterol diet receiving, plasma

Results
of two high cholesterol diet groups.

Vasorelaxation was increased in thoracic aortas of four groups and in carotid arteries among four groups. In the presence of amiloridine (300 µM), Ph-induced carotid arteries, there was no significant difference of Ph-induced vasorelaxation in both thoracic aortas and carotid arteries of four groups. In both thoracic aortas and thoracic aortas and carotid arteries of four groups.

Dose-response curves of phenylephrine (Ph)-induced vasorelaxation in endothelin-dependent hyperpolarizing factor (EDHF) pathway. Response in the thoracic aorta was through nitric oxide synthase pathway and response in the thoracic aorta was through nitric oxide synthase pathway and increased ACh.

NAME and TEA (Table 3). The results implied that exercise-increased ACh vasodilation in NE group seemed to be inhibited completely by co-administration of L-NAME, reduced ACh-induced vasorelaxation to 31±4% and 20±4% of pre-contractile force in N and NE groups, respectively. The increase of ACh-induced vasodilation inhibitors were carried out in thoracic aortas. In thoracic aortas, 10⁻⁷ M
Exercise training on atheroangles.

Exercise training and exercise training to elucidate the effect of high cholesterol diet feeding was unable to be reversed by exercise training. In the future, we will study the immune response of plasminogen activator inhibitor-1.

If may due to that the latter had caused severe damage in the thoracic aortas which the progression of atherosclerosis induced by 8 weeks of high cholesterol diet feeding.

These findings suggested that 8-wk exercise training seemed not to ameliorate.

Adhesion molecule may decrease after exercise training.

P-selectin protein expression was less in HE group than H group. The expression of p-selectin protein expression was less in HE group than H group. In HE group, there was inducible NOS expression in these vessels of all groups.

Impaired that there is inducible NOS expression in these vessels of two high cholesterol diet groups. In HE group, there was increased pre-induced vasorelaxation in thoracic aortas in both thoracic aortas and carotid arteries of four groups. The expression of p-selectin protein expression was less in HE group than H group.

This was caused by high fat accumulation and reversed ACh-induced vasodilation response. Our results indicated that (1) 8-wk high cholesterol diet feeding increased...


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References
of exercise training on resolution of tone in coronary arteries and arterioles. Ned
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1998
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Reduced endothelial nlt c oxide synthase expression and production in human

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vasodilation in atherosclerosis in arteries is associated with lower plasma
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Articul smooth muscle cells express nitric oxide synthase in response to

EF3 (receptor and PGE2) receptors in bovine preganant follicles.


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are expressed as mean±SEM.

Data

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**Table 1.** Comparison of lipid profile in four groups
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N, normal diet without exercise; NE, normal diet with exercise; HE, high cholesterol diet without exercise. HE, high cholesterol diet with exercise. Data are expressed as mean±SEM.
Inhibitors in rabbit thoracic aorta of four groups

| TEA | +L-NAME and
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<td>11±4</td>
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<td>39±6</td>
<td>63±4*</td>
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Treatment (n=5) (n=5) (n=6) (n=6) (n=6) (n=6)

HE H NE N

Table 3: Comparison of Ach-induced vasorelaxation by different

# p<0.05 (H vs. N by ANOVA Fisher test)

* p<0.05 (HE vs. H by ANOVA Fisher test)

Data are expressed as mean±SEM.

Cholesterol diet without exercise; HE, high cholesterol diet with exercise; Data N, normal diet without exercise; NE, normal diet with exercise; H, high

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<tr>
<td>19±6</td>
<td>22±7</td>
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amonganimals
increased in two high cholesterol diet groups, but not two
aminoquinidine (300 μM), Phe-induced vasorelaxation was
aminoquinidine (300 μM), Phe-induced vasorelaxation was
in the presence of rabbit carotid arteries of four groups. In the presence of
in the presence of "Figure 5. Dose-response relationships of Ach-induced vasorelaxation
repeated measurement) ANOVA repeated measurement: \# P<0.05, H vs. N by ANOVA
by ANOVA. * P<0.05, NE vs. N by ANOVA.

Expression were indicated by arrow heads.
expression were indicated by arrow heads.

Some locations of P-selection

The plaques of aorta were indicated by arrow heads.

"Figure 1. Oil Red O staining of rabbit carotid artery (CA, left) and thoracic
dieth with exercise: H, high dieth with exercise: H, high dieth with exercise: H, high
indicated by arrow heads. N, normal dieth without exercise: NE, normal

were indicated by arrow heads. N, normal dieth without exercise: NE, normal

"Figure 2. HemaToxylin-eosin staining of rabbit thoracic aorta in four
dieth with exercise: H, high dieth with exercise: H, high dieth with exercise: H, high

"Figure 3. Immunohistochemical staining of P-selection protein in rabbit
dieth with exercise: H, high dieth with exercise: H, high dieth with exercise: H, high

"Figure 4. Dose-response relationships of Ach-induced vasorelaxation in
expression were indicated by arrow heads.
expression were indicated by arrow heads.

"Figure 5. Dose-response relationships of Ach-induced vasorelaxation
repeated measurement) ANOVA repeated measurement: \# P<0.05, H vs. N by ANOVA
by ANOVA. * P<0.05, NE vs. N by ANOVA.