*Original Article*

# Low Frequency Regular Exercise Improves Flow-Mediated Dilatation of Subjects with Mild Hypertension

Jiro MORIGUCHI, Hiroshi ITOH*, Sanae HARADA, Kazuo TAKEDA, Tsuguru HATTA**, Tetsuo NAKATA***, and Susumu SASAKI**

**Although exercise is recommended for the primary prevention of hypertension, and although it is generally known to have a beneficial effect on endothelial function, working individuals often find it difficult to maintain a consistent exercise regimen. In the present study, therefore, we examined the effects of infrequently performed exercise on flow-mediated dilatation (FMD), which is an index of endothelial function, in 15 subjects with hypertension (mild hypertensives) and 10 normotensive subjects (normotensives). All subjects performed mild bicycle exercise twice a week for 12 weeks. To assess the FMD, the diameter of the brachial artery was measured using ultrasound at baseline, during reactive hyperemia, and following sublingual administration of nitroglycerin. Measurement of these parameters was performed twice, at the beginning and the end of the exercise program. At the baseline, FMD was significantly lower in the mild hypertensives than in the normotensives. Nitroglycerin-mediated dilatation (NTG-D) was similar in the two groups. The exercise decreased blood pressure in the mild hypertensives, and increased high-density lipoprotein (HDL) cholesterol in both groups. The exercise improved FMD without altering NTG-D in the mild hypertensives, but did not result in any change in the normotensives. Multiple regression analysis revealed that the elevation in FMD was positively associated with changes in HDL cholesterol, and negatively associated with changes in plasma norepinephrine and systolic blood pressure. These findings suggest that regular exercise at a low frequency improves FMD, and thereby endothelial function, and lowers blood pressure in mild hypertensives. (*Hypertens Res* 2005; 28: 315–321)**

***Key Words*: exercise, endothelium, mild hypertension, nitric oxide, vasodilation**

## Introduction

The endothelium of blood vessels plays an important role in the regulation of vascular tone and the maintenance of cardiovascular homeostasis (*1*). Impaired endothelium-dependent vasodilatation has been linked to the pathogenesis of atherosclerotic vascular diseases and acute cardiovascular events (*2*). In another study, impairment of endothelium-dependent vasodilatation was found to be already present in the forearm arteries of hypertensive patients who did not yet have apparent atherosclerotic disease (*3*).

It has been reported that flow-mediated dilatation (FMD) occurs in response to the release of nitric oxide (NO) from endothelial cells (*4*). Accordingly, FMD has recently been used to study the endothelial function of blood vessels in a

From the Kyoto Industrial Health Association, Kyoto, Japan; *Ritsumeikan Medical Service Center, Kyoto, Japan; **Division of Hypertension and Nephrology, Kyoto Prefectural University of Medicine, Kyoto, Japan; and ***Department of Clinical Pharmacology, Kyoto Pharmaceutical University, Kyoto, Japan.

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Address for Reprints: Jiro Moriguchi, M.D., Kyoto Industrial Health Association, 1–7 Narita, Hirono-cho, Uji 611–0031, Japan. E-mail: moriguchi@kyotokojohokenkai.or.jp

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noninvasive manner (*5*). Moreover, it has been reported that impairment of FMD is related to an accumulation of coronary risk factors (*6*). Node *et al*. reported that the plasma concentration of NO in borderline hypertensive patients was lower than that in a control group, but still higher than that in their hypertensive subjects (*7*). Therefore, it would be important to decrease the blood pressure (BP) and to improve the endothelial function in order to prevent cardiovascular diseases in these subjects.

Regular aerobic exercise is recommended for the primary prevention of hypertension and cardiovascular diseases (*8*). Although the beneficial effects of regular exercise on endothelial function in experimental animals (*9*) and healthy young men (*10*) have been reported, the effects of exercise on endothelial function in hypertensive subjects have not been fully clarified. According to the results of the national nutrition survey in Japan in 2002, less than 30% of middle-aged individuals exercised more than twice weekly, a percentage lower than that for the other age brackets. This report suggests that a high frequency of exercise is difficult for the working population in Japan. It is thus important to investigate the effect of low-frequency exercise—*i.e.*, exercise that might easily be carried out by full-time workers—on endothelial function.

In the present study, to determine the effects of regular exercise at relatively low frequency on FMD in subjects with mild essential hypertension, the endothelium-dependent dilatation in the forearm artery was measured by a noninvasive ultrasound method before and after a 12-week exercise program, and comparison was made with the normotensive subjects.

## Methods

### Subjects

Seventeen subjects with mild essential hypertension (mild hypertensives; 13 men and 4 women; mean age±SD, 44.4±10.6 years) were selected from among the office staff of an electric company in Kyoto. Mild hypertension was defined as BP meeting the criterion of hypertension grade 1 of the World Health Organization/International Society of Hypertension blood pressure classification (1999), *i.e.*, systolic BP (SBP) between 140 and 159 and/or diastolic BP (DBP) between 90 and 99 mmHg. BP was measured in a seated position on at least two different occasions during one of the health checkups that are performed biannually for workers in Japan. Four patients who were diagnosed with mild hypertension showed a lower BP, which was classified as a high normal BP from the baseline measurement. We included these data for evaluation purposes. Patients with secondary hypertension, however, were excluded on the basis of clinical history and physical examination. Fourteen age- and sex-matched normotensive healthy subjects (normotensives; SBP $<$130 mmHg and DBP $<$85 mmHg; 10 men and 4 women; mean age±SD, 45.3±7.4 years) were also studied as a control group. Subjects with a history of cardiovascular diseases, diabetes mellitus, or hypercholesterolemia and subjects with a smoking habit were excluded. Patients receiving anti-hypertensive drugs were also excluded. Six subjects (2 mild hypertensives and 4 normotensives) dropped out of the exercise program for various reasons, such as lower back pain, job relocation, and so on. We thus analyzed the records of a total 25 subjects (15 mild hypertensives [11 men and 4 women] and 10 normotensives [7 men and 3 women]) who completed the training program. Prior to the study, all the subjects were essentially sedentary and did not exercise regularly. The study protocol was approved by the Ethical Committee of Kyoto Industrial Health Association and written informed consent for participation was obtained from all subjects.

### Physical Examinations and Blood Sampling

Physical examinations, including measurement of the body fat percentage by biological impedance analysis (body fat analyzer TBF-102; Tanita, Tokyo, Japan (*11*)), and a blood examination were performed before and after a 12-week period of exercise. Four hours after lunch, and following 15 min rest in a supine position, samples of venous blood were taken for the measurement of total cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, plasma glucose, hemoglobin $A_{1c}$, uric acid, plasma renin activity, plasma epinephrine and plasma norepinephrine. BP and heart rate were measured at the left upper arm 3 times using an automatic sphygmomanometer (TM-2421; A&D, Tokyo, Japan) following 5 min rest in the resting position.

### Determination of Exercise Intensity and Training Methods

The maximal oxygen uptake ($V_{O_2\,max}$) was estimated using the modified (*12*) method of Åstrand and Ryming (*13*). Heart rate changes were measured at four different submaximal workloads using an electric bicycle ergometer (ML-1400; Fukuda Electronic, Tokyo, Japan). The exercise intensity for each subject was set at 50% of the estimated $V_{O_2\,max}$, and the exercise intensity was adjusted *via* real-time pulse rate monitoring to maintain a level at 50% of the estimated $V_{O_2\,max}$ during exercise. All the subjects exercised for 60 min twice a week for 12 weeks on electric bicycle ergometers (XL75; COMBI, Tokyo, Japan). According to the exercise performance record, the frequency of the exercise was similar in both groups, *i.e.*, 120.6±3.0 min/week in the mild hypertensives and 119.4±3.0 min/week in the normotensives. Throughout the study, the subjects were advised to make no changes to their lifestyles, including diet, alcohol intake, and recreational physical activity.

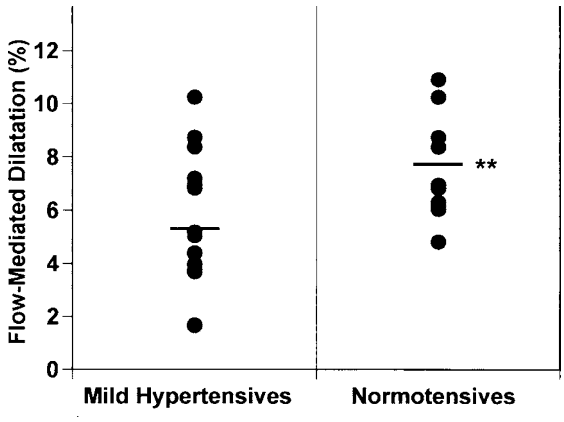


**Fig. 1.** *Baseline flow-mediated dilatation in the mild hypertensives (*n = *15) and the normotensives (*n = *10).* **p < *0.01 compared with flow-mediated dilatation in the mild hypertensives.* n *indicates the number of subjects in each group.*

## Measurement of Brachial Artery Hemodynamics

Measurement of brachial artery hemodynamics was performed while subjects were supine in a quiet, air-conditioned room (at 22°C to 24°C). An electrocardiogram was continuously recorded. The subject's right arm was comfortably immobilized in an extended position to allow consistent access to the brachial artery for imaging. Each of the imaging operations was performed by a single highly skilled sonographer. The brachial artery diameter and flow velocity were imaged using a 7.5-MHz linear array transducer ultrasound system (SSA-380A; Toshiba, Tokyo, Japan), at a location 3–7 cm above the antecubital fossa. The transducer was held at the same point on the upper arm throughout the scan using a stereotaxic clamp. The position of the transducer on the forearm was recorded on the first visit and the same point was used throughout the follow-up study. The images were obtained in a longitudinal view with great care taken to maximize the vessel diameter and provide optimal blood-vessel wall definition. The flow velocity of the brachial artery was measured using a pulsed-Doppler signal at a 70° angle to the vessel with the range gate (l.5 mm) in the center of the artery.

After the resting scan, a pneumatic cuff, placed around the forearm at 10 cm distal to the brachial artery segment for the echo imaging, was inflated above a pressure of 200 mmHg for 4.5 min. The cuff was then rapidly deflated, leading to reactive hyperemia with increasing brachial artery blood flow and resulting in the FMD. For the FMD scans, diameter measurements were taken between 30 and 120 s after cuff deflation, and the maximal diameter was taken. The flow velocity was also recorded for the initial 15 s following cuff deflation. After a 15 min period allowed for vessel recovery, the second control scan was taken at rest. The final brachial artery diameter measurement (nitroglycerin-mediated dilatation: NTG-D) was made 2 to 4 min after sublingual administration of nitroglycerin (300 μg) (*14*).

**Table 1. Baseline Clinical Characteristics in the Mild Hypertensive and the Normotensive Subjects**

| Variables | Mild hypertensives ($n$=15) | Normotensives ($n$=10) |
|---|---|---|
| Age (years) | 42.8±10.1 | 44.8±7.7 |
| Height (cm) | 166.7±8.3 | 164.4±10.2 |
| Body weight (kg) | 66.6±12.0 | 64.7±11.4 |
| Total cholesterol (mmol/l) | 5.32±0.61 | 5.28±0.69 |
| Triglyceride (mmol/l) | 1.89±1.20 | 1.40±0.86 |
| Plasma glucose (mmol/l) | 6.34±1.08 | 6.35±1.14 |
| Hemoglobin $A_{1c}$ (%) | 5.12±0.36 | 5.09±0.36 |
| Plasma renin activity (ng/l/s) | 0.30±0.29 | 0.48±0.20 |
| Plasma epinephrine (nmol/l) | 0.18±0.09 | 0.16±0.13 |
| Plasma norepinephrine (nmol/l) | 1.29±0.62 | 0.90±0.17 |
| Basal vessel diameter (mm) | 5.33±0.71 | 4.87±0.81 |
| Basal blood flow (ml/min) | 164±61 | 151±40 |
| Hyperemia (% increse in flow) | 363±104 | 363±107 |

All results are presented as mean±SD. *n* indicates the number of subjects in each group. Other parameters are shown in Table 2 (mild hypertensives) and Table 3 (normotensives).

The vessel diameter was measured at the end diastole from super-VHS video recordings taken by an observer unaware of the subjects' clinical characteristics. Measurements were taken from the anterior to posterior interface between the media and adventitia. Meanwhile, FMD and NTG-D were determined in terms of the percentage change in diameter relative to the baseline measurements. The mean flow velocity was calculated as the area under this velocity profile curve. Blood flow (ml/min) was then calculated by multiplying the mean flow velocity and the cross-sectional area of the brachial artery based on the diameter. Reactive hyperemia was calculated as the maximal flow recorded in the initial 15 s following cuff deflation divided by the flow recorded during the baseline scan.

The preliminary study of the repeatability of the ultrasound measurements was based on the 16 control subjects who underwent repeat scans. The intra-observational coefficient of variation for the brachial artery diameter at flow-mediated dilatation was 0.38±0.69%, and that for %FMD was 1.29±3.90%.

## Statistical Analyses

All data were expressed as the means±SD. The baseline characteristics of the mild hypertensive and the normotensive subjects were compared using unpaired Student's *t*-test. The parameters measured before and after the exercise training were compared using a paired Student's *t*-test. To clarify factors which affected changes in FMD, multiple regression

**Table 2. Clinical Characteristics before and after the 12-Week Period of Exercise in the Mild Hypertensive Subjects**

| Variables | Mild hypertensives ($n$=15) | |
|---|---|---|
| | Before | 12 weeks |
| Body mass index (kg/m$^2$) | 23.8±2.9 | 23.8±2.9 |
| Body fat percentage (%) | 24.3±3.4 | 24.6±3.8 |
| Heart rate (bpm) | 73.8±11.7 | 68.9±10.6 |
| HDL cholesterol (mmol/l) | 1.31±0.37 | 1.44±0.33* |
| Uric acid (μmol/l) | 338.6±99.0 | 319.6±89.1* |
| Plasma norepinephrine (nmol/l) | 1.29±0.62 | 1.58±0.71 |
| Maximum oxygen consumption (ml/kg/min) | 32.1±6.1 | 34.6±8.8* |
| Basal vessel diameter (mm) | 5.33±0.71 | 5.37±0.68 |
| Basal blood flow (ml/min) | 164±61 | 170±77 |
| Hyperemia (% increse in flow) | 363±104 | 397±129 |

All results are presented as mean±SD. bpm, beats per minute; HDL, high-density lipoprotein. *n* indicates the number of subjects in the mild hypertensives. *$p<0.05$ compared with values before the 12-week period of exercise.

**Table 3. Clinical Characteristics before and after the 12-Week Period of Exercise in the Normotensive Subjects**

| Variables | Normotensives ($n$=10) | |
|---|---|---|
| | Before | 12 weeks |
| Body mass index (kg/m$^2$) | 23.8±3.2 | 23.5±3.0* |
| Body fat percentage (%) | 24.4±4.8 | 23.3±4.9* |
| Heart rate (bpm) | 63.3±7.1 | 62.5±5.7 |
| HDL cholesterol (mmol/l) | 1.41±0.42 | 1.55±0.43* |
| Uric acid (μmol/l) | 324.5±105.0 | 314.6±96.6 |
| Plasma norepinephrine (nmol/l) | 0.90±0.17 | 0.94±0.27 |
| Maximum oxygen consumption (ml/kg/min) | 36.1±6.4 | 40.6±11.6* |
| Basal vessel diameter (mm) | 4.87±0.81 | 4.87±0.81 |
| Basal blood flow (ml/min) | 151±40 | 152±30 |
| Hyperemia (% increse in flow) | 363±107 | 345±89 |

All results are presented as mean±SD. Abbreviations are the same as in Table 2. *n* indicates the number of subjects in the normotensives. *$p<0.05$ compared with values before the 12-week period of exercise.

analysis was performed to examine the association between the change of %FMD and changes in other parameters for all subjects from both groups. The data were processed using the software package SPSS for Windows (version 7.5.1 J; SPSS Japan Incorporated, Tokyo, Japan).

## Results

### Baseline Clinical Characteristics

Both SBP and DBP were significantly higher in the mild hypertensives than in the normotensives (SBP, 142.4±8.7 mmHg *vs.* 111.3±6.0 mmHg, $p<0.001$; DBP, 93.4±7.2 mmHg *vs.* 73.9±8.2 mmHg, $p<0.001$). The FMD, meanwhile, was significantly lower in the mild hypertensives than in the normotensives (5.21±2.01% *vs.* 7.78±2.18%, $p<0.01$, Fig. 1). Other parameters, including vessel diameter and flow parameters, did not differ between the two groups (Tables 1–3). The two groups were well matched in terms of age and body mass index (mild hypertensives, 23.8±2.9 kg/m$^2$; normotensives, 23.8±3.2 kg/m$^2$).

### Effects of Aerobic Exercise on Clinical Characteristics in Mild Hypertensive and Normotensive Subjects

In the mild hypertensives, the 12-week period of exercise reduced both SBP and DBP (from 142.4±8.7/93.4±7.2 mmHg to 127.9±9.8/83.8±6.1 mmHg, $p<0.001$, Fig. 2). Uric acid decreased ($p<0.05$, Table 2), and HDL cholesterol increased following the exercise ($p<0.05$, Table 2). The maximum oxygen consumption increased after the exercise ($p<0.05$, Table 2).

In the normotensives, regular exercise did not significantly change the SBP or DBP values (from 113.3±6.0/73.9±8.2 mmHg to 110.1±5.5/72.2±7.1 mmHg) or the level of uric acid (Table 3). However, the exercise increased the HDL cholesterol ($p<0.05$, Table 3) and maximum oxygen consumption ($p<0.05$, Table 3). Furthermore, the exercise slightly decreased the body mass index ($p<0.05$, Table 3) and body fat percentage ($p<0.05$, Table 3). Other parameters did not change after the exercise program in either the mild hypertensives or normotensives (Tables 2, 3).

### Effects of Aerobic Exercise on Endothelium-Dependent and Independent Dilatation in Mild Hypertensive and Normotensive Subjects

The 12-week period of exercise improved the FMD (from 5.21±2.01% to 8.71±2.34%, $p<0.001$, Fig. 3a) in the mild hypertensives, but not in the normotensives (from 7.78±2.18% to 8.64±2.33%, $p=0.497$, n.s.). On the other hand, regular exercise did not change the NTG-D either in the mild hypertensives (from 15.11±5.25% to 15.68±5.47%, Fig. 3b) or in the normotensives (from 14.75±5.93% to 13.97±4.92%). The vessel diameter and flow parameters did not change after the exercise program in either group (Tables 2, 3).

### Multiple Regression Analysis between the Change of %FMD and Changes in Other Parameters in All Subjects from Both Groups

In the multiple regression analysis, the elevation in %FMD was positively associated with changes in HDL cholesterol, and negatively associated with changes in plasma norepinephrine and SBP (Table 4).

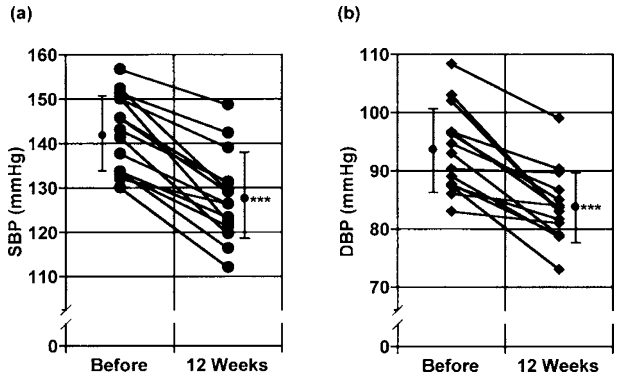


**Fig. 2.** *Individual changes in the (a) systolic (SBP) and (b) diastolic blood pressure (DBP) levels before and after the 12-week period of exercise in the mild hypertensives. Values are expressed as the mean ±SD.* ***$p < 0.001$ *compared with SBP and DBP before the 12-week period of exercise. There were 15 subjects in the mild hypertensive group.*

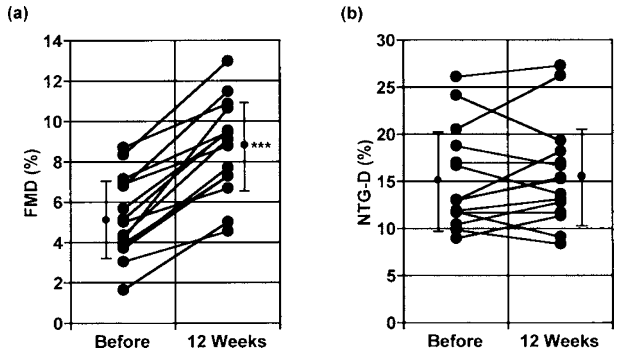


**Fig. 3.** *Individual changes in the response to reactive hyperemia and nitroglycerin before and after the 12-week period of exercise. (a) Flow-mediated dilatation (FMD); (b) nitroglycerin-mediated dilatation (NTG-D) before and after the 12-week period of exercise in the mild hypertensives. Values are expressed as the means ±SD.* ***$p < 0.001$ *compared with FMD before the 12-week period of exercise. There were 15 subjects in the mild hypertensive group.*

## Discussion

We investigated the effects of regular exercise on BP, blood profile and FMD in normotensives and mild hypertensives. In the mild hypertensives, we found that infrequent regular exercise improved FMD, which is known to depend on the ability of the vascular endothelium to release NO (*4*), and lowered BP. In contrast, BP and FMD remained unaltered in the normotensives following exercise. These findings suggest that infrequent regular exercise improves the endothelial dysfunction in the mild hypertensives.

The exercise program increased the $V_{O_2\,max}$ level equally in the normotensives and the mild hypertensives, although our exercise program was relatively less frequent (twice a week) than the exercise programs used in other reports (*15*). As we used only a single exercise protocol in this study, we cannot tell the exact amount of exercise required to improve FMD. This mild exercise protocol, however, was sufficient to improve the $V_{O_2\,max}$ and FMD, at least in the mildly hypertensive subjects. Because continuation of exercise at a high frequency is presumed to be problematic for individuals with full-time jobs, this exercise prescription may represent a new strategy for the prevention of cardiovascular diseases in this population.

To the best of our knowledge, this is the first study to focus on the effects of exercise on FMD in mildly hypertensive subjects. It is common knowledge that mortality from strokes and cardiovascular diseases gradually increases with BP level (*16*). Therefore, it is important to clarify the effects of exercise on endothelial function when using exercise therapy for mildly hypertensive subjects.

Although Higashi *et al*. reported that long-term exercise improves endothelium-dependent vasodilatation through an increase of NO in normotensive as well as hypertensive subjects (*17*), we did not find any improvement in FMD in the normotensives. This difference may have been due to a difference in the methods used to measure endothelial function: Higashi *et al*. (*17*) used plethysmography to measure changes in blood flow based on chemical-mediated vasodilatation. In addition, the relatively low frequency of our exercise program may have affected the results.

The mechanisms by which regular exercise improved FMD were not clarified in this study, but our results suggest several possibilities. The elevation in %FMD was positively associated with changes in HDL cholesterol, and negatively with changes in SBP and plasma norepinephrine by the multiple regression analysis. The HDL cholesterol level increased following the 12-week period of regular exercise. HDL cholesterol has been known to play a role in protecting blood vessels from atherogenesis by preventing the generation of oxidatively modified low-density lipoprotein cholesterol (*18*). A close link between the HDL cholesterol level and the endothelial function in forearm arteries has also been reported (*19*). Since it has been reported that the basal release of NO is increased by regular exercise in hypercholesterolemic patients, and that this effect is independent of the lipid profile modification (*20*), further investigations are necessary to determine the effects of regular exercise on endothelial function related to the HDL cholesterol.

Whether the improvement of the FMD is a cause or a consequence of the BP lowering remains unclear. It has been reported that vasodilatation in response to acetylcholine was blunted in the offspring of hypertensive patients before the clinical manifestation of hypertension compared to that in normotensive subjects (*21*). On the other hand, another study reported a relationship between impairment of endothelial

**Table 4. Multiple Regression Analysis between the Change of %FMD and Changes in Other Parameters in All Subjects**

| Independent variables | Partial correlation coefficient | *p*-value | $r^2$ |
|---|---|---|---|
| Change of HDL cholesterol | 0.589 | 0.000 | 0.116 |
| Change of plasma norepinephrine | −0.765 | 0.000 | 0.309 |
| Change of systolic BP | −0.878 | 0.004 | 0.733 |
| Total | | 0.000 | 0.781 |

FMD, flow-mediated dilatation; HDL, high-density lipoprotein; BP, blood pressure.

function and the relative severity of hypertension (*22*). In the present study, the elevation in %FMD was negatively associated with changes in SBP both in the single regression analysis (data not shown) and the multiple regression analysis. Therefore, we supposed that the improved endothelial function following regular exercise may have contributed to the reduction of BP in our mild hypertensives.

The presence of interaction between endothelial function and norepinephrine is well known (*23*). In the present study, because there was a negative correlation between the elevation of %FMD and the change in the level of norepinephrine in the multiple regression analysis, there is a possibility that the improvement in the %FMD by regular exercise may have been due, at least in part, to the change in norepinephrine.

Another possible mechanism is an increase in vascular shear stress resulting from increased blood flow by exercise, promoting the enhanced formation of NO. It has been reported that increased shear stress stimulates the release of NO (*24*) and that chronic exercise upregulates the expression of the endothelial NO synthase gene (*25*).

These mechanisms might affect the endothelial function of both mild hypertensives and normotensives alike. In agreement with previous studies that showed impairments of NO-dependent vasodilator system in patients with essential hypertension (*3*, *26*), we found that FMD was significantly lower in the mild hypertensives than the normotensives during the baseline examination of this study. We supposed that the effect of exercise on FMD was more marked in the mild hypertensives whose NO-dependent vasodilator system was impaired.

Although BPs still remained higher in the mild hypertensives than the normotensives following the exercise, FMD did not differ between the two groups. As described above, several factors might have affected the improvement of FMD in the mild hypertensives. Hence, FMD might have improved to a normotensive level, through not only lowered BP but also other factors. The small number of the normotensive subjects and the means of implementing the exercise in this study could have affected the results of the statistical analysis. Moreover, since we were unable to perform the overnight fasting blood examination, it is possible that we were unable to sufficiently investigate the influences of several factors.

Although we did not measure parameters concerned with insulin sensitivity, it is possible that the reduction in insulin resistance through regular exercise contributed to the improvement of FMD in the mild hypertensives. Reduced insulin sensitivity in hypertensive subjects (*27*), and reduced FMD in hypertensive patients with glucose intolerance (*28*), have also been reported. Moreover, it has been reported that mild exercise increases the insulin sensitivity in hypertensive subjects (*29*).

Regular exercise reduced uric acid in the mild hypertensives in this study. Since there were no correlations between changes in uric acid and the change in %FMD or in BP during our study, we presume that there is no specific relationship between these parameters.

There were several study limitations to this study. First, although we used a noninvasive method to gauge FMD, we did not study whether FMD was blocked by a specific blocker of NO production or a prostacyclin synthesis inhibitor. The use of such drugs would allow us to draw more specific conclusions relating to the role of NO or prostacyclin in the improvement of FMD as induced by regular exercise. Second, the influence of the menstrual cycle on FMD (*14*) was not considered in this study. Our subjects included 7 women, but 4 of them were in a postmenopausal state. We therefore consider that gender had a comparatively minor influence on the results. Third, body weight decreased slightly in the normotensives, but did not decrease in the mild hypertensives following the exercise. We confirmed that there were no significant changes in alcohol intake and recreational physical activity based on the questionnaire before and after the exercise program in both groups, but did not measure the urinary excretions of sodium. We consider that the relatively low frequency of the exercise and the differences in unmeasured lifestyle parameters in both groups may have played a role in the inconsistencies in these results. Fourth, since we did not employ a sedentary control group for either the normotensives or the mild hypertensives, it is impossible to know whether or not a 12-week sedentary period would also have affected the FMD.

In conclusion, mild regular exercise at low frequency improved the endothelial dysfunction and lowered the BP of our subjects with mild hypertension. The improvement in endothelial function may have been responsible for the reduction in BP. Considering the importance of endothelial function on cardiovascular events, this exercise might represent a therapeutic strategy for the prevention of future atherosclerotic diseases in subjects with mild hypertension, and especially in those with heavy work schedules.

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