Influence of Physical Fitness and Smoking on the Coagulation System in Hypertensive Patients: Effect on Prothrombin Fragment F1+2

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Abstract

Object Recently, prothrombin fragment F1+2 was shown to be a sensitive direct marker of thrombin formation. We examined the effect of lifestyle (including physical activity) on prothrombin fragment F1+2 levels.

Methods Using the results of a questionnaire, the subjects were classified into groups on the basis of multiple medications, smoking, exercise, and drinking alcohol. The prothrombin fragment F1+2 levels were compared between each pair of groups and differences were analyzed using the unpaired t-test. Correlations between each parameter and the systolic and diastolic blood pressure, as well as with prothrombin fragment F1+2, were examined by multiple regression analysis.

Patients The subjects were 109 patients who had essential hypertension without a past history of thrombotic events

Results Smokers (1.47 ± 0.75 vs 0.98 ± 0.46 nmol/L, $p < 0.0001$), and those without regular exercise (1.22 ± 0.59 vs 0.68 ± 0.30 nmol/L, $p < 0.0001$) had higher levels of prothrombin fragment F1+2. Age, lack of exercise, and smoking were significant predictors of a high concentration of prothrombin fragment F1+2. Of the smokers, the patient with a regular exercise had low F1+2 compared with those without regular exercise (0.75 ± 0.20 vs 2.01 ± 0.49 nmol/L, $p < 0.0001$).

Conclusions In patients with essential hypertension, age, smoking, and lack of regular exercise may increase the risk of thrombosis. Even in smokers, a regular exercise routine may reduce the tendency towards thrombus formation.

Key words: hypertension, lifestyle, smoking, F1+2, exercise

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Introduction

Many studies have demonstrated the efficacy of physical fitness for preventing cardiovascular disease and the cost-effectiveness of exercise (1-5). Prothrombin fragment F1+2 was shown to be a sensitive direct marker of thrombin formation (6). In the present study, we examined the effect of lifestyle, including the level of physical activity, on prothrombin fragment F1+2.

Subjects

The subjects were 109 patients with well controlled essential hypertension (the mean blood pressure in an automatic ambulatory monitor was 140 mmHg or less in systole and 90 mmHg or less in diastole) who had no complications (no hyperlipidemia or diabetes mellitus) and no past history of thrombotic events (including elevation of D-dimer levels). Written informed consent for this study was obtained from all subjects. Approval of the study was also obtained from

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Figure 1. The prothrombin fragment F1+2 levels of each pair of groups.

the research ethics committee of St. Marianna University School of Medicine.

Methods

The blood concentration of prothrombin fragment F1+2 was measured using sandwich enzyme immunoassay method (Enzygnost F1+2, Höchst, Frankfurt.). From the results of a questionnaire, the subjects were classified into pairs of groups based on the number of medications taken, smoking status, exercise, and alcohol intake. Regular exercise was defined as physical activity for more than 30 minutes per day or manual labor, and habitual drinking was defined as an intake of more than 20 g of ethanol per day. The prothrombin fragment F1+2 levels were compared between each pair of groups and differences were analyzed using the unpaired t-test. Correlations of the systolic and diastolic blood pressure, body mass index, and other parameters with the prothrombin fragment F1+2 levels were examined by multiple regression analysis. A probability value <0.05 was considered significant. Statistical analysis was done on an Apple Macintosh computer (Japan Apple Computer, Inc., Tokyo, Japan), with the Stat View 5.0 program (SAS Institute, Inc., Cary, NC).

Results

Smokers (1.47 ± 0.75 vs 0.98 ± 0.46 nmol/L, $p<0.0001$, and those without regular exercise (1.22 ± 0.59 vs 0.68 ± 0.30 nmol/L, $p<0.0001$) had higher levels of prothrombin

Table 1. Predictors of a Higher Concentration Prothrombin Fragment F1+2

	β	p
Age	0.314	<0.0001
Smoking(+)	0.589	<0.0001
Regular exercise	-0.524	<0.0001
Systolic blood pressure	0.027	0.7311
Diastolic blood pressure	-0.106	0.1883
Body mass index	0.002	0.8947

fragment F1+2 (Fig. 1). There were no significant differences in body mass index and other parameters between the pairs of groups.

Multiple regression analysis using the concentration of prothrombin fragment F1+2 as the dependent variable versus age, systolic blood pressure, diastolic blood pressure, body mass index, smoking and exercise as independent variables showed that age, smoking, and lack of regular exercise were significant predictors of a higher concentration of prothrombin fragment F1+2 ($p<0.0001$) (Table 1).

Of the smokers, the patients who undertook regular exercise had low F1+2 compared with those without regular exercise (0.75 ± 0.20 vs 2.01 ± 0.49 nmol/L, $p<0.0001$) (Fig. 2).

Discussion

Various coagulation markers are being investigated as risk

Figure 2 The prothrombin fragment F1+2 levels of smokers.

factors for cardiovascular disease. During the process of coagulation, prothrombin fragment F1+2 is generated when prothrombin is activated to form thrombin by the prothrombinase complex. As a marker of thrombin formation, F1+2 has clinical utility for assessing the risk of thrombosis and for monitoring the efficacy of anticoagulant therapy (7). Daily physical activity was suggested to prevent various thrombo-embolic events examined in a cross-sectional study in a previous report (8). Additionally, it is well established that physical exercise may improve metabolic status.

In this study, we examined the influence of several lifestyle factors on the plasma level of prothrombin fragment F1+2 in hypertensive patients. Smoking, alcohol, exercise, and use of multiple medications were all examined. We found that age, smoking, and lack of regular exercise were significant predictors of a higher concentration of prothrom-

bin fragment F1+2. Previous reports regarding predictors of a higher concentration of F1+2 showed positive associations with age (9), sex (9), smoking (9, 10), race (9), and a history of ischemic heart disease (11). The relationship between lifestyle and the concentration of F1+2 was also assessed in the Caerphilly study (12), showing that smoking was a positive predictor of a higher concentration of F1+2, but so was leisure and work activity. In the Caerphilly study, leisure activity only showed a negative association with D-dimer levels. This difference between our findings and those of the Caerphilly study may result from the selection of subjects since the Caerphilly study was population-based and our study only assessed hypertensive patients.

Additionally, we found that regular exercise may reduce the tendency for thrombus formation even in smokers. This finding supports the health benefits of exercise in hypertensive smokers.

Study Limitations

The important limitations of this study are the small number of subjects and the fact that we did not evaluate other coagulation factors. In the future, investigation of other parameters, including hemolytic factors, and clinical outcome observation should be performed.

Conclusions

In patients with essential hypertension, smoking and lack of regular exercise may increase the risk of thrombosis. Regular exercise may reduce the tendency for thrombus formation even in hypertensive smokers.

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