Muscle Fiber-Type Distribution as a Predictor of Blood Pressure
A 19-Year Follow-Up Study
Miika Hernelahti, Heikki O. Tikkanen, Jouko Karjalainen, Urho M. Kujala

Abstract—The known association between physical activity and low blood pressure may be influenced by inherited characteristics. Skeletal muscle consists of type I (slow-twitch) and type II (fast-twitch) muscle fibers, with proportions highly variable between individuals and mostly determined by genetic factors. A high percentage of type I fibers (type I%) has been associated with low blood pressure in cross-sectional studies. We investigated whether type I percentage predicts future blood pressure levels and explains part of the association between physical activity and blood pressure. At baseline, in 1984, muscle fiber-type distribution, physical activity, and body mass index (BMI) were determined in 64 healthy men (age, 32 to 58 years). At follow-up, in 2003, blood pressure, physical activity, and BMI were determined in these men. In subjects without antihypertensive medication (n=43), type I percentage accounted for 5%/18% of the variation in systolic/diastolic blood pressure. A high type I percentage predicted, independent of both baseline (in 1984) and follow-up (in 2003), physical activity, BMI, and low systolic and diastolic blood pressure. Adjusted for all baseline covariates, a 20-unit higher type I percentage predicted a 11.6-mm Hg lower systolic blood pressure (P=0.018) and a 5.0-mm Hg lower diastolic blood pressure (P=0.018). High levels of physical activity in 1984 predicted low diastolic blood pressure, but this association was lost when type I percentage was included into the model. A high proportion of type I fibers in skeletal muscle is an independent predictor of low blood pressure and explains part of the known association between high levels of physical activity and low blood pressure. (Hypertension. 2005;45:1019-1023.)

Key Words: blood pressure ■ exercise ■ hypertension ■ muscles

Hypertension, an important risk factor for cardiovascular diseases, shortens life expectancy. Low blood pressure (BP) levels and reduced risk for hypertension are associated with leisure time physical activity (LTPA) and fitness. These associations may, however, be influenced by inherited characteristics.

BP is the product of cardiac output and total peripheral resistance. Peripheral resistance, and thus also BP, is influenced by the properties of skeletal muscle, more specifically its percentage of type I fibers (type I%). Skeletal muscle consists of type I (slow-twitch) and type II (fast-twitch) muscle fibers. The type I% in the vastus lateralis muscle (the muscle most commonly studied) is highly variable between individuals, ranging from 13% to 96%, with a population mean of 50%, and is mostly determined by genetic factors. Type I fibers have a higher oxidative capacity than type II fibers. Muscle fiber-type proportions differ between elite athletes in various types of sports. Endurance sports athletes have a high type I%, but speed and power sports athletes have a preponderance of type II fibers. In nonathletes as well, high, mainly endurance-type, LTPA levels are associated with a high type I%. Former elite endurance athletes have lower risk for hypertension in middle age than do controls, and those with natural ability in endurance sports use less medication for hypertension than do those with natural ability in speed and power sports.

Hypertensive subjects show a lower type I% than do normotensive subjects, and type I% and BP are negatively correlated in cross-sectional studies. To our knowledge, no studies have examined type I% as a predictor of future BP. Our hypothesis was that type I% is a predictor of BP and partly explains the known association between high LTPA and low BP. To test this hypothesis, we analyzed, in a group of Finnish males, type I% and assessed their body composition and LTPA; after a follow-up of 19 years, we measured BP.

Methods

Subjects
In 1984, 79 apparently healthy men, using no regular medications, participated in our baseline examinations. They were originally...
recruited from private companies in Helsinki and were offered a guided exercise program supported by their employers. Their LTPA level varied from sedentary to regular jogging, but none was a competitive athlete. Of these 74, 64 (86%) agreed to participate in a new set of measurements went out to 74 subjects: 4 had died and 1 had moved abroad. Of these 74, 64 (86%) agreed to participate in examinations in 2003.

**Collection of Data**

At baseline, in 1984, the type I% of each subject was analyzed from samples taken from the vastus lateralis muscle by needle biopsy. The muscle samples were stained for actomyosin ATPase and preincubated at pH 4.3. Type I and type II fibers can then be separated.

At baseline, body mass index (BMI) was calculated as weight divided by height squared (kg/m²). A personal interview provided the data for assessment of LTPA as intensity (in metabolic equivalents of oxygen consumption [MET]) \( \times \) duration \( \times \) frequency of activities, expressed as MET-hours/week.

At follow-up, in 2003, BP was measured in the morning by the same person, a trained nurse, by use of a standard mercury manometer. After a 5-minute rest, the measurements were made from the right arm, with the subjects sitting in a quiet room. Two measurements were made for each subject, with the lower result (lower mean arterial pressure) was recorded. The subjects were asked to refrain from drinking alcohol for 24 hours and from smoking or exercise for 8 hours before the measurements.

At follow-up, BMI was calculated similarly as at baseline. LTPA, in MET-hours/week, was assessed by the Kuopio Ischemic Heart Disease Study (KIHDS) 12-month physical activity questionnaire. Both total LTPA volume and volume of exercise activities (household activities and such excluded) were calculated. The subjects’ use of alcohol was recorded as frequency and quantity of different beverage types, and then converted into grams of absolute alcohol per day.

All measurements and interviews were made blinded to baseline data. The study was approved by the ethics committee of the Joint Authority for the Hospital District of Helsinki and Uusimaa. The subjects gave informed consent. The procedures followed were in accordance with institutional guidelines.

**Statistical Analyses**

Analyses were designed to test the hypothesis that type I% predicts BP levels. Multiple regression analyses were used. Age was included as a covariate in all analyses. Systolic BP (SBP) and diastolic BP (DBP) were dependent variables. The main analyses were made with type I% as a predictor of physical activity was assessed by Pearson correlation tests and multiple regression analyses with total LTPA and exercise activities in 2003 as dependent variables. Furthermore, the percentage of variation in BMI that type I% accounted for was assessed by \( r^2 \) (Pearson correlation coefficient). All statistical significance tests were 2-tailed.

**Results**

The characteristics of study subjects are shown in Table 1. Mean type I% was 57.3% among subjects without antihypertensive medication (n=43) compared with 53.2% among those using medication (n=21); \( P=0.35 \) for difference in means.

Type I% accounted for 5% of the variation in SBP and for 18% of the variation in DBP in subjects without any antihypertensive medication.

In subjects without any antihypertensive medication, high type I% was significantly associated with low SBP and low DBP (Table 2 and Figure). After adding baseline covariates, ie, LTPA and BMI in 1984, into the model, type I% was the only significant predictor of both SBP and DBP. SBP was 0.58 mm Hg and DBP 0.25 mm Hg lower per 1 U higher type I%, corresponding to a 11.6/5.0-mm Hg lower SBP/DBP per every 20 U higher type I%. When cross-sectional data on LTPA (including alternately either exercise activities or total LTPA), BMI, and alcohol use in 2003 served as confounding factors, type I% was still inversely associated with both SBP and DBP. Furthermore, including subjects with antihypertensive medication changed no results (Table 2).

When analyzed separately from type I%, high LTPA at baseline was associated, adjusted for age and baseline BMI, with low DBP. With only those using no antihypertensive medication included, an increase of 1 MET-hour/week was associated with 0.099 mm Hg lower DBP (95% confidence interval, 0.19 to 0.01; \( P=0.040 \)), corresponding to a 2.0-mm Hg lower DBP per every 20 MET-hours/week higher (corresponding to \( \approx \) 2 hours of jogging per week). LTPA at baseline was not associated with SBP; the regression coefficient, adjusted for age and baseline BMI, was \( -0.15 \) (95% confidence interval, \(-0.37 \) to 0.08; \( P=0.19 \)). When type I%
was added to the model, type I% was a significant predictor of DBP (Table 2) and the association between LTPA in 1984 and DBP was actually lost (regression coefficient for LTPA −0.24 [95% confidence interval, −0.13 to 0.08; P = 0.66).

Table 2. Association Between Muscle Fiber-Type Distribution (Type I%) and Follow-Up SBP and DBP

Adjusted for Baseline and Follow-Up Data

<table>
<thead>
<tr>
<th>Subjects without antihypertensive medication (n = 43)</th>
<th>Model</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>−0.40 (−0.77, −0.03), P = 0.006</td>
<td>−0.23 (−0.38, −0.07), P = 0.005</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>−0.58 (−1.06, −0.11), P = 0.018</td>
<td>−0.25 (−0.45, −0.05), P = 0.018</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>−0.53 (−0.97, −0.10), P = 0.017</td>
<td>−0.25 (−0.44, −0.06), P = 0.011</td>
</tr>
<tr>
<td>All subjects (n = 64)</td>
<td>1</td>
<td>−0.39 (−0.71, −0.08), P = 0.016</td>
<td>−0.15 (−0.27, −0.03), P = 0.014</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>−0.42 (−0.74, −0.10), P = 0.011</td>
<td>−0.16 (−0.28, −0.04), P = 0.011</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>−0.65 (−1.06, −0.25), P = 0.002</td>
<td>−0.17 (−0.33, −0.01), P = 0.034</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>−0.48 (−0.83, −0.12), P = 0.010</td>
<td>−0.16 (−0.30, −0.02), P = 0.025</td>
</tr>
</tbody>
</table>

Adjusted regression coefficients (with 95% confidence intervals and P) for type I%.

Exercise activities or total LTPA at follow-up were not associated with BP.

Type I% was a significant predictor of exercise activities in 2003, with a correlation of 0.47 (P < 0.001) between these 2 characteristics (all subjects, n = 64). The correlation between type I% and volume of total LTPA (including household activities) in 2003 was 0.27 (P = 0.031). These results persisted also when adjusted for age. Among those whose type I% was <50% (n = 19), mean volume of exercise in 2003 was (in MET-hours/week) 19.4 (standard error of mean, 3.3), whereas among those whose type I% was ≥50% (n = 45), it was 35.9 (standard error of mean, 3.5; P = 0.006 for difference between groups).

Discussion

Muscle fiber-type distribution at baseline was a significant predictor of BP at follow-up 19 years later. A high type I% was associated with low SBP and low DBP. And interestingly, after adjusting either for other baseline data, ie, LTPA and BMI in 1984, or for cross-sectional data, ie, LTPA, BMI, and use of alcohol in 2003, this association persisted.

To our knowledge, no reports on type I% as a predictor of future BP or risk of hypertension as yet exist. Only 1 study has taken LTPA into consideration when investigating the cross-sectional association between type I% and BP or hypertension. Our findings are in accordance with cross-sectional reports in which type I% and BP are inversely correlated, and hypertensive subjects have a type I% lower than that of normotensive subjects. Both these studies found a correlation between mean arterial pressure and type I% when examining hypertensive subjects and normotensive subjects separately; however, no results were reported for the groups combined. Correspondingly, Hedman et al reported no correlation in the whole study group between BP and type I%, but in the hypertensive group, a high type I% was related to low mean arterial pressure. This result persisted also when controlling for obesity and LTPA. Type I% did not differ between hypertensive subjects and normotensive subjects in that study, nor in another study that also found no association between the proportion of IIb fibers and mean BP.
The fact that type I% is associated with volume of baseline LTPA, mainly of endurance type, as reported earlier for this sample,17,18 and that the association between baseline LTPA and DBP was lost when including type I% into the model suggest that the known association between LTPA and low BP, or low risk of hypertension,7,8 may at least in part be caused by fiber-type distribution. Hence, type I% may cause a genetic selection bias in observational studies on LTPA and hypertension, and also on LTPA and coronary heart disease or stroke,24 because hypertension is an important risk factor for both.32–35 These conclusions require the assumption that type I% does not change significantly with aerobic training. Although the metabolic characteristics, such as the oxidative capacity or mitochondrial density, of the muscle fibers do change with training and some findings indicate that minor changes in fiber type distribution may occur with training, the current conclusion is that type I% is rather resistant to change along with alterations in aerobic activity.12,36,37

A mediating factor for the association between a high type I% and low BP is that the higher the type I%, the lower the total peripheral resistance.15 Factors behind the low resistance are poorly known. One possible explanation has been reported: compared with type II fibers, the number of capillaries surrounding type I fibers is higher.38 Whether this association is independent of LTPA remains, however, unknown. Furthermore, compared with normotensive subjects, hypertensive subjects have a lower capillary density,29,39 and the lower the capillary density, the higher the increase in BP from 50 to 70 years of age.29 Other mechanisms explaining the low peripheral resistance may exist.

We studied the main muscle fiber types: type I and type II. Type II fibers can be further classified by ATPase staining into IIa and IIb fibers.25 The metabolic characteristics of type IIa fibers are intermediate between type I and type IIb fibers.25 Studies investigating the association between fiber type distribution and BP or occurrence of hypertension have, however, found the proportions of the main fiber types to be important, whereas the subclassification of type II fibers into IIa and IIb provides no additional information.10,22,20,30

A limitation of the present study is that the subjects were not a randomly selected population sample. They were a sample likely to provide variation concerning type I% because both sedentary men and active joggers were recruited. Some bias may be present because the subjects volunteered to participate in an exercise training program. If any, the effect of such bias should, however, be that the result is diluted, not exaggerated. Furthermore, at baseline, in 1984, data were collected to study the interrelations between type I% and physical activity, blood lipids, and sex hormones. Unfortunately, BP measurements were not performed at that time. Another limitation of the present study is the lack of follow-up muscle biopsies. Thus, we were not able to assess whether environmental factors may have influenced type I%. Nor were changes in oxidative properties of the muscle fibers assessed. The aim of the present study was, however, to investigate type I% as a predictor of future BP.

Perspectives

A high proportion of type I muscle fibers in skeletal muscle is a predictor of low BP levels. This association between type I% and BP is independent of age, LTPA, and BMI. Because type I% seems to explain part of the association between endurance-type LTPA and low BP, the possibility of selection bias in observational studies on LTPA and hypertension should be taken into consideration. Intervention studies have shown that individual responses of resting BP to exercise training are highly variable, and in part family-aggregated and genotype-dependent.40,41 The possible role of type I% in predicting this response should be investigated.

Acknowledgments

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References


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