Statistical Evaluation of Endurance-training Effects on Systolic Blood Pressure in Elderly People Using a Single-case Design

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We evaluated the effects of endurance training on systolic blood pressure (SBP) in elderly people individually, by using a single-case study design and a statistical technique, e.g., the randomization test. Six people (4 females and 2 males, 60-77 yr) participated in 12-week endurance exercise training (cycling at 80% of the work rate corresponding to the ventilatory threshold, 30-min, 5-day/wk) and recorded their own daily SBP. The mean SBP in all subjects was significantly lower than the baseline after the 7th training week ($P < 0.05$). Individual changes in SBP with training varied among subjects. The earliest and latest occurrences of significant training effects were in the 3rd training week (-6 mmHg) and the 11th training week (-5 mmHg). In the subject who had the highest SBP at the baseline, SBP decreased 12 mmHg in the 12th training week. The subject who had the lowest SBP at the baseline (99 mmHg) did not show significant changes in SBP throughout training. We concluded that the randomization test in the single-case study design was useful to evaluate individual training effects on SBP.

Keywords: blood pressure, endurance training, aging, randomization test

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1. Introduction

Regular exercise inhibits the decrease in physiological (e.g. cardiorespiratory, musculoskeletal) function with aging. To make such training more effective, it is essential to evaluate changes in physiological function with training individually and regularly revise the training program. For this purpose, it is efficient to evaluate the training effect individually and objectively (i.e., using statistical analysis).

In time-series data for a single subject, the assumption of independence of observations often is not met. Successive observations in a time series tend to be serially dependent [Kazdin (1984)], so in conventional analysis, the method was to assess the serial tendency by visually observing graphs. This method involves a serious problem in objectivity and reliability of the assessment of experiment effects [Kazdin (1984)]. To

cope with these problems, recently, statistical analysis methods have been developed for use in single-case study design. One is the randomization test, which is a nonparametric test having no assumption concerning the population [Edgington (1995)]. This method is not premised on random sampling of data from the population and normal distribution, and serial dependence of data can be disregarded. Because of these factors, the randomization test has been applied to evaluate the condition of athletes in which individual variation is more important than the variation of the group average [Nishijima et al. (2000)].

Increases in systolic and pulse pressure with aging may be independent risk factors in cardiovascular diseases [Millar et al. (1999), Franklin et al. (1999)], making it important to control blood pressure in the elderly people adequately. Validity of regular exercise training for reducing systolic pressure is substantiated by

studies with hypertensives [Boyer and Kasch (1970), Kiyonaga et al. (1985), Nelson et al. (1986), Motoyama et al. (1998)] and normotensives [Braith et al. (1994)] as the subject. Kiyonaga et al. (1985) reported that a reduction of 20 mmHg in systolic pressure was seen in 50% of patients with essential hypertension after 10 weeks and in 78% after 20 weeks of aerobic exercise training (50% of maximal oxygen uptake). These results partly suggested that the time of occurrence and degree of the training effect vary with the individual.

Using the randomization test for single-case study design, we evaluated the depressor response in systolic pressure with endurance-training in the elderly, examining whether this method is valid for assessing individual training effects.

2. Methods

2.1. Subjects

Subjects were 6 elderly people (3 males and 3 females, 60-77 years) who had no cardiovascular disease and satisfactorily completed initial screening were studied. None were smokers or took any pharmacological agent. We explained the contents and risk of the experiment and obtained their written consent.

2.2. Training

Subjects performed endurance training for 30 minutes using a bicycle ergometer for 12 weeks (May to July 2001). The training intensity was 80% of the exercise load corresponding to the ventilatory threshold measured before the beginning of training. Training was five times a week (training in exercise class: twice a week, at home: three times a week).

2.3. Body Mass, Body Fat, and Peak Oxygen Uptake

Body mass, %body fat, peak oxygen uptake ($\dot{V}O_2$ peak) and oxygen uptake at VT ($\dot{V}O_{2VT}$) were measured before the beginning of training and after 12 weeks. Body mass was measured using a digital weight scale (UC-300, AND Co.) and %body fat was measured using an impedance body fat meter (HBF-302, Omron Co.). $\dot{V}O_{2peak}$ and $\dot{V}O_{2VT}$ were measured by exercising an incremental load test (ramp fashion). Criteria for exercise suspension included at least one of the following: (1) achievement of age-predicted maximum heart rate, (2) systolic pressure > 250mmHg, and (3) impossible to continue pedaling because of limb fatigue. No subject in the study had a rise in blood pressure that was a condition for exer-

cise suspension. Electrocardiography from the rest phase to the finish of exercise was recorded by an electrocardiograph (ML-4500, Fukuda Electronic Co.), blood pressure by a continuous automatic tonometer (Portapres, TNO-TPD, Biomedical Instrumentation Co.), and expiration gas by an aeromonitor (AE300S, Minato Medical Science Co.). Oxygen uptake and carbon dioxide output were recorded breath by breath and the average for 15 seconds each was calculated. $\dot{V}O_{2peak}$ was defined as the highest $\dot{V}O_2$ achieved during the test. $\dot{V}O_{2VT}$ was determined with gas-exchange data using the V-slope method [Beaver et al. (1986)].

2.4. Blood Pressure Measurement

Subjects measured daily blood pressure themselves using an automatic tonometer (HEM-634, Omron Co.) at home from at least 2 weeks before the beginning of the training period to the end as daily as possible. Measurement was done once a day, sitting, with sufficient rest. For measurement time, we directed subjects to take measurements, if possible, 30 minutes after breakfast as the standard.

2.5. Randomization Test

The randomization test is not premised on normal distribution of data and random sampling of data from a population, but it is statistical analysis based on random assignment of intervening conditions Edgington (1955), Nishijima et al. (2000)]. Serial dependence of data is not a problem. It assesses how extreme observations are, obtained on the hypothesis that there is no effect of intervention, when compared to statistics calculated in each combination of probable random assignment. Actual procedures are as follows:

(1) To state hypothesis (the null hypothesis is that there is no difference in processing effects by the difference between baseline and intervention phase), (2) To set the level of significance α , (3) To decide assignment of intervening conditions, (4) To collect data and obtain statistics (difference of selected variables between baseline and intervention phase), (5) To randomly assign intervening conditions and calculate test statistics for all combinations, and obtain the distribution of descriptive statistics, (6) To investigate how many combinations of intervening conditions there are which are capable of obtaining the value over actual observations, and to calculate P .

Assignment of intervening conditions included assigning intervening conditions (with intervention and without intervention, intervention A and intervention B, etc.) perfectly at random (perfect random alterna-

tion) and dividing intervening conditions by a certain period (blocked random alternation), as advanced analysis of the former. In both cases, the significance of the intervening effect is assessed by what extreme value the test statistics, obtained by actual experiment conditions, shows among all test statistics obtained by randomly assigning intervening conditions. For example, if four data points are obtained with each of intervening conditions A and B, the number of possible combinations is $8!/4!4!=70$, assuming that intervention is at random. If the difference between actual intervening conditions A and B is the third largest among 70 combinations, P is $3/70(=0.04)$.

Test statistics are the difference of the average of systolic pressure between the baseline period (without intervention) and the training period (with intervention), and when this value is significantly large, training is assessed effective. To detect the occurrence phase of blood pressure reduction, data was blocked by units of two weeks because a previous study by a group study model [Kiyonaga et al. (1985)] showed that blood pressure decreased from the relatively early phase after the beginning of training. The baseline period is two weeks just before the beginning of training. If long consecutive holidays are included in this period, the baseline period was set for two weeks before them. The training period was divided into 6 phases of two weeks each after beginning, and when at least 8 observation data points were obtained, the test was done. For one subject, blood pressure measurement and training were not done at all in the fifth phase, so the observation period was prolonged for two weeks.

2.6. Statistics

The measurement values are shown in average $\pm$ standard error. In analysis of the group study model, t-test with correspondence was used, and body mass, %body fat, $\dot{V}O_{2peak}$ and $\dot{V}O_{2VT}$ were compared before and after the training period. For the systolic blood pressure, the variation of averages during the baseline period and each training phase was evaluated by using analysis of variation by replication measurement.

In the examination of the single-case study model, to verify serial dependence of variation of systolic pressure throughout the observation period, auto-correlation coefficient with a lag of 1 was calculated for data of each day. Next, to detect the occurrence phase of the blood pressure reduction effect individually, by using the randomization test, the difference of averaged systolic pressure between the baseline period and training period of each subject was calculated. Application software RANDIBM.EXE [Edgington (1987)]

Table 1. Auto-correlation of systolic blood pressure.

Subject	Auto-correlation coefficient	P value
A	0.069	0.568
B	0.310	0.004
C	0.329	0.002
D	-0.053	0.653
E	0.334	0.002
F	0.491	< 0.0001

was used for this test. The statistical level of significance was set at 5%.

3. Result

The training frequency was five days a week in principle, but the level of attainment varied with the individual. The maximum was 4.4 days/week, the minimum 2.4 days/week, and the overall average 3.1 days/week.

The result of the group study model is shown below. Body mass and %body fat decreased with training (body mass: 56.2 ± 1.7 vs. 54.8 ± 2.3 kg, $P=0.094$; %body fat: 27.7 ± 2.2 vs. $24.3 \pm 2.9\%$, $P=0.086$). $\dot{V}O_{2peak}$ and $\dot{V}O_{2VT}$ showed a significant increase ($\dot{V}O_{2peak}$: 24.4 ± 1.9 vs. 27.3 ± 1.1 ml/kg/min, $P<0.05$; $\dot{V}O_{2VT}$: 13.2 ± 1.1 vs. 17.2 ± 1.1 ml/kg/min, $P<0.05$). Systolic pressure decreased gradually after the beginning of training and was significantly low after the fourth phase compared to the baseline period (**Fig.1**).

The result of the single-case study model is shown below. **Table 1** shows the auto-correlation coefficient of systolic blood pressure of each subject during the observation period. For four subjects, a significant auto-correlation coefficient was observed. **Fig.2** shows individual results of examination of variations in systolic pressure throughout the training period using the randomization test. Except for one subject with the lowest value in the baseline period (99mmHg), significant depressor responses were found in all subjects. However, the phase of occurrence of significant reduction varied with the individual. The occurrence phase and the number were: the second phase (third to fourth week after the beginning of training), one; the third phase, (fifth to sixth week), two; the fourth phase (seventh to eighth week), one, and the sixth phase (eleventh to twelfth week), one. One subject with occurrence of a significant depressor response in the second phase and one of two with occurrence of a significant depressor response in the third phase had high systolic pressure in the baseline period (142mmHg and 137mmHg).

Fig. 1. Changes in systolic blood pressure with endurance exercise training. Data are mean values of whole subjects and SE. *: $P < 0.05$ vs. baseline.

The oldest subject (77 years) who had the highest training frequency (4.4 days/week) showed the highest increasing in VO_2peak and the largest depressor response.

4. Discussion

We examined the variation of systolic pressure with endurance training in the elderly, using two experiment designs of the group study model, the single-case study design. After the beginning of training, systolic pressure gradually decreased, and in the group study model, a significantly low value was shown after the fourth phase (seventh to eighth week). When examining the variation of systolic pressure individually in single-case study design, except for the subject with the lowest value in the baseline period, systolic pressure was reduced by training in all subjects. For the subject with the earliest occurrence of reduction, it was reduced by 6mmHg in the second phase (third to fourth week) and statistical significance was confirmed. The phase of occurrence of such significant reduction varied from the third phase to the sixth phase. Thus, the effect of training on systolic blood pressure and its occurrence greatly depended on the individual. Analysis using the single-case study design assesses the individual training effect more objectively, so it is considered to be a useful for providing exercise programs for individuals.

When examining the previous study using the group study model for the occurrence of reduction, in the study with old normotensives as subjects [Braith et al. (1994)], when endurance training of moderate intensity (for 45 minutes at 70% of heart rate reserve) and high intensity (for 35 minutes at 80-85% of heart rate reserve) were done three times a week for 6 months, both training conditions showed significantly low value at

Fig. 2. Individual fluctuations of systolic blood pressure with endurance exercise training. Horizontal dot line is the level of mean systolic blood pressure during the baseline period. Parenthesized numerical value is mean value of systolic blood pressure during each phase. *: $P < 0.05$ vs. baseline.

three months after the beginning of training. In the examination by Motoyama et al. (1998), with old hypertensives as subjects, when aerobic exercise training at an intensity corresponding to the lactate threshold (LT) (30 minutes, 3-6 times/week) was done, a significant low was shown in 12 weeks after the beginning of training and the value was stable at a low level after that. Kiyonaga et al. (1985), with mild hypertensives as subjects, conducted training at an intensity corresponding to LT, three times a week, for 60 minutes, and observed the variation of systolic pressure in detail. Systolic pressure decreased after the beginning of training, and was stable at a significantly low value in 5 weeks after beginning. Although there is some difference depending on the age of subjects and the blood pressure level before training, the depressor effect of endurance training in the elderly is considered to occur within 3 months. As a result of the group study model in this study, too, the average of blood pressure decreased linearly after the third phase (fifth to sixth

week) and showed a statistically significant low after the fourth phase, which supports the results of previous studies.

The study to examine the variation of blood pressure with endurance training statistically using a single-case design is, as far as we know, the first of its kind. Concerning systolic pressure, we calculated the auto-correlation coefficient of lag 1 individually, and a significant auto-correlation coefficient was obtained in four subjects. This suggests that systolic pressure has serial dependence. Although not all cases showed a significant auto-correlation, since there is a possibility of the systolic pressure having serial dependence, it is desirable to apply the randomization test, not a general statistical method by random sampling from the population [Edgington (1955), Nishijima et al. (2000)]. By individual examination of the occurrence of the reduction by the randomization test, the existence of the effect and the occurrence phase differ from subject to subject, so differences between individuals are big in the response of blood pressure variation in the training process. Based on this result, we concluded that, by applying the single-case study design to the statistical method, the individuality of trainability that cannot be clarified by the general statistical method can be evaluated more objectively.

This study can not clarify the cause of differences between individuals in depressor response with the training process. For the subject with the lowest systolic pressure in the baseline period, no significant reduction was observed throughout the training period, and for subjects with high systolic pressure, the effect occurred quickly and the depressor response was large. The blood pressure level before training may be a factor regulating the occurrence of reduction by training and the existence of the depressor response. That is, as estimated from previous studies by group study design, the higher the blood pressure before training, the more prominent the reduction of blood pressure. Further, the attainment of training may affect the reduction in blood pressure. The subject with the largest increase in VO_2 peak and reduction in systolic pressure had the most practicing time in training. These results suggest that trainability in aerobic capacity and blood pressure reduction is possible even in the elderly.

Single-case study design includes the method of interrupted time series analysis (ITSA) [Crosbie (1995)]. In this method, the effect of intervention is examined by comparing the intercept and slope of each regression line from 2 successive time series data points -- the baseline period (without intervention) and the intervention period. By using this method, the variation of systolic pressure in the training period can be evaluated individually and quantitatively. For the subject in

our study who interrupted training for about two weeks, systolic pressure tended to rise after resuming training. If ITSA is applied to such a case, useful information can be obtained concerning deconditioning and retraining. ITSA has the limitations that (1) observed time series data must have a linearity in variation, and (2) linearity becomes discontinuous in comparison of the variation tendency between periods [Nishijima et al. (2000)], so it is necessary to apply the method taking these limitations into consideration.

Because blood pressure is sensitively affected by the environment, measurement conditions should be strictly controlled, but this is not usual and is difficult to continue. Given daily health care, convenient measurement that smoothly fits into everyday life is easy to continue and realistic. Even if measurement accuracy is a little lower, by accumulating everyday data and analyzing it by a statistical method for single-case design such as the randomization test, objective and useful information for exercise prescription for individuals can be obtained.

5. Conclusion

We examined the variation in systolic pressure with endurance training in the elderly, using two experiment designs of the group study model, the single-case study design. The average of systolic blood pressure of all subjects showed a significant depressor response after the fourth phase (seventh to eighth week) compared to the baseline period before training. Next, we examined the occurrence of the depressor response individually by single-case study design using the randomization test, and, for the earliest subject, systolic blood pressure was significantly low (-6mmHg) in the second phase (third to fourth week). The subject who had the lowest SBP at the baseline (99 mmHg) did not show significant changes in SBP throughout training. Thus, blood pressure variation in the training process varies with the individual. Using a statistical method applicable for single-case study design such as the randomization test, the individuality of training effect could be clarified, which cannot be clarified simply by the group study design. This method can thus be useful for providing exercise programs for individuals.

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