Original Article

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Effect of Low-Intensity Physical Activity on Aortic Pulse Wave Velocity in Elderly Hemiplegics: A Randomized Controlled Trial

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Abstract

Because of the increasing number of hemiplegics with diabetes mellitus and hyperlipemia, the focus of the current study was on the prevention of the associated adverse angiopathic effects of these conditions on their activities of daily living (ADL). The aim of the study was to investigate the effect of low-intensity physical activities (LIPAs) on aortic deterioration in elderly hemiplegics. The method of study was a randomized controlled trial. The participants were 25 elderly hemiplegics independent in ADL and were residing at home or utilizing daycare nursing home facilities. They had a mean age ± standard deviation of 73 ± 8 years. The length of time elapsed from the onset of the stroke was greater than 5 years. All of the participants required a walking aid outdoors, and 22 (88%) of them also used a walking aid indoors. The participants' associated medical conditions included hypertension (92%) and diabetes mellitus (80%). The intervention was to increase the energy consumption from baseline physical activity (PA) by means of LIPAs (i.e., approximately 40 kcal/day; 3.3% of daily calories). LIPAs required the body's center of gravity to move up and down while the participant was in a standing position (intervention group [IG]; n=13) and, at the same time, to cause an effect of passive motion to the affected leg. Only the amount of PA was measured for the control group (CG; n=12). Outcomes were evaluated by the brachial-ankle aortic pulse wave velocity (baPWV), body weight, body mass index, resting heart rate (restHR), systolic blood pressure (SBP), calculated PA from daily activities, and the ankle-brachial pressure index (ABI). The differences between the baseline of IG and CG at the 1st week and after 4 and 8 weeks of intervention were compared and analyzed by an independent t-test. Multiple regression analysis was used to clarify the factors affecting the changes in baPWV at the time periods described above. The baPWV values in the affected leg were significantly different in IG compared to CG (1,973 vs. 2,419 cm/s; $p < 0.05$) on termination of the trial at 8 weeks. No significant differences were detected in respect to ABI, restHR, SBP, and PA_{PI} (amount of physical activity based on the participant's posture and exercise intensity) between the 2 groups before and after the trial. LIPAs were carried out safely among elderly hemiplegics over an 8-week period. These findings demonstrated that LIPAs were effective in improving aortic stiffness, as reflected by a decrease in baPWV on the hemiplegic participants' affected side.

Key words

brachial-ankle aortic pulse wave velocity, physical activity, hemiplegics, low-intensity physical activities, randomized controlled trial

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Introduction

There have been many reports regarding aortic pulse wave velocity (PWV) and the development of deconditioning[1-4]. Many studies have shown that resistance training and aerobic exercise improve the aortic PWV in healthy persons and in persons with aortic risk factors[5-12]. These studies have also reported on which exercises influence the aortic PWV in persons with degeneration of the aorta. However, the evidence is inconclusive regarding the effect of exercises on the aortic PWV in hemiplegics with degeneration of the aorta. A short-term positive effect on the aortic PWV has been reported as a result of resistance training and aerobic exercise, although their long-term effects are unknown[6-8]. In addition, no past study has clarified the quantity of physical activity (PA) required to achieve such an effect[5-8].

The number of hemiplegics with diabetes mellitus and hyperlipemia is increasing yearly. In order to prevent the occurrence of angiopathic conditions associated with these conditions and, consequently, allow the hemiplegic to remain independent in their activities of daily living (ADL), one must maintain an appropriate level of PA. In addition, the exercises that are effective for healthy persons may be inappropriate for hemiplegics with motor impairment. However it is important for the hemiplegic, especially the elderly one, to move their limbs bilaterally to maintain and/or increase muscle strength. Furthermore, to ensure patient adherence to the exercise regimen it must be feasible for the hemiplegic patient to carry out the prescribed exercise without too much difficulty.

In the current study, we investigated the effect of increased baseline PA values on aortic stiffness resulting from of long-term, low-intensity physical activities (LIPAs) . The brachial-ankle aortic pulse-wave velocity (baPWV) is an indicator of aortic stiffness[1-3]. In healthy, sedentary persons, aerobic exercise reduces the stiffness of the central and peripheral arteries, consequently decreasing blood pressure[9]. Thus, sign of changes in the measurements of baPWV may possibly be used as a warning of an incipient recurrent cerebrovascular accident in patients, such as elderly hemiplegics. The aim of the current study, therefore, was to clarify the effect of LIPAs in either preventing or delaying the deterioration of aortic PWV in such a condition.

Materials and Methods

Participant recruitment and screening

Strategies for recruitment of potential participants included dissemination of information on the project by distribution of brochures, in addition to verbal information by professional members of staff to daycare attendees at the nursing home. Fifty-six hemiplegic patients with a wide range of associated diseases were screened out of 198 individuals who were either residing at home or utilizing a daycare nursing home facility in a rural area of Japan. Prospective participants were excluded from the study if they had: 1) functional limitations so severe that an increase in PA was impossible; 2) associated cardiovascular conditions such as uncontrolled hypertension or angina; or 3) undiagnosed or untreated health conditions that manifested abnormal findings in their laboratory tests, contraindicating exercise testing. Thirty-one of the chosen participants withdrew after 1 week of intervention, leaving 25 participants, all of whom were men and left-sided hemiplegics. Their most commonly associated medical conditions were hypertension and diabetes mellitus. The participants' mean ± standard deviation age was 65.2 ± 9.5, ranging from 65 to 81 years old. The reported time that had elapsed from the onset of the stroke was greater than 5 years. Twenty-two (88%) of the participants required some form of walking aid indoors, and all of them required one outdoors (Table 1).

Before the commencement of the program, all of the participants underwent a medical examination by a physician to assure that their health status would not deteriorate with the prescribed exercise. Informed consent was obtained from each participant for the trial in accordance with the provisions of the Declaration of Helsinki, 1995 (as revised in Edinburgh, 2000). The ethics committee of the nursing home also approved the study.

The 25 participants were randomly divided into

Table 1. Background characteristics of the participants

	Intervention n (%)	Control n (%)	Total n (%)
Number of participants	13	12	25
Age (year)*	73±8	73±8	73±8
Medication			
>4 different drugs per day	8 (61.5)	7 (58.3)	15 (60.0)
Onset of CVA			
>5 years ago	13 (100.0)	12 (100.0)	25 (100.0)
Hypertension	12 (92.3)	11 (91.6)	23 (92.0)
Diabetes mellitus	11 (84.6)	12 (100.0)	20 (80.0)
Dizziness	1 (7.6)	1 (8.3)	2 (8.0)
BSR (lower leg)			
I	0 (0.0)	0 (0.0)	0 (0.0)
II	3 (23.0)	2 (16.6)	5 (20.0)
III	8 (61.5)	8 (66.6)	16 (64.0)
IV	2 (15.3)	2 (16.6)	4 (16.0)
V	0 (0.0)	0 (0.0)	0 (0.0)
VI	0 (0.0)	0 (0.0)	0 (0.0)
Use of a walking aid			
Indoor	12 (92.3)	1 (83.3)	22 (88.0)
Outdoor	13 (100.0)	12 (100.0)	25 (100.0)
Non-supervised exercise	2 (15.3)	1 (8.3)	3 (12.0)
Body height (cm)*	161.2±5.6	160.9±5.2	161.0±5.2
Body weight (kg)*	57.6±8.6	55.8±7.8	56.6±8.1
Body mass index (kg/m2)*	22.1±2.9	21.5±2.4	21.8±2.6

*: mean±standard deviation. CVA: cerebrovascular accident. BSR: Brunnstrom's stage of recovery.

2 groups: an intervention group (IG) and a control group (CG). A total of 5 participants withdrew over the course of the 8-week intervention, resulting in an attrition rate of 20%. Therefore, only 20 participants were included in the final data analysis (Table 1). A greater number of participants withdrew from IG (12%) than CG (8%). No significant difference existed between IG and CG at baseline, as was determined by independent *t*-tests.

A randomization code was created with equal numbers for the alternative protocol, using undisclosed random numbered tables that were given to the physical therapists who allocated the treatment to the participants. Randomization was carried out by means of sequentially numbered, sealed envelopes using the randomized code for either IG or CG.

Intervention program and the control protocol

The intervention program required additional energy consumption by the participants of approximately 40 kcal per day, which was equivalent to 3.3% of their daily calories. The program was under the supervision of either a physical therapist or nurse as LIPAs were added to the IG baseline PA. By means of a weekly interview, the participants' PA was recorded so as to calculate their baseline PA. LIPAs were carried out daily for 8 weeks and involved movement of the body in such a way that the center of gravity moved up and down while the participant remained in the standing position. This half-squatting movement involved flexing the knees to approximately 30 degrees in 1 sec and returning to full extension of both knees in the same amount of time. This created a passive motion of the ankle, knee, and hip joints in the affected leg, and this exercise session lasted for approximately 20 min. In addition to this exercise, passive dorsi-plantar flexion of the ankle in the supine position was performed 30 times over a period of 2 min. Only the amount of PA was measured for CG. Each participant's physical fitness values and reported PA were assessed before the trial and weekly thereafter.

Measurements

Uninterrupted PA over an 8-week period was represented by PA_{PI} that was the energy consumption of PA measured by means of participant's posture and exercise intensity[13]. PA_{PI} measures PA based on an energy expenditure coefficient in 9 lattices categorized into 3 postures of lying, sitting and standing in combination with 3 exercise intensities of low, moderate and high. PA_{PI} describes any human motion or activity based on 2-dimensional elements, that is, participant's posture and perceived exertion. The former element was divided into 3 postures, and the latter element was the perceived exertion brought about by the 3 exercise intensities. The coefficient energy consumption of any movement of a normal, able person is category 9. PA_{PI}, expressed as kcals, is the cumulative data for 24 hours, which is multiplied by the coefficients and body weight (BW), and the duration of the motion for each PA.

As for the PA_{PI} method, correlation with the heart rate (HR) is high at the time of movement in a disabled person. For example, when an obese person moves, it is known that their energy consumption is high, for it is in accordance with their BW, which is determined by metabolic equivalents (METs). With PA_{PI} converted from METs, the calculated energy consumption is closer to a physiological measurement, as in the case of disabled persons such as hemiplegics[13].

Several outcome measures were employed so as to know whether the participants experienced any physiological changes. These outcome measures included the following: BW, body height (BH), body mass index (BMI), resting HR (restHR), and systolic blood pressure (SBP).

The ankle-brachial pressure index (ABI) and bilateral baPWV were measured in each participant using a state-of-the-art device, the ABI/PWV (BP-203RPE; Nihon Colin-Omron, Kyoto, Japan). The ABI/PWV is a device with 4 cuffs that can simultaneously measure blood pressure in all 4 limbs and automatically calculate ABI. It can also record pulse waves through sensors in the cuffs, store data from the starting point of each pulse wave in the right arm and both legs, record the time difference between the transmission time to the arm and to the ankle, calculate the distance of transmission from the right arm to each ankle according to BH, and automatically compute and display the baPWV values based on the time and distance of transmission. This device is useful for reliable medical examinations and clinical studies because it enables ABI and baPWV measurements in a short period of time without operator bias.

Statistics

Independent *t*-test was employed for the fitness parameters (i.e., BW, BH, BMI, restHR, SBP, and PA_{PI}) and pulse wave data (baPWV and ABI) to examine the differences between IG and CG at the 1st, 4th and 8th week of intervention. Furthermore, multiple regression analysis was used to clarify the factors affecting the changes in baPWV at the same time periods. The level of significance was set at $p < 0.05$, and the Statistics Package for Social Sciences version 11.0 (SPSS Japan Inc.) was used for the data analysis.

Results

LIPAs resulted in no injuries in IG. One (7.6%) participant in IG withdrew during the 6th week because of personal reasons involving his family, and 2 (15%) participants in the 7th week because of falls in their homes. Two (16%) participants in CG were withdrawn in the 3rd week because they did not adhere to the amount of activity that was required of them in the program. These parameters are shown in chronological order during the 1st, 4th and 8th weeks.

Outcome data

Table 2 shows deconditioning data for LIPAs. The baPWV values in the affected leg 8 weeks after the commencement of the trial were found to be significantly different in IG compared to CG. However, no significant differences were found between the 2 groups in respect to ABI, restHR, SBP, and PA_{PI} before and after the trial. Figure 1 illustrates the difference in the distributions of the baPWV values in the affected leg of the 2 groups at the 8th week of the trial. The horizontal line represents the number of each group's

Table 2. Values for LIPAs

Parameters	Groups	1st week n	1st week mean ± SD	4th week n	4th week mean ± SD	8th week n	8th week mean ± SD
R baPWV (cm/sec)	I	13	1844 ± 524	13	1836 ± 512	10	1995 ± 207
	C	12	1849 ± 456	10	2029 ± 209	10	2101 ± 293
L baPWV (cm/sec)	I	13	1999 ± 651	13	1937 ± 600	10	1973 ± 289 *
	C	12	2105 ± 460	10	2277 ± 452	10	2419 ± 552
R ABI	I	13	1.05 ± 0.20	13	1.01 ± 0.22	10	1.09 ± 0.11
	C	12	1.06 ± 0.09	10	1.06 ± 0.09	10	1.09 ± 0.11
L ABI	I	13	1.01 ± 0.19	13	1.00 ± 0.19	10	1.12 ± 0.14
	C	12	1.05 ± 0.05	10	1.02 ± 0.09	10	1.05 ± 0.09
restHR (bpm)	I	13	81 ± 14	13	78 ± 16	10	78 ± 10
	C	12	83 ± 10	12	79 ± 8	10	77 ± 9
SBP (mmHg)	I	13	151 ± 16	13	143 ± 20	10	140 ± 17
	C	12	143 ± 19	12	142 ± 13	10	136 ± 11
PA_{PI} (kcal)	I	13	1134 ± 261	13	1159 ± 263	10	1269 ± 288
	C	12	1238 ± 150	10	1244 ± 177	10	1213 ± 177

R: right. L: left. baPWV: brachial-ankle aortic pulse wave velocity. ABI: ankle-brachial pressure index. restHR: resting heart rate. SBP: systolic blood pressure. PA_{PI}: amount of physical activity on the participant's posture and exercise intensity. * $p<0.05$ I: intervention group. C: control group.

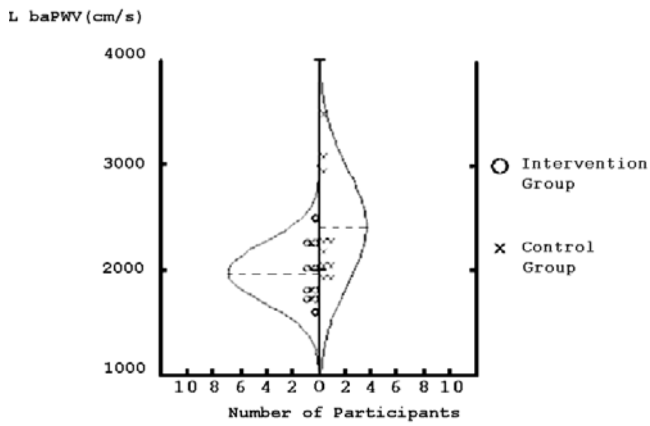

Figure 1. The cumulative curves in both groups. The graph shows the result of the baPWV values for the affected leg 8 weeks after the commencement of the trial; they were found to be significantly slower in IG compared with CG (1,973 vs. 2,419 cm/s; $p<0.05$).

participants and the cumulative curves show normal distribution patterns.

A comparison of the left baPWV values between the 2 groups with other parameters showed that the baPWV value in the affected leg was large with decreasing PA_{PI} (Table 3).

Discussion

Change in the values of PA_{PI} in IG and CG

The results of the current study demonstrated no difference in PA_{PI} between IG and CG, although the values in CG were higher than in IG at baseline. The reason for this finding may be a reflection on the small number of participants in the current study. However, the mean values in IG at the 8th week were higher than for those at their baseline, and this was reversed for the CG at the 8th week. The intervention with 40 kcal in IG may have statistically caused a beta error in the mean values for PA. The participants' understanding and performance of the exercise regimen was appropriate and, therefore, LIPAs may thus serve as a long-term, continuous form of activity for elderly hemiplegics.

Preventing deterioration of arterial stiffness on the affected side

Eight weeks of LIPAs demonstrated that baPWV on the affected side was relatively slow compared to baPWV of the non-LIPAs participants; therefore, baPWV can be directly related to PA_{PI}. The arterial stiffness noted on the affected side of

Table 3. Results for LIPAs calculated by means of multiple linear regression models and relative risk for each parameter *vis-á-vis* left baPWV

	1st week (n=25)	4th week (n=23)	8th week (n=20)
L baPWV	1.0	1.0	1.0
BW	−	−	−
Age	−	−	−
BMI	−	−	−
R baPWV	−	0.49 (0.36 to 3.72)*	−
R ABI	−	−	−
restHR	−	−	−
SBP	−	−	−
PA_{PI}	−	−	−0.71 (−1.22 to −0.21)*

baPWV: brachial-ankle aortic pulse wave velocity. BW: body weight. BMI: body mass index. R: right. L: left. ABI: ankle-brachial pressure index. restHR: resting heart rate. SBP: systolic blood pressure. PA_{PI}: Amount of physical activity based on the participants' posture and exercise intensity. *: Significant effects (β coefficient; 95% CI) on L baPWV. −: non-significant parameter.

CG is evidence of its deterioration. Fast baPWV resulting from deconditioning can be improved by local blood flow, together with an independent effect on SBP. As a result, these activities were seen to significantly retard the deterioration in aortic stiffness. Another possible reason for this finding is the fact that 80% of the participants were diabetic, and that there was an improvement in insulin resistance with LIPAs. It is believed that improvement in insulin sensitivity results in better control of the viscosity of blood due to an improvement in function of the blood vessel endothelium[14]. A past study[14] has shown that, by reducing the blood glucose level with low-intensity exercise, there may have been a significant effect on endothelial status in a 4-week period in patients of middle-to-advanced age. Therefore, there is a possibility that these findings were related to insulin sensitivity, and an additional time period of 8 weeks' intervention was needed to effectively improve distensibility of blood vessels in order to show any functional improvement.

Several studies have indicated that atherosclerosis develops primarily in the aorta and secondarily in the cerebral and coronary arteries[1-3,15-22]. PWV evaluates 2 factors: namely, the physical hardness of the vascular wall and the vasodilatation characteristics in response to blood flow[23-29]. Therefore, the risk of recurrence of a cerebrovascular accident could be prevented by control of a hemiplegic patient's PWV. In order to further validate the use of LIPAs as a means of prevention, it will be necessary to develop a large-scale prospective cohort study. The risk of a recurrence of a cerebrovascular accident could be reduced by such knowledge that PWV is shown to be reversible by PA.

Micro-physiologic considerations

Blood flow causes irritation through contact (i.e., shear stress) against the vascular endothelial bed, and blood vessels expand by producing nitrous oxide (NO)[30-32]. However, the acute effect of exercise does not decrease the hard texture of the vascular walls. But, the hardness of the vascular wall is affected by SBP[33]. In the current study SBP did not change in the 2 groups. Half-squatting does not allow isolated knee and ankle movement, but it does facilitate some voluntary muscle contraction even in a partially paralyzed leg. The authors believe that this closing and opening of blood vessels by voluntary muscle contraction is effective in increasing vasodilatation, in addition to the same effect brought about by means of the passive joint movements facilitated by LIPAs. A recent study[34] suggests that distensibility of the blood vessel is independent of the blood pressure. Passive motion by means of ankle dorsi-plantar flexion automatically increases blood flow. It is very likely that the reflex vasodilatation in response to blood flow resulted in changes in PWV in the current study. LIPAs are similar in effect to such a mechanism of induced vasodilatation in response to ankle movements[34].

McAllister and Laughlin[35] reported that NO formed in the vascular endothelium and derived from a biochemical reaction catalyzed by endothelial NO syntheses (eNOS) appears to play a role in exercise-induced dilatation of blood vessels supplying blood to the cardiac and skeletal muscles.

Exercise training augments endothelium-dependent and NO-mediated vasodilatation. Increases in eNOS gene transcription, eNOS mRNA stability, and eNOS protein translation appear to contribute to increased NO formation and, consequently, enhance NO-mediated vasodilatation after training. Enhanced endothelial NO formation may also play a role(s) in the prevention and treatment of atherosclerosis because NO inhibits several steps in the atherosclerotic disease process. A growing body of work suggests that physical exercise, perhaps via increased capacity for NO formation, retards atherosclerosis. It is, therefore, encouraging to find that nearly 80% of elderly hemiplegics with diabetes mellitus can reduce their risk of stroke recurrence[36-40].

Limitations

One of the limitations of the current study pertains to the applicability of administering LIPAs to other elderly patients with various diseases and conditions, because, in this study, the relatively small number of participants increased the beta error. Another limitation included recall bias in measurements of physical activities.

Conclusions

Daily 40 kcal-LIPAs were performed safely among the elderly hemiplegics who participated in the study over an 8-week period. These activities carried out by the participants resulted in significant improvement in the aortic stiffness, as reflected by a change in the baPWV on the affected side. However, further studies are required on the physiological effects of LIPAs, together with behavioral responses, to clarify the long-term effect on aortic stiffness in a larger number of elderly hemiplegics than participated in the current study.

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無作為化比較対照試験による高齢片麻痺患者の大動脈脈波伝播速度の改善に対する低強度身体活動の効果

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要　　旨

糖尿病や高脂血症等を起因とする血管障害由来の脳血管障害後遺症による片麻痺者の血管機能増悪の予防は健康管理において重要である。この増悪には身体活動の低下が影響を及ぼしていると考えられる。本研究では大動脈脈波伝播速度（PWV）を血管機能の指標として用い、それに対する低強度身体活動の有効性を明らかにすることを目的とした。対象者は、５年以上の発症歴を持ち、歩行が自立している25名の高齢片麻痺者であり、その80%は糖尿病と高血圧を合併していた。実験の手法として無作為化比較対照試験を用い、13名の介入群には開始前の日常生活の身体活動量に約40kcalの低強度身体活動として立位で体の重心を上下動する動作を毎日行わせた。12名の対照群には身体活動量を測定しただけであった。効果指標には体重、体格指数、安静時収縮期血圧、日常的な身体活動の量、上腕動脈-足背動脈間のPWV（baPWV）を記録した。解析の手段として独立したt検定および、１、４、８週間時点における前述した各要因の影響について重回帰分析を用いた。その結果、８週間後の患側のbaPWV値には介入群と対照群の間で有意差が認められた（1973cm/s 対 2413cm/s、p＜0.05）ものの、健側ではそうではなかった。また重回帰分析では、４週間の時点で健側のbaPWV値が、８週間時点で身体活動量が患側のbaPWVに有意な影響を及ぼした。結論として、毎日実施する40Kcalの低強度身体活動は８週間以上継続した高齢片麻痺者においてbaPWVの増悪を抑制する効果が示唆された。