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Differential Response of Central Blood Pressure to Isometric and Isotonic Exercises

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Central blood pressure may be more closely associated with cardiovascular events than peripheral blood pressure. The aim of the present study was to investigate central blood pressure responses to exercise. Apparently healthy 18 subjects were enrolled in the study (38 ± 6 years) and changes in central and brachial blood pressure were recorded in response to ergometer and hand-grip exercises. Central blood pressure was estimated using an automated device (Omron HEM-9000AI). Systolic brachial blood pressure was increased after both ergometer (from 119 ± 10 to 172 ± 16 mmHg; $P < 0.001$) and hand-grip (from 118 ± 8 to 122 ± 9 mmHg; $P = 0.001$) exercises, but central systolic blood pressure was increased only after hand-grip exercise (from 117 ± 11 to 121 ± 12 mmHg; $P = 0.002$). The radial augmentation index was increased after hand-grip exercise, whereas ergometer exercise reduced this index. Heart rate was increased only after ergometer exercise. Thus, isometric, but not isotonic, exercise may increase central blood pressure in overall healthy subjects. The response of central blood pressure, which is a better index of cardiac load than peripheral blood pressure, to hand-grip exercise may be useful in evaluating cardiovascular risk.

A chronic increase in blood pressure is a major risk factor for cardiovascular disease, whereas reducing blood pressure reduces cardiovascular events¹. Arterial pressure varies depending on the site in the arterial tree due to amplification of systolic blood pressure (SBP), and pulse pressure, from central to peripheral sites; thus, central blood pressure differs from peripheral blood pressure. Blood pressure measured over the brachial artery (peripheral blood pressure) is routinely used for individual risk evaluation and management of hypertension because it has been established as a powerful predictor of cardiovascular morbidity and mortality^{2–5}. However, recent studies suggest that central blood pressure is more closely associated with target organ damage than peripheral blood pressure^{6–8}. Furthermore, cardiovascular events are more closely associated with central rather than peripheral blood pressure^{9–14}.

Most evidence on blood pressure as a surrogate marker of cardiovascular events was derived from blood pressures obtained at rest. However, blood pressure changes every moment in response to physical and mental stress, and peripheral blood pressure measured during exercise has been recognized as a marker of cardiovascular risk independent of resting peripheral blood pressure^{15–18}. The risk related to a hypertensive response to exercise may be better assessed by central blood pressure given the greater impact of central compared with peripheral blood pressure on left ventricular afterload and myocardial oxygen consumption¹⁹. There have been a few studies investigating the effects of isotonic ergometer exercise on central blood pressure, but little is known about the effects of isometric exercise on central blood pressure. Hemodynamic responses to isometric exercises differ from those to isotonic exercises, and central blood pressure may respond differently to isometric and isotonic exercises. Thus, the aim of the present study was to compare the effects of isometric and isotonic exercise on central blood pressure. Drug therapy, especially for cardiovascular diseases, may modify the response of central and peripheral blood pressure to exercises and, thus, the present study included overall healthy subjects who were not taking any medication.

Results

The characteristics of the study subjects are given in Table 1. The blood pressure of all subjects in the study was within the normal range, indicating effective lifestyle modification. Central blood pressure tended to be lower



Table 1 | Characteristics of the study subjects

Age (years)	37.8 ± 6.7
Height (cm)	171.8 ± 5.0
Weight (kg)	68.7 ± 9.0
BMI (kg/m ²)	23.3 ± 3.2
SBP (mmHg)	119.4 ± 10.2
DBP (mmHg)	68.3 ± 10.3
HR (b.p.m.)	61.7 ± 11.3
Central SBP (mmHg)	114.4 ± 12.0
SBP2 (mmHg)	103.1 ± 11.2
Radial AI (%)	61.5 ± 11.6
Serum creatinine (mg/dL)	0.8 ± 0.1
Uric acid (mg/dL)	6.2 ± 0.8
FPG (mg/dL)	94.8 ± 9.0
LDL-C (mg/dL)	108.7 ± 22.8
HDL-C (mg/dL)	61.3 ± 12.1
Triglyceride (mg/dL)	105.4 ± 48.5

Data are given as the mean ± SD or as the number of subjects in a group with percentages in parentheses.

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; AI, augmentation index; FPG, fasting plasma glucose; SBP2, late systolic pressure in the radial artery; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol.

than peripheral blood pressure measured over the brachium ($P = 0.05$), whereas late systolic blood pressure in the radial artery (SBP2) was lower than peripheral blood pressure ($P < 0.0001$).

Ergometer exercise markedly increased peripheral systolic blood pressure (from 119 ± 10 to 172 ± 16 mmHg; Figure 1), but not diastolic blood pressure (from 68 ± 10 to 73 ± 13 mmHg; Figure 2). Heart rate was also increased by ergometer exercise (from 62 ± 11 to 118 ± 11 b.p.m.; Figure 3). The augmentation index (AI) obtained from the radial arterial pressure waveform was markedly reduced by isotonic exercise (from $61.4 \pm 12.4\%$ to $42.2 \pm 7.7\%$; Figure 4). Ergometer exercise did not affect central blood pressure (from 114 ± 12 to 116 ± 13 mmHg; $P = 0.39$; Figure 5). Hand-grip exercise also increased peripheral systolic blood pressure (from 118 ± 8 to 122 ± 9 mmHg; Figure 1), but the increase was significantly smaller after hand-grip than ergometer exercise (4.0 ± 4.6 vs 54.5 ± 16.0 mmHg, respectively; $P < 0.0001$). Peripheral diastolic blood pressure was not altered by hand-grip exercise (from 74 ± 12 to 74 ± 12 mmHg; Figure 2). Furthermore, hand-grip exercise did not have any significant effect on heart rate (from 59 ± 9 to $59 \pm$

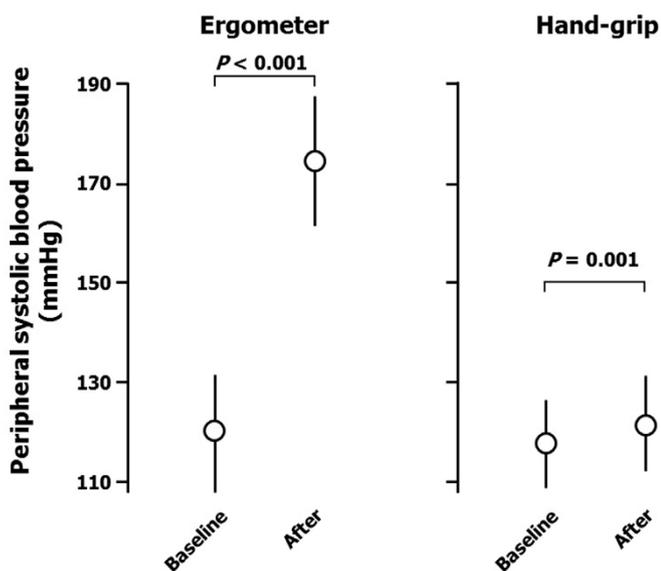


Figure 1 | Peripheral systolic blood pressure responses, measured over the brachium, to ergometer and hand-grip exercises. Data are the mean ± SD. The P -values shown were calculated by paired t -tests.

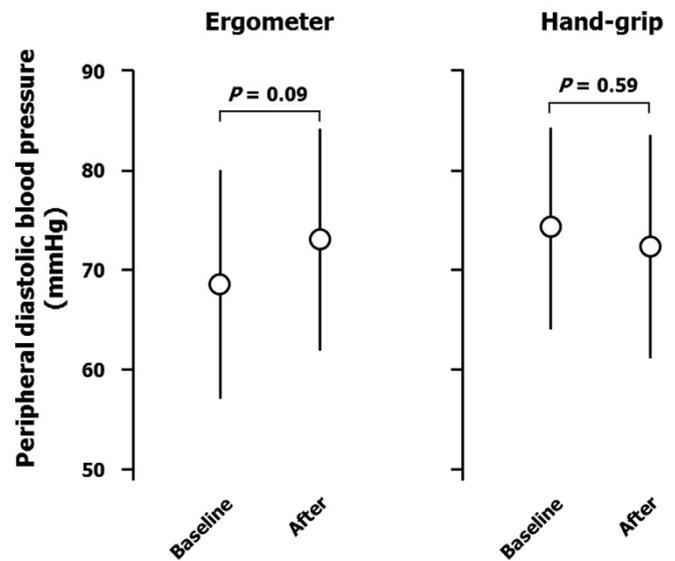


Figure 2 | Peripheral diastolic blood pressure responses, measured over the brachium, to ergometer and hand-grip exercises. Data are the mean ± SD. The P -values shown were calculated by paired t -tests.

8 b.p.m.; Figure 3). In contrast to the response to ergometer exercise, hand-grip exercise slightly, but significantly increased both radial AI (from 66.4 ± 9.2 to $69.2 \pm 9.4\%$; Figure 4) and central blood pressure (from 117 ± 11 to 121 ± 12 mmHg; Figure 5).

Central and peripheral blood pressures are different indices, but the two are closely associated in individuals. Thus, the ratio of central systolic blood pressure to peripheral systolic blood pressure was calculated in each individual and changes in this variable were compared after ergometer and hand-grip exercises (-0.29 ± 0.08 vs 0.00 ± 0.02 , respectively; $P < 0.0001$). The results confirm the differential responses of central blood pressure to hand-grip and ergometer exercises.

Discussion

In the present study, central systolic blood pressure was increased after isometric hand-grip, but not isotonic ergometer, exercise.

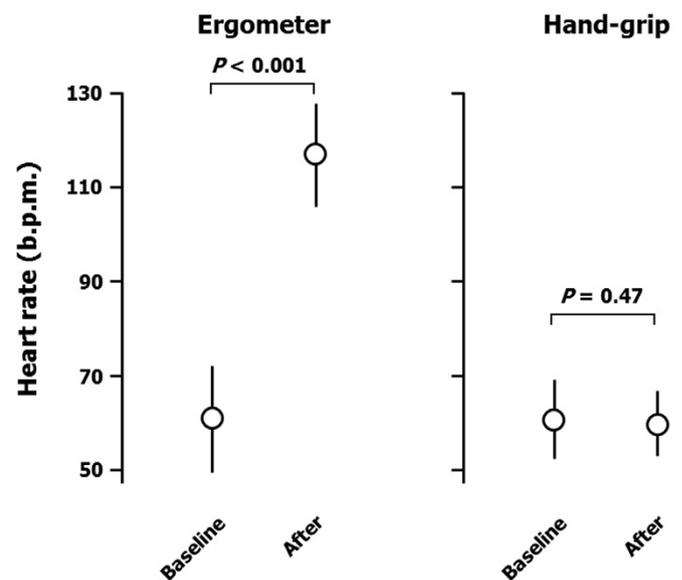


Figure 3 | Heart rate responses to ergometer and hand-grip exercises. Data are the mean ± SD. The P -values shown were calculated by paired t -tests.

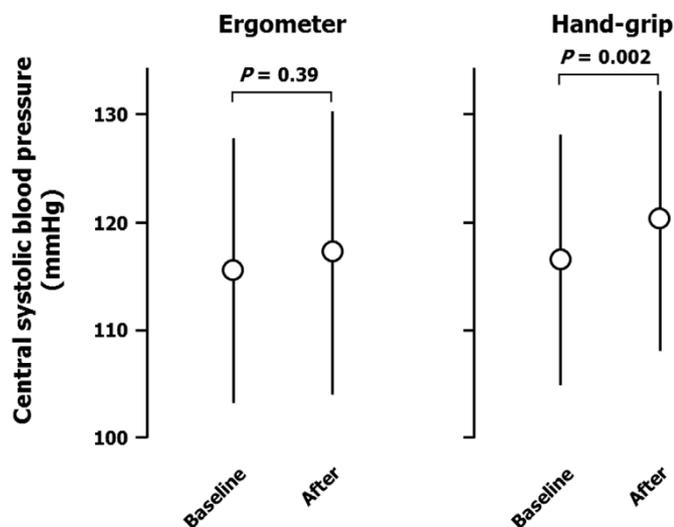


Figure 4 | Central systolic blood pressure responses to ergometer and hand-grip exercises. Data are the mean \pm SD. The *P*-values shown were calculated by paired *t*-tests.

Because central blood pressure is a better index of cardiac load than peripheral blood pressure, the response of central blood pressure to hand-grip exercise may provide useful information when evaluating cardiovascular risk in overall healthy individuals.

The most important finding of the present study is that central blood pressure responded differently to ergometer and hand-grip exercises. The precise mechanism underlying the different responses of central blood pressure to isotonic and isometric exercises is not clear, but changes in the pressure waveform of the radial artery and peripheral blood pressure after the exercises provide some clues as to the mechanism involved. Ergometer exercise increased cardiac output and thereby increased the amplitude of the forward traveling wave. This may have resulted in an increase in the amplitude of the reflected wave. However, peripheral arterial dilatation caused by the isotonic exercise may have reduced the amplitude of the reflected wave^{26,27}. Indeed, radial AI was markedly reduced although the amplitude of radial pulse pressure was increased after ergometer exercise. Central blood pressure may have been determined by the balance between an increase in cardiac output (increased forward traveling wave) and that in vascular relaxation (decreased reflected wave). Alternatively, the reduction in radial AI may be due to an increase in heart rate after exercise²⁸. It is also possible that the elastic aorta buffered an increase in central aortic pressure caused by exercise. In contrast with the response to ergometer exercise, hand-grip exercise may have increased arterial resistance and thereby increased the amplitude of the radial reflected wave^{26,27}. This is compatible with the finding that radial AI was augmented after hand-grip exercise. Moreover, increased stiffness in the conduit artery may have augmented pulse wave velocity, resulting in an increase in radial AI and premature return of the reflected wave in late systole in the central aorta. These responses after the isometric exercise may have been related to the increase in central blood pressure observed after hand-grip exercise. Cardiac output may have been increased after hand-grip exercise, but this effect was smaller than that after ergometer exercise because peripheral blood pressure showed only a mild increase. Changes observed after hand-grip exercise can be summarized as a product of arterial contraction caused by the isometric exercise.

In the present study, central blood pressure was estimated non-invasively using the Omron device. However, the superiority of central blood pressure over brachial blood pressure in the management of hypertension has been well established using the SphygmoCor device (AtCor Medical, Sydney, NSW, Australia), which records the radial

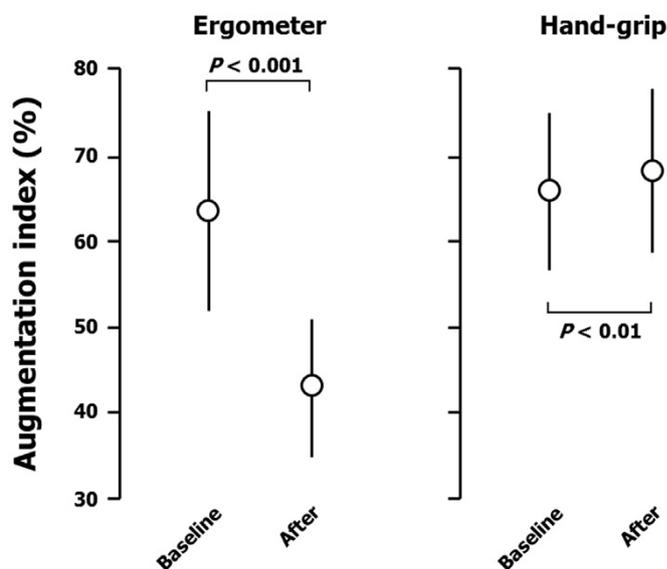


Figure 5 | Response of augmentation index obtained from pressure waveform of the radial artery to ergometer and hand-grip exercises. Data are the mean \pm SD. The *P*-values shown were calculated by paired *t*-tests.

pulse waveform and converts it to a central blood pressure waveform using a generalized transfer function^{10,11,29,30}. Central blood pressure is then estimated by calibration against brachial blood pressure^{31,32}. The Omron device records the radial pulse waveform and SBP2 is obtained by calibration against brachial blood pressure. Central systolic blood pressure is estimated using a regression equation^{21,25}. Central systolic blood pressure values estimated by the Omron device are highly correlated with those estimated by a SphygmoCor device^{22–24} and these non-invasive estimations show close correlation with invasive measurements of central blood pressure^{21,24,25}. However, both devices underestimate central systolic blood pressure, with the SphygmoCor device producing a larger deviation than the Omron device (average -15 vs -2 mmHg, respectively)²⁴. Thus, the central blood pressure response observed in the present study may reflect the response of arterial pressure in the ascending aorta. The finding that the central blood pressure value estimated by the Omron device was not significantly lower than peripheral blood pressure measured over the brachium may sound strange. However, this is quite natural, because the measurement of peripheral blood pressure using a cuff over the brachial artery underestimates brachial arterial blood pressure³³.

In contrast with the results of the present study, increases in central blood pressure after ergometer exercise were observed in a previous study in which a SphygmoCor device was used to estimate central blood pressure³⁴. In the present study, central blood pressure was measured after ergometer exercise to minimize artifact due to exercise, whereas in the previous study the hemodynamic measurements were performed during exercise. This may explain, at least in part, the differences between these two studies. Alternatively, the discrepancy between the present and previous studies may be attributable to differences in the methods used to estimate central blood pressure.

Several studies have reported that peripheral blood pressure measured during exercise is a marker of cardiovascular risk independent of resting peripheral blood pressure^{15–18}. However, central blood pressure has been shown to be a more important determinant of vascular function and cardiovascular risk than peripheral blood pressure. An increase in central blood pressure means increased pulsatile stress in the aorta, as well as increased left ventricular afterload and myocardial oxygen consumption, which can be detected only after measurement (estimation) of central blood pressure because marked



differences exist between central and peripheral blood pressure²⁰. Thus, evaluation of the response of central blood pressure to exercises is quite important and may provide useful information for risk assessment.

Interpretation of the results of the present study is limited by the following concerns. First, the accuracy of central blood pressure estimation using the Omron device during exercise has not been validated. Although central blood pressure was estimated after, but not during, exercise, in the present study, it is possible that a measurement artifact related to the exercise may have affected the results. Second, the intensity of the exercises was not considered in the present study although the response to exercise may vary depending on exercise intensity. Indeed, heart rate was not increased after hand-grip exercise. Third, the number of subjects included in the study was too small to enable definite conclusions to be drawn and, thus, this may be a hypothesis-generating study. Further studies with a greater number of subjects and different exercise intensities are needed to confirm the conclusions of the present study.

In conclusion, isometric, but not isotonic, exercise may increase central blood pressure in overall healthy subjects. Because central blood pressure is a better index of cardiac load than peripheral blood pressure, the response of central blood pressure to hand-grip exercise may be useful in evaluating cardiovascular risk.

Methods

Study population. Individuals were eligible for inclusion in the study if they: (1) were ≥ 25 years of age; (2) had normal blood pressure ($< 140/90$ mmHg); (3) were not receiving any medication; and (4) were in a stable condition. All subjects had been diagnosed with essential hypertension based on clinical blood pressure measured on at least two different occasions and attained target blood pressure ($< 140/90$ mmHg) following lifestyle modification without any antihypertensive medication. Blood pressure was measured by a doctor using a validated oscillometric technique (HEM-7070; Omron Healthcare, Kyoto, Japan) after subjects had been seated for 2 min with their back supported and their arms supported at heart level. Proper cuff size was determined based on arm circumference. Three consecutive blood pressure measurements were taken at 2-min intervals and the mean of the second and third measurements was recorded as the blood pressure. Exclusion criteria for the study were office blood pressure $\geq 140/90$ mmHg while being untreated, and a history of target organ damage, cardiovascular disease, dyslipidemia, or impaired glucose tolerance.

The study was performed in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Nagoya City University Graduate School of Medical Sciences. All subjects provided written informed consent prior to participating in the study.

Study protocol. The overall healthy subjects were instructed to avoid heavy exercise for 24 h and to fast overnight before the exercise tests. Ergometer and hand-grip exercises were performed on different days in the morning in a quiet, temperature-controlled (22–25°C) room. The order of the exercises was random.

The ergometer test was started with 10 min rest in a supine position followed by 5 min rest sitting on the cycle ergometer. Subjects were first asked to pedal at 60 r.p.m. without any added load for 1 min before they were subjected to graded symptom-limited maximum exercise test (15 W/min ramping) on an electronically braked bicycle ergometer (STB-2400; Nihon Koden, Tokyo, Japan) until 80% of target heart rate ($= [220 - \text{age}] \times 0.8$) was achieved under a 12-lead electrocardiogram and peripheral blood pressure monitoring. Peripheral blood pressure was measured and central blood pressure was estimated before and after the exercise in seated subjects using an automated device (HEM-9000AI; Omron Healthcare).

On a separate day, subjects performed a hand-grip exercise using a custom-made hand-grip device. After 10 min rest, the hand-grip exercise was started with subjects in a supine position. The exercise protocol consisted of 90-s isometric exercise at 30% of the maximal grip, which had been predetermined. Peripheral blood pressure was measured and central blood pressure was estimated before and after the exercise in subjects in a supine position using the Omron device.

Estimation of central blood pressure. The detailed method for estimating central blood pressure has been published elsewhere²⁰. Briefly, radial artery pressure waveforms and brachial blood pressure were recorded simultaneously using a fully automated device (HEM-9000AI; Omron Healthcare) to calculate late systolic pressure in the radial artery (SBP2) and to estimate central systolic blood pressure^{21–25}. Brachial blood pressure was measured with an oscillometric manometer and radial pulse waveforms were recorded non-invasively using an applanation tonometer. Signals of the radial arterial pressure wave were low-pass filtered, first at a cut-off frequency of 105 Hz to remove high-frequency noise and then at 25 Hz to extract pressure waveforms. The radial arterial waveform obtained with this device is

reportedly identical to the simultaneously and invasively measured intra-arterial pulse waveform of the opposite radial artery²¹.

Inflection points or peaks that corresponded to early and late systolic blood pressure were obtained by multidimensional derivatives of the original pulse pressure waveforms. The maximal systolic and diastolic pressures in the radial artery were calibrated with brachial systolic and diastolic blood pressure, respectively. SBP2 was calculated using the following equation:

$$\text{SBP2} = (\text{P2/PP}) \times (\text{systolic blood pressure} - \text{diastolic blood pressure}) + \text{diastolic blood pressure}$$

where P2 and PP are the height of the late systolic shoulder/peak pressure and the pulse pressure of the radial arterial pressure contour, respectively. Central systolic blood pressure was estimated using a regression equation with SBP2 as a major independent variable^{21,25}. The radial augmentation index (AI) was calculated using the following equation:

$$\text{AI}(\%) = (\text{P2/PP}) \times 100$$

Statistics. All statistical analyses were performed using SPSS 19.0 (Chicago, IL, USA). Unless indicated otherwise, data in the text and tables are expressed as the mean \pm SD. The significance of differences in variables before and after exercise was determined using a paired *t*-test. $P < 0.05$ was considered significant.

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Author contributions

Y.D. designed the study, S.T. collected and analyzed data, and S.T., T.S., S.Y. and Y.D. interpreted the data. S.T. drafted the manuscript and Y.D., G.K. and N.O. revised the manuscript. All authors reviewed the manuscript.

Additional information

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