Breathing Training for Older Patients with Controlled Isolated Systolic Hypertension

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ABSTRACT

SANGTHONG, B., C. UBOLSAKKA-JONES, O. PACHIRAT, and D. A. JONES. Breathing Training for Older Patients with Controlled Isolated Systolic Hypertension. *Med. Sci. Sports Exerc.*, Vol. 48, No. 9, pp. 1641–1647, 2016. **Introduction**: Isolated systolic hypertension (ISH) is very common but difficult to manage with conventional medication. We investigated whether slow breathing training, with and without an inspiratory load, could reduce the resting blood pressure of older well-managed ISH patients. **Methods**: Thirty ISH patients (66 ± 4 yr) were randomized into loaded breathing (six breaths per min, 18 cm H_2O), unloaded breathing (six breaths per min, no load), or control (normal breathing) groups. After a 2-wk run-in, loaded and unloaded groups trained at home for 30 min every day for 8 wk. Morning home blood pressure and heart rate were measured daily throughout the study. At the end of training, all participants reverted to normal breathing, and blood pressure and heart rate were recorded for a further 8 wk. **Results**: Compared to the pretraining run-in period, systolic blood pressure was reduced by 18 ± 7 and 11 ± 4 mm Hg for loaded and unloaded groups, respectively ($P < 0.001$), the reduction being significantly larger for the loaded group ($P < 0.05$) after 8-wk training. There were no changes in the control group. After the end of training, systolic blood pressure remained below pretraining levels for a further 6 wk for the loaded group but for only 2 wk with the unloaded group. There was a small nonsignificant reduction in diastolic blood pressure with training, as there was for heart rate. Pulse pressures were reduced by 11 ± 5 and 5 ± 6 mm Hg for loaded and unloaded groups, respectively ($P < 0.01$). **Conclusion**: Slow breathing training, especially with an inspiratory load, is very effective in reducing resting systolic and pulse pressures and could be a valuable adjunct in the management of ISH. **Key Words:** ISOLATED SYSTOLIC HYPERTENSION, SLOW LOADED BREATHING TRAINING, ELDERLY, BLOOD PRESSURE, SUSTAINABILITY

Isolated systolic hypertension (ISH) is characterized by systolic blood pressure (sBP) of more than 140 mm Hg with diastolic blood pressure (dBP) less than 90 mm Hg, consequently giving rise to high pulse pressures (9). ISH is particularly prevalent among older people, affecting more than 50% of individuals older than 60 yr (10,19) and is a major cause of stroke, cardiovascular disease, and kidney disease (28,37). High pulse pressure is both a consequence and an indicator of stiff arteries in individuals with ISH and has been shown to be a predictor of decreased endothelial function, stroke, cardiovascular disease, and mortality (4–6,13).

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The pathophysiology of ISH is characterized by the decreased compliance of large and small arteries, primarily as a consequence of age-related changes in the elastin and collagen content of the vessels (21). This leads to increased total peripheral vascular resistance, decreased baroreceptor function, and dysfunction of blood flow autoregulation in important target organs such as the brain, heart, and kidney, resulting in various adverse hemodynamic consequences (8,21).

ISH is difficult to treat, possibly because the underlying problem is one of structural changes in the conduit arteries, and more than 60% of patients with ISH have poorly controlled blood pressure and fail to meet the clinical target of 140/90 mm Hg (8,31) or pulse pressure of 50 mm Hg.

With essential hypertension, reductions in blood pressure can be obtained with behavioral and lifestyle approaches, such as yoga and meditation, and it is thought that controlled slow breathing may be the common factor responsible for the improvement (34). In support of this idea, there have been several studies of slow breathing training in essential hypertension (1,22,24,29,30) with reductions in blood pressure

that are comparable with those obtained with conventional exercise training.

Although slow breathing training has been found to be effective in reducing resting blood pressure, the mechanism of this action is not understood. Broadly, there are two possibilities. Slow breathing is very effective in entraining heart rate, which is associated with changes in autonomic control and metaboreflex sensitivity (25). Entrainment of heart rate is thought to be a consequence of respiratory neurons influencing the activity of cardiac vagal neurons (15), and it is possible that this could be enhanced by the greater voluntary effort involved in breathing against an inspiratory load. Alternatively, the prolonged changes in negative intrathoracic pressure and larger tidal volumes with slow breathing may stimulate baroreceptor activity (2) or lung afferents (11), and this would be enhanced when breathing against an inspiratory load. There is, therefore a rationale for including an inspiratory load for slow breathing training with essential hypertension, but as mentioned previously, the pathology of ISH is thought to be in the structure of the arterial wall and changes in autonomic function might not be expected to be effective in reducing blood pressure in these cases. Nevertheless, in a previous study of patients with essential hypertension, but where the mean pulse pressure was 56 mm Hg (15), it was noted that adding an inspiratory resistance to the slow breathing training enhanced the reduction in sBP, suggesting that training with an inspiratory load might be useful for ISH patients. The diameter of the aorta has been shown to respond to changes in intrathoracic pressure, such as the Valsalva and Mueller maneuvers, in normotensive human subjects (20) and would be expected to do so during loaded breathing. It is uncertain whether repeated stretching in this way can modify the structural properties of the arterial wall, but the stiffness of the aorta is determined by many factors including endothelial and smooth muscle function (3) that could be modified by mechanical stress. The mechanical effects of slow deep breathing, especially with an inspiratory load, could modify these aspects of vascular function.

The purpose of the present study was to determine whether slow breathing training, particularly when combined with an inspiratory load, can reduce resting blood pressure in older patients with ISH, reducing systolic and pulse pressures, bringing the participants closer to the conventional clinical targets. A secondary objective was to determine how long any benefits of the breathing training might be sustained because, in practice, patients are unlikely to persist with training every day.

METHODS

Participants. Patients being managed for ISH were recruited from the hypertension clinic, Srinagarind Hospital, and three community hospitals in Khon Kaen Province, Thailand. Inclusion criteria were mild to moderate ISH, defined as average sBP >140 mm Hg and dBP <90 mm Hg (9) at the time of diagnosis and older than 60 yr with constant medication for at least 1 month before the study.

Patients were excluded if they regularly exercised, had active cardiovascular disease, stroke, chronic renal failure, or chronic respiratory disease or were habitually taking supplements or herbal medicines that might affect blood pressure. The study was approved by the Research Ethics Committee of the Khon Kaen University, and all patients gave their informed consent in writing. In total, 35 subjects were recruited, 5 were excluded for various reasons and the remaining 30 patients (age 60–79 yr) were randomly allocated to three experimental groups (see Fig. 1 and Table 1 for details). The study was registered as a clinical trial (NCT 02200926).

Study design and interventions. The study was a prospective randomized controlled trial (Fig. 1). Subjects were allocated to three groups before the first visit, using sealed envelopes, assigning them to a group breathing with an inspiratory load (loaded), an unloaded breathing group, or a control group. The study had three phases: a 2-wk run-in, an 8-wk breathing intervention, and an 8-wk follow-up after the end of training.

Patients in the two training groups were shown how to breathe deeply with a frequency of six breaths per minute using a pressure threshold incentive spirometer (24) in which the inspiratory resistance was set by the depth of water in the bottle. The patients in the loaded group inspired against a load of 18 cm H_2O, whereas the unloaded group used the same device but with no water and therefore no added resistance. Five seconds of rest was allowed after every six deep breaths. The breathing pattern had a duty cycle of 0.4 (inspiratory time = 4 s and total respiratory time = 10 s). The paced breathing was practiced using a metronome in the laboratory until the subjects could maintain the desired depth and pattern of breathing without the metronome, mentally counting up to four during inspiration and to six during expiration. The training program was performed at home for 30 $min \cdot d^{-1}$, every day, for 8 wk. No breathing instructions were given to the control group. All patients were instructed how to reliably measure their blood pressure and were provided with written instructions for both the breathing training, where appropriate, and blood pressure measurements to be followed when at home. Written instructions have been recommended to improve the accuracy of home blood pressure measurements (17).

After 8 wk of breathing training, the sustainability of the training effects was assessed. Patients in the two training groups (loaded and unloaded) stopped using the incentive spirometer and resumed normal breathing. All patients continued to measure blood pressure and heart rate every morning for a further 8 wk after the end of the training period.

Measurements and data collection. Patients used an oscillometric digital upper arm blood pressure monitor (Riester, ri-champion®N, Jungingen, Germany) with an appropriate sized cuff. The monitor has automatic data storage of date and time, heart rate, sBP, and dBP. Blood pressure and heart rate were measured in the early morning, sitting in a comfortable position after at least 5 min of rest. Patients were asked to refrain from caffeine or physical activity at

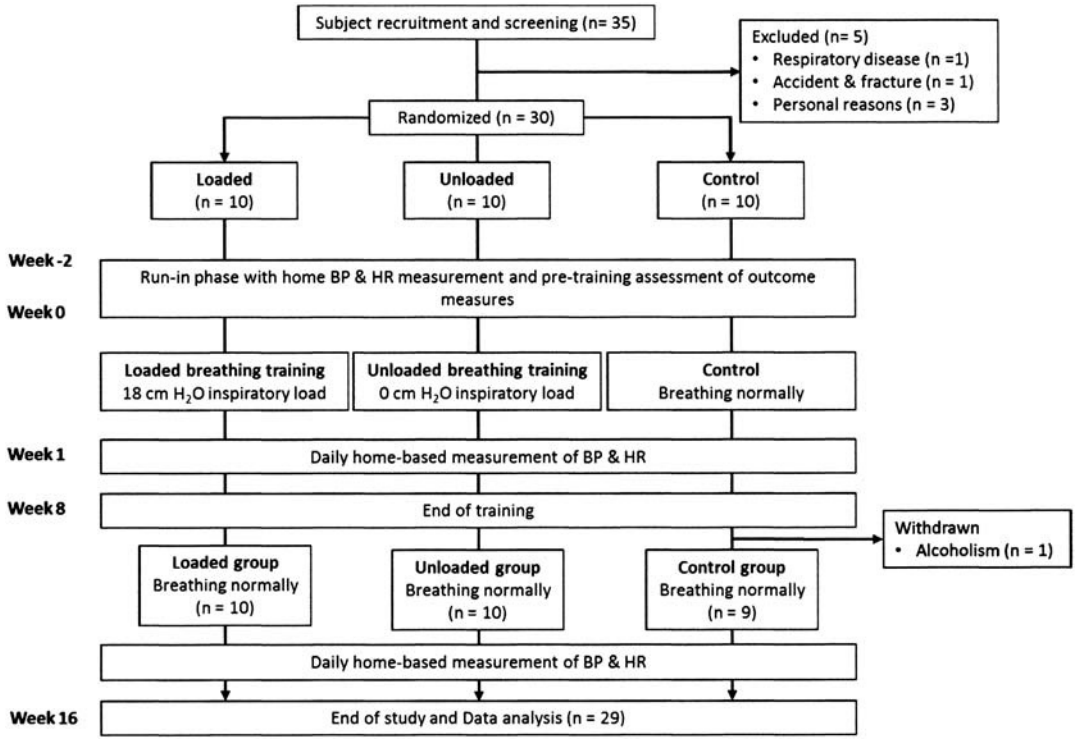

FIGURE 1—Flow of patients through the study. After a 2-wk run-in period, there were 8 wk of training followed by a further 8 wk of observation. Patients made home-based measurements of their blood pressure and heart rate every day for the entire 18 wk of the study.

least 30 min before the measurement. Data were recorded during the 2-wk run-in period before the start of training and then for the next 16 wk.

Patients were given a checklist on which they recorded whether they had undertaken the training, if appropriate, and measured blood pressure, together with any comments. They were contacted by telephone once a week and visited at home every 2 wk, partly for encouragement but also to sort out any problems and to download data from the blood pressure monitor. Compliance with the breathing training was evaluated from the number of recorded training sessions on the patient's checklist and from the time and date information downloaded from the blood pressure monitor for blood pressure and heart rate measurements.

Data analysis and statistics. The primary outcomes of the study were the change in blood pressure and heart rate, with the daily values averaged to give a single value for each week.

Data were analyzed using intention to treat (last observation carried forward imputation for three missing data) and repeated-measures ANCOVA adjusted by sex, followed by *post hoc* analysis with Bonferroni correction. All statistical analyses were performed using SPSS version 12.0.1 (SPSS, Ltd., Chicago, IL). Data are given as mean ± SD, unless otherwise specified, and significance is assumed at $P \leq 0.05$.

RESULTS

Patient characteristics. Thirty-five patients were initially recruited, five were excluded or withdrew. One patient in the control group was withdrawn from the study when he was found to have a problem with alcohol and was probably not taking his medication regularly; consequently, 29 completed the full study (Fig. 1). Details of the patients who completed the study are given in Table 1, together with their type of medication. All patients were taking antihypertensive medications; 20 were taking one drug, nine were taking two drugs, and one patient combined three drugs. Patients continued with their medication unaltered throughout the study. Although their blood pressure was well managed at the time of recruitment into the study, when first diagnosed,

TABLE 1. Subject characteristics.

Variable	Load	Unload	Control
Gender (male/female)	4/6	1/9	3/6
Age (yr)	65 (60–70)	68 (60–79)	65 (60–74)
Weight (kg)	72.1 ± 11.9	66.28 ± 11.2	67.55 ± 4.8
Height (m)	161 ± 0.1	156 ± 0.1	161 ± 0.1
BMI ($kg \cdot m^{-2}$)	28.0 ± 4.2	27.1 ± 3.9	26.2 ± 3.6
sBP (mm Hg)	144 ± 8.7	141 ± 11.1	142 ± 9.8
Diastolic blood pressure (mm Hg)	81 ± 6.7	81 ± 6.2	83 ± 9.4
Mean arterial pressure (mm Hg)	102 ± 6.6	101 ± 7.1	102 ± 8.6
Pulse pressure (mm Hg)	63 ± 7.7	64 ± 8.9	60 ± 8.7
Resting Heart rate (bpm)	72 ± 7.5	71 ± 6.4	70 ± 8.3
Other illness			
Diabetes mellitus	4	2	2
Years since diagnosis	10 (1–15)	10 (1–20)	10 (0.5–17)
Medication			
Diuretic	2	3	1
Ang II receptor blockers	4	3	6
Calcium channel blockers	3	3	5
β-Blocker	2	2	1
Metformin	4	2	2

Data are presented as mean ± SD except age and years since diagnosis, which are median and range. BMI, body mass index.

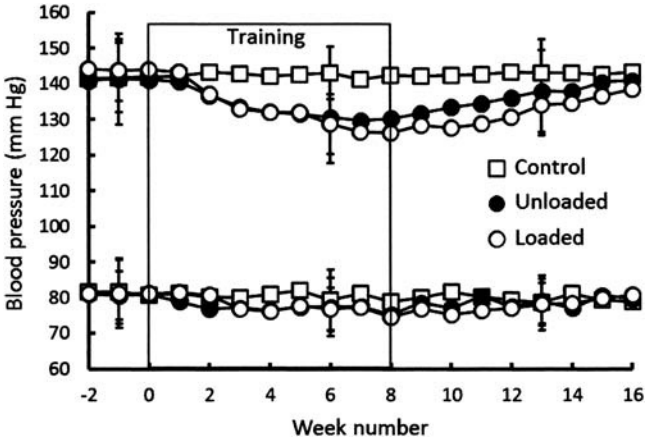

FIGURE 2—Home-based measurements of sBP and dBP. Patients made home-based measurements of their blood pressure throughout the study. The values at week 0 are the average of the 2 wk run-in period, otherwise values are weekly averages. Above are sBP measures, below dBP. *Open circles*, loaded breathing group; *Filled circles*, unloaded breathing group; open squares, *control group*. Data are mean values for each group with sample SD shown at weeks −1, 6, and 13.

in most cases several years before the trial, the mean ± SD resting sBP was 173 ± 13 mm Hg with a dBP of 80 ± 5 mm Hg, consistent with ISH.

Compliance with the loaded and unloaded breathing training was very good (92% and 95%, respectively) as was the collection of blood pressure and heart rate data. There were no differences in any of the cardiovascular variables between the three groups assessed during the 2-wk run-in period (Fig. 1, Table 1).

Effects of breathing training on blood pressure. Data for blood pressure measured during the 16-wk study period for the three groups are shown in Fig. 2. There were no changes in pressure for the control group at any stage but the sBP of both training groups declined progressively during the 8 wk of training followed by a return to pretraining levels over the following 8 wk. Part of the variance of the data in Fig. 2 was due to the differences between subjects. Consequently, in Fig. 3, the data are expressed as changes from the pretraining values averaged during the 2-wk run-in period. For sBP (Fig. 3A), between-group analysis showed loaded ($P \leq 0.0001$) and unloaded ($P = 0.001$) groups differ from the control group, and there were also differences between loaded and unloaded groups ($P = 0.004$). Within-group analysis showed the loaded group to differ significantly from pretraining run-in from weeks 6 to 14 ($P \leq 0.035$) and for the unloaded group from weeks 4 to 10 with the maximum reduction occurring after the full 8 wk of training, amounting to 18 ± 7 (95% confidence interval [CI] = −13 to −22) and 11 ± 4 (95% CI = −9 to −13) mm Hg for the loaded and unloaded groups, respectively. *Post hoc* analysis showed significant differences between loaded and unloaded groups at weeks 7 ($P = 0.049$), 8 ($P = 0.02$), and 9–14 ($P \leq 0.014$).

Data for dBP are shown in Fig. 2, and the changes from the pretraining run-in period are shown in Figure 3B. For both training groups, there was a tendency to decrease in the first few weeks of training. At week 8, the mean reductions were 7 ± 5.9 and 6 ± 4.3 mm Hg for the loaded and unloaded groups, respectively. However, statistical analysis showed no significant differences either between or within groups ($P \geq 0.20$).

The magnitude of the reductions in sBP with training did not correlate with either the initial pretraining sBP or dBP.

Pulse pressure changes followed those of sBP. Pulse pressure values at the end of training were 52 ± 7 mm Hg for the loaded group and 55 ± 13 for the unloaded group, representing reductions of 11 ± 5 mm Hg (95% CI = −8 to −14) and 5 ± 6 mm Hg (95% CI = −1 to −9) ($P = 0.01$), respectively, from the pretraining run-in.

There was a possible trend for a reduction in heart rate in the two training groups. At week 8, the resting heart rate had declined by 5 ± 3.9 bpm and 3 ± 5.1 bpm, for the loaded and unloaded groups, respectively; the change for the control group was 0 ± 13 bpm. However, there were no significant differences either between or within groups ($P \geq 0.20$).

Sustained effects of breathing training. In the 8-wk period after the end of training, resting sBP returned toward the pretraining values (Figs. 2 and 3A). For the loaded group, the pressure remained significantly lower than the

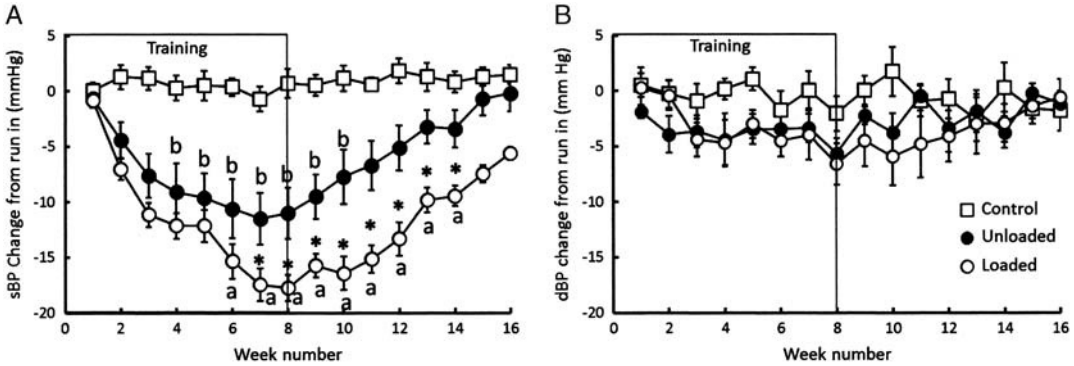

FIGURE 3—Blood pressure changes compared with the pretraining run-in values. Open circles, loaded breathing group; Filled circles, Unloaded breathing group; Open squares, Control group. A, sBP. Data differing significantly from run-in values for the [a]loaded and [b]unloaded training groups. *Significant differences between Loaded and Unloaded groups. B, Diastolic blood pressure. Data are mean and SEM.

pretraining level until week 14, whereas for the unloaded group, sBP remained significantly below pretraining levels for only 2 wk after the end of training.

Pulse pressure returned toward pretraining levels in the weeks after the end of training. The time course was similar to that of sBP, with pulse pressure being less than pretraining levels for 6 wk in the loaded group but for only 1 wk with the unloaded group.

DISCUSSION

ISH is the main form of hypertension in older people (10,19) and is frequently poorly controlled with conventional medication (31). Any treatment that helps reduce systolic and pulse pressures would have a substantial effect on the incidence of cardiovascular disease in patients with ISH. Slow breathing training has been shown to reduce resting blood pressure in patients with essential hypertension, and we have noted previously that slow breathing against an added inspiratory load was particularly effective in reducing sBP (24). This suggested that training with an inspiratory load may also be of value in treating ISH. The present study is the first to investigate the effect of breathing training in ISH, either with or without a load, and we found it to significantly reduce systolic and pulse pressure even in patients who were apparently well managed with conventional medication. The reductions were greatest when using loaded breathing, and the benefits after loaded breathing training were sustained for 6 wk after the end of training.

The patients recruited into the study were generally well controlled with conventional medication, although five patients had sBP values higher than 150 mm Hg. The patient compliance both with training and blood pressure monitoring was very good, and there was no dropout after the initial screening and randomization stage, although one control subject was withdrawn. For practical reasons, the study was not blinded, but the critical measurements of blood pressure were obtained by an automated method that requires no particular skill and gives little or no scope for observer bias. Although the patients were told about the overall purpose of the study, they were not aware of the comparison between loaded and unloaded breathing.

Early morning blood pressure measurements were chosen because there is a strong association with vascular damage, which may involve the myocardium, large arteries, and other target organs (26,27). Twenty-four–hour ambulatory measures would provide even more information of cardiovascular risk factors (36), but these measures were not available in the current study.

At the start of the study, 11 of the 20 patients in the training groups had sBP values higher than the normal treatment target of 140 mm Hg. After 8 wk of breathing training, only one subject in the unloaded group was above the target sBP, and she began the study with the highest resting sBP (165 mm Hg). All the patients using loaded breathing were well below the target sBP after 8 wk of training, the highest in this group having an sBP of 135 mm Hg. Similarly, before training, all except one patient in the training groups had pulse pressures greater than 50 mm Hg, whereas at the end of training, half the patients had pulse pressures equal to, or less than, 50 mm Hg.

The improvements cannot be ascribed to a reduction over time of anxiety about making blood pressure measurements as there was a preliminary run-in period to familiarize the patients with the procedures, nor could the improvement be due to a reduction in the "white coat" effect because all the measurements were made in the patients' own homes. Moreover, the control group, who made exactly the same blood pressure measurements, showed no change in blood pressure over the course of the study.

Although the unloaded breathing training was effective in reducing sBP, the added inspiratory load enhanced the training effect with the difference in blood pressure reduction between the loaded and the unloaded groups becoming significant toward the end of training (Fig. 3A).

The extent of the sBP reduction with training was not related to the initial blood pressure; thus, it was not just the less well-controlled patients who responded to the training.

Changes in dBP were small and variable with no differences between the two training groups (Fig. 3B). It is possible that dBP changes have a different time course compared with sBP, but the study was under powered to reveal any such subtle differences.

For a treatment based on some form of training to be truly valuable, the effects should persist for an appreciable time after the training, and as far as we are aware, this is the first study to determine how long the benefits of breathing training are sustained. Systolic blood pressure reverted to pretraining levels fairly rapidly after the end of unloaded breathing training, remaining significantly lowered for only 2 wk. However, for the loaded training group, Systolic blood pressure remained significantly lower than pretraining for 6 wk after the end of training. For this group, 8 of the 10 patients had sBP that was still lower than the 140-mm Hg target at week 14, and of the two above the target, the higher pressure was only 147 mm Hg.

The main pathology in age-related ISH is increased stiffness of the conduit arteries (21), and the fact that the breathing training reduced systolic and pulse pressures implies that this had increased the compliance of the large arteries. Although this has yet to be confirmed by direct measurement of arterial stiffness, it raises the question of possible mechanisms. There is considerable evidence, both in human subjects and in rodents, that physical activity can largely prevent age-related increases in arterial stiffness and that the age-related changes can be reversed with acute training (7,23,32,35). These changes may be due to alterations in the collagen content of the arterial wall (18) or improvements in endothelial function (12,14), and such mechanisms may be involved in the response to breathing training. However, these previous studies all involved essentially normotensive subjects or animals and in none were there any reports of significant changes in resting blood pressure. There has been

one study of exercise training specifically with ISH patients (16), which found no benefit of the type of training that other studies have found to be effective with normotensive subjects of a similar age. Although one study is not necessarily conclusive, it raises the possibility that the action of slow breathing training for ISH may not be the same as aerobic training for age-related changes in arterial stiffness.

There are other possible mechanisms whereby slow breathing, especially with an inspiratory load, might influence the neural control of blood pressure. As mentioned in the Introduction, respiratory maneuvers may activate lung afferents (11), which modulate muscle sympathetic nerve activity (33), whereas the changes in intrathoracic pressure during inspiration will expand the aorta (20) stimulating aortic baroreceptor activity (2). In addition to peripheral mechanisms, the radiation of central respiratory motor drive could influence cardiac vagal neurons as well as sympathetic nerve activity. With repetition, and over time, these effects of slow, deep, and loaded breathing may lead to modification of neural pathways regulating blood pressure.

In summary, we have shown that slow breathing training results in clinically important reductions in resting sBP and pulse pressures for ISH patients who are well managed with conventional medication. When combined with an inspiratory load of 18 cm H_2O, the benefits were greater and persisted for several weeks after the end of training. This form of training is very well tolerated and cost-effective and could be an important adjunct to the normal pharmacological management of patients with ISH.

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The authors have no conflicts of interest in publishing this study.

The results of the present study do not constitute endorsement by the American College of Sports Medicine.

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