Device-guided breathing exercises for the treatment of hypertension: An overview

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Abstract

The American Heart Association considers device-guided breathing as a reasonable treatment modality for lowering blood pressure. This review discusses all randomized controlled trials that have investigated the effects of device-guided breathing on blood pressure in patients with hypertension. Thirteen studies were included in this review. In total, 627 patients were included, of which 365 patients were allocated to device-guided breathing. Only 6 studies used acceptable control groups: listening to music, meditative relaxation exercises, or a sham-device. Two sponsored trials showed beneficial effects of device-guided breathing, both used listening to music as a control group. The remaining 4 studies, which had no employees of the manufacturer listed as co-author, observed no beneficial effects on blood pressure. There is only 1 study that used a sham device as a control group. All other studies were to some extent methodologically flawed. Based on the studies with an acceptable methodological quality, there is no clear evidence supporting a short-term beneficial effect on blood pressure by using device-guided breathing.

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Key words: Hypertension; Device-guided breathing; Review

Core tip: This review discusses all randomized controlled trials that have investigated the effects of device-guided breathing on blood pressure. There were 6 studies with an acceptable control group. Two (manufacturer sponsored) trials showed beneficial effects of device-guided breathing, both used listening to music as a control group. The remaining 4 studies observed no beneficial effects. We conclude that there is no sufficient evidence for recommending device-guided breathing in the treatment of hypertension.
tion (AHA) regarding non-pharmacological options for lowering blood pressure, device-guided slow breathing is described as a reasonable treatment modality to reduce blood pressure (Class II A, Level of Evidence B)[9]. Device-guided slow breathing aims at lowering the respiratory frequency into a so-called “therapeutic breathing zone” (less than 10 breaths per minute) through biofeedback by using an electronic device. Exercises are regarded as successful if the total exercise time is at least 45 min per week, preferably 15 min daily[8]. Sympathetic overactivity is hypothesized as an important contributing factor in the development of hypertension[6-7]. Efforts aimed at reducing this autonomic imbalance may indeed be an effective therapy for hypertension. Slow and regular breathing, guided by musical tones, will lead to a reduction of sympathetic activity and also to an increase in heart rate variability[8]. The baroreceptors measure blood pressure in the carotid arteries and the aorta, and an increase in pressure leads to parasympathetic activation and vice versa (negative feedback mechanism). As an increase in heart rate variability will lead to an increased baroreflex sensitivity[9], device-guided breathing may lead to lower blood pressure values.

The conclusions of the writing group of the AHA statement were based on a meta-analysis[8] and several other studies[9-19]. After the publication of the guideline, two additional studies have been published[20,21]. The overall effect estimate in the meta-analysis showed a small beneficial blood pressure lowering effect [a reduction of 3.7 mmHg in systolic blood pressure (SBP)], but the authors of the meta-analysis stated that the results of the overall effect estimates should be interpreted with caution because of methodological flaws in most studies. Beneficial effects were not observed after excluding studies with high risk of bias or studies that were sponsored by or involved the manufacturer of the device[9]. A previous editorial already emphasized that an independent double-blind study with a proper control group, preferably a sham device, would be necessary to answer the question whether device-guided breathing has any effect on blood pressure[22]. Recently, an investigator-initiated double-blind and sham-controlled trial was performed[23]. This review discusses all randomized controlled trials (RCTs) that have investigated the effects of device-guided breathing on blood pressure in patients with hypertension.

PREVIOUS STUDIES

Thirteen studies, of which the study and patient characteristics are presented in Table 1, were included in this review. In total, 627 patients were included, of which 365 patients were allocated to device-guided breathing. Except for 1 study in which a bi-level positive pressure device (BiPAP®) was used[10], all other studies used the Resperate® device. The Resperate® device uses a form of biofeedback with “breathe in” and “breathe out” instructions according to the listeners breathing rate to guide the respiration into a lower frequency by prolonging expiration. The BiPAP® device was used for the treatment of patients with obstructive sleep apnea and it was also capable of guiding patients’ respiratory rate to less than 10 breaths per minute. Three studies had no control group[11,12,19], 4 studies compared the intervention to usual care or frequent blood pressure measurements[13,14,17,21], 4 studies compared the intervention to listening to music[9,10,15,16], 1 study compared the intervention to meditative relaxation exercises[18], and 1 study used a sham-device in the control group[20]. Except for 3 studies[15,16,23], all other studies were sponsored by or involved the manufacturer of the Resperate® and BiPAP® devices. According to the meta-analysis by Mahtani et al[9], the Anderson paper was also not sponsored by the manufacturer[10]. However, the acknowledgements section of this manuscript states that Drs. B. Gavish, an employee of the company that manufactures the Resperate® device, had reviewed the paper.

EFFECTS OF DEVICE-GUIDED BREATHING

Table 1 presents an overview of the effects of device-guided breathing on blood pressure. Only 4 studies reported between-group-differences including the 95% confidence intervals[9,11,12,23]. Significant decreases in blood pressure were observed in all 3 studies without a control group[11,12,19]. A significant between-group-difference was observed in 2 out of 4 studies that compared device-guided breathing to daily blood pressure measurements[13], and usual care[17]. Studies comparing device-guided breathing to usual care cannot differentiate the 3 possible mechanisms through which the Resperate® could have a blood pressure lowering effect: (1) effects of guided slowing of breathing itself; (2) listening to music; and (3) sitting still. Conclusions regarding the isolated effect of device-guided breathing are only valid when a study has an appropriate control group to disentangle these 3 effects. Therefore, this review will further focus on the 6 studies that used acceptable control groups: listening to music, meditative relaxation exercises and a sham-device[9,10,13,16,18,24]. Two sponsored trials showed beneficial effects of device-guided breathing, both used listening to music as a control group[9,10]. In the study by Schein et al[9] device-guided breathing was not effective in lowering SBP compared to the control group. This study pre-defined a 5 mmHg reduction in diastolic blood pressure (DBP) as clinically relevant. The difference in DBP change between both groups was 4.4 mmHg in favour of the intervention group (P = 0.008). Although a second study failed to predefine a clinically relevant difference, it showed a significant decrease in office SBP compared to a Walkman group (between-group-difference 4.6 mm Hg, P = 0.001)[13]. The remaining 4 studies, which had no employees of the manufacturer listed as co-author, observed no beneficial effects on blood pressure[15,16,18,23]. Only the study by Landman et al[18] described the presence of 2 negative side-effects, but this was insufficient to conclude
that there was a causal relationship with device-guided breathing.

**METHODOLOGICAL QUALITY**

In order to compare the studies, we assessed the methodological quality using the criteria as described by van Tulder et al.\(^\text{[25]}\) (Table 2). The quality of the study by Anderson et al. was low; they used an open randomisation procedure without any further explanation regarding this procedure and blinding\(^\text{[9]}\). After carefully evaluating the studies by Schein et al.\(^\text{[9]}\) and Grossman et al.\(^\text{[9]}\) several methodological questions remained unanswered. It was stated in the Schein et al.\(^\text{[9]}\) study that the study had a double-blind study design\(^\text{[9]}\). Randomisation was performed by a third party and a special technician delivered and

### Table 1 Study and patients characteristics

| Ref. | Study group | Disease, therapy, patients | Number (I/C) | Period (wk) | Study arm | Interventions | Control | Endpoint | Results (mean) | Results (mean) | Results (mean) |
|------|-------------|---------------------------|--------------|-------------|-----------|---------------|---------|----------|----------------|----------------|----------------|
| Schein et al\(^\text{[9]}\), 2001; Israel | HT, medication, BP ≥ 140/90, 25-75 yr | 32/33 | 8 | Resperate® | Walkman | SBP 155.6 ± 141.4, 154.7 ± 143.4 | -2.9 (-2.8-10.6) |
| Israel | | | | 10 min/d | | | |
| Grossman et al\(^\text{[9]}\), 2001; Israel | BP ≥ 140/90, 25-75 yr | 18/15 | 8 | | Home, SBP | DBP 95 ± 91, 94 ± 92.5 | -2.5 |
| | | | | 10 min/d | | | |
| Rosenthal et al\(^\text{[9]}\), 2001; Israel | HT, medication, BP 130/85-180/110, 25-75 yr | 13/- | 8 | | | -24 h, SBP | 137.1 ± 129.9 | - |
| Viskoper et al\(^\text{[9]}\), 2003; Israel | HT, medication, SBP 140-160 or DBP 90-100, 40-80 yr | 17/- | 8 | | Home, SBP | DBP 88.9 ± 82.0 | - |
| Meles et al\(^\text{[9]}\), 2004; Italy | HT, 40-75 yr + 1) not treated, SBP 140-159 or DBP 90-99, OR = 2 | 48/31 | 8 | | | SDP 88.1 ± 84.5 | -4.5 |
| Elliot et al\(^\text{[9]}\), 2004; United States | HT, medication, SBP 140-179, DBP < 110, 40-75 yr | 89/60 | 8 | | | SDP 150.3 ± 139.7, 149.8 ± 140.6 | -1.4 |
| Logtenberg et al\(^\text{[9]}\), 2007; The Netherlands | T2DM, HT, medication, SBP 140-160, > 18 yr | 15/15 | 8 | | Discan | DBP 85.9 ± 85.3, 87.3 ± 85.3 | -0.4 |
| Altena et al\(^\text{[9]}\), 2008; The Netherlands | HT, medication, SBP 140-160, > 18 yr | 15/15 | 8 | | | DBP 83.0 ± 82.0, 87.0 ± 81.5 | 4.6 (10.4-2.3) |
| Schein et al\(^\text{[9]}\), 2009; Israel | T2DM, HT, medication, SBP > 130 | 33/33 | 8 | | | | |
| Anderson et al\(^\text{[9]}\), 2010; United States | Stage 1 HT or pre-hypertension, no medication, no CVD or T2DM. | 20/20 | 4 | | | | |
| Bertsch et al\(^\text{[9]}\), 2011; United States | HT and OSA, medication or untreated, BP ≥ 120/80-160/100, 20-75 yr | 25/- | 8 | | | | |
| Landman et al\(^\text{[9]}\), 2013; The Netherlands | T2DM, HT, medication, SBP 140-160, > 18 yr | 24/24 | 8 | | | | |
| Howorka et al\(^\text{[9]}\), 2013; Austria | T2DM, HT, medication, BP < target value, 18-78 yr | 16/16 | 8 | | | | |

\(^{a}\)P < 0.05 vs control. I: Intervention; C: Control; HT: Hypertension; SBP: (Systolic) blood pressure; DBP: Diastolic blood pressure; T2DM: Type 2 diabetes mellitus; CVD: Cardiovascular disease; OSA: Obstructive sleep apnoea.
explained the device and study procedures. Although the doctor was not aware of the group assignment, patients had weekly follow-up meetings including blood pressure measurements by that same person. Patients were requested not to talk about the specific device with their doctor or other persons who may be participating in the study. As the patients saw their doctor very regularly it is not unlikely that the doctor became aware of group assignment. Therefore, from a methodological point of view, the authors could have opted for another person performing the outcome measurements. An alternative method would have been to check the success of the blinding procedure. The authors did not explain their rationale behind this randomisation procedure. Furthermore, there were several primary endpoints instead of 1 primary endpoint and 2 secondary endpoints. Also, 5% of all blood pressure data were excluded in an unconventional and post-hoc defined 'end of treatment period' analysis.

Grossman et al[10] did not describe whether treatment allocation was concealed and who performed the outcome measurements. Also, data on compliance and whether the blinding procedure was a success, were not provided. Two patients in the control group started the study, the confidence interval ranged from -12.4 mmHg to 3.9 mmHg, and -6.5 mmHg to 11.2 mmHg, respectively, with a direction in favour of the control group.

In the control group, there was a change in antihypertensive interventions, whereas Altena et al[16] reported that 1 patient in the control group had a change in antihypertensive therapy (per-protocol analyses showing the same results).

**DISCUSSION**

Out of the 13 RCTs published, there were only a few studies with an acceptable methodological quality. All studies had a short follow-up period. In order to exert effects on cardiovascular morbidity by using device-guided breathing, the device has to be used for many months and preferably years. None of the studies investigated whether the device could be used for prolonged periods. There is 1 meta-analysis, without any involvement of the manufacturer, that showed a small beneficial effect on blood pressure with unclear clinical relevancy of using device-guided breathing[8]. As was discussed by the authors of this meta-analysis, the overall effect estimate could have been biased due to inclusion of inadequately controlled trials and sponsored studies. In studies with

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**Table 2 Randomized controlled trials with an active control group: methodological quality**

| Criteria                        | Schein[9] | Grossman[16] | Logtenberg[13] | Altena[14] | Anderson[18] | Landman[20] |
|---------------------------------|-----------|--------------|----------------|------------|--------------|-------------|
| Randomization adequate          | ✓/?       | +            | +              | +          | -            | +           |
| Treatment allocation concealed  | +         | ?            | +              | +          | -            | +           |
| Groups similar at baseline      | +         | +            | +              | +          | +            | +           |
| Patient blinded                 | ✓/?       | ✓/?          | +              | +          | -            | +           |
| Care provider blinded           | ✓/?       | ✓/?          | -              | -          | -            | +           |
| Outcome assessor blinded        | -         | ?            | -              | -          | -            | +           |
| Co-interventions avoided        | ✓/?       | ✓/?          | +              | +          | -            | +           |
| Compliance acceptable           | +         | ?            | +              | +          | +            | +           |
| Withdrawal/drop-out rate acceptable | +       | +            | +              | +          | +            | +           |
| Timing of outcome assessment similar | +       | +            | +              | +          | +            | +           |
| Intention to treat analyses     | ✓/?       | +            | +              | +          | +            | +           |

HbA1c level was higher in the intervention group of the Anderson et al[18] study, but additional analyses in which adjustments for age, gender, body mass index and HbA1c were done did not relevantly change the results[23]. The adjusted differences in SBP and DBP were 1.1 mmHg (95%CI: -7.6-9.8, in favour of the control group) and 3.5 mmHg (95%CI: -0.4-7.4, in favour of the intervention group), respectively. Finally, the Logtenberg et al[13] and Altena et al[16] studies had a single-blind design.

Sample size calculations were described in 4 studies[13,16,20], and lacking in the Anderson et al[18] and Grossman et al[10] studies[16,20]. Although Grossman et al[10] mentioned that the group size was large enough, they didn't provide a calculation[10]. The Logtenberg study based the calculation on mean SBP and standard deviation (SD) in their clinic[13]. Altena et al[16] used the mean blood pressure and SD that were observed in the Logtenberg et al[13] study. The most conservative and optimal calculation was performed in the Landman study, as they based their sample size on the highest SD of the change in SBP in the Logtenberg et al[13] (SD 9.4 mm Hg) and Altena et al[16] (SD 10.9 mm Hg) studies[20]. Comparable to their data analysis, Schein et al[9] used an unconventional method for the estimation of their sample size. The standardised detectable difference was based on a previous study[24] while they could have used the change in blood pressure and its SD.
an acceptable methodological quality, no beneficial effects were seen. Sensitivity analysis showed that studies, performed without involvement of the manufacturer, showed no beneficial effects of device-guided breathing. Since the meta-analysis was published, 1 additional study has been completed. This study, which had a successful double-blinding procedure and a sham control group, showed no beneficial effects and even possible adverse events. Unfortunately, the writing group of the AHA guideline on non-pharmacological hypertension treatment finished writing the guideline before publication of this latest trial. As this latest study has the highest level of evidence, the writing group from the AHA was asked to reconsider their recommendation from Class II A, Level of Evidence B into class III, Level of Evidence B (evidence that treatment is not effective). The committee responded that they didn’t believe that the recommendation should be changed. Despite the fact that the latest study showed possible adverse events, the writing group focused on a small positive general effect estimate from the meta-analysis by Mahtani et al. and a meta-analysis that was performed by themselves. This positive recommendation by the guideline committee does not seem to be in line with the evaluation of the authors of the Mahtani et al. study who criticized the methodological quality of most studies and the sponsor involvement in the discussion section of that paper. Since 1 member, who was involved in evaluating the topic of device-guided breathing for the AHA guideline, previously received funding from the manufacturer of the Resperate device, the response of the AHA guideline committee is of potential concern. We agree with Mahtani et al. that there is a real possibility that bias was introduced in the overall effect estimate from combining not adequately controlled studies and by including studies with a high level of sponsor involvement.

CONCLUSION

We conclude that, based on studies with acceptable methodological quality, there is no evidence for a short-term beneficial effect on blood pressure by using device-guided breathing. A meta-analysis of individual patient data combining studies with adequate control groups should be performed in the near future. Since there are no trials, not even uncontrolled, with sufficient follow-up on the feasibility and safety of using the device for many months or years, this device cannot safely be advised for treating hypertension in daily practice.

REFERENCES

1. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2003; 42: 1206-1252 [PMID: 14656957 DOI: 10.1161/01.HYP.0000107251.49515.2]
2. Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Riuilope L, Ryneckiwicz A, Schneider RE, Struijker Boudier HA, Zanchetti A, Vahanian A, Camm J, De Caterina R, Dean V, Dickstein K, Filippatos G, Funck-Brentano C, Hellemans I, Kristensen SD, McGregor K, Sechtem U, Silber S, Tendera M, Widimsky P, Zoromaro JL, Kjeldsen SE, Erdine S, Narkiewicz K, Kiowski W, Agabiti-Rosei E, Ambrosoni E, Cifkova R, Dominiczak A, Fagard R, Heagerty AM, Laurent S, Lindholm LH, Mancia G, Manolis A, Nilsson PM, Redon J, Schmieder RE, Struijker-Boudier HA, Vignaia M, Filippatos G, Adamopoulos S, Agabiti-Rosei E, Ambrosoni E, Bertomeu V, Clement D, Erdine S, Farsang C, Gaita D, Kiowski W, Lip G, Mallion JM, Manolis AJ, Nilsson PM, O’Brian E, Ponikowski P, Redon J, Ruschitzka F, Tamargo J, van Zwielen P, Vignaia M, Waebber B, Williams B, Zamo- rano JL. 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2007; 28: 1462-1536 [PMID: 17562668 DOI: 10.1093/eur- heart/jem226]
3. Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JP, Sever PS, Thom SM. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV). summary. BMJ 2004; 328: 634-640 [PMID: 15001698 DOI: 10.1136/bmj.328.7440.634]
4. Brook RD, Appel LJ, Rubemfire M, Ogedegbe G, Bisognano JD, Elliott WJ, Fuchs FD, Hughes JW, Lackland DT, Staffele- no BA, Townsend PK, Rajagopalan S. Beyond medications and diet: alternative approaches to lowering blood pressure: a scientific statement from the American Heart Association. Hypertension 2013; 61: 1360-1383 [PMID: 23608661 DOI: 10.1161/HYP.0b013e318293645f]
5. Brook RD, Julius S. Autonomic imbalance, hypertension, and cardiovascular risk. Am J Hypertens 2000; 13: 1125-1129 [PMID: 10921530 DOI: 10.1016/S0895-7061(00)00228-4]
6. Pitzalis MV, Mastrospasqua F, Massari F, Passantino A, Colombo R, Mannarini A, Forleo C, Rizzon P. Effect of respiratory rate on the relationships between RR interval and systolic blood pressure fluctuations: a frequency-dependent phenomenon. Cardiovasc Res 1998; 38: 332-339 [PMID: 9709393 DOI: 10.1001/s0008-6363(98)00029-7]
7. Lanfranchi PA, Somers VK. Arterial baroreflex function and cardiovascular variability: interactions and implications. Am J Physiol Regul Integr Comp Physiol 2002; 283: R815-R826 [PMID: 12228049 DOI: 10.1152/ajpregu.00051.2002]
8. Mahtani KR, Nunan D, Heneghan C. Device-guided breathing exercises in the control of human blood pressure: systematic review and meta-analysis. J Hypertens 2003; 21: 852-860 [PMID: 12205126 DOI: 10.1097/01.HJH.0b013e282520077]
9. Schein MH, Gavish B, Herz M, Rosner-Kahana D, Naveh P, Knishkowy B, Zlotnikov E, Ben-Zvi N, Melmed RN. Treating hypertension with a device that slows and regularises breathing exercises. Eur J Hum Genet 2007; 15: 271-278 [PMID: 17319676 DOI: 10.1038/sj.ejhg.5210618]
10. Grossman E, Grossman A, Schein MH, Zimlichman R, Gavish B. Breathing control lowers blood pressure. J Hum Hypertens 2001; 15: 263-269 [PMID: 11319675 DOI: 10.1038/sj.ejhg.5210618]
11. Rosenthal T, Alter A, Peleg E, Gavish B. Device-guided breathing exercises reduce blood pressure: ambulatory and home measurements. Am J Hypertens 2001; 14: 74-76 [PMID: 11206685 DOI: 10.1016/S0895-7061(00)01255-8]
12. Viskoper R, Shapira I, Priluck R, Mindlin R, Chornia L, Lasz T, Dicker D, Gavish B, Alter A. Nonpharmacologic treatment of resistant hypertension: results by device-guided slow breathing exercises. Am J Hypertens 2003; 16: 484-487 [PMID: 12799098 DOI: 10.1016/S0895-7061(03)00571-5]
13. Meles E, Giannattasio C, Failla M, Gentile G, Capra A, Mancia G. Nonpharmacologic treatment of hypertension
by respiratory exercise in the home setting. *Am J Hypertens* 2004; 17: 370-374 [PMID: 15062893 DOI: 10.1016/j.amjhyper.2003.12.009]

14 Elliot WJ, Izzo JL, White WB, Rosing DR, Snyder CS, Alter A, Gavish B, Black HR. Graded blood pressure reduction in hypertensive outpatients associated with use of a device to assist with slow breathing. *J Clin Hypertens* (Greenwich) 2004; 6: 553-559; quiz 560-561 [PMID: 15470284 DOI: 10.1111/j.1524-6175.2004.03553.x]

15 Logtenberg SJ, Kleefstra N, Houweling ST, Groenier KH, Bilo HJ. Effect of device-guided breathing exercises on blood pressure in hypertensive patients with type 2 diabetes mellitus: a randomized controlled trial. *J Hum Hypertens* 2009; 23: 325-331 [PMID: 19005477 DOI: 10.1038/jhh.2008.135]

16 Schein MH, Gavish B, Baevsky T, Kaufman M, Levine S, Nessing A, Alter A. Treating hypertension in type II diabetic patients with device-guided breathing: a randomized controlled trial. *Blood Press* 2009; 18: 273-279 [PMID: 19919399 DOI: 10.3109/08037050903272925]

17 Anderson DE, McNeely JD, Windham BC. Regular slow-breathing exercise effects on blood pressure and breathing patterns at rest. *J Hum Hypertens* 2010; 24: 807-813 [PMID: 20200548 DOI: 10.1038/jhh.2010.18]

18 Bertisch SM, Schomer A, Kelly EE, Baloa LA, Hueser LE, Pittman SD, Malhotra A. Device-guided paced respiration as an adjunctive therapy for hypertension in obstructive sleep apnea: a pilot feasibility study. *Appl Psychophysiol Biofeedback* 2011; 36: 173-179 [PMID: 21523471 DOI: 10.1007/s10484-011-9158-x]

19 Landman GW, Drion I, van Hateren KJ, van Dijk PR, Logtenberg SJ, Lambert J, Groenier KH, Bilo HJ, Kleefstra N. Device-guided breathing as treatment for hypertension in type 2 diabetes mellitus: a randomized, double-blind, sham-controlled trial. *JAMA Intern Med* 2013; 173: 1346-1350 [PMID: 23752780 DOI: 10.1001/jamainternmed.2013.6883]

20 Howorka K, Pumprla J, Tamm J, Schabmann A, Klomfar S, Kostineak E, Howorka N, Sovova E. Effects of guided breathing on blood pressure and heart rate variability in hypertensive diabetic patients. *Auton Neurosci* 2013; 179: 131-137 [PMID: 24021938 DOI: 10.1016/j.autneu.2013.08.065]

21 Parati G, Carretta R. Device-guided slow breathing as a non-pharmacological approach to antihypertensive treatment: efficacy, problems and perspectives. *J Hypertens* 2007; 25: 57-61 [PMID: 17143174 DOI: 10.1097/HJH.0b013e328012bf0f]

22 van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the Cochrane collaboration back review group. *Spine* (Phila Pa 1976) 2007; 32: 1290-1299 [PMID: 12811274 DOI: 10.1097/00007632-20030615-00014]

23 Patel C, North WR. Randomised controlled trial of yoga and bio-feedback in management of hypertension. *Lancet* 1975; 2: 93-95 [PMID: 49737 DOI: 10.1016/S0140-6736(75)90002-1]

24 van Dijk PR, Landman GW, van Hateren KJ, Logtenberg SJ, Bilo HJ, Kleefstra N. Call for a re-evaluation of the American Heart Association’s standpoint concerning device-guided slow breathing using the RESPeRATE device. *Hypertension* 2013; 62: e17 [PMID: 23959556 DOI: 10.1161/HYPERTENSIONAHA.113.02022]

25 Elliott WJ, Brook RD. Response to Call for a re-evaluation of the American Heart Association’s standpoint concerning device-guided slow breathing using the RESPeRATE device. *Hypertension* 2013; 62: e18 [PMID: 24156102 DOI: 10.1161/HYPERTENSIONAHA.113.02042]
