Meta-Analysis of Effects of Voluntary Slow Breathing Exercises for Control of Heart Rate and Blood Pressure in Patients With Cardiovascular Diseases

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Rising heart rate (HR) and elevated blood pressure (BP) cause a greater frequency of cardiovascular events. Many patients cannot maintain target HR and BP using pharmacological therapies. To evaluate the effectiveness of voluntary slow breathing exercises in reducing resting HR and BP, we searched Embase (1974 to April 2016), PubMed (1966 to April 2016), the Cochrane Central Register of Controlled Trials (issue 4, April 2016), and PEDro (www.pedro.org.au; 1999 to April 2016). The primary outcome was the mean change in HR at rest. Secondary outcomes included changes in systolic blood pressure (SBP) and diastolic blood pressure (DBP) as well as compliance with the breathing training. Finally, we included 6 studies consisting of 269 subjects. Practice of the breathing exercises resulted in statistically significant HR reduction (mean difference: $-1.72$ beats/min, 95% CI $-2.70$ to $-0.75$). Reductions were seen in SBP (mean difference: $-6.36$ mm Hg, 95% CI $-10.32$ to $-2.39$) and DBP (mean difference: $-6.39$ mm Hg, 95% CI $-7.30$ to $-5.49$) compared with the controls. Trial durations ranged from 2 weeks to 6 months. In conclusion, the existing evidence from randomized controlled trails demonstrates that short-term voluntary slow breathing exercises can reduce resting HR, SBP, and DBP for patients with cardiovascular diseases. © 2017 Elsevier Inc. All rights reserved. (Am J Cardiol 2017;120:148–153)

Voluntary slow breathing exercises (VSBEs) are defined based on a self-controlled breathing rate to achieve decreased respiratory rate and increased respiratory amplitude (tidal volume).\textsuperscript{1} It is an easy-operated/practical method for patients with cardiovascular disease. However, its effects on reductions in heart rate (HR) and blood pressure (BP) are still controversial. Silva et al.\textsuperscript{2} found that there was no significant reduction in HR or systolic blood pressure (SBP) after deep breathing exercises for patients with coronary artery disease, hypertension, and diabetes mellitus. Meanwhile, a study by Dixhoorn et al.\textsuperscript{3} revealed that slow breathing was related to beneficial effects on resting HR for myocardial infarction patients. Another recent study also demonstrated that slow breathing training produced a valuable reduction in resting HR and SBP in hypertensive patients.\textsuperscript{4} Thus, we performed a meta-analysis to analyze the impact of VSBE on HR and BP for patients with cardiovascular disease.

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Methods

Studies were eligible if they met the following standards: (1) studied cardiovascular disease mainly including coronary heart disease, hypertension, and heart failure; (2) patients were aged over 18 years; (3) HR and (or) BP was an outcome; (4) the language of the studies was English; and (5) were randomized controlled trails (RCTs) with designs involving VSBE and natural breathing as the intervention and control arms, respectively. Exclusion criteria were: (1) abstracts, review studies, case reports, or editorials; (2) repeated reports or low-quality studies; (3) studies not involving VSBE and natural breathing as the intervention and control arms, respectively. Terms used included “breathing exercise/slow breathing” and “heart rate/blood pressure.” We also searched the citations of full-text studies retrieved. Two reviewers screened studies through the titles and abstracts independently to confirm whether the study met the inclusion criteria. Data extracted independently by 2 investigators included study characteristics and intervention information. Disagreements were resolved in consultation with an arbitrator. We contacted the investigators of original studies for missing information when necessary.

Primary outcomes included the mean change in resting HR. Secondary outcomes included changes in SBP and
diastolic blood pressure (DBP) as well as compliance with the intervention. When data were shown only in graphical form, we extracted information from the figures using the Getdata Graph Digitizer, version 2.25 (http://getdata-graph-digitizer.com/). When the trial provided only the mean and SD before and after the intervention in each group and those change between baseline and final measurement were missing, the SD of the change could be transformed by the formula in the Cochrane Handbook 4.2.2 (SD(C) = \sqrt{SD(B)^2 + SD(F)^2 - 2 \times R \times SD(B) \times SD(F)}; C, change value; B, baseline value; F, final value). The R values for HR, SBP, and DBP were 0.75, 0.76, and 0.76 in the experimental group and 0.93, 0.8, and 0.54 in the control group, respectively. Because the R value was estimated using data from other studies, we chose sensitivity analysis to test the stability of the result.

We used the Physiotherapy Evidence Database scale to evaluate the methodological quality of each included study. For assessing bias, the tool involves 11 items (Table 1). The total scale score is 10. The second item to the eleventh item each count as a point. Item 1, used to evaluate the external reality, is not accounted for in the total score. Scores of 9 to 10 represent the best quality, scores of 6 to 8 represent good quality, scores of 4 to 5 represent general quality, and scores < 4 represent poor quality.

The meta-analysis was performed using Review Manager 5.3 software. We used it to calculate the mean difference
and 95% CI. Heterogeneity was evaluated by testing the clinical characteristics of the enrolled studies as well as by formal statistical testing using chi-square and I² tests. Where no heterogeneity was present, we performed a fixed-effect meta-analysis. If substantial heterogeneity (I² > 50%) was detected, we sought the direction of effect, and where applicable, used a random-effects analysis.

Results

Our initial search revealed a total of 2,549 records. Screening progress was shown in Figure 1. Six RCTs were ultimately included; characteristics of patient populations from included studies are presented in Tables 2 and 3. Study with a low risk of bias was defined as a study fulfilling 6 or more of the 11 criteria, whereas a study meeting < 6 of the criteria had a high risk of bias. The scores of the 6 RCTs for risk of bias ranged from 5 to 8 (Table 1), indicating a low risk of bias.

HR results of 229 patients were reported on 5 studies included.Overall, VSBE resulted in an HR decrease of 1.72 beats/min (95% CI −2.7 to −0.75, p = 0.0005) with low heterogeneity (I² = 13%; Figure 2, 1.1.1). According to the N$_{fo.05}$ = (ΣZ/1.64)$^2$−S (Z representing the Z value of each single study; S representing the number of all enrolled studies) to calculate a fail-safe number ($N_{fo.05}$). The $N_{fo.05}$ was 182. That is, that another 182 negative studies would be needed to reverse this result, thus indicating that the result is stable.

Five studies including data from 193 patients showed the effect of VSBE on BP. SBP was reduced by 6.36 mm Hg (95% CI −10.32 to −2.39; p = 0.002) with significant heterogeneity (I² = 80%; Figure 3, 2.1.1). By reviewing the studies, we conducted a subgroup meta-analysis after excluding a study by Mourya et al. The result revealed that the heterogeneity (I² = 29%; Figure 3, 2.1.2) and SBP (mean difference: −4.63 mm Hg, 95% CI −7.47 to −1.79) were significantly reduced. The $N_{fo.05}$ for SBP was 23, which indicated that the result was stable. DBP was reduced by 6.39 mm Hg (95% CI −7.30 to −5.49; p < 0.00001), and the heterogeneity was moderate (42%; Figure 4, 3.1.1). The $N_{fo.05}$ regarding DBP was 183, which indicated that the result was stable.

Data on compliance with VSBE were reported on 3 studies. In the study by Dixhoom and Mourya, 79% and 90% compliance rates were reported, respectively. In the study by Modesti et al., patients performed exercises 5.1 times/week (of the 7 requested), for 22 min/day (of 30 minutes) on average.
There were 3 studies\textsuperscript{3,4,12} that did not include the original data we needed. After contacting the investigators, an investigator\textsuperscript{4} provided the relevant results. Therefore, we used the formula to calculate the SD of mean change. We performed sensitivity analysis, excluding 2 studies\textsuperscript{3,4} from the HR comparison and another 2 studies\textsuperscript{4,12} from the BP comparison. The results indicated there were still significant effects on improving resting HR, SBP, and DBP (Figure 2, 1.1.2; Figure 3, 2.1.3; and Figure 4, 3.1.2).

### Discussion

Based on the inclusion and exclusion standards, we selected all RCTs published in English to explore the effect of VSBE on resting HR and BP. To avoid missing the studies of the effects of VSBE on HR and BP, we did not include “diseases of participants” in the search strategy. Ultimately, the diseases of the participants in the included studies were hypertension and coronary artery disease.

Many experimental and clinical observations have shown that ischemic heart disease and heart failure can reduce baroreflex sensitivity, which leads to sympathetic overactivity and suppression of parasympathetic activity.\textsuperscript{13} The origin of hypertension is characterized by such a characteristic of autonomic imbalance.\textsuperscript{14} A low breathing rate through activating the Hering-Breuer reflex could improve baroreflex sensitivity,\textsuperscript{14} improve cardiac vagal tone, and modulate sympathetic overactivity, thereby decreasing resting HR and BP.\textsuperscript{15} Changes of autonomic imbalance and baroreflex sensitivity promptly vanish after the restoration of a normal breathing rate.\textsuperscript{16} However, recently a randomized study\textsuperscript{17} has demonstrated that VSBE can induce chronic autonomic changes in the modulation of baroreflex sensitivity, ambulatory BP, renal resistive index, and HR variability.

Resting HR reduction was closely related to the decreased risk of cardiovascular events and all-cause death for patients with coronary heart disease and hypertension.\textsuperscript{18,19} The risk of cardiovascular death or hospital admission increased by 3\% with every beat increase from baseline HR and 16\% with every 5 beats/min increase in patients with heart failure.\textsuperscript{20} When resting HR increased by 5 beats/min in patients with coronary heart disease and left ventricular dysfunction, risks increased by 8\% for cardiovascular death, 7\% for myocardial infarction, and 16\% for admission for heart failure.\textsuperscript{21} In addition, data from 4,065 patients suggested that for each beat of HR change, there was a 1\% change in mortality risk for hypertensive patients.\textsuperscript{19} Our meta-analysis showed that the practice of VSBE had the overall effect of reducing resting HR by an average of 1.7 beats/min. Therefore, VSBE is a useful intervention to reduce the resting HR of patients with cardiovascular diseases.

Uncontrolled hypertension could lead to a higher risk of heart failure, coronary heart disease, and major cardiovascular disease events.\textsuperscript{22} With every 3.6 mm Hg reduction of mean BP, the relative risks of total cardiovascular events, strokes, coronary events, cardiovascular deaths, and total deaths were 0.86, 0.72, 0.91, 0.75, and 0.78 times, respectively, that of a 2.4 mm Hg reduction. These findings indicated that reduction of BP is important for cardiovascular patients. In our results, the practice of VSBE could reduce SBP by 6.36 mm Hg and DBP by 6.39 mm Hg on average. Therefore, VSBE could provide beneficial effects of BP reduction for patients with hypertension and coronary heart disease.

Only one study tested the effect of HR and BP at 6 months among the 6 included studies. Three\textsuperscript{3,9,12} studies reported the adherence to slow breathing exercises and patients in 2 studies\textsuperscript{3,12} reported good adherence to the intervention. In the study by Modesti et al,\textsuperscript{7} the number of practice sessions (7 times/week requested) decreased from 5.1 times/week at baseline to 3.3 times/week at 6 months.
Thus, monitoring of long-term adherence is required to obtain accurate information on the benefits of this intervention.

The review was limited by the methodological quality of the 6 studies, which were suggested to have a low to moderate risk of bias. The blinded methods of allocation concealment, blinding of patients, therapists, and evaluators were not completely provided by the enrolled studies. Furthermore, we did not create funnel plots to show publication bias because the number of included studies was limited. Further
limitations are that the SD of mean change before and after the intervention within the groups was transformed by a formula; the extracted data were not very accurate; and the sample was small, which could influence the interpretation of the results.

Disclosures

The authors have no conflicts of interest to disclose.

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