

The effect of slow breathing exercise on heart rate and blood pressure in patients undergoing percutaneous coronary intervention: a randomized controlled trial

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Aim

To determine the effects of slow breathing exercise (SBE) on heart rate (HR) and blood pressure (BP) in patients after percutaneous coronary intervention (PCI).

Methods and results

The study is a single-blind, randomized controlled trial. Seventy-eight eligible patients after primary PCI were divided randomly into either the control group or the trial group. The control group only received routine post-PCI care. In addition to routine care, participants in the trial group performed SBE at home, two to three times for a total of 30 min every day for 12 weeks. The main outcomes were HR and BP measured in the office and at home. The secondary outcome was compliance with the breathing exercise. Patients allocated to the trial group, on average, performed 5.21 days/week for 26.00 min/day. The trial group showed a significant reduction in HR of 3.95 b.p.m. ($P = 0.004$) measured in the office. The reduction in HR measured in the office was greater for the trial group, with a significant difference between the two groups ($P = 0.005$). There was no significant difference between the two groups in HR measured at home. There was also no significant difference in BP measured in the office or at home between the two groups.

Conclusion

Slow breathing exercise is an effective non-pharmacological method to reduce HR in patients undergoing PCI. Further study is needed to confirm whether the intervention is effective on BP.

Registration

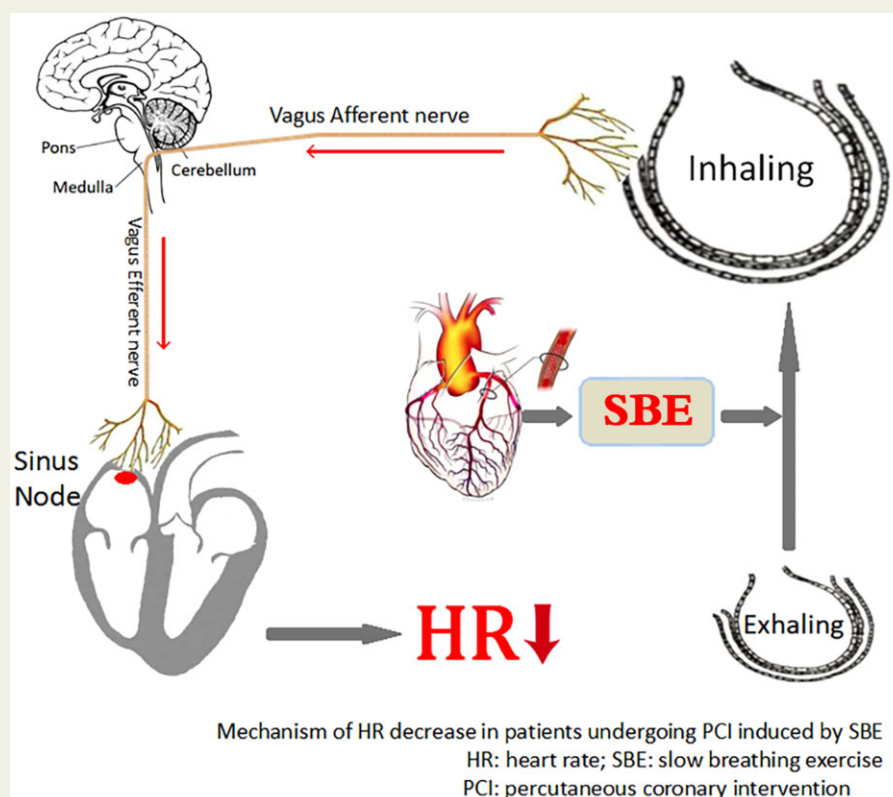
The trial was registered at the Chinese Clinical Trial Registry: ChiCTR-IOR-17012525

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Graphical Abstract



Keywords

Slow breathing exercise • Percutaneous coronary intervention • Coronary heart disease • Heart rate • Blood pressure

Implications for practice

- Slow breathing exercise (SBE) is an effective non-pharmacological method to reduce the heart rate (HR) of patients undergoing percutaneous coronary intervention (PCI).
- Slow breathing exercise can effectively decrease the HR in patients undergoing PCI, which may be benefit for them.
- Compliance with SBE is good, and this easy practical exercise may be adapted as part of a self-management program to complement pharmacological treatment.
- More studies are needed to establish the effect of SBE in reducing blood pressure in patients after primary PCI.

Introduction

Percutaneous coronary intervention (PCI) is a widely used method that can restore coronary artery blood flow and has become the cornerstone treatment for coronary heart disease.¹ Although PCI can effectively improve myocardial ischaemia symptoms and reduce the incidence of cardiovascular events, some high-risk factors for recurrent cardiac events might remain.^{2,3} Elevated heart rate (HR) and blood pressure (BP) after PCI are essential and alterable risk factors associated with an increased risk of cardiac events.^{4,5} A clinical study found that there was a two-fold increased risk of cardiovascular mortality in the 1- and 4-year follow-up for patients with a HR of 70

b.p.m. or more compared with patients with a HR <70 b.p.m. on discharge after PCI.⁶ Additionally, patients with hypertension after PCI were 10% more likely to suffer subsequent myocardial infarction (MI) and 2% more likely to stroke.⁷ It is essential to keep HR and BP in patients after PCI at appropriate levels.

At present, some medications such as beta-blockers, angiotensin-converting enzyme inhibitors, and angiotensin II antagonists are prescribed to patients with PCI to control HR and BP. The American guidelines in 2012 for the diagnosis and management of patients with stable ischaemic heart disease recommended that the HR and BP should be kept between 55 and 60 b.p.m. and <140/90 mmHg, respectively; otherwise, the risk of cardiovascular events will increase.⁸

However, the current situation of the control of HR and BP by medication after PCI is not very optimistic. A prospective cohort study conducted at 13 hospitals in mainland China showed that only 30.03% of the patients met the target HR and BP after PCI.⁹

Slow breathing exercise (SBE), a behavioural technique, is used as an adjunct to medication to control HR and BP in patients with cardiovascular diseases.¹⁰ The mechanism of the reduction of HR and BP by SBE in cardiovascular diseases is that a low breathing rate could increase the baroreflex sensitivity, improve cardiac vagal tone, and modulate sympathetic overactivity, thereby decreasing HR and BP.^{11–13} However, in previous studies,^{14,15} the autonomic nervous system is disordered in patients with coronary heart disease who receive conservative treatment or thrombolysis, whereas now those receiving PCI are better able to preserve autonomic nervous function.¹⁶ Therefore, whether SBE can still help to control HR and BP by improving autonomic nerves function in patients undergoing PCI needs to be addressed.

Methods

Study design and settings

The investigation conforms with the principles outlined in the Declaration of Helsinki. The study was approved by the Ethics Committee of First Affiliated Hospital of Soochow University (No. 2017140). In brief, the study was a randomized controlled trial with concealed allocation and partial blinding, conducted in the cardiovascular department of a tertiary hospital in Suzhou, China. The trial was registered at the Chinese Clinical Trial Registry with the number: ChiCTR-IOR-17012525. The structure of the methodology conformed to the CONSORT guidelines.¹⁷

Participants

From August 2017 to August 2018, participants were recruited from the Department of Cardiology, The First Affiliated Hospital of Soochow University and were screened by trained researchers in the Department of Cardiology. Inclusion criteria were as follows: age ≥ 18 years; primary PCI; HR > 60 b.p.m. with or without beta-blockers after PCI; essential hypertension Stage I or II [systolic BP (SBP) 140–179 mmHg, diastolic BP (DBP) 90–109 mmHg] with or without antihypertensive agents based on the JNC-VII;¹⁸ good understanding of SBE and good communication with researchers. Exclusion criteria: (i) left main coronary arteries still narrowed $\geq 70\%$ or $\geq 50\%$ after PCI;¹⁹ (ii) operation only consisted of thrombus aspiration or balloon angioplasty; (iii) cardiac arrhythmia: second-degree atrioventricular block, atrial fibrillation, tachycardia, or sick sinus syndrome; (iv) New York Heart Association (NYHA) cardiac function Class $\geq$ III; (v) chronic respiratory disease, severe liver, kidney disease, or hyperthyroidism; and (vi) severe cognitive impairment and mental illness. The participants' HR and BP were adjusted by changing the beta-blocker dosage and antihypertensive medication or dosage during the intervention. Because patients after PCI were required to come to the hospital every month for a doctor's visit within 3 months of discharge, the doctor could adjust the medication according to the patient's condition.

Sample size calculation

A 4 b.p.m. HR improvement is considered to be clinically meaningful.²⁰ Thus, to detect a minimal clinically significant difference of 4 b.p.m. with 80% power (type I error = 5%, two-side test), assuming a standard deviation (SD) of 5 b.p.m.,¹⁰ a total sample size of 64 across both groups of

the study would be required. Allowing for a 20% loss to follow-up, we planned to recruit a total of 78 participants into this study.

Randomization

A study assistant generated the random allocation sequence with a table of random numbers. Informed consents have been collected for all participants before the random allocation. Following provision of consent, random allocation was carried out by an unbiased intern in the Department of Cardiology who was not connected with the research, to blindly assign each participant fulfilling the study to the control or trial group, according to the information provided by the assistant.

The intervention

Participants in the control group only received routine care provided by a research assistant. Post-PCI routine care involves brief inpatient health education, medication management, and weekly follow-up phone calls regarding patients' cardiovascular health.

In addition to routine care, participants in the trial group also received 12-week SBE practice at home. Before discharge, SBE was taught by a certified technician in a single 2-h session in the meeting room of the ward on the day after PCI. After 20 min of quiet rest, patients were requested to slowly inhale through the nostrils for 4 s and slowly exhale through the mouth for 6 s in a breathing cycle, reaching 4–6 breaths/min, and then to keep the same rate to breath.²¹ Patients were instructed to estimate the respiration rhythm by counting number silently from 1001 to 1004 (a time of ~ 4 s) when inhaling and 1001–1006 (a time of ~ 6 s) when exhaling in a breathing cycle. During the training period, the time of the patient's chest and abdomen movement was calculated with a stopwatch to determine whether the patients had achieved the required breathing rate. To check the correctness of patients' breathing exercise method, they were required to show the exercise to the technician and necessary corrections were given for their mistakes. After 2 days of practice in the hospital, patients who could still not perform SBE properly for 10 min at a time were excluded because they might not be able to complete the breathing exercise at home independently. After discharge, participants were asked to perform SBE at home two to three times for a total of 30 min every day for 12 weeks.

Data collection and study outcomes

Heart rate and BP were measured both by blinded researchers in the office and by the participants themselves in their home setting. Measurements at home: participants were instructed to measure their BP at home with a digital upper-arm sphygmomanometer validated by the Suzhou Institute of Metrology. Participants were asked to rest in a chair for at least 5 min and then made three measurements in the morning between 9.00 and 10.00 a.m. Patients were required to eat a light breakfast and refrain from physical activity, caffeine, and hot water for at least 30 min before the measurement. When BP was being measured, HR was measured by the same sphygmomanometer. The values of three measurements were averaged to form single the BP and HR for that day, and the measurements made on one workday and one weekend, respectively, during each of these weeks were averaged to form single values for each participant. The compliance with SBE, the adjustment of medication, and the overall well-being during the training were collected from weekly follow-up phone calls of a study assistant. Measurements in the office: measurements of office HR and BP were made in the meeting room of ward at baseline and at 3 months post-intervention (12 weeks after baseline) with the same validated digital sphygmomanometer (HEM-8102A, OMRON HEALTH CARE Co., Ltd, Dalian, China) between 9.00 and

12.00 a.m. Patients were required not to smoke or drink caffeine and hot water for 30 min before the measurement. Measurements were taken by blinded researchers after at least 15 min rest when sitting. Three measurements were taken for every patient, and values were averaged to form single values.

Data analysis

Statistical analyses were performed with SPSS (version 18.0; SPSS, Inc., Chicago, IL, USA). For continuous variables, the results are described as the mean ± SD, and comparisons were analysed using the independent samples *t*-test, paired samples *t*-test, or repeated measures analysis of variance. Categorical variables presented as frequencies (percentages) were compared with the χ^2 test or Fisher’s exact test. Additionally, the intention-to-treat (ITT) analysis was performed by filling in the data of

drop-outs with the values at baseline or those closest to the measurement time point.

Results

Of the 126 participants recruited from 28 August 2017 to 27 August 2018, 48 patients were excluded due to various reasons (Figure 1) in the screen for eligibility. A total of 78 patients, aged 33–83 years, with a mean (SD) age of 61.40 (9.88) years, were included. Table 1 shows the characteristics of the participants at enrolment. There were no statistically significant differences for their characteristics between the two groups.

Some reasons for the attrition of patients during the follow-up are also shown in Figure 1. Finally, 73 patients accomplished the 12-week

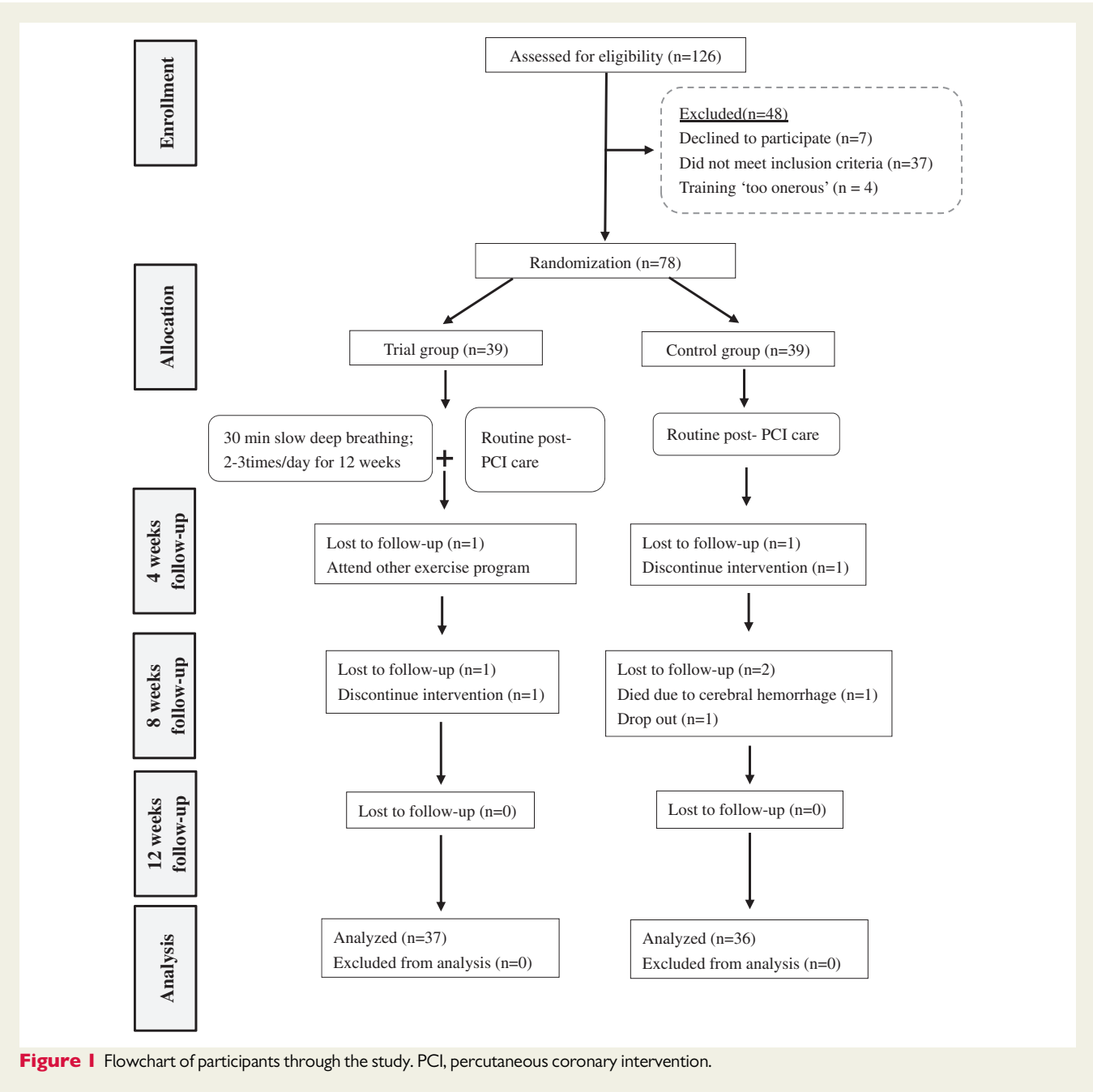


Figure 1 Flowchart of participants through the study. PCI, percutaneous coronary intervention.

Table 1 Characteristics of participants at enrolment

Variables	Control group (n = 39)	Trial group (n = 39)	t/ χ^2	P-value
Age (years), mean (SD)	61.13 (10.43)	61.67 (9.43)	-0.24	0.812
Gender (male), n (%)	34 (87.2)	35 (89.7)	<0.01	1.000
Education status, n (%)				
Primary school	9 (23.1)	9 (23.1)	0.76	0.846
Junior high school	9 (23.1)	12 (30.8)		
High school	15 (38.5)	12 (30.8)		
University	6 (15.4)	6 (15.4)		
Smokers, n (%)	10 (25.6)	10 (25.6)	0.00	1.000
Drink alcoholic beverage, n (%)	6 (15.4)	2 (5.1)	1.25	0.263
Low salt and low-fat diet, n (%)	29 (74.4)	27 (69.2)	0.25	0.800
Walk (min/d), mean (SD)	32.69 (7.59)	33.85 (15.58)	-0.42	0.679
BMI (kg/m ²), mean (SD)	24.31 (2.47)	23.32 (2.67)	1.70	0.094
Creatinine (μ mol/L), mean (SD)	71.14 (13.96)	73.11 (9.88)	-0.72	0.474
Coronary artery stenosis status, n (%)				
Left	11 (28.2)	18 (46.2)	2.71	0.302
Right	5 (12.8)	4 (10.3)		
Both	23 (59.0)	17 (43.6)		
Stents, n (%)	1.67 (1.01)	1.69 (0.98)	-0.11	0.910
Left ventricular ejection fraction (%), mean (SD)	58.43 (8.97)	55.66 (10.55)	1.25	0.214
Duration of hypertension (years), mean (SD)	7.42 (7.60)	7.54 (8.81)	-0.03	0.951
Duration of medication (years), mean (SD)	7.22 (7.40)	7.28 (8.66)	-0.04	0.972
Number of patients on beta-blocker, n (%)	28 (71.8)	29 (74.4)	0.07	1.000

BMI, body mass index; SD, standard deviation.

Table 2 Comparison of heart rate at baseline, at 4 weeks, at 8 weeks and at 12 weeks in control group and trial group

HR (b.p.m.), mean (SD)	Control group (n = 36)	Trial group (n = 37)	t/F	P-value
Office				
Baseline	70.67 (6.92)	68.68 (5.56)	1.36	0.179
Week 12	69.74 (8.48)	64.73 (6.12)	2.90	0.005*
t and P	t = 0.71, P = 0.438	t = 3.10, P = 0.004*	—	—
MD	-0.93 (7.89)	-3.95 (7.74)	1.65	0.104
Home				
Baseline	70.56 (5.81)	69.86 (6.18)	0.49	0.625
Week 4	70.94 (7.40)	69.30 (8.22)	0.90	0.372
Week 8	70.75 (6.91)	67.28 (7.98)	1.76	0.189
Week 12	70.61 (6.43)	65.35 (6.68)	3.92	0.052

P-value for comparison by independent sample t-test, paired samples t-test, or repeated measures analysis of variance.

HR, heart rate; MD, mean difference; SD, standard deviation.

*P < 0.05.

follow-up by the end of August 2018. Two patients in the control group and one patient in the trial group experienced angina during the study.

According to the patients' self-report, patients allocated to the trial group on average performed 5.21 days/week (out of the seven

requested), for 26.00 min/day (out of the 30 min requested) during the entire study period. During the first, second, and third months of the intervention, patients on average practiced 6.05 days/week for 23.62 min/day, 6.36 days/week for 27.33 min/day, and 6.23 days/week for 27.06 min/day, respectively.

Table 3 Comparison of heart rate measured in the office between control and trial groups in which patients who had not changed their medications and intention-to-treat analyses for the comparison of office heart rate

HR (b.p.m.), mean (SD)	Comparison of office HR between two groups in which patients who had not changed their medications		t	P-value	Intention-to-treat analyses for the comparison of office HR		t	P-value
	Control group (n = 29)	Trial group (n = 26)			Control group (n = 39)	Trial group (n = 39)		
Baseline	69.72 (5.56)	68.88 (5.83)	0.55	0.587	71.21 (7.49)	68.90 (5.61)	1.54	0.128
Week 12	68.50 (6.65)	65.15 (5.12)	2.07	0.043*	69.11 (9.27)	65.15 (6.34)	2.20	0.031*

HR, heart rate; SD, standard deviation.

*P < 0.05.

Table 4 Comparison of blood pressure between control and trial groups

BP (mmHg), mean (SD)		Control group (n = 36)	Trial group (n = 37)	t/F	P-value
Office					
SBP	Week 0	119.69 (13.20)	124.57 (16.13)	−1.41	0.163
	Week 12	121.47 (12.97)	122.54 (11.28)	−0.38	0.708
DBP	Week 0	72.11 (7.54)	75.57 (10.02)	−1.67	0.100
	Week 12	75.24 (7.16)	76.62 (8.03)	−0.78	0.439
Home					
SBP	Baseline	125.89 (14.18)	124.57 (13.94)	0.40	0.689
	Week 4	123.92 (14.27)	122.95 (13.61)	0.30	0.767
	Week 8	123.61 (13.54)	122.59 (13.08)	0.15	0.697
	Week 12	123.03 (13.75)	121.68 (12.02)	0.18	0.671
DBP	Baseline	74.39 (7.61)	74.46 (9.01)	−0.04	0.971
	Week 4	74.58 (8.53)	74.35 (7.54)	0.12	0.902
	Week 8	73.78 (6.84)	74.27 (8.29)	0.01	0.944
	Week 12	72.89 (6.27)	73.57 (7.67)	0.03	0.861

P-value for comparison by independent sample t-test or repeated measures analysis of variance.

BP, blood pressure; DBP, diastolic BP; SBP, systolic BP; SD, standard deviation.

P < 0.05.

Table 5 The comparison of beta-blocker and antihypertensive agents used in two groups during the study period

Variables	Change of agents	Control group (n = 36)	Trial group (n = 37)	χ^2	P-value
Number of patients on beta-blockers, n (%)	Reduction or cessation	2 (5.6)	6 (16.2)	2.11	0.372
	Increase	5 (13.9)	4 (10.8)		
	No change	29 (80.6)	27 (73.0)		
Number of patients on antihypertensive agents, n (%)	Reduction or cessation	3 (8.3)	5 (13.5)	1.31	0.507
	Increase	2 (5.6)	4 (10.8)		
	No change	31 (86.1)	28 (75.7)		

Study outcomes

Data on HR before and after the intervention are presented in [Table 2](#), together with differences within and between groups. Patients in the control group presented a minimal change in both HR measured in the office and HR measured at home. The trial group showed a significant reduction in HR of 3.95 b.p.m. ($P = 0.004$) ([Table 2](#)) in the measurement made in the office. The reductions in HR measured in the office were somewhat higher for the trial group, with a significant difference between the two groups ($P = 0.005$) ([Table 2](#)). Heart rate measured in the office also fell significantly among the patients whose medications had not changed ($P = 0.043$) ([Table 3](#)). The trial group also presented significant reductions in the measurements of HR made in the office by the ITT analysis ($P = 0.031$) ([Table 3](#)). Heart rate measured at home displayed a decreasing trend in the trial group, but did not reach statistical significance between the two groups ([Table 2](#)).

[Table 4](#) shows the comparison of BP between the control and trial groups. In general, BP in both the control group and the trial group remained within the normal range, changing relatively minimally during the study period. Although SBP and DBP in the trial group were higher than those in the control group, the difference between the two groups was not statistically significant. Besides, both SBP and DBP measured at home showed a downward trend, but no significant changes between the two groups were detected.

[Table 5](#) presents the comparison of beta-blockers and antihypertensive agents used in the two groups during the study period. Although some of the patients changed doses of beta-blockers and antihypertensive agents during the study, no difference presented statistical significance between the two groups.

Discussion

Elevated HR is closely related to further cardiovascular events, especially the increased risk of heart failure and all-cause mortality.²² A clinical study showed that there was a two-fold increased risk of cardiovascular mortality in 1- and 4-year follow-up for patients with a HR of 70 b.p.m. or more compared with a HR <70 b.p.m. on discharge after PCI.⁶ Moreover, every increase of 5 b.p.m. in HR at discharge was associated with a 29% and 24% increased risk of cardiovascular mortality at the 1- and 4-year follow-ups, respectively.⁶ Another meta-analysis also confirmed that an increased HR would raise the risk of death after PCI.²³ In the study, HR at baseline in the two groups was around 70 b.p.m., so the participants after PCI may have a relatively high risk of various cardiovascular events. At the same time, HR in the trial group decreased from nearly 70 to 64.73 b.p.m., suggesting a roughly two-fold reduction in the risk of cardiovascular mortality in the trial group. In the present study, HR measured in the office of the trial group was slightly lower than that of the control group. However, there was no statistical difference in HR, so the HR of the two groups were still comparable.

Interestingly, Jones *et al.*²⁴ found that the reduction of HR could be replicated in home-based HR monitoring by the participants and in laboratory measurements, which was not consistent with our findings. The possible reason may be that the BP monitoring devices used by patients at home were different, including brand and model

differences, leading to some deviation in the measurement of HR made at home.²⁵ In addition, one study about the effect of MediYoga on HR in patients with paroxysmal atrial fibrillation showed that there were no differences in HR between the groups,²⁶ which is inconsistent with our results. One possible reason lies in the different participants of the two studies. Our participants were patients after PCI who had the imbalance of the autonomic nervous system, while the study on MediYoga examined patients with paroxysmal atrial fibrillation, of which increase in HR during the onset of atrial fibrillation is related to the re-entry of the cardiac conduction bundles, but not to the increase in sympathetic excitability. Therefore, SBE may lower the HR of patients undergoing PCI, while being ineffective for patients with paroxysmal atrial fibrillation.

Slow breathing exercise can repair the imbalance of the autonomic nervous system, then gradually recover the autonomic nervous function.²⁷ Some clinical observations have shown that ischaemic heart diseases such as MI can reduce baroreflex sensitivity, which leads to overactivity of the sympathetic nervous system and suppression of parasympathetic activity, which result in an increase in HR.^{13,28} Although PCI can relatively well preserve autonomic nerve function in patients with MI, patients in the early stage after PCI still exhibit partial autonomic nervous imbalance.¹² Additionally, the inhalation time of 4 s in SBE fully expands the thoracic cavity and produces negative thoracic pressure during SBE. Hence, pulmonary stretch receptors and the Hering-Breuer reflex was activated to improve baroreflex sensitivity, reduce the sympathetic activity and relevantly activate the vagus activity,^{11,29} which mitigated the elevated HR.

According to some studies, the effect of SBE on the reduction in BP has been observed,^{20,30} but no significant effect on the decrease of SBP or DBP was found in this study. The possible reasons might be that the baseline BP was controlled within the normal range and the antihypertensive agents were adjusted according to their BP changes during the period of intervention, ensuring that BP was within the normal range. In addition, as a result of myocardial damage, patients after PCI often experience reduced ventricular systolic and diastolic function, which may result in a slight or no reduction in BP.³¹ Meanwhile, the role of SBE in regulating BP often occurs when the BP is abnormal.¹¹ Therefore, the effect of SBE in lowering BP in this study did not appear.

Beta-blockers are a conventional medication for patients after PCI to control HR. The dose of beta-blockers was adjusted for some patients during the period of intervention, but the number of patients on beta-blockers was not significantly different between the two groups. Also, the number of patients who reduced or stopped using beta-blocker in the trial group was more than that in the control group, which may indicate that SBE had the effect of reducing HR.

There are some strengths and limitations to this study. First, some patients changed beta-blockers and antihypertensive agents during the study period, which limited the interpretation of SBE's effectiveness on HR and BP. Second, a measurement bias might exist in HR and BP measured at home, which are monitored by the patients themselves using different digital BP monitoring devices. We can use 24-h BP monitoring and 24-h Holter electrocardiogram in future research to ensure the accuracy of the measurements. Third, there are still some improvements to be made in the implementation of SBE

and the setting of the study. The average age of the participants in this study was 61 years, and part of the population was elderly. Elderly people in China are generally not good at using smartphones, so this study adopted a way of silent counting that most people can use to control their breathing speed, which may not be very accurate. In future studies, we could train patients to use smartphone apps, which can provide reliable support to help control the breathing rate. In general, the compliance of patients in this study with SBE was relatively good, but there was still a problem that SBE guidelines required patients to complete the breathing exercise in two or three times every day, while some patients took more than three times to complete SBE, which may have decreased the effect of SBE. Finally, the sample size was small, which may influence the interpretation of the results.

Conclusion

The HR of patients undergoing PCI in the trial group decreased obviously, which meant that SBE is an effective non-pharmacological method to control HR and could be used in combination with prescribed medications. As for the lack of effect on BP in this study, further studies will be designed to address this problem.

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Conflict of interest: The authors declare that there is no conflict of interest.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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