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A randomized controlled trial of a controlled breathing protocol on heart rate variability following myocardial infarction or coronary artery bypass graft surgery

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Objectives: To determine whether a controlled breathing programme increases heart rate variability following an acute myocardial infarction and/or coronary artery bypass graft surgery.

Rationale: Heart rate variability is reduced following a myocardial infarction, and low heart rate variability is associated with a high mortality risk. By changing tidal volume and rate of breathing, individuals can alter beat-to-beat heart rate variability. It is hypothesized that heart rate increases with inspiration and decreases with exhalation, and that deep slow breathing enhances respiratory sinus arrhythmia, increasing heart rate variability.

Design: Randomized controlled trial.

Setting: Cardiac rehabilitation programme at a large academic medical centre in North Texas.

Subjects: From 2001 to 2005, 44 patients, age 46–65 years, who had a myocardial infarction and/or undergone coronary artery bypass graft surgery 1–8 weeks previously and were referred to the Cardiac Rehabilitation Program.

Intervention: Patients were randomized to either usual cardiac rehabilitation or cardiac rehabilitation with controlled breathing (6 breaths/min for 10 minutes twice daily during the eight-week treatment period).

Main measures: Weekly measurements of total power and standard deviation of the mean normal to normal RR interval (SDNN), and fortnightly measurements of respiratory sinus arrhythmia were taken using Biocom Technologies Heart Rhythm Scanner and Tracker software.

Results: No significant difference in change were seen between groups in SDNN ($P=0.3984$), baseline respiratory sinus arrhythmia ($P=0.6556$) or total power ($P=0.6184$).

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Conclusion: Results suggest participation in the controlled breathing programme offered no additional benefit in increasing heart rate variability following myocardial infarction or coronary artery bypass graft surgery. However, 77% of study patients were on heart rate-lowering medications, which may have masked changes in heart rate variability.

Background

Cardiovascular autonomic tone, as indicated measurement of heart rate variability, is severely altered in all patients immediately after an acute myocardial infarction. Heart rate variability is the oscillation in the interval between consecutive instantaneous heart rates and is an accepted, non-invasive marker of cardiovascular autonomic tone.^{1,2} Changes in heart rate occur secondary to physical or mental stress, exercise, respiration, metabolic changes and various other influences. Both the basic heart rate and its modulation are primarily due to alterations in autonomic tone: parasympathetic stimulation decreases and sympathetic stimulation increases heart rate.

Low heart rate variability is associated with high risk of mortality in myocardial infarction patients.³ The correlation observed between a greater occurrence of sudden cardiac death after an acute myocardial infarction and signs of increased sympathetic activity and/or of impaired parasympathetic vagal activity led to the idea that increased parasympathetic tone may provide protection against sudden cardiac death.⁴ If correct, cardiac rehabilitation programmes could be enhanced if a practical means to 'train' patients to achieve increased parasympathetic tone could be devised. Related work includes a randomized controlled trial in 46 patients with coronary heart disease which showed cognitive-behavioural training with heart rate variability biofeedback can augment vagal heart rate regulation.⁵

Spontaneous fluctuations in heart rate that have been shown to occur in relation to the phase of respiration (i.e., respiratory sinus arrhythmia) are mediated primarily by the parasympathetic system. In short-term recordings under

experimental conditions, an increase of sympathetic activity (usually with concomitant lowering of parasympathetic activity) was shown to reduce total heart rate variability, primarily in the breathing-related component.³ It has been theorized that, with respiratory sinus arrhythmia, heart rate increases with inspiration and decreases with expiration.⁶ Individuals can change their levels of respiration by altering their tidal volume and rate of breathing, and these respiratory changes subsequently alter the beat-by-beat variability of their heart rate. For example, deep, slow breathing enhances the respiratory sinus arrhythmia, thus increasing heart rate variability.⁶ This theory has important implications with regard to the implementation of behavioural treatments for coronary artery disease, as it potentially provides a mechanism through which heart rate variability 'training' can be achieved. Studies conducted in patients under severe stress have shown some success in improving heart rate variability through participation in controlled breathing programmes.^{6,7} We investigated whether a similar effect could be demonstrated in cardiac rehabilitation patients following a myocardial infarction and/or coronary bypass graft surgery.

Methods

Setting

This study was conducted within the Cardiac Rehabilitation Program at the Baylor Hamilton Heart and Vascular Hospital in Dallas, Texas, USA between 2001 and 2005.

Outcome measures

We examined three measures of heart rate variability: the standard deviation of the mean

normal to normal RR interval (SDNN); total power (calculated as the area under the curve when the magnitude of variability is mapped as a function of frequency); and respiratory sinus arrhythmia – the cardio-acceleration during inspiration and cardio-deceleration during expiration mediated by respiratory gating of parasympathetic efferent activity to the heart: vagal efferent traffic to the sinus node occurs primarily in phase with expiration and is absent or attenuated during inspiration. The combination of these measures was chosen because 5-minute SDNN measurements can be compared over time to assess relative changes in heart rate variability, total power is an appropriate measure for short-term changes in heart rate variability and respiratory sinus arrhythmia can provide information regarding autonomic balance (or imbalance) within heart rate variability.

Study design

This was a randomized controlled trial comparing the paired differences in pre-intervention and post-intervention values on three measures of heart rate variability – SDNN, total power and respiratory sinus arrhythmia – between patients receiving usual cardiac rehabilitation and patients receiving usual cardiac rehabilitation plus a controlled breathing programme. Patients were randomized to the treatment or control group by a coin toss. The study was designed using a total sample size of 100 patients (50 per treatment arm), which provided 80% power or better to detect an incremental benefit of the controlled breathing programme of 30% for SDNN, 20% for total power and 60% for respiratory sinus arrhythmia, based on authors' estimates of expected ranges and medians for these three measures at baseline.

Patients

Patients who had a myocardial infarction and/or had undergone reperfusion (coronary artery bypass graft or percutaneous transluminal coronary angioplasty) between one and eight weeks prior to being referred to the cardiac rehabilitation programme, could read and write English at

an eighth grade level, and were age ≤ 65 years, were considered for this study. Patients were excluded if they refused consent to participate; had undergone valve surgery or had a permanent pacemaker or defibrillator implanted; had undergone an organ transplant or were under active care for a chronic medical condition that required use of immunosuppressive medications; had been diagnosed with and/or were under treatment for atrial fibrillation, atrial flutter, or valvular disease, or were prescribed antiarrhythmic medications; had chronic obstructive pulmonary disease or asthma; had stable or unstable angina without a documented myocardial infarction; or had a documented substance abuse problem, paralyzed diaphragm or lead exposure.

Intervention

Patients were randomized to the usual eight-week cardiac rehabilitation programme, or to cardiac rehabilitation plus controlled breathing by a coin toss. 'Usual cardiac rehabilitation' meant three 1-hour sessions with cardiac rehabilitation specialists each week for eight weeks. Patients in the controlled breathing group were required to breathe at a rate of 6 breaths per minute for 10 minutes twice daily during the eight-week treatment period. They were provided with a relaxation tape with tonal pacing at this rate, set against a background of nature sounds. Exercise workloads during cardiac rehabilitation sessions were incrementally adjusted by the metabolic equivalent method to ensure equality in functional capacity progress between subjects.

Data collection

Total power and SDNN were measured weekly, and respiratory sinus arrhythmia fortnightly, using Biocom Technologies Heart Rhythm Scanner and Tracker software, during cardiac rehabilitation sessions. Measurements were taken over a 5-minute period prior to the active portion of the rehabilitation session. Patients remained seated while the measurements were taken. During respiratory sinus arrhythmia measurement, patients were required to breathe at a pace of 6 breaths per minute; other measurements were

taken with spontaneous breathing. The Heart Rhythm Scanner and Tracker measures respiratory sinus arrhythmia as a 'training score' that reflects the total training period for which the patient demonstrates respiratory sinus arrhythmia. In addition to these weekly measurements, home diaries were distributed to both study groups to track changes in activity and/or return to work. Subjects in the breathing training group also logged compliance of home performance of the breathing training protocol. Researchers collecting outcome data were not blinded to patients' treatment arm allocation.

Data analysis

Each outcome was analyzed via a linear mixed model which included a variance term to account for patient-to-patient variability as well as allowing for correlation within a patient's repeated measurements. Cubic polynomials were used to

model the effect of time to avoid assuming a linear effect for time. All analyses were performed using SAS version 9.2. Analysts were blinded to patients' treatment arm allocation.

Results

A total of 44 patients (8 female, 36 male) were recruited for this study; 24 were randomized to the control group, 20 to the treatment group (Figure 1). Patients ranged in age from 46 to 65 years; 23 were post-coronary artery bypass graft patients, 2 post-myocardial infarction and coronary artery bypass graft, 15 post-myocardial infarction, 3 post-myocardial infarction with stent placement, and 1 post-percutaneous transluminal coronary angioplasty with stent placement; 77% were taking heart rate-lowering medications (metoprolol (32 patients) and carvedilol (2 patients)). Characteristics for both study

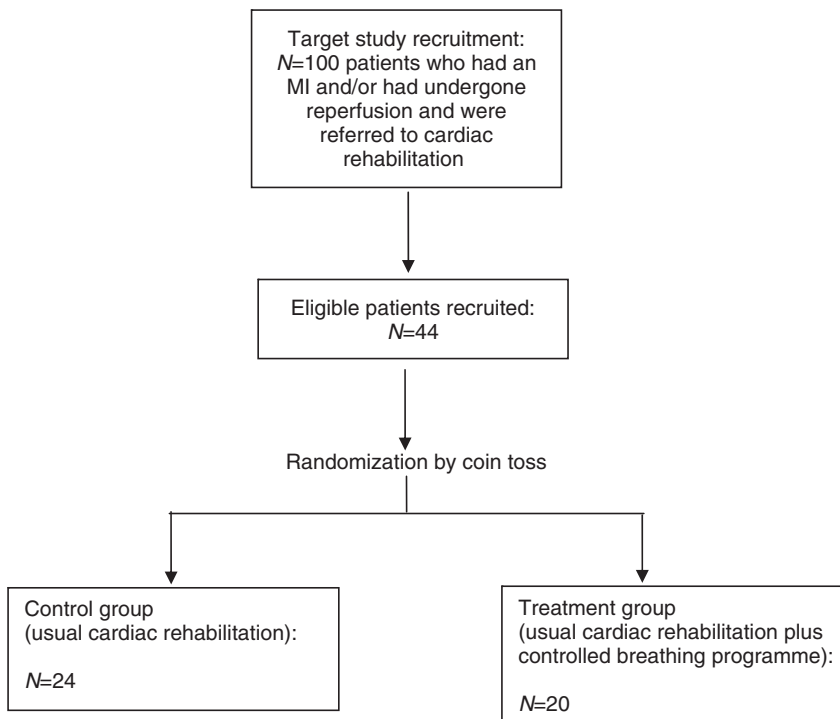


Figure 1 Flow of patients through the study. MI, myocardial infarction.

groups are shown in Table 1. All patients completed at least two-thirds of their cardiac rehabilitation exercise sessions and, based on patient logs of compliance with the home breathing protocol, all members of the controlled breathing group completed at least 85% of their breathing sessions.

Weekly changes in the three heart rate variability measures are shown for the treatment and control groups in Table 2. No significant differences

between treatment and control groups were seen for SDNN ($P=0.3984$), respiratory sinus arrhythmia ($P=0.6556$) or total power ($P=0.6184$). Figures 2–4 show average, minimum and maximum values for the treatment and control groups for these three measures, by week.

Discussion

Participation in the controlled breathing programme offered no additional benefit over usual cardiac rehabilitation in increasing heart rate variability following myocardial infarction and/or coronary artery bypass graft. There has been little previous research examining the effect of a controlled breathing programme on measures of heart rate variability over time to which we can compare our results. A few studies have compared heart rate variability under spontaneous breathing and controlled breathing at a single point in time in healthy subjects. One showed a significant change in the RR interval mean value or variability when controlled breathing (15 breaths per minute) and spontaneous breathing were compared, but a modest increase in power in the high frequency band of the RR interval spectrum.⁸ A second showed no significant change in either the RR interval mean value or variability, or the high frequency power of the RR interval,⁹ while a third found a stronger relationship between the

Table 1 Patient characteristics for the control (usual cardiac rehabilitation) and treatment (usual cardiac rehabilitation plus controlled breathing) groups

Characteristic	Treatment (<i>n</i> = 20)	Control (<i>n</i> = 24)
Age (years), mean (SD)	56.7 (4.9)	56.1 (6.0)
Gender		
Female, <i>n</i> (%)	4 (20.0)	4 (16.7)
Race, <i>n</i> (%)		
White	13 (65.0)	18 (66.7)
Non-white	7 (35.0)	6 (33.3)
Diagnosis, <i>n</i> (%)		
CABG	8 (40.0)	15 (62.5)
MI	8 (40.0)	7 (29.1)
MI/CABG	1 (5.0)	1 (4.2)
MI/STENT	2 (10.0)	1 (4.2)
PTCA/STENT	1 (5.0)	–
Beta-blocker, <i>n</i> (%)		
Metoprolol	16 (80.0)	16 (66.7)
Carvedilol	–	2 (8.3)

CABG, coronary artery bypass graft surgery; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty.

Table 2 Weekly changes in heart rate variability measures for patients in the control group (usual cardiac rehabilitation, *n* = 22) and treatment group (usual cardiac rehabilitation plus controlled breathing, *n* = 22)

	SDNN (ms ²) Mean (range)		RSA ^a (%) Mean (range)		Total power (ln[ms ²]) Mean (range)	
	Treatment (<i>n</i> = 20)	Control (<i>n</i> = 24)	Treatment (<i>n</i> = 20)	Control (<i>n</i> = 24)	Treatment (<i>n</i> = 20)	Control (<i>n</i> = 24)
Week 0	27.9 (10.7–57.1)	23.9 (4.5–51.6)	22.9 (7.6–43.9)	20.2 (5.2–42.2)	402.3 (52.0–1792.3)	289.3 (6.9–1259.4)
Week 1	26.9 (10.6–46.2)	22.2 (8.9–57.0)	–	–	377.9 (43.9–993.3)	270.5 (24.5–1374.2)
Week 2	29.5 (12.4–63.7)	22.7 (8.7–55.4)	19.9 (8.5–38.3)	22.3 (13.7–36.0)	472.4 (68.9–1886.2)	228.2 (26.4–972.3)
Week 3	30.5 (14.5–59.7)	28.5 (13.6–72.1)	–	–	446.9 (104.2–1403.2)	508.4 (74.0–2499.6)
Week 4	35.5 (16.9–63.3)	27.6 (7.6–64.9)	23.5 (7.9–39.9)	18.8 (5.1–36.9)	638.5 (126.2–1946.9)	446.2 (24.5–1827)
Week 5	33.4 (10.6–71.8)	28.3 (6.3–72.4)	–	–	637.5 (34.0–2510.4)	462.6 (18.0–2601.2)
Week 6	32.3 (13.7–58.9)	26.7 (10.1–63.6)	27.7 (9.9–53.8)	23.5 (10.2–35.5)	541.3 (32.0–1364.5)	362.7 (41.2–1354.9)
Week 7	34.1 (13.4–54.6)	27.5 (14.0–61.2)	–	–	585.2 (56.9–1350.5)	345.9 (33.1–987.9)
Week 8	36.3 (13.9–66.6)	27.2 (11.4–63.5)	27.3 (11.5–44.0)	26.4 (9.2–46.1)	640.2 (64.1–2166.8)	417.4 (39.0–1983.9)

^aMeasured bi-weekly.

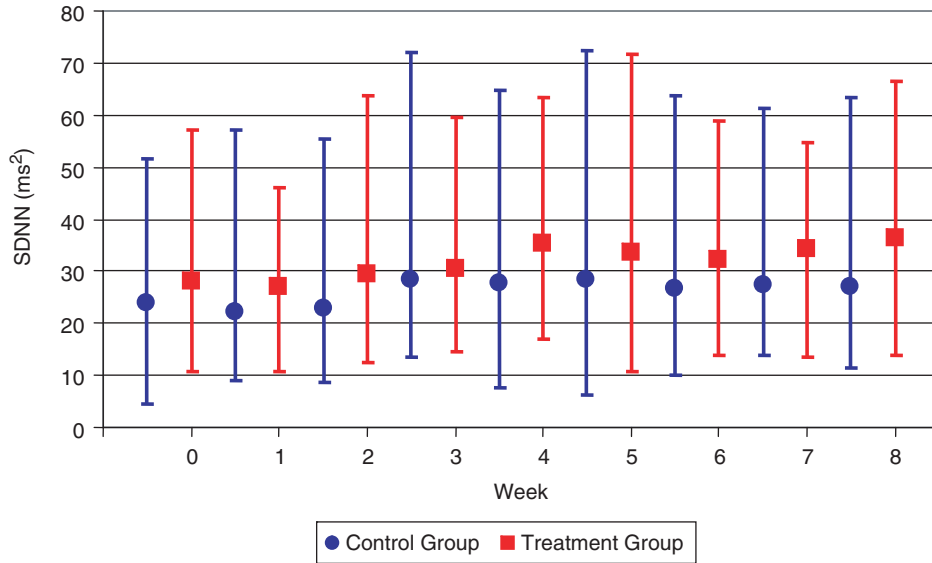


Figure 2 Standard deviation of the mean normal to normal RR interval (SDNN) (mean and range) by week for control (usual cardiac rehabilitation, $n=24$) and treatment (usual cardiac rehabilitation plus controlled breathing, $n=20$).

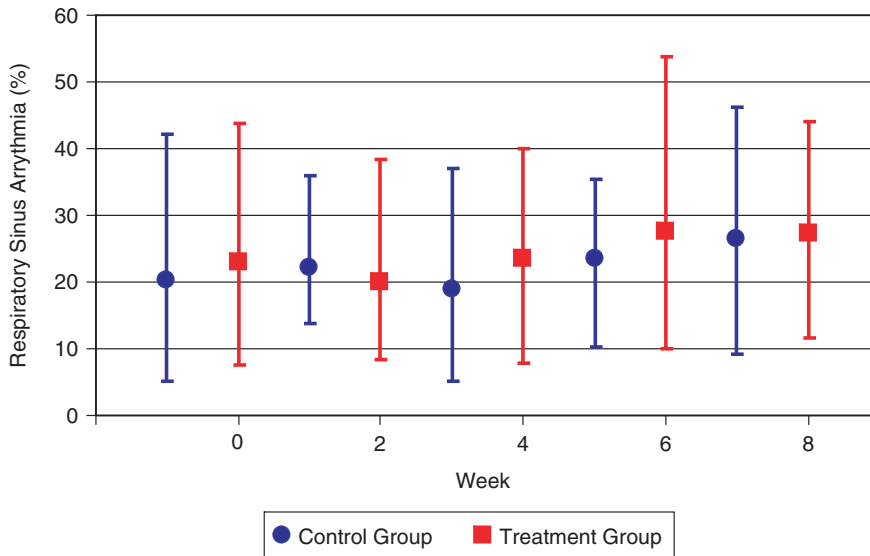


Figure 3 Respiratory sinus arrhythmia (mean and range) by week for control (usual cardiac rehabilitation, $n=24$) and treatment (usual cardiac rehabilitation plus controlled breathing, $n=20$).

natural logarithm of the high frequency oscillations and the RR interval with controlled breathing.¹⁰ Studies that have examined the impact of regularly practised slow-paced breathing over

time have shown significant reductions in blood pressure and increases in baroreflex sensitivity in hypertensive patients,¹¹⁻¹³ with effects sustained six months after the eight-week intervention,¹²

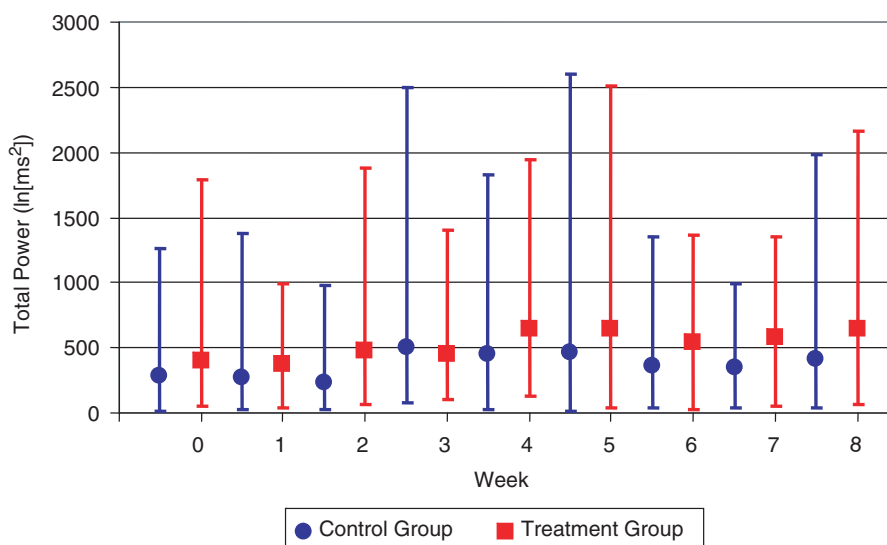


Figure 4 Total power (mean and range) by week for control (usual cardiac rehabilitation, $n=24$) and treatment (usual cardiac rehabilitation plus controlled breathing, $n=20$).

and, in healthy subjects, significant increased parasympathetic and decreased sympathetic activity (no significant changes in autonomic function was observed with the fast-breathing programme).¹⁴

Our results are surprising in the context of the short-term effects of breathing rate on heart rate variability measures and the effects observed on other autonomic physical responses – such as blood pressure. A point to consider in evaluating these results is that 77% of our study population were taking heart rate-lowering medications during the treatment period as well as participating in cardiac rehabilitation. Previous research has demonstrated the additive effect of rehabilitation and beta-blockade on heart rate variability¹⁵ and it is possible that our study did not have sufficient power to detect any incremental benefit of the controlled breathing programme. The overall lack of change in all the indicators measured in both the treatment and control groups (see Figures 1–3) suggests otherwise, however, and it should be noted that this prevalence of beta-blocker use is fairly typical of the cardiac rehabilitation population.

Other limitations to this study that cannot be ignored was the unblinded assessment of

study measures, and anecdotal reports that ‘background nature sounds’ on the relaxation tape used to pace breathing in the intervention group became annoying on repeated listening, and so may have decreased participants’ compliance with the breathing programme, or introduced unintended stresses that worked against the benefits expected from the controlled breathing, for example, by increasing blood pressure and other stress responses.¹⁶ Further research is needed regarding the impact of stress management on patient outcomes following cardiac events – even

Clinical messages

- Controlled breathing did not show incremental benefit over cardiac rehabilitation in improving heart rate variability for patients who experienced a myocardial infarction and/or underwent reperfusion.
- Medical therapy following cardiac events may interact with physical training, requiring customized rehabilitation protocols for patients on particular medications to maximize benefit.

if not specifically targeting either controlled breathing or heart rate variability – and regarding the interaction between medical therapy following cardiac events and physical training, to facilitate the design of different protocols for patients on particular medications to maximize the benefit of the rehabilitation programme.

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