

Original Article

Heart Rate Variability Biofeedback in Patients With Paroxysmal Atrial Fibrillation

Mohammad Ali Sadr-Ameli^{1*}, MD; Parisa Izadpanah¹, MD; Sadaf Sadr-Ameli³,
Keivan Maghooli³, PhD; Shabnam Madadi², MD

ABSTRACT

Background: Heart rate variability biofeedback (HRVB) is an approach to ameliorate conditions in which HRV is relatively low. Some patients with paroxysmal atrial fibrillation (AF) show increased adrenergic tone in their paroxysms.

Methods: We conducted this study to determine the effects of HRVB on patients with paroxysmal AF. Thirty-one patients (11 women) at an average age of 58 ± 10 years (38–79 y) with paroxysmal AF were included in the study. Of these, 19% had AF during exertion; 29% during rest; and in the remaining 52%, episodes were mixed. A 24-hour ambulatory Holter monitoring was done before and after 5 weeks of biofeedback training.

Results: The interpretation of Holter monitoring disclosed that high frequency changed significantly after HRVB. Clinically, 12 patients felt better, 4 patients felt worse, and 15 patients felt no obvious change. Low frequency and more importantly very low frequency decreased, which was due to a decrement in sympathetic tone.

Conclusions: HRVB in patients with adrenergic AF might reduce their episodes of paroxysmal AF and help them feel better. (*Iranian Heart Journal 2021; 22(2): 68-76*)

KEYWORDS: Heart rate variability Biofeedback, Paroxysmal atrial fibrillation, Autonomic nervous system

¹ Department of Interventional Cardiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

² Cardiac Electrophysiology Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

³ Department of Medical Engineering, Science and Research Branch, Islamic Azad University, Tehran, IR Iran.

***Corresponding Author:** Mohammad Ali Sadr-Ameli, MD; Department of Interventional Cardiology, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

Email: sadrameli_ma@yahoo.com

Tel : +98 21 2392 2141

Received: November 10, 2020

Accepted: January 20, 2021

The cyclic variances in the sinus rate over time are termed “heart rate variability (HRV)”. There are 2 methods for the analysis of HRV: time-domain analysis,¹ which is a statistical

analysis of fluctuations in the sinus rate defined in terms of sinus R-R intervals over time, and frequency domain analysis (power spectrum analysis),² which decomposes heart rate signals into their frequency

components and quantifies them in terms of their relative intensity, termed “power”.³

HRV is related to cyclical fluctuations in autonomic tone. Frequency domain studies have provided strong evidence that HRV reflects oscillations in sympathetic-parasympathetic balance.⁴ Power spectrum analysis facilitates the separation of sympathetic (low-frequency [LF]) and parasympathetic (high-frequency [HF]) activity.

The power spectrum consists of 3 major frequency bands ranging from 0 to 0.5 HZ. The HF band (0.02–0.35 HZ) is associated with parasympathetic activity, whereas the LF band (0.02–0.05 HZ) is attributed to sympathetic and parasympathetic activity, but predominantly by the latter.⁵

A very-low-frequency band (VLF, 0.01–0.04 HZ) has also been identified and proposed as a marker of sympathetic activity.⁶

The total power (TP) of the heart signal is represented by the total area under the power spectral curve.

There is a high degree of correlation between the respiratory rate and the HF component, which is associated with parasympathetic activity. Increments in sympathetic activity increase the LF component and the LF/HF ratio.

Low vagal activity, defined in terms of low HRV and low HF power, is associated with a variety of disease states and increased risks of mortality.^{7,8}

Atrial fibrillation (AF) is the most common clinically treated arrhythmia and the most common cause of arrhythmia hospitalization.⁹

With its increasing incidence and a linear incremental relationship with age,⁹ AF increases the risk of mortality, stroke, and heart failure.¹⁰

Lone AF or paroxysmal AF refers to AF that occurs in patients who have no hypertension or any evidence of structural heart disease.

Based on the autonomic setting, paroxysmal AF is classified clinically into vagotonic

(25%), which occurs during relaxation or sleep, adrenergic (15%), which occurs during strenuous exercise, and mixed form.⁹ HRV is implicated for the evaluation of the effects of the vagus nerve and the sympathetic autonomic system on the heart.

It is possible to change the rate of sinus arrhythmia by changing the tidal volume and the respiratory rate and consequently the beat-to-beat heart rate.

Recent years have witnessed substantial support for heart rate variability biofeedback (HRVB) for a variety of disorders and performance enhancement.¹¹

Since conditions as widely varied as asthma, irritable bowel syndrome, and migraine appear to respond to this form of cardiorespiratory feedback training, the issue of possible mechanisms becomes more outstanding. The most supported possible mechanism is the strengthening of homeostasis in the baroreceptor.¹²

We conducted this study to evaluate the effects of biofeedback training in patients with paroxysmal AF using a monitoring device to record physiological processes and help patients control their physiological responses.

METHODS

For the purposes of the present study, 31 patients with paroxysmal AF were trained and their HRV was measured via a 24-hour Holter monitoring before and after 5 weeks of biofeedback training. The breathing protocol was repeated twice a day (each time for a quarter of an hour).

The breathing protocol consisted of asking the subjects to observe their HRV in phase with abdominal breathing or to use a monitor (ViATOM Portable ECG/EKG Monitor CheckMe Pro Doctor with APP & PC Report) while breathing deeply at 6 to 8 breaths per minute (Fig. 1).



Figure 1: The image shows the ViATOM Portable ECG/EKG Monitor CheckMe Pro Doctor.

The subjects were encouraged to deepen and slow the expiratory phase to enhance their parasympathetic activity. They were also taught to recognize HRV and to note alterations by counting their heart rates and noting the circumstances surrounding changes. Self-regulation therapies constitute a group of behavioral approaches used to help patients exercise voluntary control over various cardiovascular diseases. These therapies include muscle relaxation, self-hypnosis, and various meditation methods. When the treatment includes the use of a monitoring device to record physiological processes and to help patients control their physiological responses, the method is termed “biofeedback”. Patients are engaged in goal-directed activities that are designed to increase their skill and efficacy in reaching a physiological target through performance-based biofeedback.

HRV was measured using standardized methods described. For instance, Kleiger et al¹³ recorded 2 leads of ECG for 24 hours on Holter tape cassette recorders. In another investigation, the power spectral analysis of the R-R interval sequence allowed the fractionation of the effects of sympathetic and parasympathetic influences on the heart rhythm.¹⁴ These patients did not take any antiarrhythmic drugs.

Statistical Analysis

Data are reported as frequencies (percentages) for categorical variables and medians (interquartile ranges) for continuous variables. The one-sample Kolmogorov–Smirnov test was used to examine normality. The χ^2 test and the Fisher exact test were applied for categorical variables. The Wilcoxon signed-rank test was utilized to evaluate the association between variables lacking normal distributions. SPSS, version 18, (SPSS, IBM) was employed to analyze the data. A *P* value of less than 0.05 was considered statistically significant.

RESULTS

Thirty-one patients with paroxysmal AF were included in this study. Twenty patients (64.5%) were male and 11 (35.5%) were female. The average age of the patients was 58.5 ± 10.5 years (38–79 y). Of these patients, 5 (19%) had paroxysmal AF during activity, 9 (29%) had paroxysmal AF during rest or sleep; and in the remaining 17 (52%), episodes were mixed.

After 5 weeks of biofeedback training, 12 patients (39%) felt better clinically (ie, they reported fewer or shorter episodes of AF), 4 (13%) felt worse, and the remaining 15 (48%) patients reported no change after biofeedback training.

The analysis and comparison of the frequency domain and the power spectrum before and after HRVB revealed a statistically significant difference in the HF band before and after training ($P < 0.000$). Nonetheless, the other components did not show such a difference (Fig. 2).

Considering TP, VLF, LF, and HF, despite a statistically significant difference in terms of HF, all the other components based on the mean rank were improved and the patients felt better. In those who reported better conditions (fewer episodes, shorter episodes,

or better tolerance) HF, LF, and VLF showed significant differences: HF was high, whereas LF and VLF were low by comparison with the same parameters before training.

In the patients who reported feeling worse, HF, LF, and VLF were higher than the same parameters in the control state. In the patients who did not notice any change, all the parameters were higher than the same parameters in the control state (Table 1). Among the patients who reported AF during rest, 33% felt worse, 11% felt better, and 56% felt no change. HF and LF exhibited a rise after training.

Among the patients who reported AF during exercise, 66% felt better, while 34% noticed no change. In these patients, whereas HF demonstrated a rise, LF and VLF had a drop following training (Table 2).

Among the patients who did not report a correlation between AF and either activity or rest, 43% felt better, 7% felt worse, and 50% had no change. In this group, HF increased and LF decreased after training.

There was no difference between both sexes regarding biofeedback training.

Table 1: Analysis of mean + SD based on the clinical status of the patients

Clinical Status		Mean	SD	Minimum	Maximum	Percentiles (25-75)
unchanged (n=15)	HF0	515.1	1042.9	23	3986	174 (70-384)
	HF1	626.1	1225.3	46	4505	143 (88-405)
	LF1	610	612.3	18	2521	483 (209-745)
	LF2	667.8	604.5	8	2112	454 (226-1185)
	VLF0	1036.7	588.9	80	1914	1219 (610-1439)
	VLF1	1125.8	573.5	57	1965	1375 (510-1541)
	TP0	2461.9	2414.2	174	10473	1919 (1449-2316)
	TP1	2943	2916	128	11262	1938 (1733-2630)
Better (n=12)	HF0	1670	3804.7	56	13228	175 (58-939)
	HF1	3390.7	9251.7	77	32456	251 (89-1153)
	LF1	1846.8	3942.3	120	14131	365 (232-1698)
	LF2	782.8	890.5	110	2967	329 (202-1140.8)
	VLF0	2094.8	3491.2	506	13064	1081 (699-1379)
	VLF1	1185.8	806.9	403	3091	914.5 (611.5-1737.5)
	TP0	7340.6	16208.6	730	58088	1837 (1005.8-4330)
	TP1	3476.4	3993.9	678	12278	1642.5 (1060.8-3539.3)
Worse (n=4)	HF0	526.3	697.2	50	1531	262 (52.3-1264.5)
	HF1	953.3	1424	81	3063	334.5 (87-2438.3)
	LF1	639.3	518.4	204	1243	555 (205.5-1157.3)
	LF2	1048.3	816	184	2095	957 (310.5-1877)
	VLF0	1114.8	632.1	590	1952	958.5 (608.5-1777.3)
	VLF1	1158.8	488.8	687	1833	1057 (755.3-1663.5)
	TP0	2516.5	1800	976	5064	2013 (1130-4406)
	TP1	3750.8	4368.5	1272	10288	1721.5 (1319-8211.8)

In patients with clinical improvement, HF was higher, whereas LF and VLF were lower than the values before training. HF, High frequency; LF, Low frequency; VLF, Very low frequency

Table 2: Comparison of the response in different types of AF (upper) and clinical status (lower) to HRVB

Type of AF		HF1 - HF0	LF2 - LF1	VLF1 - VLF0	TP1 - TP0
Mixed	Z	-2.068b	-0.310c	-0.569c	-0.362b
	P value	0.039	0.756	0.569	0.717
Rest	Z	-2.666b	-0.652b	-1.125b	-1.718b
	P value	0.008	0.515	0.260	0.086
Exercise	Z	-2.201b	-1.992c	-2.201c	-1.992c
	P value	0.028	0.046	0.028	0.046

Frequency components in 3 groups of AF before and after HRVB

HF, High frequency; LF, Low frequency; VLF, Very low frequency; TP, Total power; AF, Atrial fibrillation; HRVB, Heart rate variability biofeedback

Clinical Status		HF1 - HF0	LF2 - LF1	VLF1 - VLF0	TP1 - TP0
Unchanged	Z	-2.442b	-0.625b	-0.511b	-1.193b
	P value	0.015	0.532	0.609	0.233
Better	Z	-2.275b	-1.726c	-2.040c	-1.098c
	P value	0.023	0.084	0.041	0.272
Worse	Z	-1.826b	-0.730b	0.000d	-0.365b
	P value	0.068	0.465	1.000	0.715

Frequency components in different clinical responses after HRVB

HF, High frequency; LF, Low frequency; VLF, Very low frequency; TP, Total power; AF, Atrial fibrillation; HRVB, Heart rate variability biofeedback

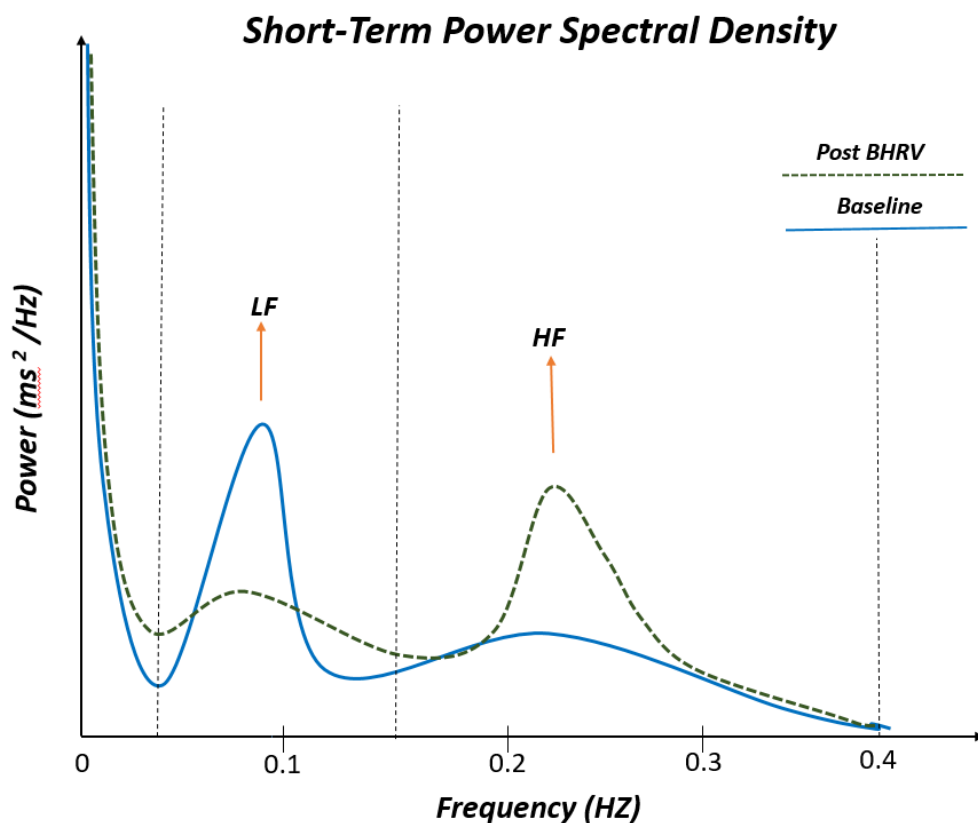


Figure 2: The image depicts the spectral analysis before and after biofeedback training. HRVB, Heart rate variability biofeedback

DISCUSSION

For all the studies on HRV in AF,¹⁵⁻²⁰ there is a paucity of data regarding HRVB in paroxysmal AF.

Of our 31 patients with paroxysmal AF, 12 patients (39%) felt better after training. Among our study population, 4 subjects had adrenergic, 1 vagal, and 7 mixed or random

forms of paroxysmal AF. In the patients who reported feeling better (ie, fewer or shorter episodes of AF), HF exhibited a rise, whereas LF and VLF had a decline after training.

Four patients felt worse: 3 had vagotonic paroxysmal AF and 1 had a mixed form. In these patients, HF increased slightly, but LF and VLF increased after training.

Sixteen patients (48%) reported no improvement after training. In these patients, HF, LF, and VLF exhibited a rise. The reason for improvement (fewer or shorter episodes or better tolerance of paroxysms) in these patients, which was not expected, could be due to the similarity of biofeedback training to meditation and decrement of inflammation offered by increasing vagal tone.²⁹

Boon et al¹⁶ reported that shorter HRV signals predicted episodes of paroxysmal AF in 80% of their cases. Wiegand et al¹⁷ reported a significant increase in the time-domain component of HRV 10 seconds before the onset of AF. Vandenberg et al¹⁸ showed that HRV in patients with AF was related to vagal tone. Vikman et al¹⁹ postulated that increased HRV in all major power spectral bands was associated with the late recurrence of AF after cardioversion. Enhanced vagal tone, reflected as increased HF, seems to predict specifically the early recurrence of AF after cardioversion. Ahsan et al²⁰ concluded that the autonomic nervous system played a crucial role in the development, propagation, and complexity of AF. Assessment of autonomic involvement may assist in explaining why certain patients with AF do not benefit from cardioversion or ablation.

Agarwal et al²¹ reported that cardiac autonomic dysfunction, as shown by low-resting short-term HRV, was associated with the increased incidence rate of AF. Friedman²² reported that an increased left atrial dimension was correlated with reduced HRV. In recent years, there has been substantial support for HRVB for a variety of disorders and performance enhancement.²³

Gevirtz²⁴ reviewed all the available literature on the outcomes of HRVB. He looked at the following application categories: asthma, chronic obstructive pulmonary disease, irritable bowel syndrome, cyclic vomiting, recurrent abdominal pain, fibromyalgia, cardiac rehabilitation, hypertension, chronic muscle pain, pregnancy-induced hypertension, depression, anxiety, post-traumatic stress disorder, insomnia, and performance.

Bernston et al²⁵ posited the effect of the vagal afferent pathway on the frontal cortical area. During HRV biofeedback, the amplitude of heart rate oscillations grows to many times the amplitude at rest, while the pattern becomes simple and sinusoidal.²⁶

Respiratory sinus arrhythmias can also reflect aspects of autonomic function. They are controlled entirely by the vagus nerve, such that the vagus nerve outputs to the sinoatrial node primarily occur only during exhalation. Greater vagus nerve traffic will, therefore, produce greater amplitudes of respiratory sinus arrhythmias, such that many investigators have equated respiratory sinus arrhythmias (or HF HRV) with cardiac vagal tone or parasympathetic influence on the heart. However, longer exhalation and slower respiration may also increase the amplitude of respiratory sinus arrhythmias, possibly independently of the vagus nerve traffic, since the vagus nerve output occurs for relatively longer periods with each breath.^{23, 27}

Lehrer et al²⁸ found large increases in baroreflex gain (number of beats per minute change in the heart rate per 1 mm Hg change in blood pressure) during HRV biofeedback (ie., the baroreflex operates more strongly).

It is known that the vagal system interacts closely with the inflammatory system, such that increases in the vagus nerve traffic (usually produced by electrical vagal stimulation) are associated with decreases in serum levels of various inflammatory cytokines.²⁹

HRV has been shown to be a good predictor of survival in severe cardiovascular diseases. This approach can be used for the management of AF, especially to control the ventricular rate. Biofeedback training helped control the ventricular rate as reported in a very small study.³⁰

Wan-Ling Chang et al³¹ concluded that HRVB was a promising intervention for improving autonomic function, cognitive impairment, and psychological distress in patients with acute ischemic stroke.³²

Cowan et al¹¹ reported the average 24-hour power spectrum of 6 patients before and after 5 weeks of training. All the patients showed a marked increase in power spectral density in the HF components (0.20–0.35 Hz) after biofeedback training. The authors concluded that after HRVB, HF peaked due to increased parasympathetic components, although these HF components were completely absent before training. Further, they showed that LF components were slightly decreased, suggestive of a decrement in sympathetic activity.

Nolan et al³⁴ studied patients with coronary artery disease who experienced psychological stress. They reported that HRVB could augment vagal recovery from acute stress and concluded that HRV biofeedback could enhance vagal HR regulation while facilitating psychological adjustment to CAD. The authors also found significant increases in HF HRV between a physical stressor task and a stress recovery period for their treatment group only.

Some studies have reported no significant differences in HF following HRVB.^{35, 36}

Wheat et al³³ argued that this finding is not against improvement in vagal tone after training as there are 2 autonomic pathways and their data are reflective of vagal activity only from 1 pathway.

Kanmanthareddy et al³⁰ discussed alternative medicines such as yoga,

acupuncture, and biofeedback. They argued that biofeedback could be implicated in the management of AF, especially to control the ventricular rate.

We think that our training sessions and periods were relatively more encompassing than those in the aforementioned studies.

CONCLUSIONS

HRVB may be implicated in paroxysmal AF, especially adrenergic paroxysmal AF (if LF and VLF decrease after training), to alleviate symptoms. The results of the present study should be verified by investigations recruiting larger numbers of patients with paroxysmal AF.

Limitations: The limitations of our study are its small study population, nonrandomized design, and short follow-up.

REFERENCES

1. Kleiger RE, Bigger JT, Bosner RJ et al: Stability over time of variables measuring heart rate variability in normal subjects. *Am J Cardiol* 68: 626-630, 1991
2. Bloomfield P :Fourier Analysis of Time-Series: An Introduction. New York, John Wiley, 1976
3. Cohen L :Time-frequency distribution-A review. *Proc IEEE*, 77 :941-981,1989
4. Malliani A, Pagani M, Lombardi F et al : Cardiovascular neural regulation explored in the frequency domain. *Circulation* 84:482-492, 1991
5. Akselrod S, Gordon D, Ubel FA et al :Power spectrum analysis of heart rate fluctuation: A quantitative probe beat-to-beat cardiovascular control. *Science* 213: 210-222 1981
6. Perini R, Orizio C, Baselli G et al: Time influence of exercise intensity on power

- spectrum of heart rate variability. *Eur J Appl Physiol* 61: 143-148 1990
7. Bigger JT, Kleiger RE, Fleiss JL and The Multicenter Post-Infarction Research Group: Components of heart rate variability measured during healing of acute myocardial infarction. *Am J Cardiol* 61:208-215, 1988
 8. Ewing DJ, Campbell IW, Clarke BF: Mortality in diabetic autonomic neuropathy. *Lancet* 1:601-603, 1976
 9. Morady F and Zipes DP :Atrial Fibrillation: Clinical Features, Mechanisms and Management in Braunwald's Heart disease. Elsevier, 730-731, 2019
 10. Roger VL, Go AS, Lloyd-Jones DM et al Heart disease and stroke statistics-2012 update: A report from the American Heart Association. *Circulation*, 125-220, 2012
 11. Marie J. Cowan, Helen Kogan, N, Robert Burr MSEE, et al : Power Spectral Analysis of Heart Rate Variability after Biofeedback Training. *J Electrocardiography* vol. 23, 85-94, 1990
 12. Vaschillo E. Lehrer P, Rishe N et al : Heart rate variability biofeedback as a method for assessing baroreflex function: A preliminary study of resonance in the cardiovascular system. *Appl Psychophysiol Biofeedback* 27, 1-27, 2002
 13. Kleiger RE, Miller JP, Bigger JT et al: Decreased heart rate variability and its association with increased mortality after acute myocardial infarction. *Am J Cardiol* 59:256, 1987
 14. Myers GA, Martin GJ, Magid NM et al: Power spectral analysis of heart rate variability in sudden cardiac death: comparison to other methods. *IEEE Trans Biomed Eng* 33: 1149, 1986
 15. David W Young : Self-measure of heart rate variability and arrhythmias to monitor and to manage atrial arrhythmias: personal experience with high intensity interval exercise (HIIE) for the conversion to sinus rhythm. *Front. Physiol.*, 08 July 2014
 16. Boon KH, Hani Khalil, Malarvili MB: Paroxysmal atrial fibrillation based on heart rate variability analysis and non-dominated sorting genetic algorithm III Computer Methods and programs in Biomedicine. Vol 153, 171-184, 2018
 17. Wiegand UK, Bonnemeier H :Heart Rate Variability preceding atrial fibrillation. *Hertz* 26 (1), 49-54, 2001
 18. Vandenberg MP, Haaksma J, Brouwer J : Heart Rate Variability in patients with Atrial Fibrillation is related to vagal tone. *Circulation* 1997, Aug 19: 96(4) 1209-16
 19. Vikman S, Makikallio TH, Yli-Mayräs et al : Heart rate variability and recurrence of atrial fibrillation after electrical cardioversion. *Ann Med*, 35(1) 36-42, 2003
 20. Ahsan A Khan, Gregory YH Lip, Alena Shantsila et al : Heart Rate Variability in Atrial Fibrillation: The balance between sympathetic and parasympathetic nervous system. :*Europ J of Clinical Investigation* vol, 49, issue 11, 2019
 21. Agarwal SK, Goldberger JJ, Mitrani RD et al: Low Heart Rate Variability linked to higher atrial fibrillation risk. *J AM Coll Cardiol*, 1016, 2017
 22. Friedman H S : Heart Rate Variability in Atrial Fibrillation, related to atrial size. *Am J Cardiol*, March 15, 93(6) 705-9, 2004
 23. Lehrer P M and Gevirtz R: Heart rate variability biofeedback : How and why does it work? *Front Psychol* vol 5 article 75, 21 July 2014
 24. Gevirtz R. The Promise of heart rate variability biofeedback: evidence-based applications. *Biofeedback* 41, 110-120 , 5298/1081-3937-41, 2013
 25. Bernstein G, Bigger J, Eckberg D L et al : Heart rate variability: Origins, Methods and

- Interpretive caveats. *Psychophysiology* , 34, 623-648,1997
26. Lehler P and Eddie D: Dynamic processes in regulation and some implications for biofeedback and biobehavioral interventions. *Appl Psychophysiol Biofeedback*, 38(2), 143-155, 2013
 27. Paul Grossman, Edwin W. Taylor: Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and biobehavioral functions *Biological Psychology* 74 , 263–285, 2007
 28. Lehrer P M, Vaschillo E, Vaschillo B et al : Heart rate variability biofeedback increases baroreflex gain and peak expiratory flow. *Psychosom Med* 2003, 65, 796-805
 29. Borovikova L V , Ivanova S, Zhang M et al :Vagus nerve stiulation attenuates the systemic inflammatory response to endotoxin. *Nature*, 2000, 404, 458-462
 30. Arun Kanmanthareddy, Madhu REDDY, Gopi Ponnaganti et al :Alternative medicine in atrial fibrillation, Yoga, Acupuncture, Biofeedback and more. *J Thorac Dis* 2015, Feb 7(2) 185-192
 31. Wan-Ling Chang, Jiunn Tay Lee, Chi Rongli et al : Effects of Heart rate variability Biofeedback in patients with acute ischemic stroke : A randomized controlled trial . *Biological Research for Nursing*, 2020, vol 22 Issue1
 32. Wan-Ling Chang, Jiunn-Tay Lee, Chi-Rong Li et al: Effects of Heart Rate Variability Biofeedback in Patients With Acute Ischemic Stroke: A Randomized Controlled Trial, *Biological Research for Nursing*, 2019
 33. Amanda L. Wheat • Kevin T. Larkin : Biofeedback of Heart Rate Variability and Related Physiology: A Critical Review. *Appl Psychophysiol Biofeedback* 35:229–242, 2010
 34. Nolan R, Kamath M, Floras J et al: Heart rate variability biofeedback as a behavioral neurocardiac intervention to enhance vagal heart rate control. *American Heart Journal*, 149, 1137–1137, 2005
 35. Hassett A, Radvanski D, Vascillio E : A Pilot Study of the Efficacy of Heart Rate Variability Biofeedback in Patients with Fibromyalgia. *Appl Psychophysiol Biofeedback* 32:1–10, 2007
 36. Karavidas M, Lehrer P, Vascillio E :Preliminary results of an open label study of heart rate variability biofeedback for the treatment of major depression. *Appl Psychophysiol & Biofeedback* 32, 19-30, 2007