

# Effect of Isometric Exercise on Heart Rate Variability in Prehypertensive Young Adults

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## Abstract

**Background and Objective:** Heart rate variability (HRV) is a sensitive and specific non-invasive tool to evaluate the degree of heart rate variation under the balanced influence of sympathetic and parasympathetic components of the cardiac autonomic nervous system. The aim was to study the effect of isometric hand grip exercise on HRV in prehypertensive young adults and to find a correlation of HRV with body mass index (BMI). **Materials and Methods:** This observational study was done on 60 healthy young adults aged 18–30 years. All the subjects were divided into three groups of 20 each on the level of their BMI and systolic and diastolic blood pressures. Group I were subjects with BMI <25 and normotensive, group II with BMI <25 and prehypertensive, and group III with BMI >25 and prehypertensive. HRV analysis (Chart HRV module, ADInstruments Pty Ltd) was performed with the following parameters calculated: low-frequency power (LF), high-frequency power (HF), and LF/HF ratio. **Results:** LF/HF ratio was significantly increased ( $P < 0.001$ ) in prehypertensive subjects (groups II and III) when compared with the normotensive subjects (group I), which indicates a heightened sympathetic discharge in prehypertensives. A positive correlation between anthropometric parameters and cardiac autonomic activity parameters and increased sympathetic activity in obese subjects were noted. **Conclusion:** An increase in anthropometric indices is associated with a change in cardiac autonomic activity, especially toward sympathetic activity. Regular anthropometric assessment can prevent the development of cardiac abnormalities and the incidence of sudden cardiac death.

**Keywords:** Body mass index (BMI), heart rate variability, isometric hand grip exercise, obesity, prehypertensive

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of death and debility.<sup>[1]</sup> Hypertension, obesity, diabetes, dyslipidemia, poor diet, smoking, alcohol consumption, and physical inactivity are the universal risk factors for heart attack and stroke.<sup>[2,3]</sup> Hypertension is the major risk factor for premature disability and death in Western and Asian populations. Asian Indians are at increased risk of diabetes, hypertension, and heart diseases.<sup>[4]</sup>

People suffering from hypertension worldwide are approximately 1 billion, and it is responsible for 7.1 million deaths each year. According to the World Health Organization (WHO), prehypertension is responsible for approximately 62% of CVD and 49% of ischemic heart disease. Thus, WHO along with the Joint National Committee (JNC7) have categorized prehypertensives

as individuals with systolic blood pressure (SBP) of 120–139 mmHg and a diastolic blood pressure (DBP) of 80–89 mmHg, whereas JNC8 have categorized prehypertensives as SBP of 120–129 mmHg. The aim of reclassification is to limit the rate of progression of prehypertension to hypertension level.<sup>[5]</sup> Hypertension is a multifaceted progressive disease process spanning several decades of life. Hypertension is familial, and parental history increases the risk of developing hypertension, especially if both the parents are hypertensives.<sup>[6]</sup> Though hypertension is more common in middle-aged and elderly

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populations, prehypertension is relatively more common in young adults, especially those with a family history of hypertension.<sup>[7]</sup>

Obesity is a global problem, and it is a significant contributor to morbidity and mortality. The prevalence of overweight and obesity is increasing in children and adolescents in India.<sup>[8,9]</sup> The contribution of obesity to the genesis of hypertension has been fully established.<sup>[10]</sup> However, studies have not yet thoroughly evaluated the link of body mass index (BMI) with the causation of prehypertension.<sup>[11]</sup> Therefore, in the present study, we have attempted to assess the nature and magnitude of autonomic imbalance after doing isometric hand grip (IHG) exercise and the role of BMI as an independent contributor to the genesis of sympathovagal imbalance in prehypertensives.

## MATERIALS AND METHODS

### Study design and setting

This was an observational study of Indian young adults aged >18 years without any comorbidity. Appropriate approval was obtained from the Institutional Ethics Committee, and informed consent was obtained from all the recruited subjects before conducting the study.

### Study subjects

A total of 60 healthy young adults were included in this study, ranging from 18 to 30 years. The study was conducted in the Department of Physiology at a tertiary care center in North India from 2014 to 2015. Subjects were physically and mentally fit, non-smoker, non-alcoholic, with SBP and DBP < 140/90 mmHg. The exclusion criteria were: (i) subjects with SBP  $\geq$  140 and/or DBP  $\geq$  90 mm/Hg, (ii) undergoing regular physical training, (iii) subjects on antihypertensive drugs or any other medication, (iv) history of acute or chronic illness such as diabetes, renal disease, or any neuropsychiatric disorder which can affect autonomic function, and (v) smokers.

### Measurement of BMI

BMI was calculated as body weight in kilograms divided by square root of body height in meter, using the Quetelet index.<sup>[12]</sup> Normal weight was defined as BMI 18.5–22.9 kg/m<sup>2</sup>, overweight as BMI 23 to  $\leq$  24.9 kg/m<sup>2</sup>, and obesity as BMI  $\geq$  25 kg/m<sup>2</sup>, as per revised body type classification for Indian population recommended by the Health Ministry and Diabetes Foundation of India in 2008.<sup>[13]</sup>

All the subjects were divided into three groups, each 20 on the level of their BMI as per recommendations and SBP and DBP.

Group I: Subjects with BMI <25 kg/m<sup>2</sup> and normotensive (having SBP in the range of 100–119 mmHg and DBP of 60–79 mmHg).

Group II: Subjects with BMI <25 kg/m<sup>2</sup> and prehypertensive (having SBP of 120–139 mmHg and DBP of 80–89 mmHg).

Group III: Subjects with BMI >25 kg/m<sup>2</sup> and prehypertensive (having SBP of 120–139 mmHg and DBP of 80–89 mmHg).

### Procedure

A detailed history and a general physical examination of all the subjects were done, with the main emphasis on CVD. All the subjects were explained about the procedure of tests and tested in a comfortable environment under similar laboratory conditions. Subjects were instructed to refrain from heavy meals/tea/coffee at least 2 h before the test and were rested just before the commencement of the test. All the basal parameters such as heart rate, blood pressure, and respiratory rate were measured. Continuous ECG was recorded in sitting position during the whole procedure by Power Lab, ADInstruments Pty Ltd, Bella Vista, New South Wales, Australia. ECG was initially recorded in a resting state. Then, the subject was asked to perform isometric exercise with a hand grip dynamometer. The subjects were asked to hold the hand dynamometer in their right hand to fully grasp it. Then the subject was instructed to compress the dynamometer with maximum effort, and developed tension was measured. This was maximal isometric tension (Tmax). Three readings were recorded, each with maximum effort; finally mean of the three was taken. The subject was again asked to perform the isometric exercise up to 30% of his/her maximum strength till he/she got exhausted. ECG was re-recorded immediately after the stoppage of exercise and again 5 min after exercise to observe its immediate effect.

### HRV analysis

HRV analysis was obtained from a “Lab Chart Recording” of heartbeat signal from a pulse transducer at 1000 samples/s with LAB CHART PRO-7. The results were shown in a Poincaré plot, period histogram, delta RR histogram, tachogram, spectrum, and statistical report. HRV was recorded for 5 min, three times during the procedure: (1) in resting condition, i.e., before isometric hand grip exercise; (2) immediately after stoppage of exercise; and (3) 5 min after isometric hand grip exercise.

The following HRV parameters were noted and compared in different groups.

Low-frequency power (LF): It is determined by both sympathetic and parasympathetic activity and provides an index not of cardiac sympathetic tone but of baroreflex function.

High-frequency power (HF): It reflects mainly respiratory sinus arrhythmia as an index of cardiac vagal control.

LF/HF ratio: It reflects a cardiac sympathovagal balance.

### Ethical consideration

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients' verbal and analytical approval before the sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a Local Ethics Committee according to the document number IEC/SGRRMC/2017-121 dated July 17, 2017.

### Statistical analysis

Qualitative variables were expressed as a proportion, whereas quantitative variables were expressed as means  $\pm$  standard deviation. For analysis of the data, descriptive and univariate analytic techniques were used. The  $\chi^2$  test or Fisher's exact test was used to compare categorical variables, whereas Student's *t*-test for independent observations was used for continuous variables. Pearson's correlation was used to find the correlation. *P*-values less than 0.05 were considered statistically significant. All the analyses were performed by the statistical software SPSS Version 21 (IBM SPSS Statistics for Windows, version 21, IBM Corp., Armonk, NY, USA).

### RESULTS

Table 1 shows the demographic and anthropometric parameters of different groups. The mean age of subjects was  $21.28 \pm 2.82$  years, with a mean BMI of  $26.96 \pm 5.1$  kg/m<sup>2</sup>. The mean BMI of group III was significantly more than that of groups I and II.

Table 2 shows the comparison of the effect of hand grip exercise on HRV between groups I and II. No significant difference was seen in the LF, HF, and LF/HF ratio at rest, immediately after hand grip exercise, and 5 min after isometric hand grip exercise between group I and group II.

Table 3 compares the effect of hand grip exercise on HRV between group I and group III. The LF/HF ratio was significantly higher in group III than in group I immediately after hand grip exercise and 5 min after isometric hand grip exercise.

Table 4 compares the effect of hand grip exercise on HRV between group II and group III. The LF/HF ratio was significantly higher in group III than in group II

immediately after hand grip exercise and 5 min after isometric hand grip exercise.

Table 5 shows the correlation of BMI with HRV. A significant positive correlation was found between BMI and LF/HF ratio and LF.

### DISCUSSION

The spectral analysis of HRV revealed the sympathovagal alteration in the form of sympathetic overactivity and vagal withdrawal, which contributes to the development of prehypertension and hypertension in the Indian population. Many studies have revealed that prehypertension is more prevalent among males, and vagal withdrawal is a more prominent component than sympathetic overactivity in male prehypertensives.<sup>[4]</sup> Our previous study in young adults showed increased sympathetic reactivity in prehypertensive subjects on traditional autonomic testing,<sup>[14]</sup> with higher sympathetic activity in males compared with females.<sup>[15]</sup> However, to our knowledge, there is no study that has thoroughly evaluated the link of BMI with the causation of prehypertension.

In the present study, the values of HRV parameters at rest do not differ between groups I, II, and III. The LF/HF ratio is a sensitive measure of sympathovagal balance. An increase in this ratio indicates increased sympathetic activity.<sup>[16,17]</sup> The LF/HF ratio was significantly increased (*P*<0.001) in prehypertensive subjects (groups II and III) when compared with the normotensive subjects (group I), which indicates an intensified sympathetic discharge in prehypertensives. Despite modest sample size in the present study, we found a significant difference in the LF/HF ratio between prehypertensive and normotensive groups, which was not observed in previous studies.<sup>[18,19]</sup> This difference could be due to the racial difference in basal LF/HF ratio or due to the difference in altered cardiac autonomic tone in response to rise in blood pressure, supported by a previous report on ethnic variation in HRV indices and the autonomic responses to stress.<sup>[20]</sup> The study has also previously shown that alteration in sympathovagal balance tilts towards augmented sympathetic activity in prehypertensives.

In the present study, there is increased sympathetic activity during IHG. This is in accordance with other studies in which adrenergic activation in hypertension is not a

**Table 1: Anthropometric parameters of different groups**

Parameters	Total	Group I	Group II	Group III
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
Age (years)	21.28 $\pm$ 2.82	22.26 $\pm$ 2.12	20.3 $\pm$ 1.62	22.15 $\pm$ 3.85
Height (cm)	160.26 $\pm$ 8.25	158.92 $\pm$ 6.29	168.30 $\pm$ 8.23	162.5 $\pm$ 9.13
Weight (kg)	70.38 $\pm$ 20.32	55.96 $\pm$ 4.47	63.76 $\pm$ 6.09	90.15 $\pm$ 30.22
BMI (kg/m <sup>2</sup> )	26.96 $\pm$ 5.11	22.19 $\pm$ 1.47	23 $\pm$ 1.1	31.93 $\pm$ 2.48

BMI: body mass index

**Table 2: Comparison of effect of hand grip exercise on HRV between group I and group II**

Group		At rest			Immediately after IHG			At 5 min post IHG		
		LF	HF	LF/HF	LF	HF	LF/HF	LF	HF	LF/HF
I	Mean±SD	5,103.0±11.6	6,564.3±14.3	1.2±0.8	6,673.3±12.3	10,177.4±10.6	0.9±1.2	10,102.8±18.2	10,625.9±21.5	0.9±0.8
II	Mean±SD	3,691.6±15.1	4,737.7±12.1	1.7±1.4	6,359.5±10.2	12,003.6±11.6	0.9±0.9	5,939.3±12.3	9,129.7±10.3	1.0±1.1
	P-value*	0.35	0.50	0.16	0.88	0.76	0.98	0.22	0.68	0.36

\*P-value <0.05 is considered statistically significant

HRV: heart rate variability, LF: low-frequency power, HF: high-frequency power, IHG: isometric hand grip exercise

**Table 3: Comparison of effect of hand grip exercise on HRV between group I and group III**

Group		At rest			Immediately after IHG			At 5 min post IHG		
		LF	HF	LF/HF	LF	HF	LF/HF	LF	HF	LF/HF
I	Mean±SD	5,103.0±11.6	6,564.3±14.3	1.2±0.8	6,673.3±12.3	10,177.4±10.6	0.9±1.2	10,102.8±18.2	10,625.9±21.5	0.9±0.8
III	Mean±SD	5,950.1±13.6	6,736.0±10.4	2.0±1.3	3,147.9±14.5	5,593.8±15.3	3.9±0.9	4,690.5±15.4	90,092.5±12.3	2.6±1.2
	P-value*	0.76	0.96	0.01	0.10	0.23	0.04	0.13	0.001	0.001

\*P-value <0.05 is considered statistically significant

HRV: heart rate variability, LF: low-frequency power, HF: high-frequency power, IHG: isometric hand grip exercise

**Table 4: Comparison of effect of hand grip exercise on HRV between group II and group III**

Group		At rest			Immediately after IHG			At 5 min post IHG		
		LF (ms <sup>2</sup> )	HF (ms <sup>2</sup> )	LF/HF	LF (ms <sup>2</sup> )	HF (ms <sup>2</sup> )	LF/HF	LF (ms <sup>2</sup> )	HF (ms <sup>2</sup> )	LF/HF
II	Mean±SD	3,691.6±15.1	4,737.7±12.1	1.7±1.4	6,359.5±10.2	12,003.6±11.6	0.9±0.8	5,939.3±12.3	9,129.7±10.3	1.0±1.2
III	Mean±SD	5,950.1±13.6	6,736.0±10.4	2.0±1.3	3,147.9±14.5	5,593.8±15.3	3.9±0.9	4,690.5±15.4	90,092.5±12.3	2.6±1.2
	P-value*	0.44	0.60	0.39	0.05	0.30	0.04	0.50	0.001	0.001

\*P-value <0.05 is considered statistically significant

HRV: heart rate variability, LF: low-frequency power, HF: high-frequency power, IHG: isometric hand grip exercise

**Table 5: Correlation of BMI with HRV**

Parameters	Correlation coefficient (r)	P-value*
LF (ms <sup>2</sup> )	0.357	0.006
HF (ms <sup>2</sup> )	-0.256	0.048
LF/HF	0.297	0.024

\*P-value <0.05 is considered statistically significant

consequence of a high blood pressure state but instead plays a pathogenic role in its occurrence. It triggers the elevation in blood pressure and favors the maintenance of a hypertensive state. Normotensive individuals with a genetic predisposition for hypertension showed increased sympathetic activity only in response to autonomic perturbations such as IHG, leading to increased LF/HF ratio during IHG, which is in accordance with the present study.<sup>[21-23]</sup>

HRV is used as a non-invasive tool to estimate cardiac autonomic activity quantitatively and has proved to be of prognostic significance in hypertension.<sup>[18,19]</sup> HRV has been reported to be decreased in hypertensive state, and the magnitude of the decrease in HRV predicts the severity of hypertension.<sup>[18]</sup> HRV has also emerged as a cardiovascular risk marker.<sup>[17]</sup> It has been noticed that decreased HRV has a greater risk for developing hypertension among

normotensive men, as autonomic dysregulation has been documented in the early stage of hypertension.<sup>[24]</sup> Thus, decreased HRV in prehypertensive subjects in the present study supports these earlier findings and could also be used as a predictive tool for the future development of hypertension in these subjects.

The present study revealed that reduced vagal tone plays a critical role in shifting this sympathovagal balance from the conversion of normotensive state to prehypertensive state, as evident from the decrease in LF/HF in prehypertensives. The intensity of sympathovagal imbalance (degree of increase in the LF/HF ratio) was more prominent in prehypertensive subjects with higher BMI than those with normal BMI. The study also reported that the magnitude of change in the vagal drive was more than the change in sympathetic drive in prehypertensives with higher BMI. From this study, the exact cause of sympathovagal



imbalance in prehypertensive subjects cannot be definitively ascertained. Increased adiposity can be a crucial determinant for the development of prehypertension in susceptible individuals, as obesity is associated with increased sympathetic and decreased parasympathetic activity.<sup>[25,26]</sup> Studies have shown that alteration in plasma levels of leptin, neuropeptide-Y, and  $\alpha$ -MSH (melanocyte-stimulating hormone) might alter autonomic activity that leads to hypertension in obese patients.<sup>[27]</sup> Therefore, we assume that the sympathovagal imbalance caused by increased adiposity is among the major predictors of increased blood pressure in prehypertensives. This was further supported by the study of Schmid *et al.*<sup>[28]</sup> that an increase in BMI is significantly associated with an increase in sympathetic tone and increased blood pressure in young healthy overweight subjects. Also, previous studies have identified that sympathetic activity normalizes in overweight subjects following a 6-month calorie restriction combined with exercise.<sup>[29]</sup>

The main limitation of our study is the relatively small number of subjects. Another limitation is that the sample was drawn from one limited geographical area, which is inadequate for extrapolating these findings to the general population.

## CONCLUSION

It can be deduced from the present study that there is enhanced sympathetic activity during IHG. This indicates an early existence of malfunctions in the autonomic nervous system in individuals at increased risk of hypertension. By identifying elevated sympathetic activation at an early stage, methods such as lifestyle modification for prevention and treatment of hypertension can be devised. We recommend further large-scale longitudinal studies to access the effect of lifestyle modifications on altered autonomic function in young prehypertensive subjects.

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## Conflicts of interest

There are no conflicts of interest to be declared.

## REFERENCES

- Mendis S, Puska P, Norrving B. Global Atlas on Cardiovascular Disease Prevention and Control. Geneva, Switzerland: World Health Organization; 2011.

- O'Donnell MJ, Xavier D, Liu L, Zhang H, Chin SL, Rao-Melacini P, *et al.* Risk factors for ischaemic and intracerebral haemorrhagic stroke in 22 countries (the INTERSTROKE study): A case-control study. *Lancet* 2010;376:112-23.
- Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, *et al.*; INTERHEART Study Investigators. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): Case-control study. *Lancet* 2004;364:937-52.
- Pal GK, Chandrasekaran A, Hariharan AP, Dutta TK, Pal P, Nanda N, *et al.* Body mass index contributes to sympathovagal imbalance in prehypertensives. *BMC Cardiovasc Disord* 2012;12:54.
- Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, *et al.*; National Heart, Lung, and Blood Institute Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure; National High Blood Pressure Education Program Coordinating Committee. The Seventh Report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: The JNC 7 report. *JAMA* 2003;289:2560-72.
- Wang NY, Young JH, Meoni LA, Ford DE, Erlinger TP, Klag MJ. Blood pressure change and risk of hypertension associated with parental hypertension: The Johns Hopkins Precursors Study. *Arch Intern Med* 2008;168:643-8.
- Pal GK, Pal P, Nanda N, Lalitha V, Dutta TK, Adithan C. Sympathovagal imbalance in prehypertensive offspring of two parents versus one parent hypertensive. *Int J Hypertens* 2011;2011:263170.
- Arifa QA, Nabi T, Rafiq N. Socio-demographic correlation with overweight and obesity among children of North India. *Indian J Child Health* 2019;6:278-82.
- Arifa QA, Kumar D, Rafiq N, Nabi T. Association of overweight and obesity with dietary and physical activity behaviour among school-aged children in North India: A cross-sectional study. *Int J Community Med Public Health* 2018;5:2944-51.
- Foulds HJ, Bredin SS, Warburton DE. The relationship between hypertension and obesity across different ethnicities. *J Hypertens* 2012;30:359-67.
- Rafiq N, Nabi T, Nazeer M. Effect of body mass index on cardiac autonomic functional status in healthy young adults. *Blood pressure. Int J Contemp Med Res* 2019;6:6-10.
- Garrow JS, Webster J. Quetelet's index (W/H<sup>2</sup>) as a measure of fatness. *Int J Obes* 1985;9:147-53.
- India reworks obesity guidelines, BMI lowered. 2008. Available from: <http://www.igovernment.in/site/Indiareworks-obesity-guidelines-BMI-lowered/>. [Last accessed on 2012 Sep 16].
- Rafiq N, Nabi T, Nazeer M. Cardiac autonomic dysfunction contributes to prehypertension status. *Indian J Appl Res* 2018;8:19-21.
- Rafiq N, Nabi T, Aara S, Arifa Q. Influence of gender on cardiac autonomic reactivity in young adults. *JMSCR* 2018;6:810-7.
- Malliani A. Heart rate variability: From bench to bedside. *Eur J Intern Med* 2005;16:12-20.
- Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability. Standard and measurement, physiological interpretation and clinical use. *Circulation* 1996;93:1043-65.
- Schroeder EB, Liao D, Chambless LE, Prineas RJ, Evans GW, Heiss G. Hypertension, blood pressure, and heart rate variability: The Atherosclerosis Risk in Communities (ARIC) study. *Hypertension* 2003;42:1106-11.
- Liao D, Cai J, Barnes RW, Tyroler HA, Rautaharju P, Holme I, *et al.* Association of cardiac autonomic function and the development of hypertension: The ARIC study. *Am J Hypertens* 1996;9:1147-56.
- Li Z, Snieder H, Su S, Ding X, Thayer JF, Treiber FA, *et al.* A longitudinal study in youth of heart rate variability at rest and in response to stress. *Int J Psychophysiol* 2009;73:212-7.
- Noll G, Wenzel RR, Schneider M, Oesch V, Binggeli C, Shaw S, *et al.* Increased activation of sympathetic nervous system and endothelin by mental stress in normotensive offspring of hypertensive parents. *Circulation* 1996;93:866-9.

22. Grassi G. Role of the sympathetic nervous system in human hypertension. *J Hypertens* 1998;16:1979-87.
23. Davrath LR, Goren Y, Pinhas I, Toledo E, Akselrod S. Early autonomic malfunction in normotensive individuals with a genetic predisposition to essential hypertension. *Am J Physiol Heart Circ Physiol* 2003;285:H1697-704.
24. Singh JP, Larson MG, Tsuji H, Evans JC, O'Donnell CJ, Levy D. Reduced heart rate variability and new-onset hypertension: Insights into pathogenesis of hypertension: The Framingham Heart Study. *Hypertension* 1998;32:293-7.
25. Lambert E, Sari CI, Dawood T, Nguyen J, McGrane M, Eikelis N, *et al.* Sympathetic nervous system activity is associated with obesity-induced subclinical organ damage in young adults. *Hypertension* 2010;56:351-8.
26. Esposito K, Marfella R, Gualdiero P, Carusone C, Pontillo A, Giugliano G, *et al.* Sympathovagal balance, nighttime blood pressure, and QT intervals in normotensive obese women. *Obes Res* 2003;11:653-9.
27. Baltatzis M, Hatzitolios A, Tziomalos K, Iliadis F, Zamboulis Ch. Neuropeptide Y and alpha-melanocyte-stimulating hormone: Interaction in obesity and possible role in the development of hypertension. *Int J Clin Pract* 2008;62:1432-40.
28. Schmid K, Schönlebe J, Drexler H, Mueck-Weymann M. Associations between being overweight, variability in heart rate, and well-being in the young men. *Cardiol Young* 2010;20:54-9.
29. de Jonge L, Moreira EA, Martin CK, Ravussin E; Pennington CALERIE Team. Impact of 6-month caloric restriction on autonomic nervous system activity in healthy, overweight, individuals. *Obesity (Silver Spring)* 2010;18:414-6.