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Research Article

Analysis of cardiac autonomic modulation in normotensive obese and eutrophic adults of Nepal

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ABSTRACT

Background: Obese people have a higher prevalence of cardiovascular disease, though unknown mechanism, supposed to be due to autonomic dysfunction which is still in controversy. This study aimed to assess and compare heart rate variability (HRV) between normotensive obese and adults.

Methods: The study was conducted on 30 normotensive obese adults (mean age 32.07±7.25 years) with BMI>30 and 29 age- and sex-matched normal weight controls (mean age 30.48±8.01 years) with BMI: 18-24 Kg/m^2. Short-term HRV variables were assessed using standard protocol. The data were compared between the groups using Mann Whitney ‘U’ test.

Results: In obese group, there was significant increase in the mean heart rate [79.17±8.80 Vs 71.48±8.41 beats/min, p=0.001], systolic blood pressure [121.20±9.89 Vs 113.24±11.07, mmHg, p=0.004] and diastolic blood pressure [84.97±7.87 Vs 74.83±10.31 mmHg, p=0.000]. The HRV parasympathetic indicators were less [RMSSD {28.75(16.72-38.35) Vs 41.55(30.6-56.75) ms, p=0.018}, NN50 {15.5(2-39) Vs 83.5(32.75-116.25), p=0.010}], and sympathetic indicator LF/HF ratio [1.2(0.65-2.20) Vs 0.79(0.5-1.02), p=0.004] was more in obese group.

Conclusions: Obese persons have increased sympathetic activity with a reduction in parasympathetic (vagal) tone indicating poor autonomic cardiac rhythm control. Moreover, the altered autonomic activity could be the reason for increased mean heart rate and blood pressures in normotensive obese persons.

Keywords: Obesity, Heart rate variability, Body mass index, Autonomic nervous system, Normotensive obese

INTRODUCTION

Obesity has several lethal consequences on cardiovascular and other systems leading to arterial hypertension, atherosclerosis, dyslipidemia, diabetes, obstructive sleep apnea, depression, and reduction in quality of life.[1-3] Studies have indicated an increase in all cause of mortality with increased body mass index (BMI), especially death from cardiovascular disease in men, though it is not uncommon in female.[4-5] Thus, obesity is leading directly or indirectly to increased morbidity and mortality.

The risk of diseases appears to increase as a function of the percent fat content in the body, above an upper limit of normal. The surrogate measures such as the Quetelet index (Body mass index – measured as weight in kg/height in metres^2) are used for grading the obesity in daily practice. This study uses the criteria suggested by WHO guidelines that BMI ≥25/30 is classified as overweight/obese.[6-8] Despite the relatively consistent findings of increased prevalence of cardiovascular disease in obesity, the reason for these associations remains obscure. Many factors have been suggested as causes for this relationship, such as insulin resistance, hypertension, and reduced high-density lipoprotein. On the other hand, it has also been suggested that a reduction in autonomic function might be the mechanism for the increased prevalence of cardiovascular disease in obesity.[9-15] The studies concentrated on the autonomic activity of the heart itself reported controversial findings. Heart rate variability (HRV) measures the effect of autonomic function on the heart alone. Decreased HRV significantly increases cardiovascular mortality. Therefore, it could be the most useful method to investigate the effect of obesity on cardiovascular health. It is important to emphasize the effect of obesity without hypertension on HRV. Therefore, this study was aimed to assess and compare Heart Rate Variability (HRV) between normotensive obese and eutrophic adults.

METHODS

This cross-sectional comparative study was conducted in the Neurophysiology laboratory in the Department of Physiology, B. P. Koirala Institute of Health Sciences (BPKIHS), Nepal. Thirty normotensive obese individuals (mean age 32.07±7.25 years) and 29 age- and sex-matched normal weight controls (mean age 30.48±8.01 years) were recruited from the medical staffs, students and the attendant of the patients at BPKIHS. The mean height of the obese patients was 1.60 ± 0.99 m and that of the controls was 1.66 ± 0.10 m. Mean BMI were 32.02 ± 2.89 and 21.87 ± 2.40 kg/m^2, respectively. As per WHO directives, obese was defined as a BMI of over 30, and normal weight was defined as a BMI of less than 25, i.e., between 18 and 24 (kg/m^2).[16,8] To be included, subjects were required to be between 18 and 75 years old and they also had to meet the BMI criteria noted above. Informed written consent was taken from all the subjects and they were screened for any history of drugs/alcohol intake, the familial history of hypertension and cardiac diseases, or medical illness likely to affect the heart rate variability parameters based on clinical history and physical examinations. Hypertensive persons were excluded from the study based on diagnostic criteria of Joint national committee (JNC) 7 on the prevention, detection, evaluation and treatment of high blood pressure.[17] The choice of the patients was very selective, to attribute a potential pathogenetic value to a metabolic alteration typical of the obese patients, represented by normal blood pressure level. The study was approved by the institutional ethical committee of BPKIHS, Nepal.

Room temperature of the laboratory was maintained at the thermo neutral zone i.e. 26±2 °C. All the required set up was checked before commencing the test. Further, subjects were made comfortable and familiar with the laboratory set up and conditions, and were advised to relax completely during recording. The subjects were instructed not to perform any exercise 40 h before the day of the experiment and to avoid drugs and caffeine 12 h before the test. The blood pressure was measured in supine position in each subject. Analysis of heart rate variability (HRV) was performed based on 5 minute ECG recorded at rest in the supine position. Recordings were taken during 08:00 am to 11:00 am to avoid any hemodynamic effect on HRV.

ECG recording and HRV analysis

For HRV, ECG at spontaneous respiration was recorded for 5 min in supine position after 15 min of supine rest. Blood pressure was recorded before taking ECG recording. ECG electrolyte gel was applied on skin underneath the standard limb leads after cleaning the skin with methyl alcohol to decrease the skin impedance so that electrical signal from the body is conducted easily to the electrodes. The subjects were instructed to take supine rest with normal breathing, relax and close their eyes but not to fall asleep to obtain steady state haemodynamics before commencement of the recording and during recording to avoid the problem of non-stationarity of the ECG signals. The ECG was taken from one of the standard limb leads having most prominent R wave. The ECG electrodes were joined to isolated ECG amplifier/ coupler of Coulbourn Instrument and its software (Windaq pro/pro+ model no. DI-400 series, USA) to capture ECG signals for HRV. The sampling frequency of the ECG was set at 2000Hz. The recordings were edited and corrected manually for ectopic beats, arrhythmias, noise and trends from the Windaq Pro/Pro+ software before any calculation of HRV. After that 'R' wave detection of normal QRS complex was completed by using Windaq Pro/Pro+ software and R wave detected ECG was edited manually to ensure all R waves. Thereafter, QRS complex occurrence times were estimated using the same software and the file was saved as lotus file, which was readable by MS Excel. The cumulative values of R-R intervals were converted into individual R-R interval series in MS excel from the Lotus file. Thus, the intervals between successive normal-to-normal QRS complexes (RR intervals resulting from sino-atrial node driven rhythm) or instantaneous heart rate values for each cardiac cycle were determined. Rechecking and editing, if required, were done manually. Thereafter, RR intervals were saved in ASCII format. It was readable to "Kubios HRV analysis software verson 2.0" which was used to calculate time domain and frequency domain measures of HRV. This software has been developed by the biomedical signal analysis group, Department of Applied physics, Ohio of Kuopio, Finland.

The HRV variables analyzed were: the time domain measures included standard deviation of normal RR interval (SDNN, ms), root mean square of differences of successive RR intervals (RMSSD, ms), NN50count and pNN50 percentage were calculated; and the frequency domain measures with low frequency power (LF ms^2, 0.04-0.15 Hz), high frequency power (HF ms^2 , 0.15-0.4 Hz), low frequency in normalized unit (LFnu), high frequency in normalized unit (HFnu), and LF/HF - ratio of absolute LF power to HF power.[18]

Statistical analysis

Statistical analysis was conducted with SPPS software (v 16.02, Chicago, IL, USA). Differences in variables between the groups were tested using Mann-Whitney U test. The data are expressed as median (interquartile range). A p-value of <0.05 was considered significant.

RESULTS

Among the studied variables between the groups weight, body mass index, mean heart rate, systolic blood pressure, and diastolic blood pressure were found to be significantly (p<0.05) more in normotensive obese groups shown in Table 1.

Table 1: Comparison of anthropometric and cardiorespiratory variables between normotensive obese (n=30) and eutrophic (n=29) groups.

Variables	Obese Mean ± SD	Normal weight Mean ± SD	P value
Age, yrs	32.07±7.25	30.48±8.012	0.429
Height, m	1.60±0.099	1.66± 0.10	0.038
Weight, kg	82.93±11.14	60.69±9.43	0.000
BMI, kg/m^2	30.02±2.89	21.87±2.40	0.000
Respiratory rate, cycles/min	16.60±2.76	16.41±2.87	0.801
Mean heart rate, beats/min	79.17±8.80	71.48±8.41	0.001
Systolic blood pressure, mmHg	121.20±9.89	113.24±11.07	0.005
Diastolic blood pressure, mmHg	84.97±7.87	74.83±10.31	0.000

Table 2: Comparison of heart rate variability parameters in time domain between normotensive obese (n=30) and eutrophic controls (n=29).

Variables	Obese Median (Q1-Q3)	Normal weight Median (Q1-Q3)	P value
SDNN (ms)	35.55(26.77-49.25)	46.15(37.22-58.57)	0.038
RMSSD (ms)	28.75(16.72-38.35)	41.55(30.6-56.75)	0.018
NN50count	15.5(2-39)	83.5(32.75-116.25)	0.010
PNN50%	6.4(0.5-17.33)	25.65(11.42-40.5)	0.012

SDNN - Standard deviation of normal RR interval; RMSSD - Root mean square of differences of successive RR intervals; NN50count – Number of RR intervals that differ by more than 50 milliseconds; pNN50% – Percentage of consecutive RR intervals that differ by more than 50 milliseconds.

Table 3: Comparison of heart rate variability (HRV) parameters in frequency domain between normotensive obese (n=30) and eutrophic (n=29) groups.

Variables	Obese (n=30) Median (Q1-Q3)	Normal weight (n=29) Median (Q1-Q3)	P value
LF power (ms^2 / Hz)	248(110.75-465)	480(187-953)	0.063
HF power (ms^2 / Hz)	216(103.5-530)	640.5(300.75-1219.75)	0.014
LF %	26.15(21.6-36.55)	27.85(18.62-36.92)	0.921
HF %	23(12.15-45.28)	34.3(23.57-45.25)	0.192
LFnu	54.5(39.65)	44.1(33.75-54.82)	0.079
HFnu	45.5(31.3-60.35)	55.9(45.17-66.25)	0.079
LF/HF	1.2(0.65-2.20)	0.79(0.5-1.02)	0.045

LF power – Low frequency power; HF power - High frequency power; LF % - Low frequency power percent; HF % - High frequency power percent; LFnu - Low frequency normalized unit; HFnu - High frequency normalized unit; LF/HF – Ratio of low frequency to high frequency.

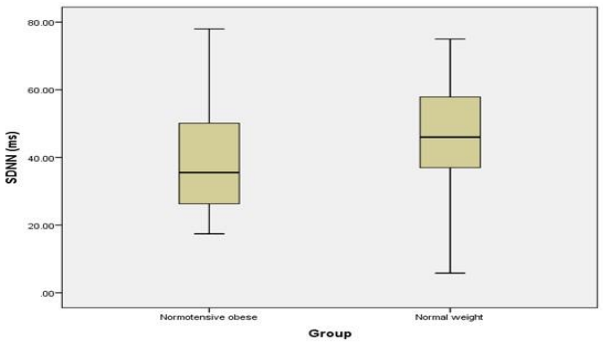

Figure 1: Standard deviation of normal RR interval for normotensive obese and eutrophic controls.

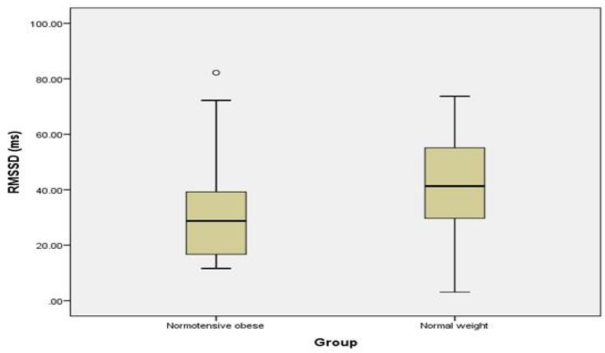

Figure 2: Root mean square of differences of successive RR intervals for normotensive obese and eutrophic controls.

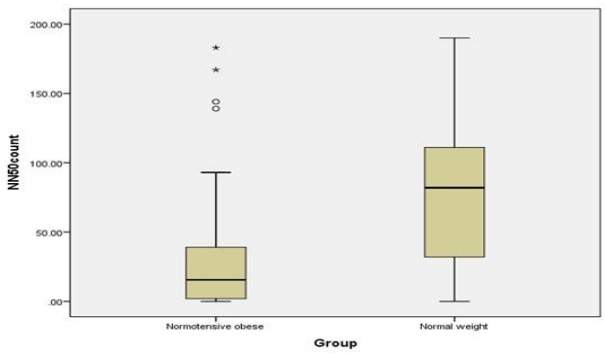

Figure 3: Number of RR intervals that differ by more than 50 ms for normotensive obese and eutrophic controls.

Heart rate variability (HRV) measures

Time domain variables of HRV: In the time domain measures, SDNN, RMSSD, NN50count and pNN50 percentage were significantly ($p<0.05$) less in obese group as compared to the normal weight group (Table 2, and Figures 1, 2, 3 and 4).

Frequency domain variables of HRV

Among the frequency domain variables, HF power (ms^2) ($HFms^2$) and LF/HF ratio were significantly ($p<0.05$) more in obese group than in normal weight controls. The other frequency domain variables were comparable between the groups (Table 3, and Figures 5 and 6).

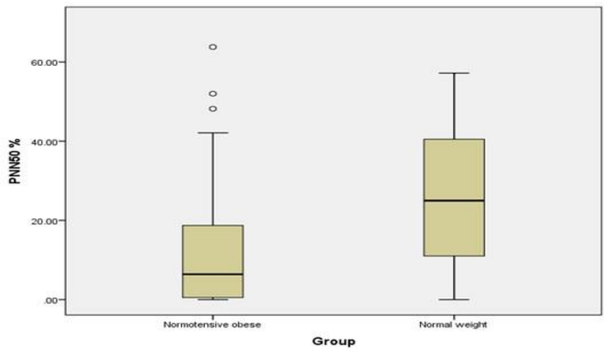

Figure 4: Percentage of consecutive RR intervals that differ by more than 50 ms for normotensive obese and eutrophic controls.

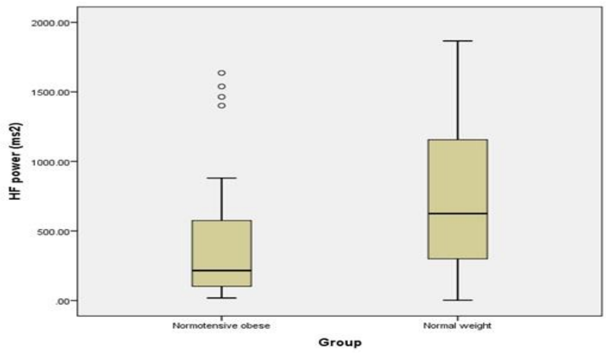

Figure 5: High frequency power for normotensive obese and eutrophic controls.

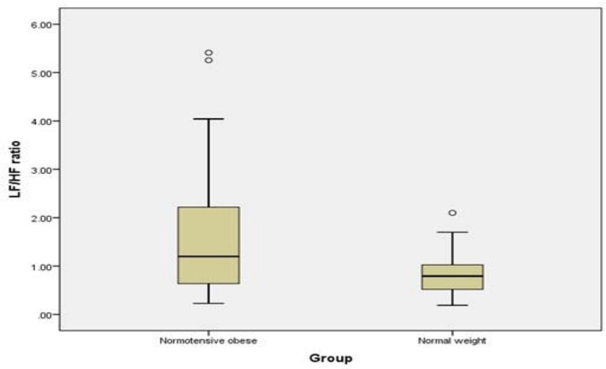

Figure 6: Low frequency-high frequency ratio for normotensive obese and eutrophic controls.

DISCUSSION

In the present study the analysis of cardiac autonomic modulation in normotensive obese and eutrophic adults were examined. The resting mean heart rate was significantly more in normotensive obese group in comparison to normal weight group. Several studies support the finding of tachycardia in obese and the reason probably being the altered autonomic modulation in intrinsic heart rate.[19-23] Increased heart rate is also imputed to relatively suppressed vagal tone.[24, 25]

This study confirmed that both SBP and DBP are significantly higher in normotensive obese persons which are supported by some epidemiological studies.[26-28] It is estimated that as much as one-third of all hypertension may be attributable to obesity in populations where hypertension and obesity are widely prevalent.[29]

In this study, all the parasympathetic markers of HRV (time domain measures: SDNN, RMSSD, NN50count, pNN50% and frequency domain measure: HF power) that estimate high frequency beat-beat variations in heart rate were lower in normotensive obese persons than in eutrophic adults. As expected the sympathetic marker of frequency domain; LF/HF ratio was increased in obese persons. This finding itself strongly supports the reason for increased heart rate in normotensive obese adults. Further, our findings are in accord with the earlier reports that obese persons suffer from an increased mortality risk supposedly due to cardiovascular disorders related to either continuously lowered parasympathetic or heightened sympathetic activation.[10,30,31] A reduction in parasympathetic activity among obese children has also been reported in another investigation.[32] Whereas, a reduction in sympathetic activity in obese is described by some other researchers which is in contrast to this study.[32,33] Moreover, Luiz Carlos reported that the obese children exhibited modifications in heart rate variability, characterized by a reduction in both sympathetic and parasympathetic activity.[34] According to Nagai & Moritani, a causal relationship between alterations in autonomic nervous system (ANS) activity and obesity cannot be confirmed.[33] However, the authors suggest that a reduction in autonomic activity may be an etiological factor in the onset and development of obesity.

This variation among the studies was partially explained on the basis of the duration of obesity.[35] It is suggested that duration of the obesity has a major role to play in determining the level of cardiac sympathetic activity.[33] Present study showed an increase in sympathetic activity, but if the obesity is of a longer duration, then it is likely to lead to overall reduction of the autonomic activity and hence a reduction in the sympathetic activity too.[35] Another report of Peterson *et al.* suggesting an association between the increase in body fat and hypo activity of sympathetic and parasympathetic components of ANS which proposes a reduced sympathetic activity is related to lower energy expenditure and, consequently, to a positive energy balance and increase of body weight.[36] Further, Yakinci *et al.* performed autonomic function tests; sympathetic (orthostatic test) or parasympathetic (Valsalva ratio, 30/15 ratio and HR responses to deep breathing) on obese children and found normal sympathetic activity and parasympathetic hypo activity.[37] Thus, the different findings in sympathetic activity of obese among studies are probably due to difference in age group or duration of obesity.

CONCLUSION

This study revealed the poor autonomic modulation control in obese persons which strongly argue in favour of the notion that the increased sympathetic activity with a reduction in parasympathetic activity affecting the cardiac mechanism acting on the sinus node. Further, it can be concluded that altered autonomic activity could be the reason for increased mean heart rate and blood pressures in normotensive obese persons. The interventional programs decreasing fat content of the individual can be advised to reduce the altered autonomic activity.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Balarajan Y, Villamor E. Nationally representative surveys show recent increases in the prevalence of overweight and obesity among women of reproductive age in Bangladesh, Nepal, and India. J. Nutr. 2009;139:2139-44.
2. Daniels SR. Complications of obesity in children and adolescents. Int J Obesity. 2009;33(Suppl 1):S60-5.
3. Lee YS. Consequences of childhood obesity. Ann Acad Med Singapore. Ind J Nutr. 2009;38:75-81.
4. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of US adults. N Engl J Med. 1999;341:1097-105.
5. Lobstein T, Baur L, Uauy R. IASO International Obesity Task Force. Obesity in children and young people: a crisis in public health. Obes Rev. 2004;5:4-104.
6. WHO. Obesity: preventing and managing the global epidemic: report of a WHO consultation (ISSN 05 12-3054): WHO; Geneva, Switzerland; 1999. WHO Tech Rep Ser, 894.
7. Han TS, Sattar N, Lean M. ABC of obesity. Assessment of obesity and its clinical implications. BMJ. 2006;333(7570):695-708.
8. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894:1-253.
9. Kaufman CL, Kaiser DR, Steinberger J, Kelly AS, Dengel DR. Relationships of cardiac autonomic

function with metabolic abnormalities in childhood obesity. Obesity. 2007;15:1164-71.
10. Tonhajzerova I, Javorka M, Trunkvalterova Z, Chroma O, Javorkova J,Lazarova Z, et al. Cardio-respiratory interaction and autonomic dysfunction in obesity. J Physiol Pharmac. 2008;59(Supply 6):709-18.
11. Lown B, Verner RL. Neural activity and ventricular fibrillation. N Engl J Med. 1976;294:1165-70.
12. Corr PB, Yamada KA, Witkowski FX. Mechanisms controlling cardiac autonomic function and their relation to arrhythmogenesis. In: Fozzard HA, Haber E, Jennings RB, Katz AN, Morgan HE, eds. The Heart and Cardiovascular System. New York: Raven Press. 1986:1343-1403.
13. Schwartz PJ, Priori SG. Sympathetic nervous system and cardiac arrhythmias. In: Zipes DP, Jalife J, eds. Cardiac Electrophysiology. From Cell to Bedside. Philadelphia: W.B. Saunders. 1990:330-343.
14. Levy MN, Schwartz PJ eds. Vagal control of the heart: Experimental basis and clinical implications. Armonk: Future, 1994.
15. Vanderlei LCM, Pastre CM, Hoshi RA, Carvalho TD, Godoy MF. Basic notions of heart rate variability and its clinical applicability. Rev Bras Cir Cardiovasc 2009; 24: 205-217.
16. Haslam DW, James WP. Obesity. Lancet. 2005;366(9492):1197-209. (WHO/obesity and overweight: fact sheet no.311, Sept. 2006).
17. The seventh report of the Joint National Committee on the prevention, detection, evaluation, and treatment of high blood pressure. National Heart, Lung, and Blood Institute. August 2004. www.nhlbi.nih.gov.
18. Task force of the European Society of Cardiology and The North American Society of Pacing and Electrophysiology. Heart rate variability. Europian Heart Journal. 1996;17:354-84.
19. Rumantir MS, Vaz M, Jennings GL, Collier G, Kaye DM, Seals DR, et al. Neural mechanisms in human obesity-related hypertension. J Hypertens. 1999;17:1125-33.
20. Messerli FH, Nunez BD, Ventura HO, Snyder DN. Overweight and sudden death. Arch Intern Med. 1987;147:1725-8.
21. Grassi G. Debating sympathetic overactivity as a hallmark of human obesity: a pro’s position. J Hypertens. 1999; 17: 1059-1060.
22. Rabbia F, Silke B, Conterno A, Grosso T, DeVito B, Rabbone I, et al. Assessment of cardiac autonomic modulation during adolescent obesity. Obes Res. 2003;11:541-8.
23. Riva P, Martini G, Rabbia F, Milan A, Paglieri C, Chiandussi L, et al. Obesity and autonomic function in adolescence. Clin Exp Hypertens. 2001;23:57-67.
24. Wong CY, O’Moore-Sullivan T, Leano R, Byrne N, Beller E, Marwick TH. Alterations of left ventricular myocardial characteristics associated with obesity. Circulation. 2004;110:3081-7.
25. Gutin B, Barbeau P, Litakar MS, Ferguson M, Owens S. Heart rate variability in obese children: relations to total body and visceral adiposity, and changes with physical training and detraining. Obes Res. 2000;8:12-9.
26. Zahorska-Markiewicz B, Kuagowsa E, Kucio C, Klin M. Heart rate variability in obesity. Int J Obes Relat Metab Disord. 1993;17:21-3.
27. Masuo K, Mikami H, Ogihara T, Tuck ML. Weight gain-induced blood pressure elevation. Hypertension. 2000;35:1135-40.
28. Macmohan S, Cutler J, Brittain E, Higgins M. Obesity and hypertension: epidemiological and clinical issues. Eur Heart J. 1987;8(suppl B):57-70.
29. Stamler R, Stamler J, Riedlinger WF, Algera G, Roberts RH. Weight and blood pressure. Findings in hypertension screening of 1 million Americans. JAMA. 1978;240:1607-10.
30. Laederach-Hofmann K, Mussgay L, Ru´ddel H. Autonomic cardiovascular regulation in obesity. J Endocrinol. 2000;164:59-66.
31. Peterson HR, Rothschild M, Weinberg CR, Fell RD, McLeish KR, Pfeifer MA. Body fat and the activity of the autonomic nervous system. N Engl J Med. 1988;318:1077-183.
32. Nagai N, Matsumoto T, Kita H, Moritani T. Autonomic nervous system activity and the state and development of obesity in Japanese school children. Obes Res. 2003;11:25-32.
33. Nagai N, Moritani T. Effect of physical activity on autonomic nervous system function in lean and obese children. Int J Obesity. 2004;28:27-33.
34. Marques Vanderlei LC, Pastre CM, Freitas Júnior IF, Fernandes de Godoy M. Geometric Indexes of Heart Rate Variability in Obese and Eutrophic Children. Arq Bras Cardiol. 2010;65(8):789-92.
35. Hambdy RC. Obesity: an epidemic. South Med J. 2003;96:531-2.
36. Spraul M, Ravussin E, Fontvieille AM, Rising R, Larson DE, Anderson EA. Reduced sympathetic nervous activity. A potential mechanism predisposing to body weight gain. J Clin Invest. 1993;92(4):1730-5.
37. Yakinci C, Mungen B, Karabiber H, Tayfun M, Evereklioglu C. Autonomic nervous system functions in obese children. Brain Dev. 2000;22:151-3.

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