**Original Article**

MEMOIRS HEALTH SCI. MED. KANAZAWA UNIV. Vol. 20
35~41 1996

# Effect of Body Fat on Cardiac Autonomic Nerve Activity in Healthy Young Subjects

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**SUMMARY**

Aim of this study was to assess the relation of generalized obesity and fat distribution to sympathetic and parasympathetic components of heart rate in healthy young subjects.

We recorded ECG continuously in the supine and standing position with pacing respiration at 0.25Hz for 5 min in 47 healthy young female.

Habitus was represented by body mass index, as an index of generalized adiposity, and by the ratio of waist-to-hip girth (waist/hip ratio), as an index of centripetal fat distribution. A spectral analysis of R-R variability from 256-sec series interbeat interval in each position provided markers of sympathetic nerve activity (ratio of low frequency component to high frequency component (LF/HF ratio) in the standing position), and vagal activity (HF power in the supine position).

LF/HF ratio in the standing position was positively correlated with both waist/hip ratio ($r=0.366$, $p<0.02$) and waist girth ($r=0.317$, $p<0.04$), but not correlated with body mass index ($p=0.904$). HF power in the supine position was not correlated with waist/hip ratio ($p=0.893$), waist girth ($p=0.907$) or body mass index ($p=0.454$).

These results suggest that, in healthy young female, centripetal fat distribution is one of the determinants of the cardiac sympathetic activity, but not the cardiac vagal activity.

**KEY WORDS**

body fat, autonomic nervous system, ECG, spectral analysis

## INTRODUCTION

The relation between obesity and hypertension has been well established. Especially, obese individuals with upper body obesity have a greater risk for hypertension than those with lower body obesity[1-3].

Sympathetic activation could contribute to increased systemic vascular resistance and hypertension through activation of $\alpha$-adrenergic vasoconstriction and stimulation of the renin-angiotensin system[4]. Such vasoconstriction could be reinforced by sympathetically mediated trophic effects on the vasculature[5].

Guzzetti et al.[6], with the spectral analysis of heart rate variability, found that in a population of hypertensive subjects, the markers of sympathetic activity was increased and those of vagal activity was decreased.

Microneurography allows direct recordings of postganglionic sympathetic nerve action potentials[7] and a recent study[8], using microneurography, found the presence of incresing

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**Table I. Characteristics of Study Subjects**

| Variables | Mean | SE | Range | |
|---|---|---|---|---|
| | | | Minimum | Maximum |
| Age (yr) | 20 | ... | 19 | 21 |
| Weight (kg) | 54.4 | 1.08 | 40.5 | 74.5 |
| Height (m) | 1.59 | 0.007 | 1.44 | 1.70 |
| Body mass index ($kg/m^2$) | 21.5 | 0.36 | 16.6 | 28.8 |
| Waist girth (cm) | 67.6 | 0.89 | 58.0 | 84.5 |
| Hip girth (cm) | 90.1 | 0.67 | 80.0 | 100.0 |
| Waist/hip ratio | 0.750 | 0.008 | 0.670 | 0.888 |
| R-R interval (msec) | 863 | 19.1 | 640 | 1300 |
| Mean blood pressure (mmHg) | 80.0 | 1.21 | 59.0 | 93.0 |

Study sample n =47.

body fat leads to increasing of the resting rate of muscle sympathetic nerve discharge in healthy subjects. Then, increasing body fat might be considered to play a part of sustained elevation of arterial pressure in humans with obesity hypertension.

The question of whether increasing body fat may affects the cardiac vagal activity as well as sympathetic one remains uncertain. We, therefore, measured the fluctuations in the heart rate using spectral analysis to assess the relation of generalized obesity and fat distribution to sympathetic and vagal components of the heart rate in the healthy subjects.

## SUBJECTS AND METHODS

**Subjects :** Fifty female students were recruited for this study. One student who had bigeminal ectopic beats or 2 students who had sequantial artifacts in the session were excluded. Generalized obesity was difined as the body mass index (BMI, weight[kg]/(height)$^2$[$kg/m^2$]) and central obesity as the waist-to-hip circumference ratio (Waist/hip ratio). Forty seven subjects had a mean age of 20 years (range, 19 to 21 years), a BMI of $21.5\pm0.4kg/m^2$ (mean ± S.E., range 16.6 to $28.8kg/m^2$), and waist/hip ratio of $0.75\pm0.08$ (range, 0.67 to 0.89). All were normotensive (mean blood pressure $80\pm$ 1.21mmHg, range 59 to 93) (Table 1). None of them was on any medication, or instructed not to ingest caffein, alcohol or nicotine for at least 9h prior. All studies were carried out between 800 and 1000hr in a quiet warm room. Informed consent was obtained from all subjects.

**Protcol :** The day before the experiment, ECG electrodes were firmly applied to the chest (lead CM5 and NASA) and continuous ECG signals were recorded on a Holter ECG recorder SM-30 (Fukuda Denshi Co., Tokyo Japan). The next morning, after 15-min quiet period in the supine position, the subject breathed synchronously with an oscilloscope beam, controlled at 0.25Hz for 5min. Then, the suject stood up and remained upright for 5min controlled respiratory was performed again for 5min in the upright position. The blood pressure was measured at the end of rest period using a automatic digital blood presure monitor HEM-709 (Omuron Co., Tokyo, Japan). At the end of experiment, body weight, height, waist girth and hip girth were measured.

**Table II. Correlation Matrix Showing Pairwise Associations of Relevant Variables**

| | Body mass index | Waist/hip ratio | Weight | Waist girth | HF Power | LF/HF |
|---|---|---|---|---|---|---|
| Body mass index | ... | | | | | |
| Waist/hip ratio | 0.173 (0.246) | ... | | | | |
| Weight | 0.876 (0.000) | 0.149 (0.318) | ... | | | |
| Waist girth | 0.573 (0.000) | 0.816 (0.000) | 0.585 (0.000) | ... | | |
| HF power | -0.112 (0.454) | -0.020 (0.893) | -0.010 (0.949) | 0.018 (0.907) | ... | |
| LF/HF | -0.018 (0.904) | 0.366 (0.011) | 0.104 (0.485) | 0.317 (0.030) | -0.261 (0.077) | ... |
| Mean blood pressure | -0.034 (0.823) | -0.066 (0.658) | -0.049 (0.745) | -0.068 (0.650) | -0.327 (0.025) | -0.013 (0.928) |

HF power indicates power of the high frequency component in the supine position. LF/HF indicates the ratio of LF-to-HF power in the standing position. Values represent r values, and corresponding p values are given in parentheses. n=47

**Data analysis :** ECG data were played back, and analog to digital conversion was performed at 10 bit 125Hz, and R-R interval measurements were converted to a heart rate time series using data processa DMW-9000H (Fukuda Denshi Co., Tokyo, Japan). A artifact-free 256-sec series R-R segments during controlled respiratory periods in each position were selected for spectral analysis. The power spectrum of fluctuations in selected R-R segments was computed by means of the autoregressive model program[9] and was integrated into it's two major components ; a high frequency component (HF), centered at 0.25Hz, reflecting mostly cardiac vagal activity[10,11], and a low frequency component (LF), centered at about 0.1Hz[12]. The LF/HF ratio in the standing position was obtained by dividing the power of the LF by the power of the HF component, as a marker of sympathetic activity[13,14].

Results are expressed as mean ±S.E.. Correlations between the dependent and independent variables were analyzed by simple linear regression. Mann-Whitney U tests were used to compare the bottom and the top of quartiles group differences for mean LF/HF values in each waist/hip ratio, waist girth and BMI group. Values of $p<0.05$ were considered significant.

**RESULTS**

A correlation matrix of relevant variables is shown in the Table 2. LF/HF in the standing position was correlated with both waist/hip ratio ($r=0.366$, $p=0.02$) and waist girth ($r=0.317$, $p=0.04$ ; Fig. 1). In contrast, there was no correlation between LF/HF in the standing position and BMI ($p=0.904$ ; Fig. 1). Increased waist/hip ratio and waist girth were associated with increased LF/HF in the standing position as a marker of sympathetic activation. Division of the sample into quartiles of waist/hip ratio indicate that the LF/HF in the top quartile was significantly greater than that in the bottom quartile (87.7±7.6 vs 62.6 ±8.6, $p<0.05$, Fig. 2).

The LF/HF in the top quartile of waist girth was 1.5-fold that of bottom quartile (86.0±9.4 vs 59.0±8.0cm, $p<0.05$). In contrast, in BMI group, we could not separate overweight from light-weight subjects (70.2±9.58 vs 65.6±6.09kg/m$^2$, $p=0.974$, Fig.2).

There was no correlation between HF power

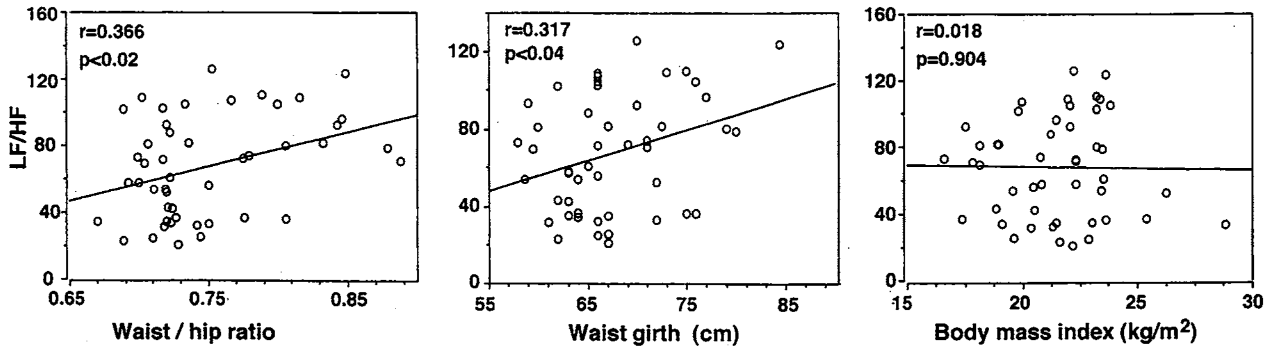


**Fig. 1. Correlation between LF/HF and waist/hip, waist girth, or body mass index (BMI). LF/HF indicates the LF/HF ratio in the standing position.**

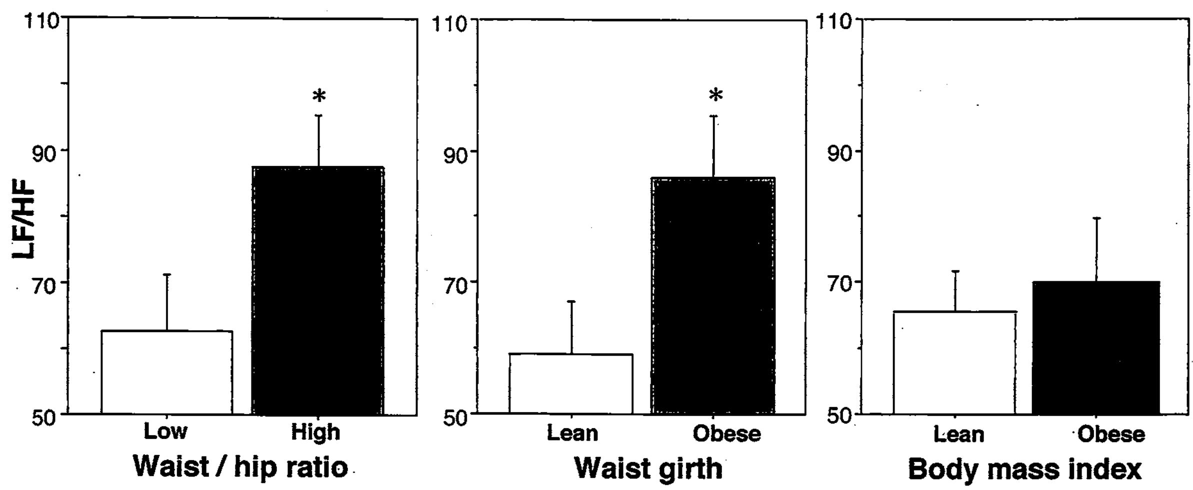


**Fig. 2. Comparison of mean LF/HF values between top (shaded bars) and bottomquartile (open bars) of waist/hip ratio, waist girth, and body mass index. Results are expressed as mean ±S.E..**
* $p<0.05$ top vos bottomquartile.

in the supine position and any of habitus variables (Fig. 3).

We found no significant relation between BMI and waist/hip ratio ($p=0.246$, Fig. 4).

## DISCUSSION

The principal findings in the present study were significant positive correlation between LF/HF in the standing position and the severity of central fat distribution as expressed by waist/hip ratio and waist girth.

However, generalized obesity as expressed by BMI showed no relation to LF/HF in the standing position. In addition, there was no correlation between HF power in the supine position and any habitus variables.

Previous reports concerning the relation between the sympathetic activation and body fat in healthy subjects have been based on measurement of 24-hour urinary norepinephrine excretion[15] and the resting firing rate of muscle sympathetic nerve activity (MSA)[8,16,17]. The former measurement is an integrated measure of sympathetic nervous system activity, discriminating norepinephrine of sympathetic nervous system origin from norepinephrine of adrenal medullary origin continues to exist as a problem[15]. In contrast, the latter has an advantage in that it gives a direct measurement of sympathetic nerve activity[7]. There is, however, also a limitation, neither of them can provide a vagal activity simultaneously. Heart rate variability is an indirect end-organ response of cardiac autonomic function and can provide not only the sympathetic activity but also the vagal activity simultaneously[10]. Previous studies have shown that HF power in the supine

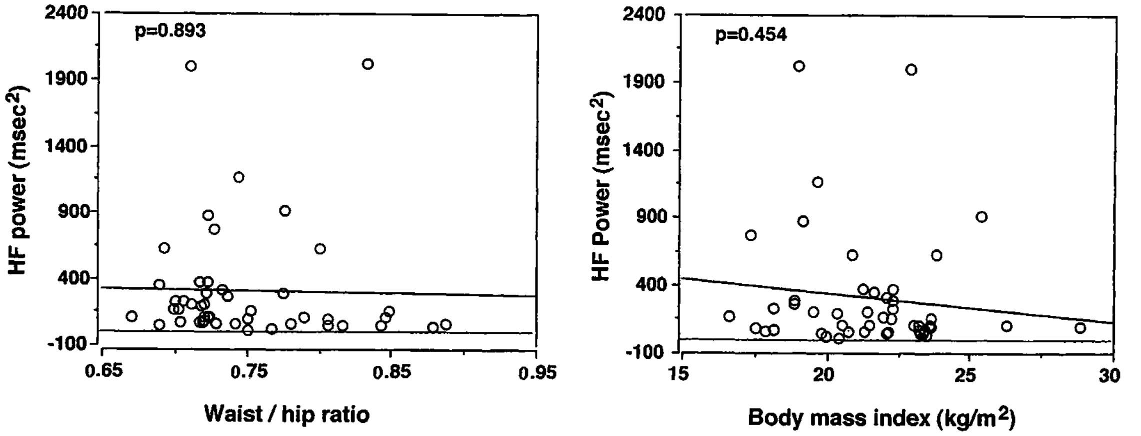


**Fig. 3. Correlation between HF power and waist/hip ratio or body mass index.**

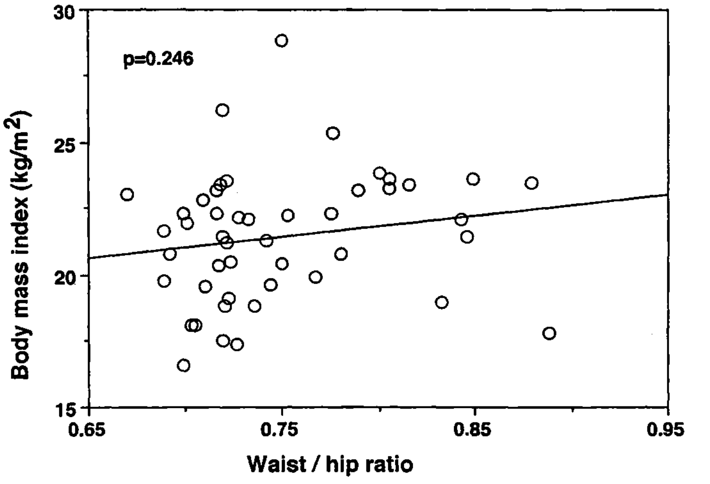


**Fig. 4. Correlation between body mass index and waist/hip ratio.**

position as a marker of cardiac vagal activity[11] and LF/HF[13] in the standing position[12] as a marker of cardiac sympathetic tone.

**Relationship between sympathetic activity and body fat** : A recent studies[8,16] found a direct correlation between the resting rate of sympathetic nerve discharge to skeltal muscle and body fat as expressed by body mass index and percent body fat. Therefore, in healthy humans, body fat is one of the major determinants of resting sympathetic nerve activity. Our present results are similar, that showed a slight but significant positive correlation between a marker of cardiac sympathetic activity and the severity of centripetal fat distribution, as expressed by waist/hip ratio and waist girth. However, there was no correlation between a marker of cardiac sympathetic activity and BMI as a marker of generalized obesity. Increase of BMI is known to be associated with severity of centripetal fat distribution in subjects covering a broad spectrum of total body weight. However, because our subjects consisted of lean and mild obese, we found no significant correlation between BMI and waist/hip ratio. These results suggest that severity of centripetal fat distribution play and important role in the cardiac sympathetic activity in healthy subjects.

It has been showed that abdominal fat cells are metabolically more active than peripheral fat cells[18], and abdominal obesity is associated with increased lipolytic activity and increased free fatty acid release and turnover[19]. Recently, Grekin[20] reported that chronic increases in portal venous free fatty acid is responsible for hypertension, mediated by increased sympatheric tone. These reports suggested that central obesity is more important determinant than generalized obesity and consisted with the present study.

**Relationship between vagal activity and body fat :** As far as we know, there is no report on the relationship between vagal activity and body fat. In the present study, we did not identify a relationship between cardiac vagal activity, as expressed by the HF power in the supine position, and indexes of generalized obesity or centripetal fat distribution. Thus, our results suggest that, in the healthy young female, body fat or body fat distribution is not the determinant of the cardiac vagal activity.

There must be other alternative explanations for the decrease in vagal activity in hypertension subjects.

It has been shown that sensitivity of baroreceptor was reduced in experimental[21] and human hypertension. Reduction of baroreflex sensitivity might be considered to play a role in reducing the cardiac vagal nerve activity in hypertension. However, precise mechanism for reduced vagal nerve activity is uncertain and further study is necessary.

## CONCLUSIONS

We have described a significant correlation between the cardiac sympathetic activity and centripetal fat distribution in healthy young female, but no relation between the cardiac vagal activity and body fat or body fat distribution. These results suggest that central obesity might be one of the major determinants of sympathetic nerve activity but not vagal nerve activity.

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# 心臓自律神経機能への体脂肪による影響

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## 要　　旨

【目的】心拍変動の交感および副交感神経活動成分と肥満および体脂肪分布との関連を検討した。
【方法】健常若年女性47名を対象とした。呼吸数を一定（0.25Hz）とし，安静臥位および直立時の心電図を各５分間記録した。体格は，全身的肥満の指標として，体格指数を，中心性肥満の指標としてウエスト／ヒップ比を計測した。臥位および立位の各256秒間の心拍変動をスペクトル分析し，立位での低周波成分パワーと高周波成分パワーの比（LF/HF 比）から交感神経活動指標を，また，臥位での高周波成分パワーから迷走神経活動指標を求めた。
【結果】直立時 LF/HF は，ウエスト／ヒップ比と正の相関（r=0.37，p=0.02），ウエスト周囲長と正の相関（r=0.32，p=0.04）を示したが，体格指数その他は有意の相関を示さなかった。安静臥位時の HF パワーは，体格指数，ウエスト／ヒップ比を含むいずれとも有意の相関を示さなかった。
【まとめ】健常女性では，中心性肥満は，心臓交感神経活動の規定因子の１つである可能性が，心臓迷走神経活動に対しては，規定因子でない可能性が示唆された。