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# RELATIONSHIP BETWEEN OBESITY DECREASE AND REGRESSION OF HYPERTENSIVE LEFT VENTRICULAR HYPERTROPHY

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**Summary**. *There is a well-known relationship between obesity and hypertensive left ventricular hypertrophy. However, little is known about the relationship between obesity decrease and regression of hypertensive left ventricular hypertrophy.*
*The aim of the study is assessment of relationship between obesity decrease and regression of hypertensive left ventricular hypertrophy.*
*73 patients with II-III stage hypertension (43 male), average age 55.9 ± 8 and LVH determined by echocardiography (average left ventricular mass (LVM) index: 164 ± 32 g/m$^2$; Penn convention) have been treated (by medication and by diet) for a year. Each subject underwent two-dimensional and Doppler echocardiography, 12-lead electrocardiogram examination (QTc interval dispersion), exercise stress testing (Bruce - protocol), 24-h ambulatory monitoring blood pressure (ABPM), 24-h Holter monitoring with Lown classification of ventricular arrhythmia's and heart rate variability. Mean body mass index (BMI) was 28.7 ± 3.6 kg/m² (23 to 39), and 28 (39%) patients were obese (BMI > 30 kg/m$^2$) (OH group).*
*After one year systolic BP (SBP) was reduced on the average been 168 ± 26 to 158.2 ± 21 mmHg, diastolic BP (DBP) from 102 ± 12.7 to 97 ± 11 mmHg. LV mass index was reduced from 163 ± 32 to 150.2 ± 27 g/m$^2$ (all p<0.001). 22 patents (30.1%) lost weight more than 5%. These patients significantly decreased LV mass 309 ± 79 vs 278.4 ± 61 g; t=3.22 p<0.004), LV mass index (161 ± 35 vs 148 ± 29 kg/m²; t=2.68; p<0.02), LV diastolic dimension (52.3 ± 4.7 vs 50.5 ± 4.4 mm; t=2.95, p<0.008), Cornell's index (1.55 ± 0.4 vs 1.41 ± 0.4, p<0.02), peak double product (DP) (27.3 ± 5 vs 24.4 ± 5, t=2.8, p<0.02), DP/METTs (2.48 ± 1 vs 1.84 ± 1, t=2,15; p< 0.05), mean 24h systolic BP (SBP) (144.1 ± 17 vs 138.6 ± 16 mmHg, t=2.2 p<0.04), mean 24h diastolic BP (DBP) (89.5 ± 11 vs 85.7 ± 12 mmHg, t = 2.2, p<0.04), mean SBP per day (148.2 ± 18 vs 141 ± 16 mmHg, t=2.6, p<0.02), mean DBP per day (92.7 ± 11 vs 88 ± 13 mmHg, t=2.6, p < 0.02) and increase of mean 24h RR intervals per night (938.2 vs 999 ms; t= 3, p<0,007).*
*Patients (51.70%) who didn't achieve significant loss of weight significantly decreased LV mass index (163 ± 30 vs 152 ± 25 kg/m²; t=2.1; p<0.05), office SBP (170.3 ± 27 vs 158.9 ± 19, t=2.2, p<0.03), grades of ventricular arrhythmias (2.73 vs 1.95, t=2.1, p<0.04), and mean VES/24h (66.6 vs 20, t=2.22, p<0.04).*
*Hypertensive patients with LVH with significant loss of weight after one year, achieved higher grade of LVH regression (on account of decrease of LV diastolic dimension), lower DP at exercise, lower values of BP during 24-hour monitoring and improvement of heart rate variability, than patients without significant loss of weight.*

**Key words**: *Obese, hypertension, left ventricular hypertrophy, regression*

## Introduction

Hypertension is a mass non-infectious disease with a prevalence of over 20% of adult population (1). One of the earliest adaptation mechanisms to increased afterload is left ventricular hypertrophy. However, the hypertrophy as an adaptation very quickly changes into a pathological condition. Nowadays there is a common agreement that left ventricular hypertrophy is an independent risk factor for cardiovascular morbidity and mortality.

High blood pressure is only one of the factors in hypertension which lead to LVH. A significant role in the development of LVH can be played by many other unhemodynamic factors such as: age, sex, sympathetic nervous system, renin-angiotesin system, genetic factors and overweight.

A correlation between hypertension and overweight has been known for a long time. As demonstrated by the results of the INTERSALT Study (2), there exists a positive correlation between body weight and blood pressure. Approximately 50% of the obese patients exhibited elevated blood pressure, whereas, in contrast, 50% of the patients with primary hypertension were

overweight. A loss of weight leads to a decrease of blood pressure and therefore constitutes a general therapeutic measure for appropriately disposed patients.

More than half a century ago Smith and Wiliams at the Mayo Clinic attempted to untangle the cardiac effects of obesity from those of hypertension (3). Messerly and co-authors showed that cardiac adaptation to obesity results in cardiac hypertrophy of the eccentric type, ie., an increase in myocardial mass combined with chamber dilatation (4).

The Framingham study has indicated that patients with left ventricular hypertrophy are at an increased risk of sudden death and other cardiovascular morbidity and mortality. The risk for sudden death is 5 to 6 times higher in patients with left ventricular hypertrophy than in those without, regardless of levels of arterial pressure. Therefore, LVH regression is the main target in the therapy of hypertensive patients. Our recently published results have undoubtedly showed the importance of LVH regression (5,6).

However, the Framingham study (7) has also indicated that obesity per se represents a higher risk of sudden death. While it is well known that weight reduction has a positive effect on high blood pressure, so that it is accepted as one of the basic therapeutic nonfarmacological methods in hypertension treatment, the effect of weight reduction on LVH is still unknown. Therefore, our study intends to find out a correlation between obesity, hypertension and LVH. We also want to examine whether there is any correlation between weight reduction and LVH regression which eventually lead to reduction of LVH risks.

## Patients and Methods

This study has included 73 patients with hypertension of 2nd and 3rd degree (43 male patients), average age 55.9 +/- 8 with echocardiographically proved LVH. This study has been designed as a long-term research but the first results have been evaluated after a year of active treatment. The active treatment means a modification of individual habits (a regular 45 minute walk, a diet, salt and alcohol reduction and smoking quitting) and antihypertensive medicament therapy. The design and the protocol of the study have been published in detail in the doctoral dissertation (6).

Average diastolic pressure of 95-115mmHg in the sitting position and systolic pressure of 160-200 mmHg after a 3 week period without therapy for treated patients and 2 week for untreated hypertensive patients have been a prerequisite for the study.

The obese patients have been classified according to the standard of the World Health Organization (8) - body mass index (BMI) higher than 30. BMI has been determined according to the formula:

$$BMI = TM/TV^2 \ (kg/m^2)$$

The average BMI has been 28.7. ± 3.6 kg/m².(23 to 39). 28 patients (39%) have had an BMI index higher than 30 and they have been classified in the group of obese hypertensive patients with LVH.

LVH diagnosis had been echocardiographically stated before it was included in the study. The criterion for LVH is made according to the method described by Devereux and Reichek and the Penn convention. The left ventricular mass index for male patients must be ≥ 134 g/m$^2$ and for female patients ≥ 110 g/m$^2$.

Exclusion criteria were:

- Known secondary hypertension of any etiology, malignant hypertension, or hypertensive encephalopathy
- History and/or signs of cardiovascular complications (eg, congestive heart failure, myocardial infarction, stroke, angina pectoris) or major target-organ damage (eg, serum kreatinin > 160 µmol/L), significant known aortic stenosis (known mean antegrade Doppler gradient ≥ 20 mmHg)
- Major cardiovascular or noncardiovascular diseases besides hypertension
- Conditions that would prevent collection of technically adequate echocardiograms, or ambulatory blood pressure monitoring, Holter monitoring, Heart rate variability or exercise testing

All the patients have undergone a complete diagnostic check up which includes sphygmomanometer recordings of blood pressure, electrocardiogram, echocardiogram, exercise testing and lab analyses (glucose, complete cholesterol, HDL cholesterol, triglycerides, creatinine), 24 hour BP monitoring and 24 EKG monitoring (Holter monitoring and heart frequency variability).

**Electrocardiogram** Standard electrocardiograms with simultaneous 12-lead recordings were obtained at 25 mm/sec and 10 mV/cm. LVH is defined by the criteria based on the product of Cornell voltage (RaVL + SV3) X QRS duration product criteria: > 2,440 mm X msec in men and the product of QRS duration times Cornell voltage plus 6 mm exceeding the same value in women. Furthermore, Sokolov-Lyon voltage combination (SV1 + RV5 or V6) > 38 m is accepted as an alternative criterion for LVH in both men and women (9).

Q-T intervals were defined from the onset of the QRS complex to the end of the T wave, which was defined as its return to the T-P baseline on all possible leads. If U waves were present, the Q-T interval was measured to the nadir of the curve between the T and U waves. Q-T intervals were corrected with Bazett's formula to compensate for their known dependence on the heart rate. The upper limit for the duration of the normal Q-T interval corrected for heart rate (Q-Tc) is often given as 0.44 sec. However, the normal corrected Q-T interval actually may be longer, 0.46 for men and 0,47 for women, with a normal range ± 15 per cent of the mean value. The QTc dispersion was determined as the difference between the maximal and minimal QTc intervals in different leads. No subjects had < 10 measurable leads (10). Literature reviews found the QT dispersion to vary mostly between 30 and 60 ms in normal subjects although average values around 70 ms were also reported.

**Two-dimensional guided M-mode echocardiography** was performed using a Sequa equipped with a 3.5-MHz transducer. All echocardiograms were taken in the left lateral position after 5 min of rest. Echocardiograms from the left ventricle were recorded at the level of the tips of the mitral valve leaflets. The left ventricular internal dimension in diastole (LVIDd) and the thicknesses of both the interventricular septum (IVST) and the posterior wall (PWT) were measured using both the American Society of Echocardiography and the Penn convention parameters. Left ventricular internal dimension in systole (LVIDs) was measured at the nadir of septal motion.

Left ventricular mass (LVM) was calculated according to the formula of Devereux and Reichek (11): LVM(g)=1.04 [(IVST+PWT+LVIDd)3−(LVIDd)3]−13.6. All measurements were obtained in at least five cardiac cycles. Measurements of left ventricular mass were divided by body surface area, to obtain left ventricular mass index (LVMI). Cut-off values for LV hypertrophy by Penn convention ($g/m^2$) criteria were $\geq 134$ $g/m^2$ for men and $\geq 110$ $g/m^2$) for women. To assess left ventricular systolic function, left ventricular fractional shortening (%) was calculated as (LVIDd−LVIDs)/LVIDd×100.

**Exercise testing:** All subjects underwent standard treadmill exercise testing on the same day as the baseline examination according to the Bruce protocol. Exercise was stopped when subjects achieved a target heart rate (in beats per minute) defined as 85% of the age- and sex-predicted maximum heart rate. Other reasons for stopping exercise included participant request, limiting chest discomfort, dyspnea, fatigue, leg discomfort, hypotension, an excessive increase in systolic blood pressure (peak systolic pressure $\geq 250$ mmHg), $\geq 2$ mm ST-segment depression, or significant ventricular ectopy (including frequent ventricular beats and nonsustained ventricular tachycardia) (12).

**Ambulatory blood pressure measurements** were started shortly after determination of casuals blood pressure using a Del Mar Avionics Pressurometer IV device. After 24h the recorder was returned to the hospital. For the blood pressure analyses, daytime was defined as 0700-2259 h and nighttime from 2300-0659 h. Measurements were taken every 15 min during the daytime and every 30 min at night, giving a total of 80 measurements. Auscultatory measurements were used primarily, but if the auscultatory technique failed, a substitution with its matching oscillometric value was made. The results consisted of (1) calculation of 24-hour average systolic BP, diastolic BP, and heart rate, (2) separate calculations of daytime and nighttime average BP and heart rates and differences (nocturnal systolic BP and diastolic BP fall -%) and (3) the standard deviation (SD) of 24h average BP (13).

**24-hour Holter monitoring:** In the Holter ancilary study, a 2-channel 24-hour electrocardiogram was recorded before randomization and after 12 months of treatment in 73 patients. The 24-hour recordings were using the Del Mar Avionics models 5268-505 MPA/R-ACQ:2.15; Irvine, California, USA.

**Continuous electrocardiographic monitoring (14)**: ventricular arrhythmias were classified in a manner similar to that of Lown and Wolf (14) according to the presence of the following arrhythmia types: ventricular premature complex (VPCs), multiform extrasystoles, ventricular couplets, ventricular tachycardia and R-on-T ventricular premature complexes). A summary category of the presence of a frequent ($\geq 30$ VPCs/hr) or a complex (presence in 24 hours of any of the following: multiform extrasystoles, ventricular couplets, ventricular tachycardia and R-on-T VPC) ventricular arrhythmia was also created.

**Heart rate variability:** The program automatically detects abnormal QRS complex and filters them out, so that the HRV is calculated only on RR intervals with normal QRS complexes. The time domain parameters studied have already been described:

- Standard deviation of all 24-hour RR intervals (SDNN, ms);
- SD of the average RR intervals in all 5-minute segments (SDANN, ms); and
- Root-mean-square of successive differences between adjacent normal RR intervals (rMSSD, ms)
- The percentage of differences between adjacent normal RR intervals > 50 ms (pNN50, %)

**Statistical analyses.** Clinical values are presented as mean ± SD and HRV parameters as mean (95% confidence interval of the mean). Student's *t* test and linear regression were performed for comparisons of variables between groups. Significance was set at a p value < 0.05.

## Results

### Obesity and LVH

The two groups of hypertensive patients with LVH, the obese patients and the patients with normal weight, have been compared according to their age, sex, heart frequency and BP (Table 1). Echocardiographic parameters have been different for slim and obese patients. (Table 2) The obese patients have the greater LV mass and the thicker septum and the posterior wall. The relative thickness of the walls, ejection fraction, shortage fraction as well as diastolic function parameters have been similar in the two groups.

Table 1. Clinical Characteristics of Lean and Obese Patients With Left Ventricular Hypertrophy (LVH)

| Characteristic | Obese | Lean |
|---|---|---|
| No. of patients | 28 | 43 |
| Age, y | 52.8 ± 8.6 | 56.9 ± 8.3 |
| Sex (M:F) | 17:11 | 26:17 |
| Weight, kg | 93 ± 12.7 | 79.6 ± 7** |
| Height, cm | 170.2 ± 9.1 | 170.4 ± 6.3 |
| Body surface area m² | 2.04 ± 0.2 | 1.91 ± 0.1 ** |
| Systolic BP, mmHg | 168.9 ± 27.3 | 167.9 ± 29.2 |
| Diastolic BP, mmHg | 104.8 ± 13.3 | 98.7 ± 14 |
| Heart rate, beats per minute | 78.4 ± 12.8 | 76.4 ± 20 |

Values are means ±SD; *<0.05; **<0.01

Table 2. Echocardiographic Measurements (Mean ± SD) of Lean and Obese Patients with Left Ventricular Hypertrophy (LVH)

| Echocardiographic Measurements | Obese | Lean |
|---|---|---|
| Septal thickness, mm | 14.05 ± 2.4 | 12.6 ± 1.6** |
| Posterior wall thickness, mm | 12.05 ± 1.2 | 11.1 ± 1.1* |
| Relative wall thickness | 0.49 ± 0.1 | 0.46 ± 0.15 |
| Left ventricular diastolic diameter, mm | 53.7 ± 4.3 | 51.8 ± 4 |
| Left ventricular systolic diameter, mm | 33.3 ± 4 | 32.3 ± 4 |
| Left ventricular mass, g | 361.8 ± 95 | 295.6 ± 58.2** |
| Left ventricular mass index, g/m² | 177.6 ± 40.5 | 156.8 ± 28.7 |

Values are means ±SD; *<0.05; **<0.01

The obese patients have had higher average 24 hour systolic BP (150.97 ± 19 vs 142.8 ± 11, p < 0.02), average day systolic BP (154.1 ± 18 vs 145.8 ± 12, p < 0.009), and average night systolic BP (141.2 ± 0.6 prema 132.8 ± 13.2, p < 0.02) than the slim patients with LVH. Other parameters obtained after 24 hour BP monitoring have been similar in the two groups.

Table 3. Time Domain Analysis of Heart Rate Variability (Mean ± SD) of Lean and Obese Patients with Left Ventricular Hypertrophy (LVH)

| Parameters HRV | Obese | Lean |
|---|---|---|
| RR (Over 24h) (ms) | 803.4± 117.4 | 888.9± 127.3** |
| RR (daytime) (ms) | 769.8± 115.4 | 850.7± 126.7** |
| RR (nighttime) (ms) | 883.4± 148.7 | 970.3± 100.8** |
| SDNN (Over 24h) (ms) | 119.7± 23.7 | 125.2± 22.7 |
| SDNN (daytime) (ms) | 104.1± 17 | 110± 19* |
| SDNN (nighttime) (ms) | 101.4± 33.8 | 106.9± 32.1 |

Values are means ±SD; *<0.05; **<0.01

The obese patients have had a greater left ventricular myocardium vulnerability. Namely, the average degree of ventricular extrasystole (Lown) has been higher in the obese patients than in the slim ones. (3.11 ± 1.6 prema 2.21 ± 1.6, p < 0.02). A possible cause of VES in obese patients may be a hyperactivity of the sympathic nervous system. Table 3 shows the results of heart rate variability where it can be seen that the obese patients with LVH have had significantly lower values of HRV.

BMI in our patients has significantly correlated with LV mass. (r = 0.34; p = 0.003; fig. 1), septum thickness (r = 0.28; p = 0.015), posterior wall thickness (r = 0.31; p = 0.007), LA diameter (r = 0.27; p = 0.02), diabetes mellitus (r = 0.26; p = 0.02), and serum creatinine level (r = 0.38; p = 0.01).

### Weight Reduction and LVH Regression

After a year long treatment 22 (30%) patients have reduced their weight for more than 5% (from 81 ± 13.to 76 ± 13 kg). The average age of the first group has been 57.3 ±8.5 g., which is not different from the second group of patients who have not significantly reduced their weight (55.9 ± 8 g. from 85 ± 13 to 86 ± 13 kg). BMI has been reduced in the first group from 27.9 ± 3 to 26.6 ± 3 (ns) while in the second group BMI has not been significantly increased from 29 ± 4 to 29.6 ± 4.

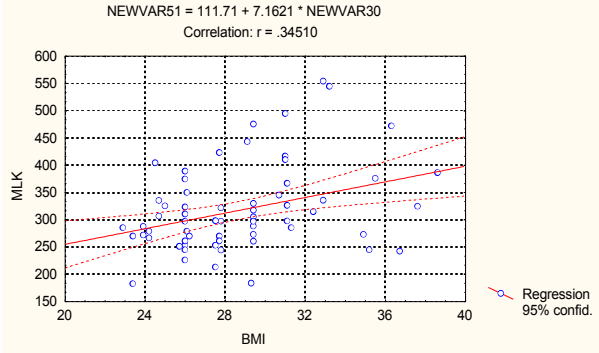


Fig. 1 Correlation Between Body Mass Index and Left Ventricular Mass.

### Left Ventricular Mass

The first group of patients have significantly reduced LV mass, LVM index and LV diastolic diameter (Table 4). LVH regression in the second group has been significantly lower than in the first group. In the patients with reduced weight significant changes have been registered on electrocardiogram. Namely, the sum of RaVL +SV3 has been significantly reduced (16.4 ± 5 in relation to. 14.6 ± 5; p < 0.02) as well as the sum of RV5 + SV1 (26.8 ± 6.6 in relation to 23.7 ± 6.97; p < 0.003) and the Cornel index (1.55 ± 0.4 in relation to 1.41 ± 0.4; p<0.02).

Table 4. Echocardiographic Measurements (Mean ± SD) at baseline and changes after first year treatment for each treatment group.

| Echocardiographic Measurements | I group before | After 12 months | II group before | After 12 m |
|---|---|---|---|---|
| Septal thickness, mm | 12.8 ± 1.6 | 12.5 ± 1.7 | 13.3 ± 2 | 12.8 ± 1.6 |
| Posterior wall thickness, mm | 11.2 ± 1.3 | 11 ± 0.4 | 11.5 ± 1.2 | 11.1 ± 1.3 |
| Relative wall thickness | 0.46 ± 0.05 | 0.43 ± 0.06 | 0.47 ± 0.06 | 0.47 ± 0.7 |
| Left ventricular diastolic diameter, mm | 52 ± 5 | 50.5 ± 4 | 52.4 ± 4 | 51.8 ± 4 |
| Left ventricular systolic diameter, mm | 32.2 ± 4.7 | 31.9 ± 4.5 | 32.9 ± 3.9 | 32.1 ± 3.9 |
| Left ventricular mass, g | 309 ± 79 | 278 ± 61** | 321 ± 72 | 301 ± 61 |
| Left ventricular mass index, g/m² | 161 ± 35 | 148 ± 29* | 163 ± 30 | 152 ± 26* |

Values are means ±SD; *<0.05; **<0.01

**Blood pressure**

Office blood pressure in the first group has been reduced but not statistically significant. Contrary to this, systolic blood pressure in the second group, ambulatory measured, has been statistically significantly reduced (170.3 ± 27 in relation to 158.9 ± 19; $p < 0.03$). However, 24 ambulatory monitorings of BP showed a significant reduction of blood pressure in the patients with reduced weight (Table 5). This group of patients at the end of one-year period had the lower maximal double product (DP) in the exercise test (27.3 ± 5 in relation to 24.4 ± 4.7; $p < 0.02$) as well as DP/METTa (2.5 ± 1.4 in relation to 1.84 ± 0.5; $p < 0.05$).

**Ventricular Arrhythmias and Heart Rate Variability**

An average degree of ventricular arrhythmia (Lown) has not been significantly changed in the first group (2.3 ± 1.5. in relation to 2.4 ± 1.6; n.s) while the frequency of ventricular arrhythmia has been significantly reduced in the second group (2.7 ± 1.6 in relation to 1.95 ± 1.5; $p<0.04$). The night RR interval has been significantly prolonged after a yearlong treatment in the first group (938.2 ± 162 in relation to 999 ± 132; $p<0.007$). Both groups have improved HRV but statistically not significantly (table 6). QT dispersion has been improved in both groups but statistically not significantly.

## Discussion

Obesity is associated with numerous comorbid conditions such as hypertension, diabetes, dyslipidemia, atherosclerosis, osteoarthritis, cancer, and chronic renal failure. Epidemiologic studies suggested that up to 50% of obese individuals, as defined by body mass index (BMI) > 27 kg/m$^2$, have concomitant HTN. Obesity-associated HTN has a complex, multifactorial mechanism including activation of sympathetic and rennin systems, insulin resistance, abnormal renal sodium handling, and possibly leptin-resistance and natriuretic peptide downregulation. The influence on the hypertensive cardiomyopathy is also very complex.

The hemodynamic changes in obese-hypertensive subjects have a mixed profile resulting from the interplay of the individual components of obesity and HTN. In the obese-hypertensive patient, intravascular volume, total peripheral resistance and cardiac output are all elevated. However, due to the effect of the obesity component, total peripheral resistance is less elevated than would be expected in the lean hypertensive subject, and may be completely normal in some obese-hypertensive patients (15,16).

The coexistence of both obesity and HTN in the same patient results in a mixed "eccentric–concentric" hypertrophy. Obesity-HTN produces an extensive rise in left ventricular stroke work, as the result of increased afterload associated with HTN and increased preload associated with obesity. The combined hemodynamic burden increases the risk for congestive heart failure (17). Autopsy data from the Mayo Clinic (3) revealed that the average heart weight was 467 g in obese hypertensive subjects, compared with 367 g in obese individuals without heart disease and only 272 g in nonobese hypertensive subjects.

Our results have showed that obese hypertensive patients have greater LV mass and thicker walls than slim hypertensive patients. The diastolic diameter is also

Table 5. Ambulatory blood pressure values (Mean ± SD) at baseline and changes after first year treatment for each treatment group.

| | I group before | After 12 m | II group before | After 12 m |
|---|---|---|---|---|
| 24-h average SBP, mmHg | 144.1 ± 17 | 138.6 ± 16* | 147.9 ± 15 | 142.7 ± 14 |
| 24-h average DBP mmHg | 89.5 ± 11 | 85.7 ± 12 | 92 ± 11 | 88.1 ± 9 |
| Daytime average SBP, mmHg | 148.2 ± 18 | 141.4 ± 16* | 150.9 ± 15 | 145.8 ± 15 |
| Daytime average DBP, mmHg | 92.7 ± 11 | 88 ± 13* | 94.1 ± 11 | 90.7 ± 4 |
| Nighttime average SBP, mmHg | 132.7 ± 18 | 130 ± 16 | 138.7 ± 16 | 132.6 ± 14 |
| Nighttime average DBP, mmHg | 80.5 ± 13 | 78 ± 12 | 85.2 ± 12 | 80.9 ± 11 |
| Day/night diference SBP % | 16.2 ± 8.2 | 11.5 ± 9* | 12.3 ± 7 | 13.6 ± 10 |
| Day/night diference DBP % | 10.96 ± 5 | 8 ± 6* | 8.4 ± 5 | 8.7 ± 7 |

Values are means ±SD; *p<0.05; **p<0.01

Table 6. Time domain Analysis of Heart Rate Variability (Mean ± SD) at baseline and changes after first year treatment for each treatment group.

| Parameters | I group before | After 12 m | II group before | After 12 m |
|---|---|---|---|---|
| RR (Over 24h) (ms) | 855.8 ± 155 | 856.7 ± 217 | 848.6 ± 121 | 888.7 ± 133 |
| RR (daytime) (ms) | 817.7 ± 149 | 856.4 ± 144 | 811.6 ± 121 | 851.3 ± 132 |
| RR (nighttime) (ms) | 938.2 ± 162 | 999 ± 32** | 931.3 ± 140 | 967 ± 142 |
| SDNN (Over 24h) (ms) | 125.9 ± 27 | 131.4 ± 24 | 116.7 ± 23 | 121.8 ± 28 |
| SDNN (daytime) (ms) | 106.2 ± 24 | 111.2 ± 20 | 103.6 ± 20 | 109.5 ± 27 |
| SDNN (nighttime) (ms) | 110.5 ± 34 | 110.9 ± 21 | 95.8 ± 29 | 105.2 ± 35 |

*p<0.05; **p<0.01

higher but statistically not significant. Thus, our obese hypertensive patients have had a mixed "eccentric-concentric" LVH.

These hypertrophic changes can cause heart arrhythmia. Our results have proved this hypothesis. Our obese hypertensive patients with LVH have had a greater VES frequency than slim hypertensives with LVH. A possible cause of the greater VES frequency can be the increased activity of the sympathic nervous system. Our results have showed that obese patients with LVH have significantly lower HRV values.

A recent study of obese individuals showed the presence of mononuclear cell infiltration in and around the sinoatrial node, with marked fat throughout the conduction system. Lipomatous hypertrophy of the interatrial septum has also been noted in obesity. Such changes may contribute to the high rate of sudden cardiac death in morbidly obese patients (17).

Parallel with the facts about LVH risks an idea has been developed about LVH regression as a possible protection against bad effects. Our recently published results have showed undoubtedly the positive effect of LVH regression. However, when hypertension, LVH and obesity are combined, the problem becomes more complex. It has been known for 20 years that excessive weight loss with ketogenic (high protein-low carbohydrate) diets can be associated with prolongation of the QT interval, ventricular tachycardia, and sudden death (18).

Can weight reduction improve the prognosis for LVH obese patients? MacMahon et al (19) recently demonstrated that a small weight loss of merely 8 kg in mildly obese and hypertensive patients was associated with a decrease in posterior wall and septal thickness, as well as in left ventricular mass.

Our results also show that weight reduction of 5% in medium obese, hypertensive patients with LVH leads to a more significant LVH regression than in patients without any weight reduction. Weight reduction also leads to a significant BP reduction, not only in casual conditions but also in 24 hour monitoring. There has been night BP reduction which has important implications for it diminishes the risks in this group of hypertensive patients. Heart rate variability has also been improved which indirectly shows the diminished effect of the sympathic nervous system.

Weight reduction in our patients has not been accompanied by more frequent ventricular arrhythmia, or any worsening of QT dispersion. This weight reduction has not had any significant effect on lipid status or sugar in blood.

However, our study has showed a deficiency we are regularly faced with in the treatment of hypertensive patients. Every third patient has reduced weight for 5% although all of them have been submitted to a diet and physical exercise. Since this is a group of patients with high risks (hypertension of 1$^{st}$ and 2$^{nd}$ degree, LVH, 40% with BMI 30) the approach to these patients must be more rigorous. Recent studies have showed that long-term use of orilstat (1-2 years), a new lipase inhibitor, not only improves lipid profile, blood pressure and the quality of life but is similar to placebo when its tolerability is in question (20). Future studies should answer the question whether this medicament can have an even greater effect on blood pressure reduction and elimination of the risks which accompany it (ventricular arrhythmia and sudden death.)

## Conclusion

A year long antihypertensive treatment (diet, physical activity, salt reduction, alcohol reduction) in patients with LVH has reduced their weight for 5 % in 30% of the examined patients. With weight reduction there is more significant LVH regression and BP regulation than without it.

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# ODNOS IZMEĐU SMANJENJA GOJAZNOSTI I REGRESIJE HIPERTENZIVNE HIPERTROFIJE LEVE KOMORE

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Kratak sadržaj: *Dobro je poznat odnos između gojaznosti i hipertenzivne hipertrofije leve komore (HLK). Međutim manje je poznat odnos između smanjenja stepena gojaznosti i regresije hipertenzivne HLK*
*Cilj ove studije bio je da utvrdi vezu između smanjenja gojaznosti i regresije HLK.*
*73 bolesnika sa hipertenzijom II-III stepena (43 muškaraca), prosečne starosti 55.9 ± 8 i sa ehokardiografski utvrđenom HLK (prosečni indeks mase leve komore 164 ± 32 g/m², Penn konvencija) lečeno je (medikamentima I dijetom) godinu dana. Svakom ispitaniku rađen je Dopler ehokardiografija, 12 kanalni EKG (QTc disperzija), test fizičkim opterećenjem (Brusov protokol), 24h ambulatorni monitoring KP, 24h Holter monitoring sa Lownovom klasifikacijom ventrikularnih aritmija i varijabilnost srčane frekvence. Prosečni indeks mase tela iznosio je 28.7 ± 3.6 kg/m² (23-29), a 28 (39%) je bilo gojazno (IMT > 30 kg/m²)*
*Posle jednogodišnjeg tretmana sistolni KP (SKP) snižen je sa 168 ± 26 na 158.2 ± 21 mmHg, sijastolni KP (DKP) sa 102 ± 12.7 na 97 ± 11 mmHg. Indeks MLK smanjen je sa 163 ± 32 na 150.2 ± 27 g/m² (sve p<0.001).*
*22 (30.1%) bolesnika je smanjilo težinu za više od 5%. Ovi bolesnici značajno su smanjili MLK sa 309 ± 79 na 278 ± 61 g; t=3.22, p<0.004. indeks MLK (161 ± 35 prema 148 ± 29; kg/m², t=2.68, p<0.02), dijastolni dijametar LK (52.3 ± 4.7 prema 50.5 ± 4.4 mm; t=2.95, p<0.008), Cornell-ov indeks (1.55 ± 0.4 prema 1.41 ± 0.4; p<0.02), maksimalni dvostruki proizvod (DP) (27.3 ± 5 prema 24.4 ± 5; t=2.8, p<0.02), odnos DP/METTa (2.48 ± 1 prema 1.84 ± 1; t=2.15; p<0.05), srednji 24h SKP (144.1 ± 17 prema 138.6 ± 16 mmHg; t=2.2, p<0.04), prosečni 24h DKP (89.5 ± 11 prema 85.7 ± 12 mmHg; t=2.2, p<0.04), srednji dnevni SKP (148.2 ± prema 141 ± 16 mmHg; t=2.6, p<0.02), srednji dnevni DKP (92.7 ± 11 prema 88 ± 13 mmHg; t=2.6, p<0.02) i povećali srednji 24h RR interval u toku noći (938.2 prema 999 ms; t=3, p<0.007). Pacijenti (51.7%) koji nisu značajno smanjili težinu takođe su značajno smanjili indeks MLK (163 ± 30 prema 152 ± 25 kg/m², t=2.1; p<0.05), ambulantni SKP (170.3 ± 27 prema 158.9 ± 19, t=2.2, p<0.03), stepen ventrikularnih aritmija (2.73 prema 1.93, t=2.1, p<0.04), i srednji VES/24h (66.6 prema 20, t=2.22, p<0.04).*
*Hipertenzivni bolesnici sa HLK i sa značajnim smanjenjem težine posle jedne godine, postigli su veći stepen regresije HLK (prevashodno na račun smanjenja dijastolnog dijametra LK), manji DP na opterećenju, manji KP u toku 24h monitoringa i poboljšali varijabilnost srčane frekvence, nego bolesnici bez značajnog smanjenja težine.*

Ključne reči: *Gojaznost, hipertenzija, hipertrofija leve komore, regresija*