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THE INFLUENCE OF WEIGHT LOSS ON ARTERIAL STIFFNESS IN OBESE AND OVERWEIGHT SUBJECTS

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Abstract

Objectives: *The Metabolic Syndrome (MetS) and obesity are among the proven causes of vascular dysfunction. The cardio-ankle vascular index (CAVI) was developed as a method to assess arterial stiffness. The aim of the study was to establish the influence of weight loss on arterial stiffness parameters.* ***Material and Methods:*** *135 subjects completed a 6 months standardized life style intervention study. Average initial weight was 96.63kg with a BMI of 34.34kg/m2. CAVI and the ankle-brachial index (ABI) were measured and body composition was assessed. Some biochemical markers were also determined.* ***Results:*** *The average weight decreased to 84.61kg, with fat mass loss of 9.6 kg. Mean CAVI decreased from 7.92±1.28 to 7.21±1.08. The decrease in CAVI correlates with the total weight and fat loss rather than the speed of weight loss.* ***Conclusions:*** *Our results show that weight loss can influence arterial stiffness, mainly by decreasing fat tissue mass.*

key words: *obesity, arterial stiffness, weight loss, lifestyle intervention.*

Background

The prevalence of obesity, at a global scale, is steadily rising. In 2008 The World Health Organization estimates that over 500 million obese persons existed (9,8% of adult population) and that their number will be greater than 700 millions in 2015 [1]. Obesity is a well-known risk factor for the development of cardiovascular disease [2,3]. It is a metabolic status caused by the failure of the homeostatic mechanisms that regulate energy intake and expenditure and it involves alterations of both carbohydrate and lipid metabolisms [4]. The cardio-vascular risk evaluation of obese patients is a necessity and it involves determining the characteristic markers influencing the atherosclerosis process. The classical approach involves evaluating the markers for the alteration of carbohydrate metabolism (glycemia, HbA1c) and lipid metabolism (total, HDL and LDL cholesterol, triglycerides). However, the first homeostatic modification in obesity

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influencing the cardiovascular system appears to be the immune-inflammatory process that accelerates atherosclerosis and endothelial dysfunction [5,6].

The interventions based on lifestyle changes, promoting physical activity and a balanced diet represent, according to current medical guidelines, the initial treatment for both non-complicated obesity and diabetes [7-9]. The results of several studies suggest that weight loss may be effective in reducing large artery stiffness [10-12].

The aim of this study was to test the hypothesis that weight loss via a lifestyle intervention would reduce arterial stiffness in overweight and obese adults. We further hypothesized that the reduction in total body or abdominal adiposity would be associated with the reduction in arterial stiffness (if observed).

Material and Method

We have performed a prospective, interventional study on 210 overweight and obese patients (40 Male/170 Female) consisting in a 6 months standardized life style intervention. The following inclusion and exclusion criteria were used:

Inclusion criteria - patients aged from 18 to 65 years; BMI between 27 and 40 kg/m^2; able and willing to give informed consent; residence in Bucharest during the study and being able to attend weekly meetings with the nutritionist.

Exclusion criteria - uncontrolled hyper-tension (> 160/90 mmHg) or the usage of Angiotensin Converting Enzyme (ACE) inhibitors; concomitance of serious medical conditions (neoplasia recently diagnosed or in treatment, chronic renal disease stage III-V, hepatic failure, cardiac failure class III-IV NYHA, severe respiratory failure; psychiatric conditions including acute depression, neurotic bulimia, illicit drug abuse, etc.); weight loss of more than 5 kg during the previous 3 months; history of weight-loss medication use during the last 3 months; initiation of treatment with statin, anti-hypertensives, aspirin, C and E vitamins during the last 3 months; pregnant or breastfeeding females; intention to become pregnant in the next 6 months.

Withdrawal criteria: patients request; impossibility to monitor; necessity of initiation (or dose adjustment) of therapy with statin, anti-hypertensive medication, aspirin, oral anti-diabetics or insulin; change of the smoking or non smoking status; onset of a medical pathology, linked or not to the study, proving to be life threatening and requiring adequate medical intervention.

The nutritional intervention included individual weekly meetings explaining general nutritional and behavior principles, promoting the replacement of high caloric content foods with more nutritionally valuable choices (hypo-caloric diet) and adequate liquid consumption. Also, the patients were instructed to exercise 30 minutes daily or 1 hour 3 times a week, and being monitored with pedometers. Patients received also psychological counseling.

The following anthropometric parameters have been recorded: height, weight, waist circumference and hip circumference. Also, bio-impedance was performed using GAIA 359 (Jawon Medical) to determine exact weight, the quantity of fat, water and muscular tissue.

The following vascular parameters were measured using VASERA 1000 (Fukuda Denshi): blood pressure, cardio-ankle vascular index (CAVI), ankle-brachial index (ABI) and pulse wave velocity (PWV). Blood pressure was determined at all 4 limbs.

Biological determinations were also performed: Complete Blood Count (CBC), total, LDL and HDL cholesterol, triglycerides, Alanine transaminase (ALT) , Aspartate transaminase (AST), creatinine, urea, uric acid, glycemia, as well as biochemical markers for endothelial dysfunction: vascular cell adhesion molecule 1 (VCAM-1), intercellular adhesion molecule 1 (ICAM-1).

Out of the 210 enrolled patients, 135 subjects (104 women and 31 men) completed the intervention. This corresponds to a drop-out rate of 35.7 %, comparable with that already reported in other studies [13]. Out of the patients that dropped-out, a greater percentage was represented by females (40%). The most frequent cause of drop-out was the low study intervention compliance (missing the weekly visits).

At baseline, the average weight was 96.63 kg with a BMI of 34.34 kg/m2. The mean age was 38 years. The patients were divided in 4 groups based on the BMI value, as presented in Table 1.

Table 1. Baseline characteristics of the study group according to BMI.

Parameter	**Total**	**BMI <30**	**BMI 30-35**	**BMI 35-40**	**BMI 40-45**
Height (cm)	167.8 ± 8.15	167.07 ± 7.17	168.31 ± 7.89	168.08 ± 9.62	167.81 ± 9.14
Weight (kg)	96.63 ±12.05	79.38 ± 7.55	92.51 ± 9.44	105.25 ± 13.13	117.95 ± 13.66
SBP (mmHg)	130.7 ±14.01	124.58 ± 12.14	129.36 ± 12.92	134 ± 14.27	147.55 ± 23.9
DBP (mmHg)	76.51 ±7.47	74.1 ± 12.53	75.98 ± 7.31	79.12 ± 9.81	89.6 ± 14.6
HR (bpm)	68.94±11.64	67.78 ± 9.54	67.22 ± 14.01	70.25 ± 10.84	74 ± 9.97
Waist circumference (cm)	105.02 ±11.03	92.15 ± 7.72	100.96 ± 6.71	110.34 ± 8.4	119.13 ± 11.42
Hip circumference (cm)	113.55±14.39	99.05 ± 16.01	110.54 ± 7.69	116.43 ± 8.16	127 ± 5.49

Statistical Analysis

Descriptive statistics were calculated and the normal distribution was verified for all continuous variables. Simple correlations were performed to assess relations among variables of interest. Pairs observations were used to compare subjects characteristics and dependent variables at baseline and after the intervention. For all the parameters t-student test was performed for pairs observations between initial and final results. Linear regression was used to test the independent effects of measures of total body and abdominal adiposity on the reduction in arterial stiffness. Our study was not powered to test sex differences, so that pooled data are presented.

All of the data are expressed as mean ± standard deviation. The significance level was set a priori at the $p < 0.05$ level.

The analyses were performed using Epi Info (Centers for Disease Control and

Prevention, 1600 Clifton Rd. Atlanta, GA 30333, USA) and Excel 2007.

Results

After 6 months of life-style change intervention, an average weight loss of 12.02 kg was recorded. Regarding the adipose tissue, measured by bio-impedance, an average decrease of 9.6 kg was obtained. The waist circumference also decreased in these 6 months with 12.8cm.

Following intervention, an improvement of the lipid profile was observed, with a significant (p<0.05) decrease of the total cholesterol and triglycerides levels as shown in Table 2. The HDL cholesterol change was highly significant. There were no significant changes in ALT, AST, creatinine, urea, uric acid and glycemia due to the intervention.

The vascular parameters showed an improvement for both the vascular stiffness (ABI, CAVI) and its effects (BP) as shown in Table 3. A CAVI decrease of 0.71 was registered, indicating an improvement of arterial elasticity. This result is supported also by the ABI improvement with 0.04. The average decrease of systolic BP was 8.1 mmHg and the average decrease of diastolic BP was 5.2 mmHg, suggesting an improvement of the vascular stiffness.

Table 2. Change of anthropometric, arterial stiffness and lipid profile parameters following intervention.

Parameter	Baseline	After intervention	Δ After - Before	Statistical significance
Weight (kg)	96.63 ±17.05	84.61 ±16.04	**-12.02**	p<0.01
Fat tissue (kg)	38.04 ±8.86	27.44 ±9.29	**-9.6**	p<0.01
Waist (cm)	105.02 ±11.03	93.65 ±9.82	**-11.55**	p<0.01
Systolic BP (mmHg)	130.7 ±14.01	122.6 ±13.16	**-8.1**	p<0.05
Diastolic BP (mmHg)	76.51 ±7.47	71.31 ±7.64	**-5.2**	p<0.05
CAVI	7.92 ±1.28	7.21±1.08	**-0.71**	p<0.05
ABI	1.02 ±0.08	1.06 ±0.04	**0.04**	ns
Total Cholesterol (mg/dl)	219.51 ±34.47	195.88 ±34.13	**-23.63**	p<0.05
Triglycerides (mg/dl)	158.86 ±75.97	136.47 ±67.5	**-22.39**	p<0.05
HDL Cholesterol (mg/dl)	40.09 ±9.42	48.7 ±10.57	**8.61**	P<0.01

Table 3. Change of arterial stiffness parameters according to baseline BMI.

Parameter	Total	BMI<30	BMI 30-35	BMI 35-40	BMI 40-45
CAVI	-0.71	-0.67	-0.63	-0.75	-0.73
ABI	0.04	0.031	0.038	0.064	0.062

When analyzing the change of arterial stiffness parameters in the subgroups of patients divided according to baseline BMI, we found a trend of increased benefit with higher initial BMI, with a maximum for the patients having BMI in the range 35-40 kg/m^2.

Analyzing the effect of the lifestyle intervention we found strong statistical correlations between weight loss and: fat mass loss, decreases in waist circumference, diastolic blood pressure and total cholesterol, increases in HDL cholesterol as well as decrease in cellular adhesion molecules (VCAM-1 and ICAM-1) as seen in Table 4.

Table 4. Correlations between weight loss and some clinical and biochemical parameters.

Parameter	Pearson correlation	p value
Fat tissue	0.840	0.000
Waist	0.802	0.000
Systolic BP	0.062	0.512
Diastolic BP	0.317	0.001
Total Cholesterol	0.617	0.000
HDL Cholesterol	-0.502	0.000
VCAM-1	0.643	0.000
ICAM-1	0.612	0.000

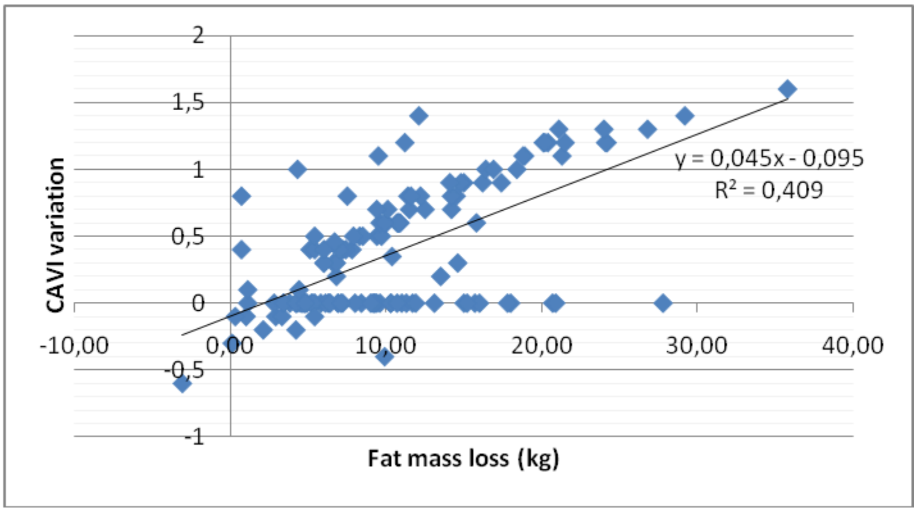

Figure 1. Correlation between CAVI variation and fat mass loss.

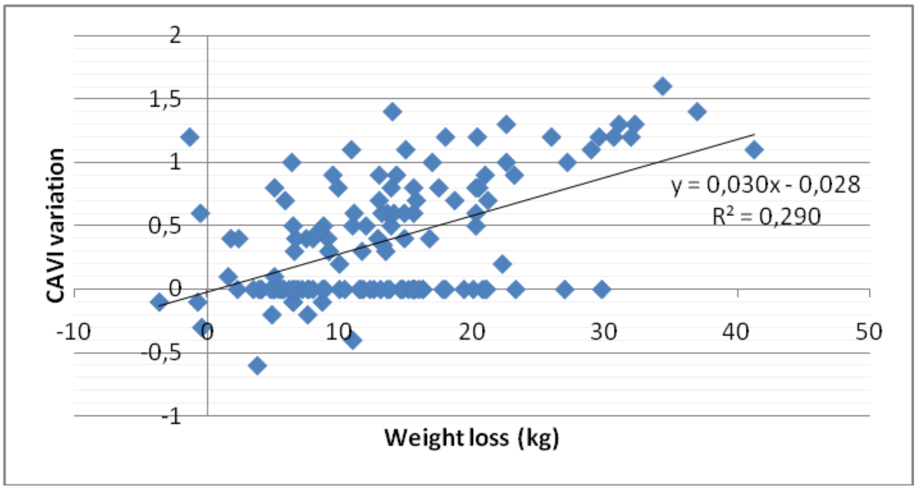

Figure 2. Correlation between CAVI variation and total weight loss.

After the statistical analysis of the data, a significant correlation between CAVI variation and the loss of adipose tissue can be observed (Fig. 1). The association with the decrease of total weight was also significant (Fig. 2).

We found a weak relation between the change in CAVI and the change in systolic blood pressure (Fig. 3).

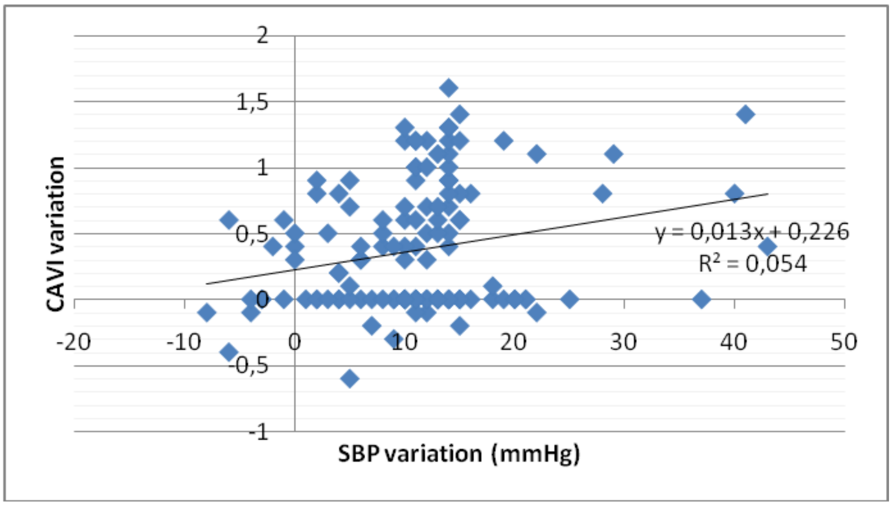

Figure 3. Correlation between systolic BP change and CAVI change.

Discussions

The starting premise of our study was that the arterial damage (expressed by arterial stiffness parameters) existed in overweight and obese subjects before manifesting itself through major cardiovascular events. We wanted to determine if this process can be influenced by weight loss.

The results showed that weight loss leads to the improvement of vascular parameters (CAVI, ABI), reducing the arterial stiffness in overweight and obese patients. The association of a hypocaloric diet with physical exercise and the change of eating habits has led to weight loss and the decrease of fat tissue mass, both correlated with CAVI improvement. There are studies [11,14,15] in the literature that proved a decrease in artery stiffness through weight loss, but the mechanisms by wich this occurs are still under research. Dengo et al. in a recent randomized, placebo-controlled study proved that weight loss through a hypocaloric diet can reduce arterial stiffness in major arteries in older patients [16]. Hughes et al. demonstrated that young overweight and obese adults who lower their insulin levels and lose weight over 6 months experience decreased vascular stiffness measured by pulse wave velocity (PWV) [17].

At this moment, the mechanisms that lead to the decrease of arterial stiffness through weight loss are not entirely clear. In our study, both the weight loss and more important, the decrease of adipose tissue mass were correlated with the improvement of arterial stiffness. The limitations of this study are the relatively small number of patients and their young age. The vascular alteration in young patients is incipient and the modifications after 6 months of intervention are limited compared with those obtained in older patients that already manifest vascular damage. Sex differences were not analysed, because the studied patients were predominantly females. Taking into account the gender-based different distribution of adipose tissue, we consider that a further sex differentiated analysis is required (whenever a sufficient number of cases will be achieved). In a future study, we aim to analyze the influence of weight loss on the inflammatory and cellular adhesion markers, as well as the correlations with the vascular stiffness.

Conclusion

Our study showed that weight loss is associated with significant improvements in sysolic blood pressure and lipid profile. Weight loss was significantly associated with a decrease of the cardio-ankle vascular index (CAVI), suggesting an improvement in arterial stiffness. The association was even stronger with the decrease of fat mass, raising the hypothesis of some metabolically active substances (adipo-cytokines) in this process.

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