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Cardiac Changes in Overweight and Obese Patients

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Background. Obesity and overweight are two pathologies that are more and more frequent in the XXI[st] century diagnosis and are causing high morbidity and mortality rates in the general population, especially through cardiovascular complications.

Aims. Identification and early diagnosis of cardiac changes in overweight and obese patients. **Material and method**. We carried out a sectional, analytical and observational study on 111 subjects: 27 normal weight subjects and 84 overweight and obese patients, which were submitted to a clinical exam, biochemical exams and 2D ultrasound.

Results. The presence of diastolic dysfunction is twice more frequent in overweight patients in comparison to normal weight ones (30% *vs* 15%) and 5 times more frequent in obese patients than normal weight ones (75% *vs* 15%). The size increase of the interventricular septum is correlated with the body mass index, there being statistically significant differences between normal weight *vs* overweight *vs* obese patients, as well as between overweight and obese ones. Within the whole group and within the groups, both the left ventricle mass (g) as well as the left ventricle mass to body surface ratio (g/m²) are statistically significantly higher in patients with present diastolic dysfunction (E/A < 1). This indicates a relation between the presence of diastolic dysfunction, increased left ventricle mass and body mass index ($p < 0.05$).

Conclusions. Overweight and obese patients, unlike normal weight ones, present early cardiac changes, such as: a decrease of left ventricle ejection fraction, diastolic dysfunction, thickening of the interventricular septum, increase of the left ventricle mass both per se as well as in ratio to body surface.

Key words: Obesity, ejection fraction, left ventricle mass, diastolic dysfunction.

INTRODUCTION

Obesity and overweight are two pathologies that are more and more frequent in the XXI[st] century diagnosis and are causing high morbidity and mortality rates in the general population, especially through associated complications. It is well known that the heart response through left ventricle hypertrophy in obese individuals is, in the absence of other additional cardiovascular risk factors, due mainly to the increase of muscular mass, circulating blood volume and visceral fat mass [1]. Given the well documented connection between obesity, left ventricular hypertrophy and mortality, these findings have an important prognosis potential, as well as therapeutic implications in the primary and secondary prevention of cardiovascular diseases [1]. The objective of the study was identification of early cardiac changes in overweight and obese patients through noninvasive methods.

MATERIAL AND METHODS

We carried out a sectional, analytical and observational study on a group of 111 subjects, divided as follows: Group I consisting of 27 normal weight subjects – NW; group II consisting of 84 overweight and obese subjects – OW + O: 36 overweight patients – OW; 33 patients with I[st] degree obesity – O-I; 13 patients with II[nd] degree obesity – O-II; 2 patients with III[rd] degree obesity – O-III.

The scientific research ethics committee approved the study protocol and all participants gave their informed consent.

Prior to being included in the study, no participant had any clinical complaints or a cardiac disease diagnosis.

For each participant, a research sheet was prepared, containing:

- Personal data: Age, gender

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- Personal medical history
- Family medical history (FMH)
- Anthropometric data: Weight, height, abdominal circumference
- Medication
- Smoking and alcohol intake
- Daily physical activity
- Food habits
- Internet usage
- Objective exam and Blood test
- EchocardiographyALOKA S4000 2D Doppler ultrasound.

Patients were divided into three classes, according to the body mass index (BMI): Normal weight (IMC = 18.5–24.9 kg/m²), overweight (IMC = 25.0–29.9 kg/m²) and obese (IMC ≥ 30 kg/m²), according to the current international standards [2-4].

Left ventricle mass was calculated through an ultrasound exam carried out with an ALOKA S4000, using Devereux's formula: LVM (g) = 0.8 × (1.04 × ([DTDVS + PPVS + SIV]3 – [DTDVS]3)) + 0.6 g, the results were expressed both in grams (LVM), as well as in grams/m^2 (LVM/Sc), by adjusting the left ventricular mass to the individual's body surface [5-7].

Statistical analysis was carried out using the SPSS 13.0 software for Windows and Microsoft Excel.

Kolmogorov-Smirnov and Shapiro-Wilk tests were used to verify the normality of continuous numerical variable distribution. The differences between continuous quantitative variable average values were assessed with the Student test (t-test), as well as the ANOVA test (in the case where several categories were present). The analysis of differences between continuous variable average values whose distribution does not comply with the normality condition was carried out with the Mann-Whitney U test, as well as the Kruskal Wallis test in the case of several categories being present. In order to analyze the differences between qualitative variables the Z (Z-test) and Chi-squared ($\chi 2$) tests were used. A $p < 0.05$ was considered to be statistically significant.

RESULTS

The group structure based on body mass index is presented in Figure 1.

In the following charts we present the two main subgroups, normal weight patients (NW) and overweight and obese patients (OW + O), based on the following characteristics: Average age, gender distribution, body weight (kg), blood pressure measured at brachial level (arm BP), smoker status, family history of early cardiovascular disease (AHC) (Figure 2, Figure 3, Figure 4, Figure 5, Figure 6, Figure 7).

With the exception of weight, whose average value is significantly higher in overweight and obese *versus* normal weight patients ($p < 0.05$); there are no significant differences between the two studied groups regarding average age, gender distribution, presence of early family history (unmodifiable cardiovascular risk factors) and on some modifiable risk factors (smoking status, average blood pressure). This shows a strong homogeneity of the studied groups, thereby allowing a better statistical analysis.

Analyzing statistically the ejection fraction (EF), it does not follow a normal distribution in the weight status (normal weight and overweight and obese) and detailed weight status (NW, OW, O-I, O-II, O-III) categories. Because of this, by using the Mann-Whitney test, we can notice statistically significant differences ($p < 0.05$) (Figure 8).

In order to study the differences between the average values of the ejection fraction according to the detailed weight status, the Kruskal Wallis statistical test was applied. We obtained a $p < 0.05$ value between normal weight and overweight patients, as well as a highly significant statistical value ($p < 0.001$) between normal weight and I^{st} and III^{rd} degree obese patients (Figure 9).

Overweight and obese patients have diastolic dysfunction, represented in the E/A ratio, which is 4 times higher than in normal weight patients ($p < 0.001$). There is also a significant statistical difference between overweight and obese patients ($p < 0.05$), which implies early cardiac changes (Figure 10).

By analyzing the size if the interventricular septum (IVS) as initial modification prior to ventricular hypertrophy, one notices that the interventricular septum is in average significantly thicker ($p < 0.05$) in overweight and obese patients than in normal weight ones, as the Mann Whitney test indicates (Figure 11).

In detail, according to obesity types, normal weight patients present a significantly lower IVS modification than overweight, I^{st} degree and II^{nd} degree obese patients do (Figure 12).

Also, a $p < 0.05$ indicates a statistically significant difference of average IVS modification between overweight patients and Ist degree obese ones, the latter showing a higher value (Figure 12).

The left ventricle (LV) mass calculated both per se (g) as well as relative to body surface (g/m^2) is significantly lower ($p < 0.001$) in normal weight patients in comparison to overweight and obese ones (Figure 13).

Highly statistically significant differences ($p < 0.001$) of the left ventricle mass calculated in both ways were also observed in sub-categories: The left ventricle mass is significantly smaller in normal weight patients than in overweight, Ist degree and IInd degree ones, as it is between overweight and obese ones (Figure 14, Table 1).

In the case of the entire group, as well as the normal weight, overweight and obese categories, both the left ventricle mass (g) and the left ventricle mass relative to body mass (g/m^2) is significantly statistically higher in patients with diastolic dysfunction (E/A < 1). This indicates a relation statistically significant ($p < 0.05$) between the presence of diastolic function and left ventricle mass increase (Figure 15)

Overweight and obese patients with subunit values for the E/A ratio, therefore with diastolic dysfunction, have the highest left ventricular mass value (calculated in both ways), it being significantly higher ($p < 0.05$) than in overweight and obese patients without subunit values for the E/A ratio and in normal weight individuals with over unit E/A (Figure 16, Table 2). Moreover, normal weight patients that do not show subunit values for the E/A ratio have a statistically significant lower left ventricle average mass ($p < 0.05$) in comparison with normal weight patients with subunit values for the E/A ratio.

In order to study whether the left ventricle mass increase is influenced, in the obese and overweight, by the presence of systemic high blood pressure, the early heart disease family history or the current smoker status, a statistical analysis through multiple linear regression was applied. The Spearman non-parametric coefficient was tested, coefficient which allows the measurement of the correlation between a continuous and an ordinal variable (Table 3). One noticed that there is a linear relation only between the left ventricle mass and high blood pressure, which was also proved by the ANOVA multifactorial analysis (Table 4).

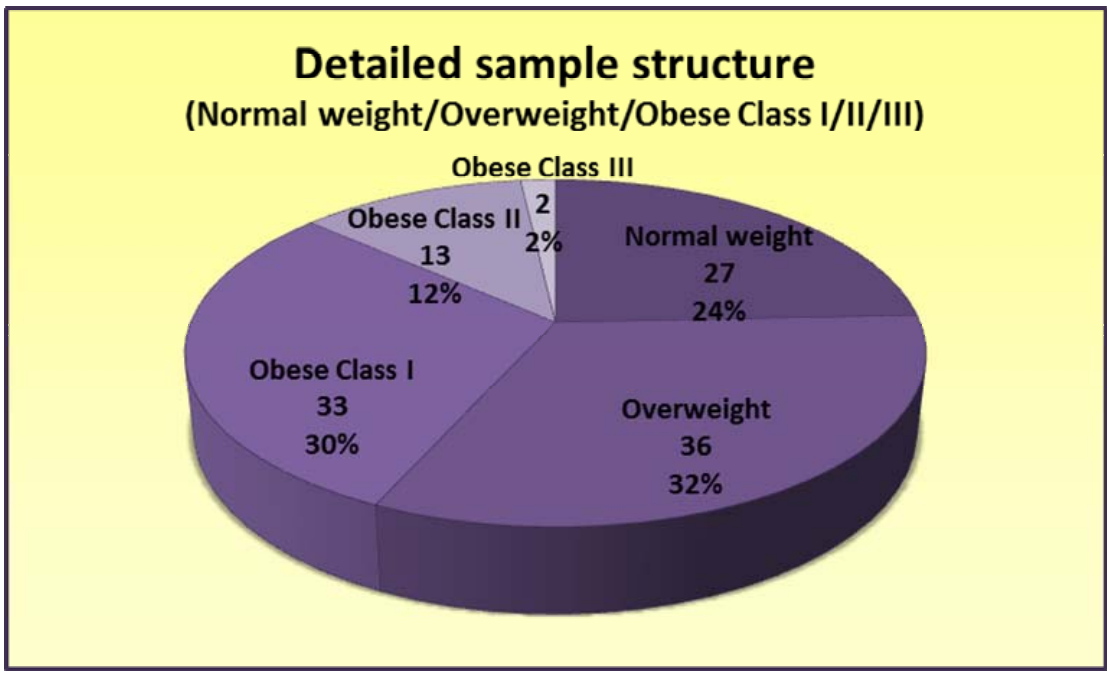

Figure 1. Group structure based on obesity degrees.

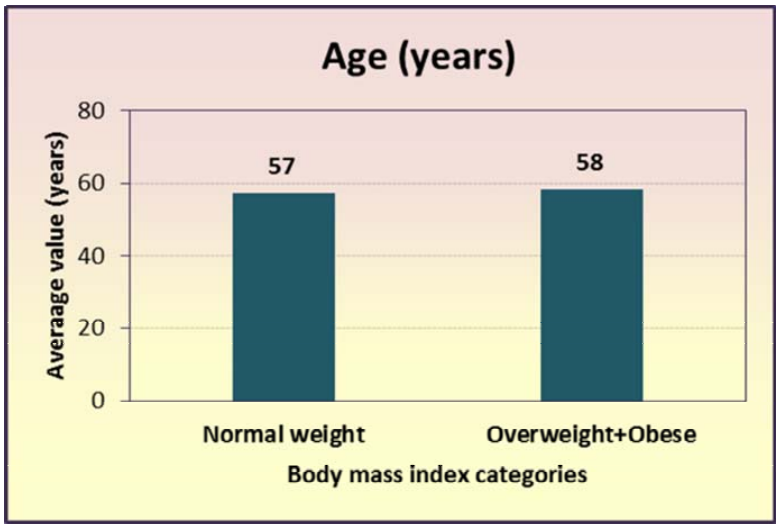

Figure 2. Average age based on weight status.

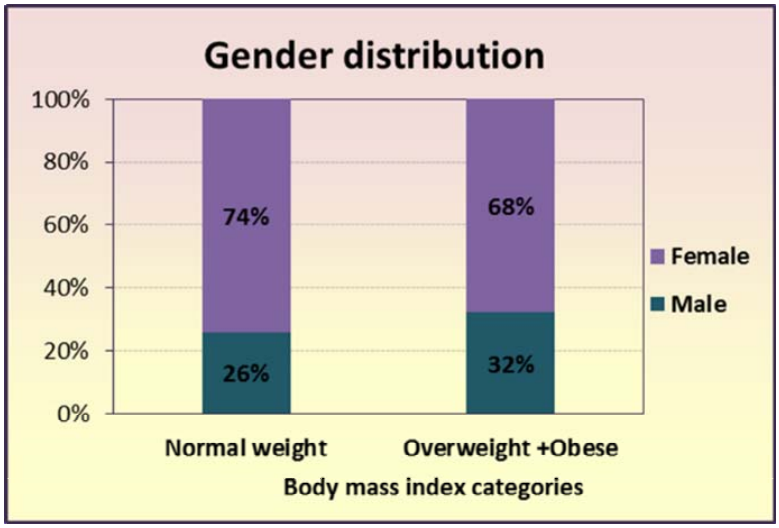

Figure 3. Gender distribution based on weight status.

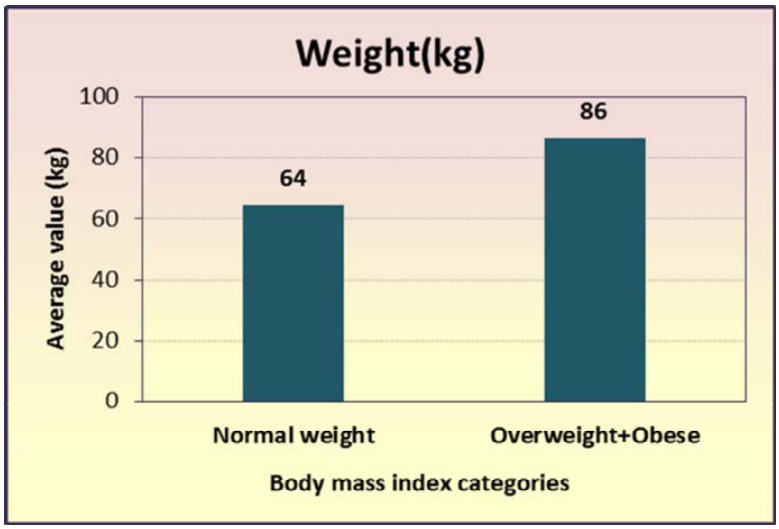

Figure 4. Average weight in the groups studied.

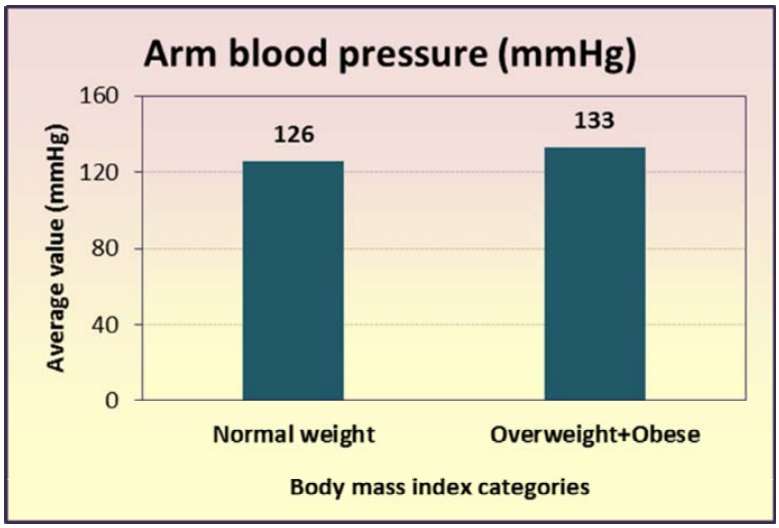

Figure 5. Average blood pressure value based on weight status.

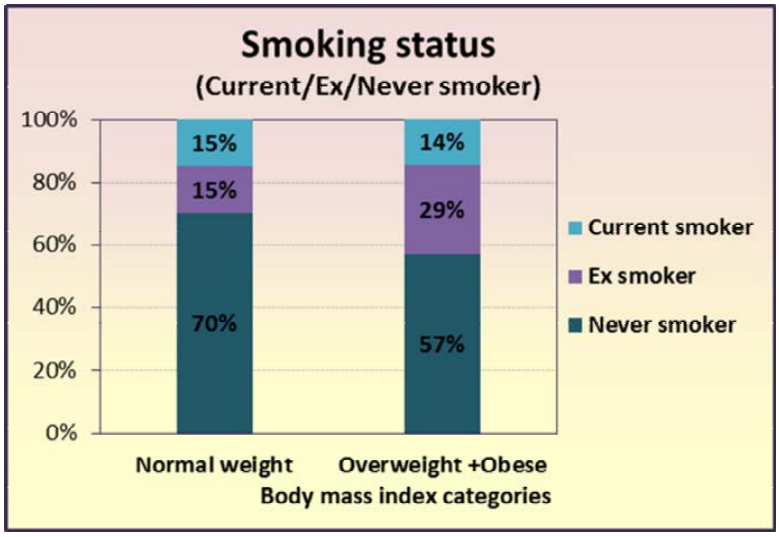

Figure 6. Smoking status based on weight status.

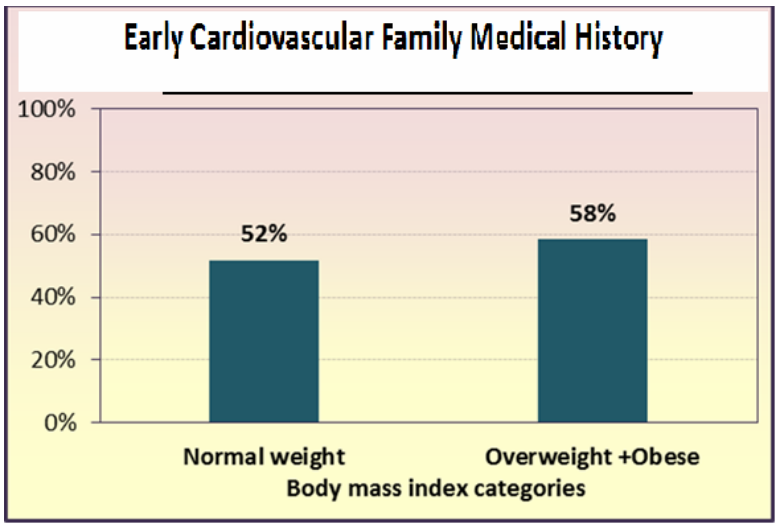

Figure 7. Presence of early cardiovascular family medical history based on weight status.

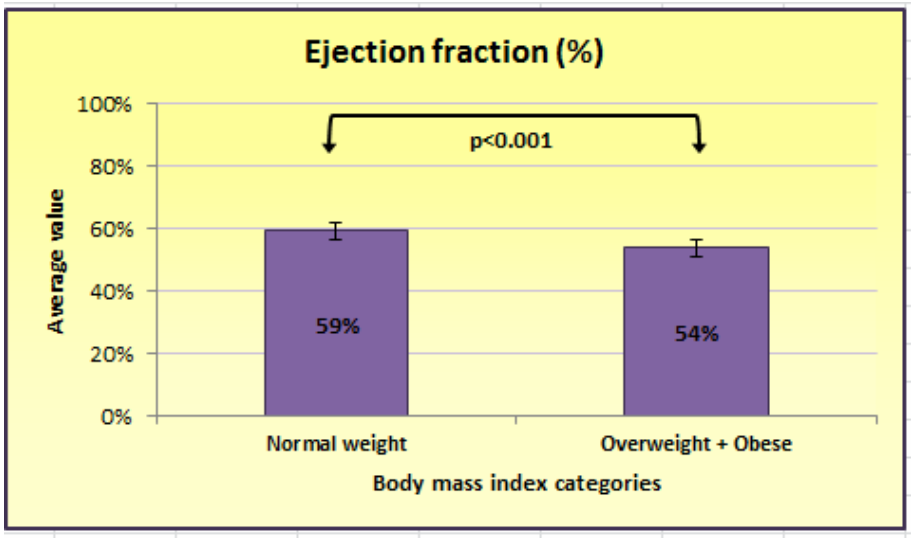

Figure 8. Average value of ejection fraction (%) relative to the weight status.

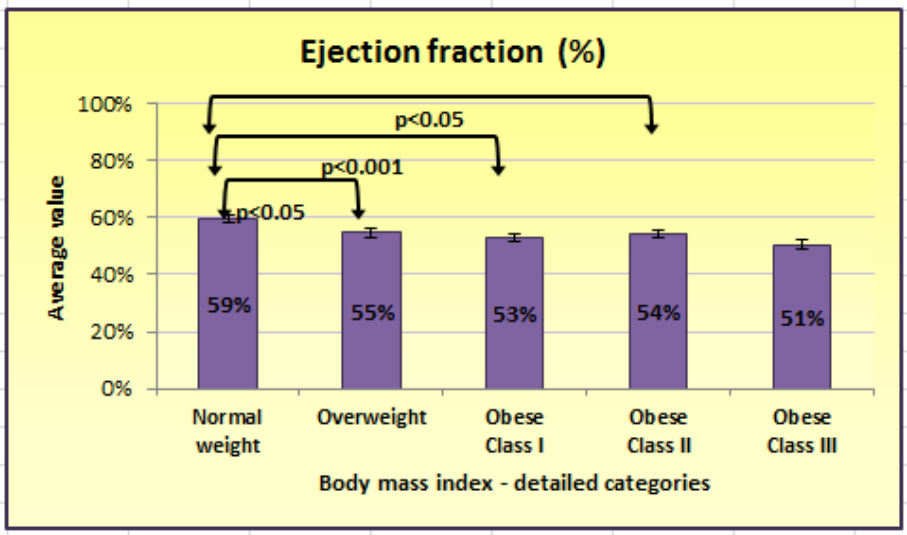

Figure 9. Average percentage of ejection fraction (%) based on the detailed weight status.

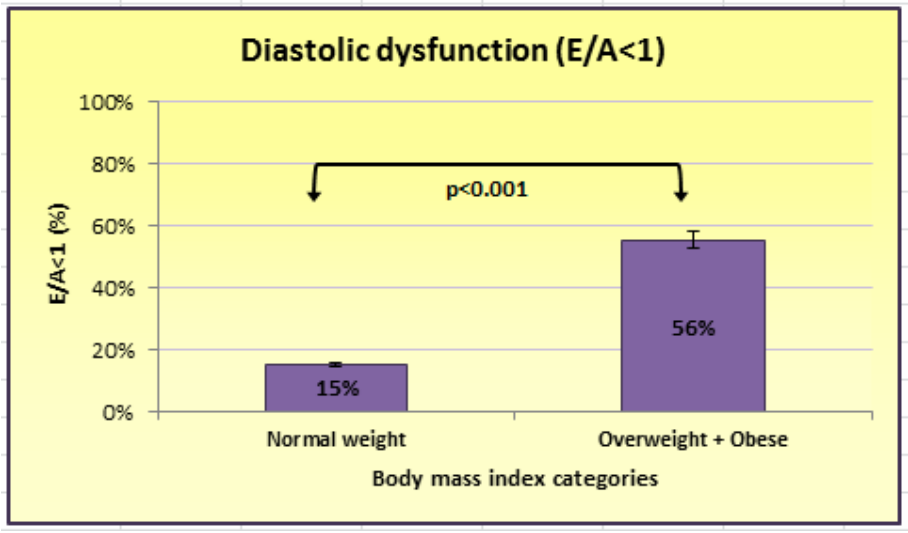

Figure 10. Presence of diastolic dysfunction (E/A < 1 ration) in the studied group.

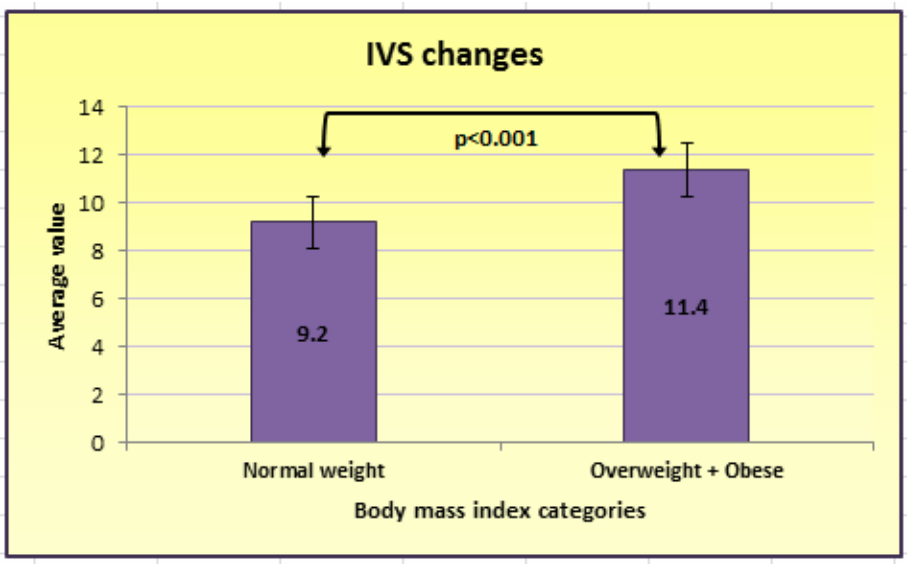

Figure 11. IVS modification based on the weight status.

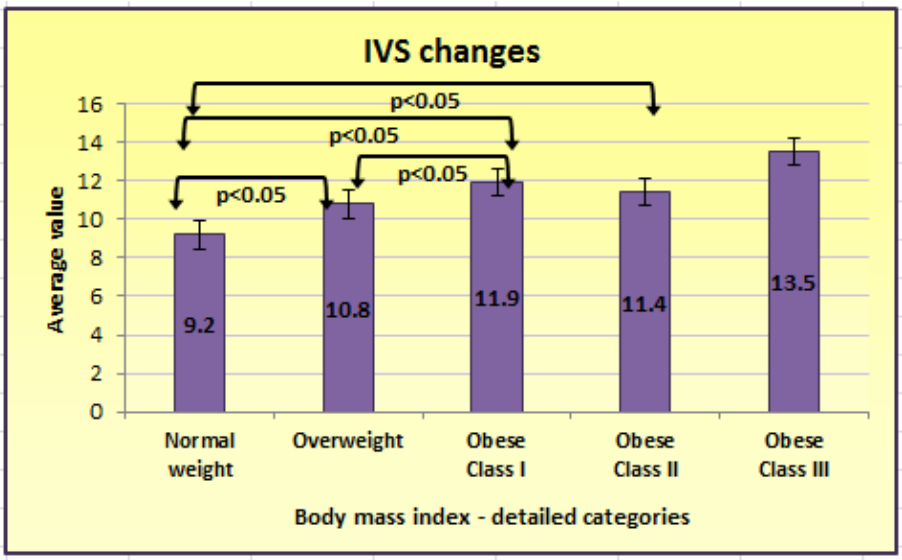

Figure 12. IVS modification based on the detailed weight status.

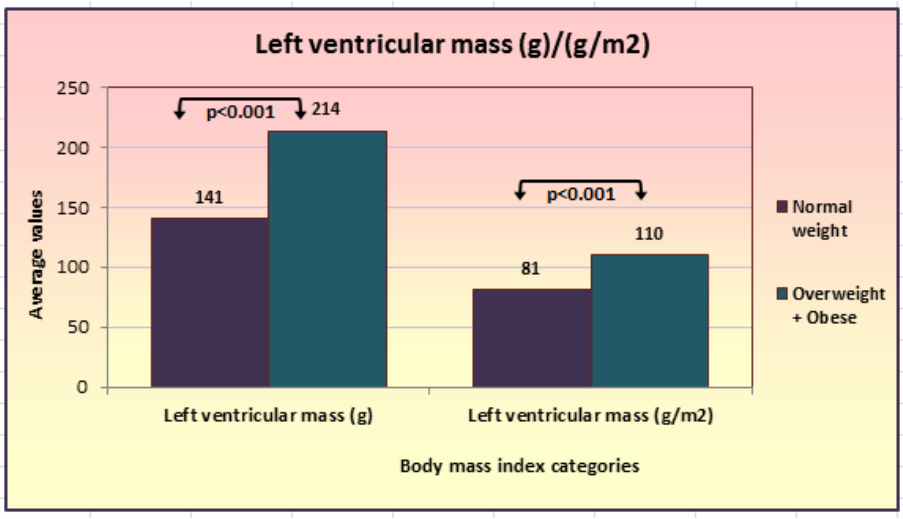

Figure 13. Left ventricle (LV) mass based on the weight status.

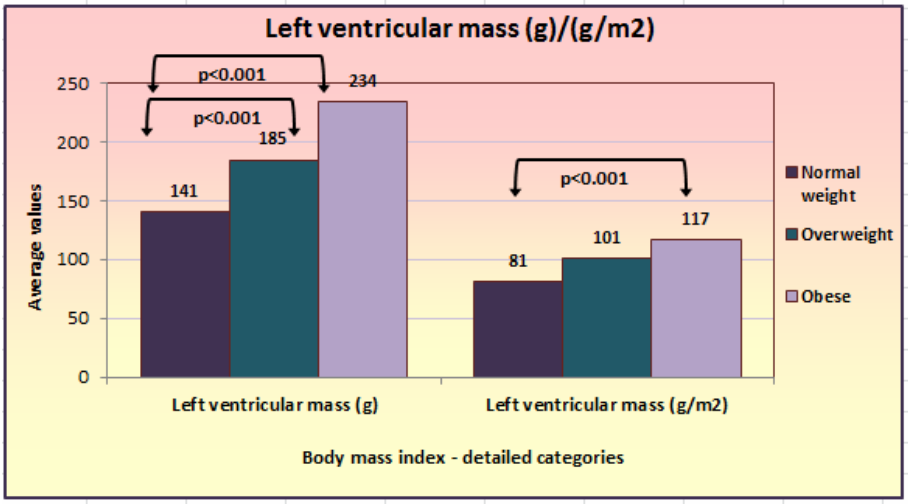

Figure 14. Relation between left ventricle mass (g) and weight status.

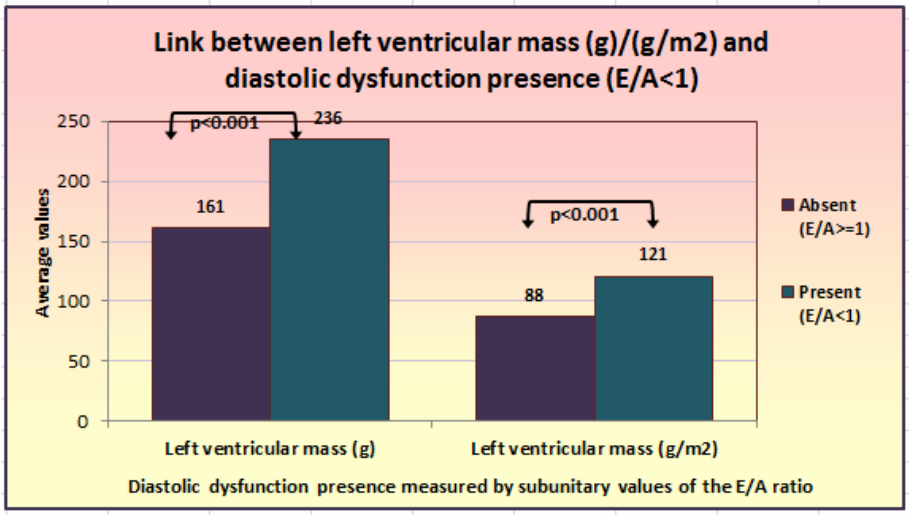

Figure 15. Relation between left ventricle mass (g)/(g/m^2), diastolic dysfunction and weight status.

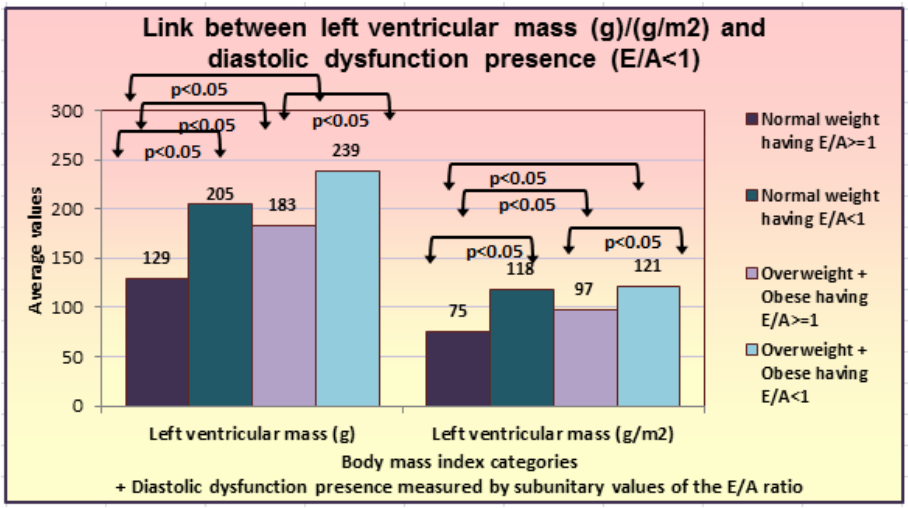

Figure 16. Relation between left ventricle mass (g)/(g/m^2, diastolic dysfunction and detailed weight status relation.

Table 1
Kruskal Wallis test result on the left ventricle mass
based on detailed weight status

Test Statistics[a,b]

	LV mass (g)	LV mass (g/m2)
Chi-Square	44.241	33.857
df	4	4
Asymp. Sig.	.000	.000

a. Kruskal Wallis Test

b. Grouping Variable: Body mass index detailed categories

Table 2
Student test applied on the left ventricle mass – diastolic dysfunction – detailed weight status relation

Comparisons of Column Means[a]

	v2_v22			
	Normal weight+ E/A>=1	Normal weight+ E/A<1	Overweight& Obese+E/ A>=1	Overweight& Obese+E/A<1
	(A)	(B)	(C)	(D)
LV mass (g)		A	A	A C
LV mass (g/m2)		A	A	A C

Results are based on two-sided tests assuming equal variances with significance level 0.05. For each significant pair, the key of the smaller category appears under the category with larger mean.

Table 3
Spearman correlation coefficient for linearity testing

Correlations

			HBP (mm Hg-yes/no)	FMH (yes/no)	Current smoker	LV mass (g)
Spearman's rho	HBP (mmHg-yes/no)	Correlation Coefficient	1.000	.213*	-.082	.355**
		Sig. (2-tailed)	.	.025	.390	.000
		N	111	111	111	98
	FMH (yes/no)	Correlation Coefficient	.213*	1.000	-.004	.108
		Sig. (2-tailed)	.025	.	.965	.290
		N	111	111	111	98
	Current smoker	Correlation Coefficient	-.082	-.004	1.000	.124
		Sig. (2-tailed)	.390	.965	.	.223
		N	111	111	111	98
	LV mass (g)	Correlation Coefficient	.355**	.108	.124	1.000
		Sig. (2-tailed)	.000	.290	.223	.
		N	98	98	98	98

*. Correlation is significant at the 0.05 level (2-tailed).

**. Correlation is significant at the 0.01 level (2-tailed).

Table 4
Results of the ANOVA multifactorial analysis

Tests of Between-Subjects Effects

Dependent Variable: LV mass (g)

Source	Type III Sum of Squares	df	Mean Square	F	Sig.
Corrected Model	63048.684[a]	7	9006.955	2.806	.011
Intercept	1762069.809	1	1762069.809	549.008	.000
HBP	21332.729	1	21332.729	6.647	.012
FMH	.016	1	.016	.000	.998
Current_smoker	9498.604	1	9498.604	2.959	.089
HBP * FMH	7482.522	1	7482.522	2.331	.130
HBP * Current_smoker	181.879	1	181.879	.057	.812
FMH * Current_smoker	718.241	1	718.241	.224	.637
HBP * FMH * Current_ smoker	6129.497	1	6129.497	1.910	.170
Error	288859.858	90	3209.554		
Total	4057413.855	98			
Corrected Total	351908.542	97			

a. R Squared = .179 (Adjusted R Squared = .115)

The LV mass increase (g) in the obese and overweight is not influenced by the current smoker status or the presence of early heart disease family history, nor by these two factors combined. There is a linear link between the presence of systemic high blood pressure and the LV mass increase (g), but it is a very weak one: Only 12.9% of the LV mass (g) variation is explained by HBP. While analyzed more in detail, on the weight status categories (OW+O and NW) this link ceases to exist.

DISCUSSION

The current study brings convincing statistical arguments that overweight and obese subjects have significant early changes, observed through transthoracic ultrasound, in comparison with normal weight ones, such as: decreased left ventricular ejection fraction, early diastolic dysfunction, thickening of the interventricular septum, left ventricular mass increased both per se and relative to body surface area.

The presence of diastolic dysfunction is twice more frequent in overweight patients in comparison to normal weight ones (30% *vs* 15%) and 5 times more frequent in obese patients than in normal weight ones (75% *vs* 15%).

The interventricular septum size increase is correlated to body mass index, there being statistically significant differences both between normal weight patients *vs* overweight vs obese, but also between overweight and obese. The data obtained in our study are consistent with several international publications, which concludes that obesity-related with left ventricular hypertrophy is a powerful risk factor for systolic/diastolic dysfunction [8, 9].

In the case of the entire group, as well as the normal weight, overweight and obese categories, both the left ventricle mass (g) and the left ventricle mass relative to body mas (g/m^2) is significantly statistically higher in patients with diastolic dysfunction ($E/A < 1$). This indicates a relation between the presence of diastolic function, left ventricle mass increase and body mass index ($p < 0.05$).

The data of our study are consistent with data from a 2009 study which showed that, by means of nuclear magnetic resonance, the response of the heart through left ventricular hypertrophy in the obese, in the absence of additional factors of cardiovascular risk, is mainly due to increased muscle mass, circulating blood volume and visceral fat mass [10].

In another study of 702 adults one has shown that in female subjects, the left ventricular mass expressed both in grams and in relation to body surface, the aortic augmentation index and the pulse wave velocity in the aorta increased, the E/A ratio decreased, while the number of metabolic syndrome components met in the same individual increased [11]. Moreover, the number of metabolic

syndrome components is found to be strongly correlated with the geometric cardiac changes that lead to left ventricle hypertrophy, with left ventricular dysfunction and diastolic blood pressure changes, regardless of age and blood pressure, mainly in women. In men, although there are differences between the studied groups, these were not statistically significant [11].

A multiethnic study conducted in the United States of America (MESA) that began in 2000 brings some very interesting data [12]. This study was conducted in 6 centers with adequate representation of the multiethnic population, with an average age of 61 years, similar to that in our study, with equal numbers of participants of both genders, with no symptoms of heart disease. The authors concluded that in those asymptomatic subjects, the division in risk classes for certain cardiovascular events has to be also done by other methods than the classic ones, such as measuring the left ventricular mass by ultrasound or measuring the calcium levels in coronary arteries [12]; data consistent with our study regarding the calculation of left ventricular mass by transthoracic echocardiography in overweight and obese subjects with no cardiovascular disease symptoms.

This research provides evidence about the necessity of establishing an investigational plan of subjects overweight and obese, where transthoracic echocardiography, a noninvasive method, should be part of; to be able to detect early cardiac changes and thus to take the best treatment decisions for each patient.

Study limitations

1. Few IIIrd degree obese patients were included in the study, in order to prove the early cardiac changes in low and moderate weight gains.

2. The number of smokers or former smokers in the study group is low, in order to have a proper and correct statistical interpretation.

CONCLUSION

1. Overweight and obese subjects present significant early cardiac changes, observed by transthoracic ultrasound, in comparison with normal weight subjects, such as: decrease of left ventricle ejection fraction, early diastolic dysfunction, interventricular septum thickening, left ventricle mass increase, both per se as well as relative to body surface.

2. There is a certain directly proportional relation between body mass index – left ventricle mass – diastolic function.

3. The correlation between left ventricle mass and weight gain continues to be maintained after the multifactor regression analysis, taking into account the smoker status, early cardiovascular disease family history and the presence of systemic high blood pressure.

4. We deem as extremely useful the transthoracic echocardiography of every overweight and obese patient, in order to capture early cardiac changes, towards a good clinical and medication management.

Acknowledgment. The paper was supported by project E-ProCord: New medical and modeling approaches in IT&C age applied on cardiovascular profile evaluation at molecular level. Differences implied by gender, age, and existing pathology, CNCSIS Code ID_2246/2008, Contract No. 947/2009, NURC funder authority.

Abbreviations: Normal weight – NW, Overweight – OW, Obese – O, IVS – interventricular septum.

Introducere. *Obezitatea şi supraponderabilitatea sunt două patologii din ce în ce mai frecvente în secolul XXI. Acestea determină creşteri ale ratelor de morbiditate şi mortalitate în populaţia generală, mai ales prin complicaţii cardiovasculare.*

Scop. *Identificarea şi diagnosticul precoce al modificărilor cardiace la pacienţii supraponderali şi obezi.*

Material şi metodă. *A fost realizat un studiu transversal pe 111 participanţi: 27 normoponderali, 84 pacienţi supraponderali şi obezi. Aceştia au fost examinaţi clinic, biologic şi ecografic.*

Rezultate. *Prezenţa disfuncţiei diastolice este de două ori mai frecventă la pacienţii supraponderali comparativ cu cei normoponderali (30% vs 15%) şi de 5 ori mai frecventă la pacienţii obezi (75% vs 15%). Dimensiunile septului interventricular au fost corelate cu indicele de masă corporală, fiind diferenţe*

semnificative statistic privind dimensiunile acestuia între pacienţii normo, supraponderali şi obezi şi între pacienţii supraponderali şi obezi. Masa ventriculară stângă precum şi masa ventriculară stângă raportată la suprafaţa corporală au fost semnificativ statistic mai mari la pacienţii cu disfuncţie diastolică (E/A < 1). Aceasta sugerează o relaţie între prezenţa disfuncţiei diastolice, creşterea masei ventriculare stângi şi a indicelui de masă corporală (p < 0,05).

***Concluzii**. Pacienţii supraponderali şi obezi prezintă modificări cardiace – scăderea fracţiei de ejecţie a ventriculului stâng, disfuncţie diastolică, îngroşarea septului interventricular, şi creşterea masei ventriculului stâng.*

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