Statistical Study on Obesity Correlation - Inflammatory Status - Cardiovascular Pathology

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The mediators of inflammation are involved in the pathophysiological processes by which obesity, especially the abdominal, causes an increased cardiovascular risk. The role of inflammation is increasingly accepted in the pathogenesis of diabetes and metabolic syndrome. In type 1 DZ autoimmune lesions from the pancreatic islets play a causal role in the development of the disease. In type 2 DZ, the mediators of inflammation released at adipocyte level play a key role in the development of the cardiovascular complications of this condition. Primary obesity is conditioned by excessive dietary intake and the functional status of anabolic systems. In the last decades, the prevalence of obesity has increased dramatically worldwide but also in our country, due to the increasing adoption of a sedentary lifestyle and excessive caloric intake by the population.

Keywords: obesity, abdominal circumference (CFA), C-reactive protein, ischemic coronary artery disease.

Recent studies show that inflammation can be linked to obesity and type II DZ. Adipocytokines act directly at the vascular wall, activating the smooth muscle and thus causing vascular dysfunction [1]. Increasing the proportion of fatty tissue in the body results in the phenomenon of "cell stress A", activation of mitogenic JNK (MAP-kinase) and NF-kb signals. These signaling pathways stimulate the production of pro-inflammatory cytokines TNF-α, IL-6, leptin, resistin, chemokines such as PAI-1 or MCP-1 (monocyte chemoattractant protein-1). Through these monocytes are recruited to the adipose tissue, where they turn into macrophages and in turn produce other cytokines and chemokines that increase local inflammation and contribute to its systemic spread. All adipocytokines also act at the hepatic level where they stimulate the synthesis of acute phase proteins (fibrinogen, C-reactive protein), visceral adipose tissue being the most likely site of subclinical inflammation [1, 2]. Studies have shown that plasma levels of C-reactive protein in obesity correlate with waist circumference and visceral adiposity. Moreover, following liposuction, a process that eliminates subcutaneous fat, but not visceral fat, the persistence of high levels of C-reactive protein was found, while weight loss due to diet and physical activity decreased the plasma value of this marker.

In the onset period, obesity presents a dynamic phase in which an accelerated weight gain of 10-20 kg is achieved in a few months. After 5-10 years of evolution of obesity, type 2 diabetes appears, generalized atherosclerosis with cardiac, cerebral, peripheral complications [3, 4].

Repeated increases in blood sugar as a result of dietary abuse cause pancreatic stimulation and insulin release

These will cause blood sugar drops below the lower limit of normal. Hypoglycaemia by its effect on the hypothalamus, causes catecholamine, cortisol, and hunger discharges, which again increase blood sugar levels, with cycle resumption [5, 6].

Chronic hyperinsulinism, through hypoglycemia, induces cortisolic hyperfunction, through hypothalamo-corticotropic stimulation, progressing to pseudo-cushingoid syndrome [7, 8]. Moderate but chronic hypercortisolism induces endogenous insulin resistance, hyperglycemia and hypertriglyceridemia, and by nonspecific suppression of the gonadotropic and thyrootropic axis, induces the occurrence of hypogonadism and hypogonadotropy and secondary hypothyroidism.

This endocrine syndrome causes metabolic disorders: hypertriglyceridemia, hypercholesterolemia, decreased HDL, increased LDL, impaired glucose tolerance, type 2 diabetes, hyperuricemia [9].

Given these obesity-specific disorders, the purpose of this paper is to study the inflammatory status of obese patients and to evaluate the prevalence of cardiovascular but also endocrine-metabolic pathology in these patients.

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Experimental part

Material and methods

The study was carried out in the Cardiology Clinic of the Emergency County Clinical Hospital in Craiova, having a retrospective component (following the observation sheets), but also a prospective one (through direct supervision), for a period of 2 years (2017-2019).

The presented case is based on a number of 172 patients admitted to the Cardiology Clinic and subsequently monitored (all patients also had different degrees of obesity).

The study carried out aims:

- clinical evaluation of patients with obesity and establishing the degree of obesity according to CFA;
- paraclinical evaluation of patients with obesity: dosage of C-reactive protein, evaluation of thyroid function, cortico-adrenal, but also of cardio-vascular function through Rx cord-lung, EKG, eco cord;
- establishing the prevalence of cardio-vascular pathology but also endocrino-metabolic in obese patients.

The cases were investigated by anamnesis, by clinical examination based on a type sheet and by paraclinical examination (laboratory - usual analyzes, hormonal dosages, determination of C-reactive protein, Rx cord-lung, EKG, cardiac ultrasound).

We mention that the study included patients with primary obesity, intake, who appeared in our clinic for accusations characteristic of cardiac pathology.

Dosage of CRP (C-reactive protein) [10]

Preparation of the patient - fast (on uneaten);

Specimen harvested - venous blood;

Harvest container - vacutainer without anticoagulant; with or without gel separator;

Processing required after harvesting - the serum is separated by centrifugation;

Sample volume - minimum 0.5 mL serum;

Causes of sample rejection - intense lipemic or intensely hemolysed specimen;

Method - Latex immunoturbidimetry;

Reference values: 0.5 mg / dL*;*

In recent years, epidemiological studies have confirmed that patients with elevated baseline plasma levels of CRP have an increased risk of coronary heart disease and myocardial infarction [11]. Prospective studies in European and US countries have confirmed consistent results regarding the predictive value of CRP determinations on cardiovascular risk in both men and women. Thus, CRP is an indirect risk factor for coronary heart disease. hs-CRP is a strong predictor of future cardiovascular events and according to AHA 2003 recommendations, among the inflammatory markers currently used, the highly sensitive reactive protein C is the only one approved for clinical use. Decision intervals for cardiovascular risk assessment are set according to CDC / AHA recommendations:

-<1 mg / l - low risk;

-1-3 mg / l - moderate risk;

-> 3 mg / l - increased risk.

In the case of values> 10 mg / l a non-cardiovascular cause should be considered.

The SPSS program, specialized in scientific statistical calculations, produced by **SPSS** and the Data Analysis module of the MICROSOFT EXCEL program, together with the XLSTAT suite for MS Excel, were used for data processing.

Patient data recording with the EXCEL program produced the initial database from which significant aspects of this study were extracted [12, 13].

The actual processing was done with the help of:

-the SPSS program's CrossTab, BasicTables, General Tables, Correlate, Regression and Factor Analisys commands;

-the Pivot Tables, Functions-Statistical and Chart commands in MS Excel, and the commands in the XLSTAT module for the ANOVA test and the Cramer test.

The Chi square test was used to interpret the incidence tables; the data were appreciated from the point of view of the dependency between the two classification factors, retaining only the results below 5%, considered a sufficient significance threshold. The test shows whether there is any connection (mutual influence) between the two factors analyzed through the incidence table.

In the chi square test of dependency testing between two factors, the test result was calculated for the data from the incidence tables, a result which was compared with the threshold value indicating a significant dependence (95% or 99% threshold) or a highly significant dependence (99.9% threshold) between the two classification factors.

$$\chi^2 = \sum_{i=1}^{n} \frac{(|O_i - E_i|)^2}{E_i} \quad [14]$$

The Chi square test is valid if at least 80% of the probable frequencies exceed 5 and all the probable frequencies exceed 1. For small samples the test can be used by applying the Yates correction, also known as continuity correction, which implies the reduction by 0.5 units. of the difference between the observed frequency and the probable frequency in the chi square calculator (of the formula) before the square rise; thus, the value of Chi square decreases. By decreasing the value of Chi square, the chances of the null hypothesis being rejected decrease, so that the risk of making a Type I mistake (rejecting the null hypothesis when it is actually true) decreases significantly. However, it increases the risk of a Type II error (accepting a false hypothesis when it is actually false). Some statisticians recommend the use of continuity correction in case of a 2x2 contingency table. Others oppose correction. In the medical literature, the Chi square test is applied both with and without correction.

We used the following interpretation of the values of p, provided directly by the program with which the statistical processing of data is performed, by applying the above test:

- p <0.05, the difference between the two averages is significant (S);
- p <0.01, the difference between the two averages is highly significant (HS);
- p <0.001, the difference between the two averages is very significant (VHS);
- p> 0.05, the difference between the two averages is insignificant (NS).

Student's t-test comparing the means for two groups proposes two statistical hypotheses [15]:

- H0 hypothesis (or null hypothesis): the difference between means is random;
-Hypothesis H1: the difference between the means is statistically significant.

The result *p* of the test represents the probability of making an error if the hypothesis H0 of the test is rejected, a result provided as a number between 0 and 1. If p is less than 0.05 we reject hypothesis H0, null, and admit that hypothesis H1 is true. .

In the t test of comparison of means (Student's test), we used the following interpretation of the values of p, provided directly by the program with which the statistical processing of data is performed, by applying the above test:

- p <0.05, the difference between the two averages is significant (S);
- p <0.01, the difference between the two averages is highly significant (HS);
- p <0.001, the difference between the two averages is very significant *The correlation coefficient.*

For two sets of data, the coefficient used to measure the linear correlation is *Pearson's coefficient* [16]. Although the data distributions are not always such that the results obtained using this coefficient are the best, however, we considered it to be the most synthetic indicator of correlation. The relationship used to calculate the Pearson correlation coefficient is:

$$r = \frac{\sum_{i=1}^{n}\left(x_i - \overline{X}\right)\cdot\left(y_i - \overline{Y}\right)}{\sqrt{\sum_{i=1}^{n}\left(x_i - \overline{X}\right)^2}\cdot\sqrt{\sum_{i=1}^{n}\left(y_i - \overline{Y}\right)^2}}$$

where: $X \div x_1, x_2, \ldots\ldots x_n$ şi $Y \div y_1, y_2, \ldots\ldots y_n$ are the values measured for the two parameters a whose correlation we calculate, and the respective sampling averages, calculated with the formula given above.

Results and discussions

The studied group comprised 172 patients with obesity, in which the degree of obesity was evaluated (according to CFA), by sex, age, evaluation of cardiovascular function (presence of hypertension, coronary ischemic disease), evaluation of the thyrotropic axis and corticotropic by dosing TSH, FT4, ACTH and cortisol.

To assess cardiovascular risk in both women and men, we determined highly sensitive rectal protein C, knowing that numerous epidemiological studies have shown that patients with elevated plasma levels are at increased risk of coronary heart disease and myocardial infarction.

The patients with obesity, following the evaluation of the thyrotropic and corticotropic axis, were divided into 3 groups as follows:

- lot 1, without endocrine dysfunction
- group 2 with primary hypothyroidism
- group 3 with reactive hypercorticism, with secondary hypothyroidism.

The age distribution of the patients studied was the following (table 1):

-In group 1 the mean age of the patients was 60.65 years, with a minimum of 42 years and a maximum of 81 years at a standard deviation of 9.98;

-In group 2 the average age was 61.28 years, with a minimum of 48 years and a maximum of 80 years at a standard deviation of 7.59;

-In group 3 the average age was 55.55 years with a minimum of 47 years and a maximum of 66 years at a standard deviation of 5.52.

Table 1
DISTRIBUTION BY AGE GROUP OF PATIENTS

Age	Lot 1	Lot 2	Lot 3	Total
Nr.	89	61	22	172
Minimum	42	48	47	42
Maximum	81	80	66	81
Average	60.65	61.28	55.55	60.22
Dev.std.	9.98	7.59	5.52	8.86
CV	16.46%	12.38%	9.93%	14.71%
Student Test	L1-L2	L1-L3	L2-L3	ANOVA
p	0.67866	0.02285	0.00172	0.02632

Table 2
PERCENTAGE DISTRIBUTION OF PATIENTS BY GROUPS AND BY SEX

Sex	Women	Men	Total
Lot 1	56.18%	43.82%	100.00%
Lot 2	81.97%	18.03%	100.00%
Lot 3	81.82%	18.18%	100.00%
Total	68.60%	31.40%	100.00%

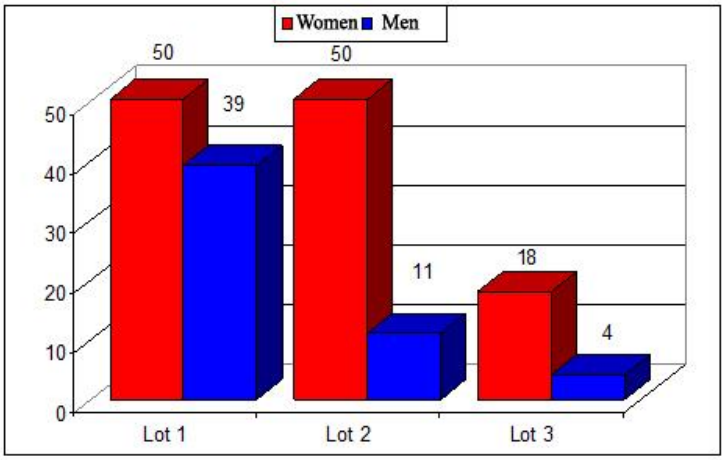


Chart 1. Graphic representation of patients by sex

The distribution by sex of the 3 groups was as follows (table 2, graph 1):

-group 1 included 50 women (56.18%) and 39 men (43.82%);

-group 2 included 50 women (81.97%) and 11 men (18.03%);

-group 3 included 18 women (81.82%) and 4 men (18.18%).

The CFA values correlated with the degree of obesity in men were as follows:

-CFA <94 cm;

-CFA = 94 -101.9 cm;

- CFA ≥102 cm.

For women, the CFA values correlated with the degree of obesity:
-CFA<80 cm;
-CFA=80-87,9 cm;
-CFA ≥ 88 cm.

CFA was measured because it correlates with intra-abdominal fat mass, CFA values over 94 cm in men, respectively over 80 cm in women, being associated with increased risk of cardiovascular morbidity and mortality (Table 3).

Table 3
DISTRIBUTION BY GROUPS ACCORDING TO THE DEGREE OF OBESITY AND ABDOMINAL CIRCUMFERENCE

CFA	CFA 1	CFA 2	CFA 3	Total
Lot 1	40.45%	43.82%	15.73%	100.00%
Lot 2	37.70%	39.34%	22.95%	100.00%
Lot 3	0.00%	59.09%	40.91%	100.00%
Total	34.30%	44.19%	21.51%	100.00%

The distribution of CRP hs values by groups is shown in table 4.

Table 4
DISTRIBUTION OF HS CRP VALUES BY GROUPS

hs CRP	Lot 1	Lot 2	Lot 3	Total
Nr	89	61	22	172
Minimum	0.3	0.4	0.5	0.3
Maximum	8	8.5	7.8	8.5
Average	2.39	3.38	4.00	2.95
Dev.std.	2.02	2.26	2.39	2.23
CV	84.48%	66.70%	59.79%	75.51%
Student Test	L1-L2	L1-L3	L2-L3	ANOVA
p	0.00567	0.00175	0.28478	0.00146

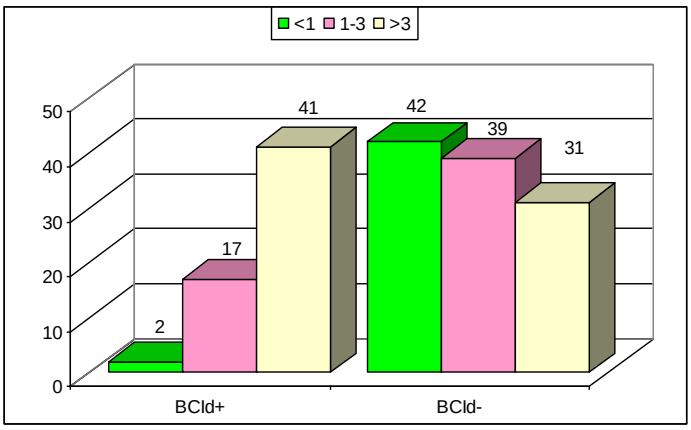
The breakdown by batch of hs CRP values is as follows (Table 4):
• in patients in group 1: 30 patients (33.71%) had hr CRP <1 mg / l (risk low), 33 patients (37.08%) had a CRP of 1-3 mg / l (moderate risk) and 26 patients had a CRP> 3 mg / l;
• in group 2, 10 patients (16.39%) had low cardiovascular risk, 19 patients (31.15%) moderate risk and 32 patients (52.46%) increased cardiovascular risk;
• in group 3, 4 patients (18.18%) had low cardiovascular risk, 4 patients (18.18%) moderate risk and 14 patients (63.64%) increased cardiovascular risk

Painful BCI-hs CRP coelation

In the case of the 60 patients with painful BCI included in the study, the following were found (table 8.134, 8.135, fig. 8.54):
-2 patients (3.33%) had hp CRP <1 mg / l (low risk);
-17 patients (28.33%) had hsp CRP between 1-3 mg / l (moderate risk);
-41 patients (68.33%) with hr CRP> 3 mg / l (increased risk).

Table 5
CORRELATION BETWEEN THE LEVEL OF CRP HS AND THE PRESENCE OF PAINFUL BCI

hs CRP	<1	1-3	>3	Total
BCId+	2	17	41	60
BCId-	42	39	31	112
Total	44	56	72	172



Graph 2. Correlation between the level of CRP hs and the presence of painful BCI**.**

At a square chi of 33,760, p<0.001, high statistical significance (tables 6, 7) was highlighted.

Statistical correlations

Table 6

Chi square	33.760
p Chi square	0.000
Cramer's V	0.443

Table 7

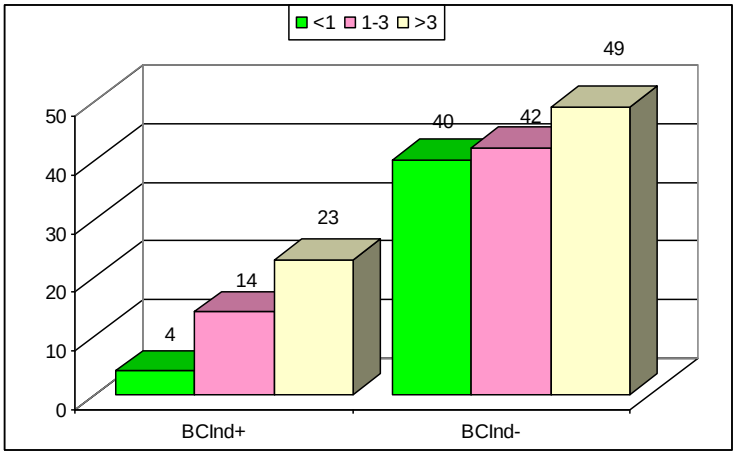
p<0.001	high statistical significance, confidence of 99.9%
V<0.5	significant association / influence between the two factors

The patients with non-painful BCI presented the following values of hs CRP (table 5):
- 4 patients (9.76%) with hs CRP <1mg / l (low risk);
- 14 patients (34.15%) with hp CRP between 1-3 mg / l (moderate risk);
- 23 patients (56.10%) with hs CRP> 3 mg /l.

Table 8

CORRELATION OF BCI PAIN-FREE HS CRP LEVEL

hs CRP	<1	1-3	>3	Total
BCId+	4	14	23	41
BCId-	40	42	49	131
Total	44	56	72	172



Graph 3. Correlation between the level of CRP hs and the presence of painless BCI.

Correlation level hs CRP-degree of obesity

Patients with obesity grade 1 presented the following values of hp CRP (table 8, graph 3):

-30 patients (50.85%) with hs CRP <1 mg / l ,,

-19 patients (32.20%) with hs CRP between 1-3 mg / l;

-10 patients (16.95%) with hs CRP> 3 mg / l;

In patients with grade 2 obesity, hs CRP had the following values:

-14 patients (18.42%) with hs CRP <1 mg / l;

-25 patients (32.89%) with hs CRP between 1-3 mg / l;

-37 patients (48.68%) with CRP> 3 mg /l.

In the case of patients with obesity grade 3 hs CRP dosage revealed:

-no patient had CRP hs <1 mg / l;

-12 patients (32.43%) had hsp CRP between 1-3 mg / l;

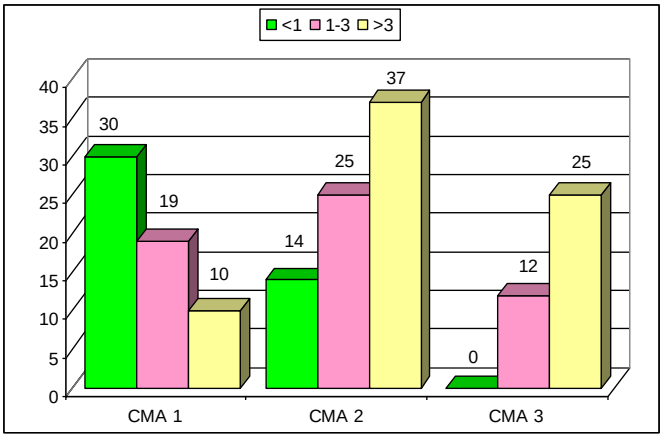
-25 patients (67.57%) had hsp CRP> 3 mg /l.

The prevalence of moderate / increased risk for cardiovascular events increases significantly (p <0.001) with obesity and especially with increased CFA (Table 9, Figure 4).

Table 9

CORRELATION BETWEEN THE LEVEL OF CRP AND THE DEGREE OF OBESITY

CFA	Obezity	hs CRP			
		<1	1-3	>3	Total
CFA 1	Grd. I	30	19	10	59
CFA 2	Grd. II	14	25	37	76
CFA 3	Grd.III	0	12	25	37
Total		44	56	72	172



Graph 4. Correlation between CRP hs level and CFA size.

At a square chi of 41,150, p<0.001, high statistical significance was highlighted (table 10, 11).

Statistical correlations

Table 10

Chi square	41.150
p Chi square	0.000
Cramer's V	0.346

Statistical correlations

Table 11

p<0.001	High statistical significance, 99.9% confidence.
V<0.5	weak association / influence between the two factors

Conclussions

Being the second leading cause of preventable death (after smoking), obesity is a major public health problem. The prevalence of obesity and overweight increases practically in all countries and age groups in the world, and the economic cost of obesity is estimated as 2-7% of all health expenses.

The group of patients studied has an average age of 60.22 years, with a standard deviation of 8.86; the minimum age was 40 years and the maximum was 81 years.

The gender distribution of the 172 patients included in the study was in favor of women (68.60% women, versus 31.40% men).

Endocrine obesity-associated tuberculosis was present in almost half of the patients in the total group (48.26%), being represented by primary hypothyroidism in 35.47% of patients and reactive hypercorticism with secondary hypothyroidism in 12.79%.

There were no statistically significant differences of the average age between groups 1 and 2 (in patients without endocrine disorders, respectively in those with primary hypothyroidism), its values being 60.65 years in group 1, respectively 61.28 years in group 2. In contrast, in patients with reactive hypercorticism the mean age was slightly lower (55.5 years).

Obesity had a statistically significantly higher prevalence in women (68.60%), compared to men; the prevalence of grade II and III obesity was also observed among women.

Reactive hypercorticism was only found in patients with high degrees of obesity (59.09% grade II obesity and 40.91% grade III obesity).

In the study performed the painful ischemic heart disease was diagnosed in 34.88 of the patients, and the painless form in 23.84%, without significant differences in its distribution ($p > 0.05$), on the 3 groups analyzed.

The prevalence of moderate / increased risk for cardiovascular events (assessed by determining hs CRP) increases significantly ($p < 0.001$) with the degree of obesity (especially with increased CFA) and its association with endocrine-metabolic changes.

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