Influence of Body Structure and Weight on Bone Mass. Obesity and Bone Mineral Density

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IAȘI
2012
Keywords: bone, body composition, osteoporosis, menopause, leptin.
# TABLE OF CONTENTS

I. Introduction ........................................................................................................... 1

II. Osteoporosis - General ......................................................................................... 2
   II.1. Epidemiology of Osteoporosis ....................................................................... 2
   II.2. Definition of Osteoporosis ........................................................................... 3
   II.3. Etiopathogenesis ......................................................................................... 3
       II.3a. Osteoblast Differentiation ..................................................................... 5
       II.3b. Osteoclast Differentiation .................................................................... 6
   II.4. Bone Mass: Factors Influencing It .............................................................. 8
   II.5. Influence of Body Weight and Structure on Bone Mass ......................... 13
       II.5a. Muscle Mass and Bone Mass ............................................................... 13
       II.5b. Endocrine Role of the Adipose Tissue ............................................... 13
   II.6. Genetics of Osteoporosis .......................................................................... 20

III. Diagnosis of Osteoporosis ................................................................................. 24
   III.1. Clinical Examination .................................................................................. 26
   III.2. Paraclinical Examination ........................................................................... 26
   III.3. Imaging Examination .................................................................................. 28

IV. Prevention and Treatment .................................................................................. 31
   IV.1. Physical Activity ......................................................................................... 31
   IV.2. Calcium ....................................................................................................... 31
   IV.3. Vitamin D ..................................................................................................... 32
   IV.4. Hormone Replacement Therapy .................................................................. 33
   IV.5. Selective Estrogen Receptor Modulators (SERM) ...................................... 35
   IV.6. Calcitonin ..................................................................................................... 35
   IV.7. Bisphosphonates ........................................................................................ 36
   IV.8. Parathormone .............................................................................................. 38
   IV.9. Strontium ranelate ...................................................................................... 39
   IV.10. Denosumab ............................................................................................... 39
   IV.11. New Therapies .......................................................................................... 40

V. Recommendations Related to Postmenopausal Osteoporosis
   Prevention and Treatment .................................................................................... 41

B. PERSONAL CONTRIBUTION
   I. Introduction ....................................................................................................... 47
   I.1. Study Substantiation ...................................................................................... 47
I.2. Research Assumption ........................................................................47
II. Study Objectives ...............................................................................48
III. Patients and Method ........................................................................48
III. Patients...............................................................................................48
III. 1.1. Inclusion Criteria ......................................................................49
III.1.2. Exclusion Criteria ......................................................................49
III.2. Methods.............................................................................................49
III.3. Research Ethics Issues .................................................................51
III.4. Statistical Processing Methods .....................................................53
IV. Results..................................................................................................54
IV.1. Characteristics of the Studied Groups ...........................................54
     IV.1.1 Group A- Postmenopausal Patients with Osteoporosis .......54
     IV.1.2 Group B- Postmenopausal Patients without Osteoporosis ...56
IV.2. Clinical Characteristics of the Patients in Group A as Compared with the Patients in Group B.................................63
IV.3. Clinical Characteristics of the Patients in Group B1 as Compared with the Patients in Group B2..............................................66
IV.4. Correlations.........................................................................................69
     IV.4.1. Relation between Various Parameters in the Patients in Group A and Group B.................................................................69
     IV.4.2. Relation between Various Parameters in the Patients in Group B1 and Group B2.................................................................72
IV.5. Clinical and Paraclinical Characteristics of the Whole Group of Pre- and Postmenopausal Women..............................................76
IV.6. Clinical and Paraclinical Characteristics of the Patients in Group C as Compared with the Patients in Group D.........................80
IV.7. Clinical and Paraclinical Characteristics of the Patients in Group C1 as Compared with the Patients in Group D1. ......................84
IV.8. Clinical and Paraclinical Characteristics of the Patients in Group C2 as Compared with the Patients in Group D2.........................85
IV.9. Clinical and Paraclinical Characteristics of the Patients in Group C1 as Compared with the Patients in Group C2.........................87
IV.10. Clinical and Paraclinical Characteristics of the Patients in Group D1 as Compared with the Patients in Group D2......................88
IV. 11. Comparative Description of the Paraclinical BMI-Dependent Characteristics of Group C2.................................................................89
IV.12. Comparative Description of the Paraclinical BMI-Dependent Characteristics of Group D2.................................................................90
IV.13 Charts Showing the Frequency of the Studied Parameters.........................................................................................................................91
IV.14 Normal Distribution Testing of the Studied Parameters P-P plot.....................................................................................................................94
V. Correlations.................................................................................................103
V. 1. Relation between BMI and Paraclinical Parameters in the Patients in Group C and D.................................................................................103
V. 2. Relation between Leptin and Paraclinical Parameters in the Patients in Group C and D.................................................................................107
V. 3. Relation between Adiponectin and Paraclinical Parameters in the Patients in Group C and D.................................................................................111
V. 4. Relation between IGF 1 and Paraclinical Parameters in the Patients in Group C and D.................................................................................115
V.5. Relation between Testosteron and Paraclinical Parameters in the Patients in Group C and D.................................................................................118
V.6. Relation between Estrone and Paraclinical Parameters in the Patients in Group C and D.................................................................................121
V.7. Relation between Estradiol and and Paraclinical Parameters in the Patients in Group C and D.................................................................................123
V.8. Relation between Physical Activity and Paraclinical Parameters in the Patients in Group C and D.................................................................................125
V.9. Relation between Lumbar T-Score and and Paraclinical Parameters in the Patients in Group C and D.................................................................................130
V.10. Relation between Lumbar Z-Score and and Paraclinical Parameters in the Patients in Group C and D.................................................................................131
VI. Discussions......................................................................................................132
VII. Conclusions....................................................................................................144
VIII. New Perspectives Brought about by the Thesis......................................................145
REFERENCES.....................................................................................................146
ENCLOSURES......................................................................................................159
List of Published Papers Related to Different Thesis Topics......165
INTRODUCTION

Osteoporosis is a chronic disease of the skeletal system consisting of bone mass diminution and osseous tissue microarchitecture abnormalities, which lead to bone brittleness and fracture risks (agreement 1991). The clinical significance of osteoporosis is given by the fracture risk, which is higher in women than in men and which varied greatly from country to country. The World Health Organization (WHO) developed an algorithm which includes clinical fracture risk factors, by means of which it is possible to calculate the 10-year likelihood of a hip or other major bone fracture due to osteoporosis (vertebrae, hip, forearm, humerus). This algorithm is called FRAX and may be accessed on the Internet at the address http://www.shef.ac.uk/FRAX (Kanis A 2000).

In 1994, the World Health Organization (WHO) Expert Committee established a lucrative definition of osteoporosis based on bone mineral density (BMD) measured by DXA (Dual X Ray Absorbtmetry) and related to the young adult score (T score).

An increasingly higher number of data collected during the last few years have shown that in addition to BMD there are other factors playing a decisive role in fracture risk increase and outlining the concept of bone quality (Crabtree et al. 2002). Thus, recent osteoporosis definitions attempt to include the two separate notions, i.e. BMD and bone quality, in the general concept of bone strength (Siao-pin S, Boloșiu H 2004)

Osteoporosis is a matter of public health, as over 150 million people have been diagnosed with osteoporosis, of whom about 1.5 million in Romania alone, according to the International Osteoporosis Foundation’s (IOF) data. Hence, the interest for more thorough knowledge of the factors causing osteoporosis, as well as for determining the involvement of various hormonal factors, the positive or negative correlation between body weight, adipose tissue or muscle mass and bone mass.
As for the costs incurred for the treatment of a bone fracture due to osteoporosis, they are extremely high, which justifies the interest for the more thorough knowledge of the factors that may cause or prevent bone loss. The total care costs calculated only for hip fractures reach about 14.7 million Euros each year, whereas the total costs of the treatment of fractures occurred on osteoporotic bones exceed 25 billion Euros per year, in Europe alone. The total costs involved by fractures due to osteoporosis are thought to reach 31.8 billion Euros per year by 2025 (Fița 2009).

**Study Substantiation**

Knowing the factors that influence bone mass and determining bone mineral density is extremely important, as they help us prevent or treat osteoporosis in patients at risk and avoid the occurrence of a possible fracture and its aftermaths.

Over the last decades, osteoporosis has become a major public health concern, which has considerable repercussions on morbidity and mortality rates. Considering the extremely high osteoporosis treatment costs, the high osteoporosis incidence rates, the high mortality rates related especially to hip fractures, as well as the degradation of the life quality of people diagnosed with osteoporosis, we find it pertinent to try and detect the factors that may influence bone metabolism and determine how they can be modified so as to prevent or delay bone mass decrease.

According to literature, there are many studies focusing on the influence that adipose tissue has over bone metabolism, which revealed that obesity is considered to protect individuals from osteoporosis. Therefore, osteoporotic fractures are inversely correlated with the BMI. The bone protection effect of obesity may be accounted for by the mass effect, as gravitational stress stimulates bone formation (Leslie WD 2008). Adipocytes and osteoblasts have a common mesenchymal origin. Therefore, the connection between the adipose tissue and locomotor system could be more than a mere mechanical interference. The adipose tissue is a source of hormones that may influence bone metabolism (Breitling R 2009). Adipocytes can synthesize by aromatization estrogens from androgen precursors
(Dieudonné MN 2006), which may turn them into an important source of estrogens able to protect the bone mass of postmenopausal women (Vulpoi C 2002). Adipocytes secrete specific peptidic hormones called adipocytokines (Breitling R 2009). They act on their own receptors, with multiple locations and effects, which have been only partly elucidated.

Defining the influence of the various body compartments, lean body mass, adipose tissue mass on bone mass and turnover, as well as elucidating the relation between bone mass and hormone factors such as leptin and adiponectin, IGF-1, testosterone, estrone, estradiol, may have an impact on the discovery of new osteoporosis prevention and therapy solutions.

**Research Assumption**

Theoretical information provides us with important data on the multitude of factors influencing bone mass. The bone is a live and ever-changing tissue, which is essential for skeleton adjustment to mechanical loads. The bone remodeling process may be affected by various factors anytime during a person’s life, which changes the balance between bone forming and bone resorption. With age, bone lysis physiologically surpasses bone formation, leading to demineralization and hence to bone quality decrease and fracture risk increase, a phenomenon which is known under the name of osteoporosis (Seeman 2008).

**The research assumption** relies on the idea that body weight influences bone metabolism both directly, by gravitational stress, and by a hormone-modulated effect. We started this research assuming that if we analyzed the connection between body weight and BMD, and also among the various body compartments, fatty mass, lean mass, as well as the various hormonal factors correlated with lean and muscle mass or hormonal factors secreted by the adipose tissue, we would gather new information able to support bone mass preservation in specific populations and during specific life periods.
Study Objectives

This paper aims to analyze the effect of weight-related, body structure and associated hormonal factors involved in bone metabolism, as well as to prioritize them in age and body weight subgroups.

The main objective was to assess the predictive role of body weight on bone mass in the entire group of women and in the various age and weight groups, and to assess the predictive role of the various body compartments, lean mass versus adipose tissue mass, on bone mass and their relative importance on age groups.

Our secondary objectives were to analyze the connection between the adipose tissue mass and adipocytokines level, the predictive role on bone mass acquisition of the hormonal factors correlated with the lean and muscle mass - IGF1 and testosterone, as well as to determine the predictive role on bone mass acquisition of the hormonal factors correlated with the adipose tissue - estradiol, estrone, leptin, adiponectin.

Patients and Methods

This study comprises two parts. The first is a prospective study conducted on 112 menopausal patients hospitalized in the Endocrinology Clinic of Iași between January and December 2009 (menopause meant the final ceasing of the menses and of the whole set of neurovegetative phenomena accompanying the final ceasing of the ovarian function). The second part of the paper describes a prospective study which included 67 pre- and postmenopausal patients in whom additional investigations were performed. The research that was conducted and described here was part of a grant awarded further to a competition held at the “Grigore T. Popa” University of Medicine and Pharmacy of Iași, entitled “Influence of Body Weight and Structure on Bone Metabolism – a Direct or Hormone-Modulated Effect?” and managed by Dr. D. Brănișteanu. Premenopause is the period when the menstrual cycle is irregular, which precedes menopause onset. These irregular menstrual cycles
are accompanied by episodes of amenorrhea and various symptoms
due to the progressive disappearance of estrogen protection.

The first part of the study divided menopausal women in four
groups, depending on their lumber T score (calculated based on
osteodensitometry performed by Dual X Ray Absorbtionetry): group
A including 33 osteoporotic patients, group B including 79 patients
without osteoporosis, the latter being later subdivided in group B1
including 49 patients with osteopenia and group B2 including 30
patients with normal bone mineral density.

The second part of the study was conducted on 67 volunteers
divided into two large groups, group C comprising 31 premenopausal
women and group D including 37 postmenopausal women. These
groups were then subdivided, depending on BMI, into subgroup C1
(16 patients) with a BMI below or equal to 24.9 kg/m² and subgroup
C2 (15 patients) with a BMI over 25 kg/m². Postmenopausal women
were divided, in their turn, depending on BMI, in subgroup D1 (8
patients) with BMI < 24.9 kg/m² and subgroup D2 (16 patients) with
BMI over or equal to 25 kg/m².

Inclusion Criteria
The inclusion criteria in the first study were:
- postmenopausal women (over one year since menopause onset)
- women that had not been previously investigated by DXA
osteodensitometry
- Caucasians
The inclusion criteria in the second study were:
I - postmenopausal women (over one year since menopause onset)
   - Caucasians
II – premenopausal women without a history of osteoporosis
   - Caucasians

Exclusion Criteria
The exclusion criteria were the same both for the first part of the
study and for the second part of the study:
1. osteoporosis in therapy other than calcium and vitamin D, for a period longer than 5 years; the bone turnover parameters will be considered in the volunteers in therapy for a shorter period of time
2. recent severe bone injury
3. women in hormone replacement therapy
4. diseases that may influence bone turnover:
   - diabetes mellitus under medication
   - severe liver or kidney conditions
   - hyperthyroidism or a history of hyperthyroidism during postmenopause, iatrogenic hyperthyroidism, suppressive treatment in patients that had undergone surgery for thyroid cancer
   - primary hyperparathyroidism
   - inborn or acquired growth hormone deficit
   - hypogonadism for which substitution therapy was administered or not during childhood, in the absence of a spontaneous triggering of puberty
   - Cushing syndrome, corticoid therapy for more than one year
   - severe malabsorption or anorexia nervosa

Methods
Thorough anamnesis and a full clinical examination of the patients were performed.
Here are the parameters that were checked in each patient in the first study:
- age
- menopause onset age
- height (m), weight (kg), BMI (body mass index)(kg/m^2),
- bone mineral density (DXA, Hologic). DXA Hologic, model DELPHI (2002), soft 11.1 osteodensitometer handled by two experienced certified technicians, 5-minute whole body checkup. The bone mineral density values were expressed in relation to the values determined in significant groups of subjects, both women and men, of various ages and races: the Z score is the relation with the same age group, whereas the T score is the relation with the healthy young (30 years) individual values.
The osteoporosis diagnosis is defined as a T score below -2.5 DS (WHO, 1994). BMD in normal bone is over 1 DS, and osteopenia is diagnosed when BMD is between -1 DS and -2.5 DS. In our study, bone mineral density was measured in the lumber spine L1-L4.

The first study was a preliminary one, as its results lay the grounds of an extended research and a second study that also included premenopausal women. The volunteers were female patients who signed an informed consent.

**Investigation Protocol**

1 to 3 volunteers per day, from Monday to Friday, were enrolled in the study according to previous appointments. On their appointment day, the patients were subjected to a clinical examination, they were weighed using electronic scales, their weight being expressed in kilograms (kg), and they were measured using a height measuring device, their height being expressed in meters (m). Then 10 ml of blood were sampled on an empty stomach, the blood was centrifuged and the serum was stored at -30 degrees until its biological examination. After blood sampling, a DXA measuring was performed.

Here are the parameters investigated in each volunteer:
- body structure (DXA, Hologic)
  * mass of lean or adipose tissue (kg)
  * percentage of lean or adipose tissue %
  * the lean mass/fat mass ratio in the whole body, in the trunk or in the limbs
- BMD bone mineral density g/cm\(^2\)
- Z score (number of DS against the average BMD for the same sex and age for Caucasian mass)
- T score (number of DS against the average BMD at the age of 25 for the same sex and Caucasian race), in the entire skeleton, in vertebrae L1-L4

Hormonal investigations
Plasma **testosterone** dosing was done by ELISA (NovaTec Immundiagnostica GmbH, Dietzenbach, Germany) at a 4.6% intradetermination variation coefficient and a 7.5% interdetermination variation coefficient. The sensitivity level reached 0.075 ng/ml, normal values ranging from 0.2 to 1.2 ng/ml.

The amounts of **adiponectin and leptin** were determined by ELISA methods using high sensitivity Quantiquine kits (R&D System Inc., Minneapolis, MN, USA). The intra- and inter-determination variation coefficients of **adiponectin** (Quantiquine Human Total Adiponectin Immunoassay) were below 6.9%, with a sensitivity of 0.246 ng/ml and normal values ranging from 0.865 to 21.424 ng/ml.

The intra- and inter-determination variation coefficients of **leptin** (Quantiquine Human Total Leptin Immunoassay) were below 5.4%, with a sensitivity of 7.8 pg/ml and normal values ranging from 3.877 to 77.273 ng/ml.

Plasma **IGF-1** dosing was done by ELISA (Demeditec Diagnostics GmbH, Kiel, Germany), with intra- and inter-determination variation coefficients below 7.22%, with a sensitivity of 1.292 ng/ml and normal values ranging from 150 to 350 ng/ml.

Plasma estrone dosing was done by ELISA (NovaTec Immundiagnostica GmbH, Dietzenbach, Germany), with a 4.8% intradetermination variation coefficient and a 8.8% interdetermination variation coefficient. The sensitivity level reached 1pg/ml, normal values ranging from 25 to 350 pg/ml.

Plasma **estradiol** dosing was done by ELISA (NovaTec Immundiagnostica GmbH, Dietzenbach, Germany), with intra- and inter-determination variation coefficients below 10%. The sensitivity level reached 8.68 pg/ml, whereas normal menopausal values were considered to be below 60 pg/ml.

Physical activity was assessed by the filling out of a physical activity questionnaire translated into Romanian and validated (GP physical activity questionnaire) - http://www.patient.co.uk/showdoc/27001115/(Appendix no. 2). These questionnaires allow the patient a self-evaluation of the physical activity done at work, of
their walking speed and of the number of hours of physical activity done over a week.

The BMI was calculated as the ratio between weight (kg) and squared height (m²).

**Statistical Processing Methods**

The data were statistically processed using SPSS Statistics 17.0. The results of the assessments are expressed as a mean +/- DS or percent. The individual parameters of the various correspondent groups are compared depending on sex, age and weight, using the Student’s t-test or χ² test. The t-test is used to check the assumptions by relating them to normally distributed population means, when the theoretical dispersions are not known. The χ² test compares an observed distribution with a known theoretical distribution and detects the possible differences between them.

Statistical processing also included the analysis of the charts showing the frequency of the studied parameters and drew the normal distribution curve (histogram). The normal distribution of the studied parameters was also tested (P-P plot). Correlation is used to point out the relation between two characteristics or between two variables. The starting point is the assumption that this correlation is linear. The degree of association is measured by Pearson’s correlation coefficient, marked r, which took the name of the person that discovered it. The correlation coefficient is measured on a scale from +1 to -1. The complete correlation between two variables is marked +1 or -1. When one variable increases and the other increases too, the correlation is positive, whereas when one increases and the other decreases, the correlation is negative.

The first stage consists of the drawing of a chart designed to provide a visual representation of the spatial distribution of the two variables to study, whereas the second stage is the calculation of Pearson’s correlation coefficient, which provides the degree of association of the two variables. A correlation relation does not automatically mean a causality relation. The percentage in which a variable depends on another is measured by r².
We used Pearson’s simple correlation between various parameters taken two by two on groups or on the entire group. We used ANOVA multiple variable regression to exclude systematic distortions. Covariate relations between groups were compared by ANCOVA multiple covariate regression. The correlation of the various factors will be repeated after their correction by blocking the influence of other factors (hierarchical regression). The differences were considered significant when p < 0.05.

Results
Relation between the Various Parameters in the Patients in Group A and Group B

Further to the analysis of the relation between the patients’ age and various clinical and paraclinical parameters (Table B17), we found a significant negative correlation between age and BMI (r = -0.614, p = 0.044) and a negative yet insignificant correlation (r = -0.429, p = 0.189) between age and lumber T score in group A. On the other hand, the correlation between age and BMI is positive, yet insignificant (r = 0.004, p = 0.973), whereas the correlation between age and lumbar T score is negative and insignificant (r = -0.144, p = 0.206) in group B.

Table B17. Relation between Age and Various Parameters in Group A and Group B

<table>
<thead>
<tr>
<th>Age versus</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>-0.614</td>
<td>0.044</td>
</tr>
<tr>
<td>Group B</td>
<td>0.004</td>
<td>0.973</td>
</tr>
</tbody>
</table>
Instead, the analysis of the BMI and lumbar T score correlation (Table B18) revealed a negative and insignificant correlation in group A ($r = -0.175$, $p = 0.607$), and a positive and significant correlation in group B ($r = 0.329$, $p = 0.003$).

Table B18. Relation between BMI and lumbar T score in the patients in group A and group B

<table>
<thead>
<tr>
<th>BMI versus</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar T score group A</td>
<td>-0.175</td>
<td>0.607</td>
</tr>
<tr>
<td>Lumbar T score group B</td>
<td>0.329</td>
<td>0.003</td>
</tr>
</tbody>
</table>

The analysis of the BMI and lumbar T score correlation (Table B20) revealed a positive, yet insignificant correlation in both group B1($r = 0.181$, $p = 0.212$) and group B2($r = 0.345$, $p = 0.062$).

Table B20. Relation between BMI and lumbar T score in the patients in group B1 and group B2

<table>
<thead>
<tr>
<th>BMI versus</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar T score group B1</td>
<td>0.181</td>
<td>0.212</td>
</tr>
<tr>
<td>Lumbar T score group B2</td>
<td>0.345</td>
<td>0.062</td>
</tr>
</tbody>
</table>

The second study was conducted on pre- or postmenopausal volunteers in whom additional investigations were done and more parameters influencing bone mass were measured, like for instance lean mass, fat mass, adiponectin, leptin, IGF-1, testosterone, estrone, estradiol, physical activity.
The patients were divided:
- on age groups:
  - premenopausal
  - postmenopausal, over one year from menopause onset
- on weight groups:
  - normal weight – BMI below 25 kg/m²
  - overweight – BMI between 25 and 30 kg/m²
  - obese - BMI over 35 kg/m²

The groups of women are as follows:
- 16 premenopausal women with BMI below 25 kg/m²
- 9 premenopausal women with BMI between 25 and 30 kg/m²
- 6 premenopausal women with BMI over 30 kg/m²
- 8 postmenopausal women with BMI below 25 kg/m²
- 11 postmenopausal women with BMI between 25 and 30 kg/m²
- 15 postmenopausal women with BMI over 30 kg/m².

They are divided in group C, premenopausal women (31 women), and group D, postmenopausal women (34 women). In their turn, they were divided, depending on their BMI, in subgroup C1 under and normal weight (16 patients) and C2 overweight and obese (15 patients). Group D was in its turn divided, depending on their BMI, in subgroup D1 under and normal weight (8 patients) and D2 overweight and obese (26 patients).

Correlations

Relation between BMI and Paraclinical Parameters in Patients in Groups C and D
The analysis of the relation between BMI and various paraclinical parameters (Table B34) revealed a positive and strongly significant correlation between BMI and leptin both in group C ($r = 0.693$, $p = 0.000$ ) and in group D ($r = 0.704$, $p = 0.000$). The correlation is strong $r > 0.6$. The correlation between adiponectin and BMI is negative and significant both in group C ($r = -0.566$, $p = 0.003$) and in group D ($r = -0.479$, $p = 0.011$). The correlation is moderate. Testosterone has a poor significant correlation only in group C ($r = 0.371$, $p = 0.068$), whereas osteocalcin has a negative weakly significant correlation only in group D ($p = -0.383$, $p = 0.048$). Fat mass has a very strongly significant positive correlation both in group C ($r = 0.963$, $p = 0.000$) and in group D ($r = 0.934$, $p = 0.000$). Lean mass has the same very strongly significant positive correlations both in group C ($r = 0.830$, $p = 0.000$) and in group D ($r = 0.810$, $p = 0.000$)

The patients in group C exhibit a moderately significant positive correlation for BMD ($r = 0.460$, $p = 0.011$), lumbar T score ($r = 0.458$, $p = 0.009$), lumbar Z score ($r = 0.510$, $p = 0.003$), whereas the patients in group D exhibit a strongly significant positive correlation for BMD ($r = 0.631$, $p = 0.000$), lumbar T score ($r = 0.653$, $p = 0.000$) and lumbar Z score ($r = 0.632$, $p = 0.000$).

Table B34. Relation between BMI and paraclinical parameters in patients in groups C and D

<table>
<thead>
<tr>
<th>BMI versus</th>
<th>Group C</th>
<th></th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>$R^2$</td>
<td>$P$</td>
</tr>
<tr>
<td>Leptin</td>
<td>0.693</td>
<td>0.4804</td>
<td><strong>0.000</strong></td>
</tr>
<tr>
<td>Adiponectin</td>
<td>0.566</td>
<td>0.3198</td>
<td><strong>0.003</strong></td>
</tr>
<tr>
<td>IGF1</td>
<td>0.404</td>
<td>0.1636</td>
<td><strong>0.045</strong></td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.371</td>
<td>0.1378</td>
<td><strong>0.068</strong></td>
</tr>
<tr>
<td>Estrone</td>
<td>0.098</td>
<td>0.0097</td>
<td>0.640</td>
</tr>
<tr>
<td>Estradiol</td>
<td>0.386</td>
<td>0.1488</td>
<td>0.057</td>
</tr>
<tr>
<td>Osteocalcin</td>
<td>0.030</td>
<td>0.0009</td>
<td>0.885</td>
</tr>
<tr>
<td>Fat mass</td>
<td>0.963</td>
<td>0.9277</td>
<td><strong>0.000</strong></td>
</tr>
</tbody>
</table>
The Relation between Leptine and the Paraclinical Parameters for the Patients in groups C and D

Looking into the statistically significant differences between the two groups (Table B35), we noticed that there is a moderately significant positive correlation in group C, insignificant in group D ($r = 0.408$, $p = 0.043$).

Highly significant positive correlations can be found between leptine and fat mass both in lot C ($r = 0.811$, $p = 0.000$) and also strong correlations in group D ($r = 0.657$, $p = 0.000$). The correlation is strongly $p > 0.6$. Significant positive correlations are also recorded, there is a moderate correlation between leptine and the light mass both in group C ($r = 0.530$, $p = 0.000$) and strong in lot D ($r = 0.758$, $p = 0.000$). Highly significant positive correlations are recorded between leptine and T lumbar score for group D ($r = 0.685$, $p = 0.000$) the same highlyly significant positive correlation is recorded between leptine and Z lumbar score in group D ($r = 0.714$, $p = 0.000$).

Table B35. The relation between leptine and the paraclinical parameters in groups C and D

<table>
<thead>
<tr>
<th>Leptin versus</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$r$</td>
<td>$R^2$</td>
</tr>
<tr>
<td>Adiponectin</td>
<td>0.375</td>
<td>0.1410</td>
</tr>
<tr>
<td>IGF1</td>
<td>0.164</td>
<td>0.0269</td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.408</td>
<td>0.1665</td>
</tr>
<tr>
<td>Estrone</td>
<td>0.059</td>
<td>0.0035</td>
</tr>
<tr>
<td>Estradiol</td>
<td>0.342</td>
<td>0.1171</td>
</tr>
<tr>
<td>Fat mass</td>
<td>0.811</td>
<td>0.6583</td>
</tr>
<tr>
<td>Lean mass</td>
<td>0.530</td>
<td>0.2814</td>
</tr>
</tbody>
</table>
The Relation Between Adiponectine and Paraclinic Parameters in groups C and D

Comparing the relation between adiponectine and various paraclinic parameters in groups C and D (Table B36), we noticed that there is a moderately significant negative correlation between adiponectine and IGFI (r = -0.405, p = 0.045), between estadiol and adiponectine (r = -0.402, p = 0.046), and highly significant negative correlations between T lumbar score and adiponectine (r = -0.727, p = 0.000), and also for the lumbar score Z and adiponectine (r = -0.705, p = 0.000) in lot C and not in lot D. Only the fat and light mass are correlated both in groups C and D, the correlation being negative, highly significant for the fat mass in lot C (r = -0.623, p = 0.001) and in lot D (r = -0.553, p = 0.003), and for the light mass the correlation is highly significant negative for group C (r = -0.611, p = 0.001) and negative correlation of little significance for group D (r = -0.389, p = 0.045).

Table B36. The relation between adiponectine and the paraclinic parameters for the patients in groups C and D

<table>
<thead>
<tr>
<th>Adiponectine versus</th>
<th>Group C</th>
<th></th>
<th></th>
<th>Group D</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>R²</td>
<td>p</td>
<td>r</td>
<td>R²</td>
<td>p</td>
</tr>
<tr>
<td>IGF1</td>
<td>0.405</td>
<td>0.1637</td>
<td>0.045</td>
<td>0.239</td>
<td>0.0571</td>
<td>0.230</td>
</tr>
<tr>
<td>Testosterone</td>
<td>0.350</td>
<td>0.1222</td>
<td>0.087</td>
<td>0.144</td>
<td>0.0208</td>
<td>0.473</td>
</tr>
<tr>
<td>Estrone</td>
<td>0.081</td>
<td>0.0066</td>
<td>0.699</td>
<td>0.144</td>
<td>0.0208</td>
<td>0.473</td>
</tr>
<tr>
<td>Estradiol</td>
<td>0.402</td>
<td>0.1615</td>
<td>0.046</td>
<td>-0.142</td>
<td>0.0202</td>
<td>0.480</td>
</tr>
<tr>
<td>Fat mass</td>
<td>0.623</td>
<td>0.3886</td>
<td>0.001</td>
<td>0.553</td>
<td>0.3054</td>
<td>0.003</td>
</tr>
<tr>
<td>Lean mass</td>
<td>0.611</td>
<td>0.3736</td>
<td><strong>0.001</strong></td>
<td>0.389</td>
<td>0.1511</td>
<td><strong>0.045</strong></td>
</tr>
<tr>
<td>-----------</td>
<td>--------</td>
<td>--------</td>
<td>-----------</td>
<td>--------</td>
<td>--------</td>
<td>-----------</td>
</tr>
<tr>
<td>BMD</td>
<td>0.732</td>
<td>0.5353</td>
<td><strong>0.000</strong></td>
<td>0.340</td>
<td>0.1159</td>
<td>0.079</td>
</tr>
<tr>
<td>T score</td>
<td>-0.727</td>
<td>0.5291</td>
<td><strong>0.000</strong></td>
<td>0.342</td>
<td>0.1171</td>
<td>0.081</td>
</tr>
<tr>
<td>Z score</td>
<td>0.705</td>
<td>0.4971</td>
<td><strong>0.000</strong></td>
<td>0.260</td>
<td>0.0678</td>
<td>0.190</td>
</tr>
</tbody>
</table>

**The Relation between IGF 1 and the Paraclinical Parameters for the Patients in the C and D groups**

Looking into the relation between IGF1 and the various paraclinical parameters in groups C and D, we noticed there are correlations only in lot C, a highly significant positive correlation with estradiol (r = 0.605, p = 0.001), and moderately significant positive correlations between IGF1 and fat mass (p = 0.411, p = 0.041) for the C lot, between IGF1 and the light mass (r = 0.505, p = 0.010), between IGF1 and T lumbar score (r = 0.437, p = 0.029), between IGF1 and Z lumbar score (r = 0.431, p = 0.032).

**The Relation between Testosterone and the Paraclinical Parameters for the Patients in Lots C and D**

Looking into the relation between testosterone and various paraclinical parameters in lots C and D (Table B38), we noticed that there is moderately significant positive correlations between testosterone and estrone in lot D (r = 0.552, p = 0.003), as well as between testosterone and estradiol, highly significant positive correlations both in lot C (r = 0.686, p = 0.000) and in lot D(r = 0.639, p = 0.000). There is a moderately significant positive correlation (r = 0.448 , p = 0.025) between testosterone and fat mass only in lot C.

**The Relation between Estrone and the Paraclinical Parameters for the Patients in Lots C and D**

Comparing estrone with various parameters in lots C and D, we noticed that there is a highly significant positive correlation (r = 0.689, p = 0.000) only between estrone and estradiol and this occurs only in lot D.
The Relation between Estradiol and the Paraclinic Parameters for the Patients in Lots C and D

Concerning the relation between estradiol and various parameters in lots C and D, we noticed that there is a moderately significant positive correlation between estradiol and the light mass \((r = 0.469, p = 0.018)\) only in lot C.

The Relation between Physical Activity and the Paraclinic Parameters for the Patients in Lots C and D

We have looked into the relation between physical activity and the various parameters in lots C and D and we have noticed that there is a moderately significant negative correlation between physical activity and leptine \((r = -0.526, p = 0.007)\) only for lot C. There is also a slightly significant negative correlation between physical activity and fat mass, though this occurs only in lot D \((r = -0.339, p = 0.050)\).

The Relation between Lumbar Score and the Paraclinic Parameters for the Patients in Lots C and D

We have looked into the relation between lumbar score, fat mass \((r = 0.463, p = 0.009)\) and lumbar score and light mass \((r = 0.630, p = 0.000)\) for the pre-menopausal women, and also the lumbar score, fat mass \((r = 0.643, p = 0.000)\) and lumbar score light mass \((r = 0.746, p = 0.000)\) for the post-menopausal ones, and we noticed that there is a significant positive correlation (Table B42). The correlation is moderate between the fat mass and lumbar score for lot C and high in the other 3 cases.

Table B42. The relation between T lumbar score and the fat mass / light mass for the patients in lots C and D

<table>
<thead>
<tr>
<th>T score versus</th>
<th>Lot C</th>
<th>Lot D</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(r)</td>
<td>(R^2)</td>
</tr>
<tr>
<td>Fat mass</td>
<td>0.463</td>
<td>0.2144</td>
</tr>
</tbody>
</table>
The Relation between Z Lumbar Score and the Paraclinical Parameters for the Patients in Lots C and D

We have noticed that there is also a significant positive correlation between the Z lumbar score and the fat mass in both lot C ($r = 0.491$, $p = 0.005$), and lot D ($r = 0.607$, $p = 0.000$), as well as between Z lumbar score and the light mass both in lot C ($r = 0.680$, $p = 0.000$), and in lot D ($r = 0.734$, $p = 0.000$). If the correlation between score Z and the fat mass in lot C is moderate, in the other 3 cases it is highly significant.

Discussions

The osseous mineral content is strongly influenced by menopause and estrogen depletion. The trabecular bone is characterized by an increased turnover, the vertebrae being the first bones where mineral loss becomes significant after menopause (Genant, Jiang 2006, Gong et al 1996). The untreated postmenopausal women lose approximately 5 percent of their osseous mineral content in the first 3 years after menopause (Gong et al 1996).

In the last years many clinical studies have been published, and they show the connection between the osseus mass, body composition and hormone parameters. The conclusions are that body weight has an important predictive effect upon osseous mass.

Reid has studied the relation between the adipose tissue and the bone. Thus, the author shows in his paper that body weight impacts both upon osseous turnover and upon osseous density, being a major hazard factor for the vertebral and hip fractures. Body weight impacts osseous mineral density both through the fat and light mass. The fat mass acts through several mechanisms, once through the skeletal pressure it exerts, then through the association with the secretion of active hormones per bone by the beta pancreatic cells.
like insulin, amylin, as well as the estrogen and leptine secretion by the adipocytes.

Weight and the body mass index are positive predictive factors of the osseous mass for adults, suggesting the idea that the overweight or obese persons might face a lower hazard of osteoporosis, while other studies hold that low body mass is an independent hazard factor for osteoporosis with the pre- and postmenopausal women (Guerrini et al 2008).

However, recent studies suggest that for children and teenagers, obesity is associated with lower osseous mass than for people of normal weight (Wang et al 2005).

Other authors suggest that the body mass influences the osseous mineral content (Gueguen et al 1995).

The obese postmenopausal women have an average of lumbar mineral osseous density which overlaps that of premenopausal women. The osteoporosis hazard for the postmenopausal women seems to be lower in the case of high body weight (Guerrini et al 2008).

At present, the way in which various compartments of the body influence osseous mass is less clear, sometimes the results of various studies being conflicting. The data in medical literature demonstrate that light mass is a better prediction factor for osseous mass than fat mass and total body weight both with the pre- and postmenopausal women. Other authors describe light mass as being more predictive in the case of women than in the case of men (Jankowska et al 2001, Jee et al 2011).

A higher muscular mass correlated with the physical activity will favour the acquisition of osseous mass for young persons (Jiang et al 2007, Jurimae et al 2006). Muscular mass does not depend only upon physical activity but also upon the hormones like IGF1 and testosterone, which impact the bone in a direct way (Jurimae et al 2007, Harris et al 1999).

Data regarding the adipose tissue and the bone are even more conflicting; certain authors suggest that fat mass seems to be more important for the prediction of osseous mass, especially in the case of postmenopausal women (Heiss et al 1995). This effect may be
mediated by adipocitokine (Herzog 2003) or by the extragonadal estrogenic reservoir represented by the adipocites (Himms-Hagen et al 1999).

Adipocites and osteoblasts share mesenchymal origins. The adipose tissue is an important hormone reservoir which influences osseous metabolism (Christian et al 1989, Clifford 2011, Cooper et al 1992). These hormones have specific receptors located in various tissues and multiple effects which are partially unaccounted for. The adipocite can synthesize estrogens through aromatisation out of androgenic precursors, and it can be an important estrogenic source in protecting the osseous mass of the postmenopausal women (Brănișteanu et al 2002).

The adipocite secretes specific peptide hormones called adipocitokines (Breiting 2009).

Leptine influences food behaviour through central mechanisms via the hypothalamic connections (Elefteriou et al 2005). Leptine is now considered to be a mediating factor between adipocites and the osseous metabolism (Huang et al 2001, Hutano et al 2009). Leptine receptors have been described on the osteoblasts, but in vitro and in vivo their effects upon metabolism are multiple and frequently antagonistic (Chikayu et al 2001).

It has been demonstrated that leptine stimulates osseous formation through direct mechanism, but it inhibits the process of recruiting the osteoclastic precursors (Farooqi, O Rahilly 2009, Filip et al 2009). However, the central effect of leptine through the stimulation of the sympathetetic nervous system causes osseous demineralization in animal patterns (Elefteriou et al 2005).

The effect of leptine upon the bone is complicated, but the central stimulating role on the somatotropic axis and the inhibition of neuropeptide Y stimulates the accumulation of osseous mass. The pleiotropic effects exerted by leptine upon the bone may be partially explained by the clinical studies (Fitzpatrick et al 2012).

Certain effects of leptine become more important in moments which are critical for the bone like puberty or after the menopause (Jankowska et al 2001, Jee et al 2011)
The benefic effects of leptine upon the bone have been described in various studies (Herzog 2003, Himms-Hagen 1999), thus while some found close connections with fat mass, others have shown that leptine normalised at fat mass unit would not have a direct impact upon the bone or there may be even negative correlations (Dieudonne et al 2006).

In vitro and for animal patterns, adinopectine seems to have direct effects mediated by the receptors located in the osteoblast, thus determining the rise of osseous turnover, the osteoclastic activity prevailing, possibly associated with the loss of osseous mass (Chikazu et al 2001). The effects noticed in vitro have been confirmed by some clinical studies (Farooqi 2009).

FRAX, the WHO instrument for calculating the fracture hazard has not been used because it had not been validated for Romania when we undertook this study. On the other hand, the patients who enrolled for the second study answered a questionnaire where they mentioned what kind of physical activity their work implies, what their walking pace is, how many hours of physical activity they had performed in the last week. Depending on the answer given, the patients were classified into inactive, moderately active and active persons.

This study is structured in two parts. The first part is a comparative analysis of the paraclinical characteristics for two lots of women in their postmenopausal period, some suffering from osteoporosis lot A and others not suffering from it lot B, subclassified in sublot B1 suffering from osteopenia and sublot B2 with normal mineral density.

It has been noticed that the patients suffering from osteoporosis are older than those with normal MOD (63 vs 56.8 years old), the group over 65 years of age being the best represented, approximately 45.4%.

The patients not suffering from osteoporosis have a higher BMI (30.13 kg/m2 versus 25.25 kg/m2). The time interval since the menopause started seems not to have influenced MOD, since there are no significant differences between the inception of menopause
for the patients suffering from osteoporosis and those with normal MOD (50.7 versus 47.09 years old).

It has been noticed that looking only into BMI and the patient’s age or the time interval since menopause started will not account for the reason why some patients develop osteoporosis while others do not, the patients suffering from osteoporosis having a lower BMI in comparison with those with normal MOD, but at the same time the time interval since menopause started was lower for the patients in group A compared to those in group B.

Starting from these data, supplementary investigations have been made to assess leptine, adiponectine, IGF 1, estrone, estradiol, testosterone, fat mass, light mass, T lumbar score, Z lumbar score for a lot of premenopausal women lot C (31 patients), subclassified according to BMI into under-weight and normal weight lot C1 (16 patients) and lot C2 overweight and obese (15 patients) and a lot of 34 postmenopausal women lot D, classified according to BMI in lot D1 of 8 women under-weight and normal weight and lot D2 of 26 women overweight and obese.

We started from the premise that, analysing the interrelations among various hormones, their relation with the fat mass, light mass, T lumbar score or Z lumbar score, we could find out new data about the factors involved in the decrease of osseous mineral density, this allowing us to influence its evolution.

**BMI**

Weight and the body mass index are positive predictive factors of osseous mass for adults, and this implies that the overweight or obese persons might run a lower risk of developing osteoporosis. However, recent studies suggest that for children and adolescents, obesity is associated with lower osseous mass than with the normal weight persons (Wand at al 2005).

Looking into the whole groups of volunteers, we noticed that BMI is positively correlated with BMD, T score and Z lumbar score. The best correlation was reached for the Z score because this parameter excluded the influence of age upon the bone. For the entire group of women there is a positive correlation between BMD and BMI ($r^2 = 0.1458$), there is also a positive correlation between the T
score and BMI ($r^2 = 0.1487$). In lot D it can be noticed that the obese postmenopausal, IMC over 30 Kg/m$^2$, have a lumbar MOD which is significantly higher than the normal weight ones and comparable with MOD for premenopausal women (lot C). Postmenopausal women with BMI $<25$ kg/ m$^2$ (lot D1) had a significantly lower MOD than that of the premenopausal women irrespective of weight ($p < 0.05$).

Analysisng the relation between BMI and various paraclinic parameters, it has been noticed that there is a highly significant positive correlation between BMI and leptine both in lot C ($r = 0.693$, $p = 0.000$) and D ($r = 0.704$, $p = 0.000$). There is a significant negative correlation between adiponectine and BMI both in lot C ($r = -0.566$, $p = 0.003$) and in lot D ($r = -0.479$, $p = 0.011$). The correlation is moderate. Testosterone is a slightly significant correlation only for lot C ($r = 0.371$, $p = 0.068$). Fat mass displays a highly significant positive correlation both for lot C ($r = 0.830$, $p = 0.000$) and for lot D ($r = 0.810$, $p = 0.000$).

For the patients in lot C there is a moderately significant positive correlation for BMD ($r = 0.460$, $p = 0.011$), T lumbar score ($r = 0.458$, $p = 0.009$), Z lumbar score ($r = 0.510$, $p = 0.003$), as well as for lot D, but here there is a highly significant positive correlation for BMD ($r = 0.631$, $p = 0.000$), for T lumbar score ($r = 0.653$, $p = 0.000$) and for Z lumbar score ($r = 0.632$, $p = 0.000$).

In a way similar with the data in medical literature (Schoenau E, Fricke O 2008) BMI is positively correlated with MOD, the overweight or obese patients having a higher MOD than the underweight or normal weight ones, irrespective of their menopausal status. BMI is positively correlated both with the fat mass and with the light mass, in accordance with the data in medical literature (Leslie WD 2008) which show that both fat mass and a well represented light mass have a protecting effect upon MOD.

**Leptine**

Leptine is the first identified hormone secreted by the adipocites, it is an aminoacid with 146 proteins which acts mainly as
a factor of signalling the adipose tissue towards the central nervous system, regulating the food quantity and energetic consumption.

Leptine, either through the fat cells or through the osteoblasts, determines the inhibition of osteoclasts by the stimulation of anti-osteoclastogenic factors. It makes the osteoblastic cells synthesize IGF1 and TGF β which in their turn stimulate the osteoprogenitor cells, stimulating the mineralization of the osseous matrix, thus preventing the apoptotic suicide of osteoblasts and osteoclasts (Thomas et al 1999).

Di Carlo et al achieved a longitudinal observation of the seric level of leptine and the mineral osseous density for women in their postmenopausal period; they conclude that there is a correlation between the leptine level and BMD in the immediate postmenopause period, this correlation diminishing along with the women’s continuing postmenopause, no matter if the therapy of hormone substitution is given or not (Di Carlo et al 2006). Other studies hold that leptine might be correlated with fat mass and might not have a direct osseous impact (Di Carlo et al 2007) or even a negative osseous impact has been noticed after the fat mass was weighed (Jiang et al 2007).

Di Carlo and his team undertook a longitudinal assessment of the seric level of leptine and the osseous mineral density for women in their postmenopausal period. They also assessed the total BMD at specific levels and determined the seric level of leptine for postmenopausal women who had been given calcium supplements, while others had been given hormone therapy of substitution. 44 women were included, 22 received calcium supplements and were classified into group A, and 22 received a transdermal treatment of 50 mg of 17 beta estradiol per day and progesterone 5 mg per day, 12 days a month in a sequential pattern, group B. For all women, BMD was determined when the study commenced and 12 months after. After 12 months, the level of leptine was significantly higher for group A than for group B, while BMD was lower for group A in comparison with group B. A significant correlation was found between the level of leptine, BMI and total BMD at the study inception. After 12 months leptine was
correlated with BMI in both groups, but the correlation with BMD disappeared. This study confirms that there is a correlation between the level of leptine and BMD in the period of immediate postmenopause, this correlation diminishing during the postmenopause period, no matter if the hormone substitution therapy was given or not (Di Carlo et al 2007).

At the same time, Jiang and his collaborators looked into the possibility of any relation between leptine, osseous mineral density and fat mass for men. They included in their study 350 Chinese men aged between 20 and 80. It has been noticed that leptine is correlated with fat mass, \((R(2) = 0.448, p < 0.001)\), is correlated with BMD at multiple skeletal levels, \(R(2) = 0.115\) for BMD at the level of the spine before, \(R(2) = 0.102\) for BMD at the level of the spine laterally and \(R(2) = 0.098\) at the level of the thigh-bone neck, but it is not a predictive factor of osseous mineral density for the Chinese men (Jiang et al 2007).

Various results, which had been a priori contradictory, were accounted for considering the multiple antagonistic effects of leptine upon osseous mass (Martin et al 2007).

Martine and his collaborators studied the opposite effects of leptine upon the osseous mineral density. They noticed that leptine may have either a negative or a positive effect upon the bone, depending on the leptine level. They made two study groups on rats, which were treated with two different doses of leptine. The group which received small doses of leptine managed to prevent the decrease of osseous mass, both at the level of the trabecular and cortical bone. The osseous mineral density was measured through three dimensional microtomography. In the other group, which was given high doses of leptine, the inhibition of osseous increase and the decrease of osseous mass were noticed, and this was due to the decrease of osseous formation and increase of resorption, one of the mechanisms seems to be the decrease of abdominal fat mass and level of IGF-1 (Martin et al 2007).

In our study, we established a positive correlation between the serum leptin and the Z lumbar score \((r^2 = 0.3642)\) in the entire
group of women, but also a positive correlation between leptin and the adipose tissue mass ($r^2 = 0.3894$).

When the leptin was normalized at the adipose tissue mass, the quantity of leptin secreted on the fat mass unit was positively correlated to the Z score ($r^2 = 0.226$), suggesting that leptin could have an additional effect on the osseous mass and it is more than a reflection of the fat mass.

Subsequently, we monitored the leptin according to the pre- or post-menopause status, in group C, respectively in group D. The average values are 7.72 +/-9.35 ng/ml with values between 0.90 and 32 ng/ml in group C as compared to 16.37 +/-29.5 ng/ml in group D, with values between 0.30 and 153.8 ng/ml. The patients belonging to the group C2 have higher leptin levels as compared to the patients from group C1, the differences being significant from a statistic point of view ($p = 0.001$); similarly, the patients belonging to group D2 have higher levels than the ones from group D1 (20.19+/-33.49ng/ml versus 5.49+/-6.39 ng/ml). Besides the significant positive correlation between leptin and BMI, both in group C and D, we noticed that there are very significant positive correlations between leptin and the fat mass for group C ($r = 0.811$, $p = 0.000$), and strong correlations for group D ($r = 0.657$, $p = 0.000$). Moreover, there are significant positive correlations, moderated between leptin and the fatless mass for group C ($r = 0.530$, $p = 0.000$), and strong for group D ($r = 0.758$, $p = 0.000$). There are very significant positive correlations between leptin and T lumbar score for D ($r =0.685$, $p = 0.000$), the same very significant positive correlation existing in group D too ($r =0.714$, $p = 0.000$).

As a conclusion, we noticed higher leptin levels in overweight and obese women, as compared to the under- or normal weight ones. In our study, leptin values are correlated not only to the BMI, but also to the fat mass and to the fatless mass and the very significant positive correlation with T score shows its protective effect on the bone.

**Adiponectin**

26
Adiponectin is a polypeptide hormone with molecular weight of 30 KDa, secreted by adipocytes, with antiatherogenics, anti-inflammatory, cardio-protective effect and with a role in regulating the sensitivity to insulin. Adipocytes and osteoblasts have common origins in the mesoderm; Berner and his colleagues proved the transcription, translation and secretion of adiponectin in vitro by the human osteoblasts. The same team proved the existence of adiponectin expression in the mandible in rats. Adipokines seem to be correlated to the visceral adipose tissue, while the leptin increases if it is positively correlated to the visceral adipose tissue, adiponectin decreased once with the reduction of the ratio between visceral adiposity and the subcutaneous adipose tissue (Breitlin 2009, Lenchik et al. 2008, Ungur-Altun, Altun 2007), adiponectin seems to have in vitro direct effects on the osteoblast, increasing the osseous turnover, possibly associated to the loss of osseous mass and inhibiting the osteoclastogenesis (Luo et al. 2006).

The studies in literature are multiple and contradictory, adiponectin being correlated to the increase of the osseous turnover and the decrease of the osseous mass (Jurimae, Jurimae 2007, Richards et al. 2007). Adiponectin was correlated with the increase of the osseous turnover and the decrease of the osseous mass (Jurimae et al. 2007, Richards et al. 2007).

The association between the serum level of adiponectin and the osseous mineral density was treated in several studies. Therefore, Richards and his collaborators studied the correlation between adiponectin level and BMD in non-diabetic women. They started from the idea that there is a positive association between BMD and body weight, which maintains also at skeleton levels which are not subject to a mechanical pressure, suggesting that a non-mechanical factor, such as the hormones secreted by adipocytes can control the BMD. We included in the study 1735 women, aged between 18 and 81 years old, the average age being of 50 years old. We used linear regression methods, in order to explain the relationship between adiponectin and the BMD. Using the analysis adjusted to the age, serum level of adiponectin was associated to an average decrease of -
2.7% of the BMD, at femoral neck level -3.1%, at lumbar column level -2.6%, at hip level total score -3.2%

After an adjustment of the potential factors which can influence the BMD, inclusively the BMI, leptin, fat mass, hormonal substitution therapy, smoking, physical exercise, the relationship persists, still with a more diminished magnitude. The relationship between BMD and adiponectin persists in post-menopause, but it disappears in pre-menopause.

Another study was carried out by Jaak and Toivo Jurimae and it aimed at monitoring the plasmatic concentration of adiponectin in 153 healthy women in pre- and post-menopause. The adiponectin concentration at the level of the entire group of women was of $12.2 \pm 6.3$ ng/ml and was positively correlated to the age, $p < 0.05$. Complementarily, a negative association was noticed between adiponectin and central obesity, mineral density and leptin. The multiple regression analyses show that only the leptin and the age can be considered as predictors of adiponectin concentration.

In other articles, we consider that adiponectin level would not have a direct causality with the osseous mass.

Kontogianni et all. studied if adiponectin and leptin can be possible mediators of the relationship between the fat mass and the BMD in women in peri-menopause. The study included 80 healthy women, 25 in pre-menopause, 55 in post-menopause, between 42 and 68 years old. We measured the osseous mineral density at the level of the lumbar column and the body mass. Adiponectin was not significantly correlated neither to the BMD nor to the body mass, while leptin was negatively correlated to the lumbar BMD (Kontogianni et all. 2004).

In our paper, the average values of adiponectin were similar in the two groups of patients, C and D (15.89 ± 5.67 ng/ml versus 15.16 ± 6.29 ng/ml). Following comparatively the average values in normal weight women in post-menopause (group D1) and those of the overweight or obese women (group D2), we noticed that there are significant statistic differences with higher average values in group D1 ($p 0.005$). In concordance with the literature, the persons with
high BMI have a smaller adiponectin value as compared to the women with normal BMI, influencing therefore the osseous mass. Comparing the average values of the normal weight patients in pre-menopause (group C1) and those of the overweight and obese women (group C2), we noticed that there are significant differences with regard to the average values of adiponectin, with higher average values in group C1 (p = 0.031). Comparing the relationship between adiponectin and different para-clinical parameters of groups C and D, we noticed the presence of a moderately significant negative correlation between adiponectin and IGF1 (r = -0.405, p = 0.045), between oestradiol and adiponectin (r = -0.402, p = 0.046) and very significant negative correlations between the T lumbar score and adiponectin (r = -0.727, p = 0.000), but also between Z lumbar score and adiponectin (r = -0.705, p = 0.000) for group C, but not for group D. Only the fat mass and the fatless mass are correlated both for group C and for group D, the correlation being negative and very significant for the fat mass for group C (r = -0.623, p = 0.001) and for group D (r = -0.553, p = 0.003); for the fatless mass the correlation is negative and very significant for group C (r = -0.611, p = 0.001) and negative and slightly significant for group D (r = -0.389, p = 0.045).

As a conclusion, adiponectin in our study is negatively correlated to the DMO only in pre-menopause, but not in post-menopause, is negatively correlated to the fatless mass, but also to the fat mass. In accordance with the literature, we noticed a negative correlation between adiponectin and the osseous mass, mentioning that in literature the correlation between adiponectin and BMD does not depend on the menopause (Jurimae J, Jurimae T 2007).

**IGF 1**

Insulin-like growth factor I (IGF-I) is a polypeptide hormone, its structure being similar to the proinsulin and insulin, causing insulin-like effects; it is synthesized mainly in the liver, but also in other tissues, under the influence of the growth hormone (hGH).

A low level of IGF 1 is considered as predictive for a reduced osseous mass and osteoporosis (Liu et all.2008). Supporting this
statement, the study carried out by Liu et al. followed the IGF-1 effect on the osseous mineral density in women at pre- and post-menopause. Besides IGF-1 level, osteoprotegerin, leptin, osteocalcin, they also determined the urinary excretion of terminal N telopeptide of type I collagen (NTx) and they studied if they can be used as markers of osteopenia or osteoporosis in women at pre- or post-menopause. Therefore, they included 282 apparently healthy women at pre-menopause and 222 women at post-menopause, between 20 and 75 years old, for whom they examined the BMD at the level of the lumbar column, of the femoral neck, measured by X-rays double absorptiometry. We noticed that IGF-1 and leptin change the first, both markers decreasing in a significant manner p 0.0001 or respectively increasing p 0.020 reported to the age. In post-menopause women, the decrease of the osseous mass is correlated to the low level of IGF-1 and low fatless mass. As a conclusion, the authors suggest that the serum level of IGF-1 in young women can help to the early identification of the risk of developing the osseous mass loss and the osteoporosis risk (Liu et al.2008).

Other authors noticed the disappearance of the correlation between the osseous mass and IGF 1 when its value was reported to the adipose tissue mass and respectively to the fatless mass (Jurimae et al.2006). Jaak and Toiovo Jurimae carried out a study where they followed the influence of IGF-1 and leptin on the osseous mineral density in pre-menopause women. Therefore, they enrolled 204 women, apparently healthy, aged between 18 and 49 years old, having a BMI under 30 kg/m^2. They noticed that leptin is significantly associated to BMC (β = 0.840, p = 0.0001), to the total osseous mineral density (β = 0.833, p = 0.0001), to BMD at the level of the femoral neck (β = 0.829, p = 0.0001) and backbone BMD (β = 0.833, p = 0.0001). IGF-1 is significantly correlated to the BMC (β = 0.920, p = 0.0001), total BMD (β = 0.918, p = 0.0001), BMD at the level of the femoral neck (β = 0.921, p = 0.0001), and of the lumbar column BMD (β = 0.917, p = 0.0001), but it is not significantly correlated when it is adjusted to the total fat (p>0.062). We found a significant association between leptin and IGF-1 (β = 0.801, p =
0.0001) and it remains significant after reporting it to the age, fat mass, but not when it was reported to BMC. To sum up, it seems like IGF-1 and leptin have no direct effect on BMC and BMD (Jurimae et al. 2006).

Therefore, notwithstanding the conflict results, we think that each study brought a correct piece of information; parameters connected to the body composition and to the adipose tissue can have a different importance in the acquisition, maintenance or loss of osseous mass in certain population categories and in certain life periods.

In our study, in group C, IGF 1 has average values of 21.8 +/- 7.75 ng/ml, and in group D of 17.9 +/- 7.96 ng/ml, knowing that the secretion of IGF-1 decreases with the age. Monitoring the relationship between the IGF1 and different para-clinical parameters in groups C and D, we noticed that there are correlations only in group C, a very significant positive correlation with oestradiol (r = 0.605, p = 0.001) and moderately significant positive correlations between IGF1 and the fat mass (p = 0.411, p = 0.041), between IGF1 and the fatless mass (r = 0.505, p = 0.010), between IGF1 and T lumbar score (r = 0.437, p =0.029), between IGF1 and Z lumbar score (r = 0.431, p = 0.032). Therefore, in accordance with the literature, we proved that there is a positive correlation with the fatless mass, with leptin, with T lumbar score and with Z lumbar score, in our study being a positive correlation with the fat mass too, these correlations existing only in pre-menopause women.

We proved that IGF1 level is positively correlated to the osseous mass, aspect which partially explains the correlation between the fatless mass, source of IGF1 synthesis and osseous mass.

**Sexual hormones**

As regards the influence of the hormonal factors, there are articles which show that the serum levels of estrogens, and of testosterone (Sun et al. 2003, Filip, Rasyewski 2009) are positively correlated to the osseous mass regardless of sex and age. Sun et al. carried out a study which aimed at monitoring the association between the osseous mineral density and the sexual hormones in
adults. In this study, they measured the sex hormone binding globuline SHBG, leptin, DHEAS dehydroepiandrosterone sulfate and insulin in 50 apparently healthy men, aged between 18 and 66 years old. The osseous mineral density was positively correlated to the oestradiol (p = 0.007). There is no significant correlation between BMD and SHBG, DHEAS or insulin. In the multiple regression analyses of BMD with the age, BMI, oestradiol, testosterone and leptin as variables, only the age (p < 0.05), the BMI (p < 0.001) and leptin (p = 0.004) were significantly correlated to the BMD (Sun et all. 2003).

Another study carried out by Filip and Raszewski was performed in order to show the existence of different correlations between leptin, oestradiol, testosterone, DHEA-S, SHBG, markers of the osseous turnover and BMD in post-menopause overweight and obese women. The study included 80 apparently healthy post-menopause Caucasian women, BMD being studied at the level of the L2-L4 lumbar column and at the level of the femoral neck. The data were analyzed by multiple regression. BMD at the level of the femoral neck was positively correlated to the weight (r = 0.52, p < 0.000001), to the body mass index BMI (r = 0.48, p < 0.000006), hips circumference (r = 0.48, p < 0.000006), waist circumference (r = 0.45, p < 0.00002) and DHEA-S (r = 0.36, p < 0.00008). There is no correlation between oestradiol, SHBG, testosterone, leptin, the markers of the osseous turnover and BMD at the level of the lumbar column L2-L4 and of the femoral neck. In the entire group, a significant predictor of the BMD at lumbar level L2-L4 was the BMI (β = 0.39, p < 0.01), the testosterone (β = 0.27, p < 0.05) and the osteocalcin (β =0.22, p < 0.05, R(2) = 0.23), while the predictor of BMD at the level of the femoral neck was the BMI (β = 0.42, p < 0.001), the testosterone (β = 0.24, p < 0.05), the oestradiol (β = 0.19, p < 0.05) and the osteocalcin (β =0.20, p < 0.05, R(2) = 0.41). In the subgroup with BMI 30-39,9 kg/m$^2$, a significant predictor of the BMD at the level of the lumbar column L2-L4 and of the femoral neck was the testosterone (β =0.32, p < 0.05, R(2) = 0.19) and respectively (β = 0.33, p < 0.05, R(2) =
0.29) and the osteocalcin (β = 0.34, p < 0.05, R(2) = 0.19 and respectively β = 0.45, p < 0.01, R(2) = 0.29). In the subgroup with WHR smaller or equal to 0.85, the predictor of the BMD at L2-L4 level was the oestradiol (β =0.38, p < 0.05, R(2) = 0.21), while the predictor of BMD at the level of the femoral neck was the BMI (β = 0.29, p < 0.05) and the testosterone (β = 0.3, p < 0.01, R(2)=0.36). Therefore, they say that the testosterone is a predictor of the BMD at the level of the lumbar column in post-menopause overweight and obese women, while for the BMD at the level of the lumbar neck, both the testosterone and the estrogens are positive prediction factors (Filip et all. 2009).

In 2000, Barrett-Connor et al. conducted a study on postmenopausal women and also men, in whom they analyzed the correlation between fractures and plasma levels of total and bioavailable estradiol, total and bioavailable testosterone, estrone, androstenedione, dihydrotestosterone and dehydroepiandrosterone. We noticed that high levels of total and bioavailable estradiol were associated with a low fracture prevalence, whereas individuals with low estradiol levels exhibited a higher rate of vertebral fracture occurrence, which suggests that, starting with a certain level, estrogens would have a protective role on BMD during postmenopause (Barrett-Connor).

**Testosterone**

The analysis of the relation between testosterone and various paraclinical parameters in groups C and D (Table B33) revealed moderately significant positive correlations between testosterone and estrone (figure B106) in group D( r = 0.552, p = 0.003), as well as between testosterone and estradiol (figure B107), strongly significant positive correlations in group C (r = 0.686, p = 0.000) and in group D (r = 0.639, p = 0.000). The correlations between testosterone and estradiol and estrone are normal, considering the aromatization process occurring in the adipose tissue. A moderately significant positive correlation is established between testosterone and fatty mass (r = 0.448, p = 0.025) (figure B109) only in group C.
Testosterone acts on the bone both directly and indirectly, further to bone aromatization in estrogens (Damien et al. 1998). Although there are suggestive data in literature of the positive correlation between androgens and bone mass in women (Dawson-Huges et al. 1997), we found no such correlation in the studied group.

**Estradiol**

As concerns the relation between estradiol and various parameters in groups C and D, we noted a moderately significant positive correlation between estradiol and lean mass ($r = 0.469$, $p = 0.018$) only in group C.

**Estrone**

By comparing estrone with various parameters in groups C and D, we noticed a strongly significant positive correlation ($r = 0.689$, $p = 0.000$) only between estrone and estradiol and only in group D.

In the group we studied, we found that neither estradiol, an estrogen secreted mainly by the ovaries, nor estrone, an estrogen produced additionally by androgenic aromatization in the adipose tissue, is correlated with the bone mass measured in the lumbar area of premenopausal and postmenopausal women, which suggests that the role presumably played by the adipose tissue, that of additional estrogenic reservoir during postmenopause, is insignificant in the preservation of an adequate bone mass. This lack of correlation may be also accounted for by the fact that estrogens influence the quality of the bone rather than BMD. The bone quality could not be determined since this would have required bone biopsies.

**Fat mass**

Concerning the relationship between the fat mass and the bone, multiple evidences support the idea that the fat mass, as a component of body weight, has benefic effects in bone mass growth and in the reduction of the risk of osteoporosis (Kholsla and associates, 1996, Gnudi and associates 2007). In pre and post menopausal women, the total fat mass is positively correlated to the bone mineral density of the entire skeleton structure (Reid and
associates 1992, Reid and associates 1992, Salomone and associates 1995). A longitudinal study shows that any modifications in the bone mineral density are positively correlated to the changes in fat mass, thus the EPIC (Moayyeri, 2012) study has shown that persons presenting a rapid loss in bone mass also possess a lower fat mass, than the persons who present a slower rate of loss in bone mass. By contrast, a few independent groups suggest that fat mass in excess does not protect a person against the decrease in bone mass (De Laet 2005). Multiple studies took on proving the direct correlation fat mass - bone. That special interest in highlighting the various correlations between fat mass and bone is triggered by the multitude of correlations between osteoporosis and obesity, both being influenced by genetic and environmental factors, by the fact that the incidence of osteoporosis increases with age, yet also that of obesity, the bone remodeling and adiposity being regulated by hypothalamic means, also by the sympatric nervous system, last yet not least it should be reminded that both the adipocytes and the osteoblasts have a common progenitor consisting in the mesenchymal stem cells.

The WHO experts have studied 4489 persons, in different weight categories, of normal BMI weight, between 18,5 şi 25 kg/m², overweight of BMI between 25 and 30 kg/m², and obese, of BMI over 30kg/m². On a cohort of 153 pre-menopausal women, the increased fat mass was negatively associated with the bone mass. A few evidences show that environmental factors may determine inverse correlations between the bone mass and the fat mass. Consuming tea or milk seems to have an effect in preventing both osteoporosis and obesity. A high milk consumption was proven to have a role in increasing the top of bone mass gain in those at the age of puberty, of slowing down bone loss and in the reduction of the incidence of osteoporosis in the elderly (Zemel 2004).

Administering a hormone substitution therapy in post-menopausal women alleviate the loss in bone mass, yet also that of lean mass. Studies have been carried out that proved the relationship between the abdomen's circumference and the hip circumference (WHR) and that of the fat abdominal mass measured through CT or
MRI, and it was noticed that there is a positive and significant correlation with the bone mass (Heiss and associates 1995). Jankowska and associates, however, have reported that in Polish men the WHT is in inverse proportion to bone mass (Jankowska and associates 2001), and also Huang and others have proven that an increased visceral mass is associated with the reduction in BMD in HIV infected men (Huang and associates 2001). Other studies carried out on healthy children show that there is a negative correlation between the bone mass and the abdominal subcutaneous tissue (Afghani, Goran 2006). These conflicting results suggest that the fat mass exerts complex influence upon the bone mass, the correlations being influenced by sex, ethnicity, the study configuration, and the methods of analysis.

A cross study undertaken by Hsu and collaborators on 7137 men, 4585 pre-menopausal women and 2248 post-menopausal women, concluded that the fat mass was a risk factor for Chinese men and women (Hsu and associates, 2006).

Another study carried out on 68 pre-menopausal Caucasian women and on 51 Caucasian men, shows that the BMD is positively correlated to fat mass in pre-menopausal women, yet not in men (Reid and associates, 1992).

The study undertaken by Pluijm and others confirm the positive effects of fat mass upon the BMD in white women, yet not in men, a study carried out on 264 pre-menopausal women and on 258 men (Pluijm and collaborators, 2001). Castro and others report that increased obesity is associated with an elevated BMD in white women, yet with a significantly lower BMD in black women (Castro and collaborators, 2005).

Afghani and Goran report an inverse correlation between the cutaneous abdominal adipose tissue and the BMC in the white race, yet not in the black race as well, and it also reports an inverse association between the intra-abdominal adipose tissue and the BMC in the black race, yet not in the white race (Afghani, Goran 2006). These differences prove that the results obtained on certain ethnic groups cannot be transferred to other ethnic groups, and that studies
on large groups have the ability of detecting associations that may not be detected on small groups.

Reid and others suggested the idea that physical exercise may dissociate the relationship between fat mass and BMD. They found a positive association between fat mass and BMD in sedentary women, yet not in those who were exercising regularly (Reid and collaborators, 1995).

The effect of fat mass on the bone may also be affected during the growth process. A longitudinal study on twin females, aged between 8 and 26, indicates that during the period of linear growth, the 4 year post-menarcheal period, the BMD at the lumbar spine level, that of the total hip and that of the femoral collar are irrespective of the fat mass. Subsequent to that 4 year period, it was noticed that the changes in fat mass exert an influence upon the mineral bone density (Young and collaborators, 2001).

Wearing and his collaborators advocate the idea that the relationship between obesity and the risk of fracture is age-related. The increased adiposity is deemed related to an increased risk of distal fracture in children, yet it seems to defend against hip and fist fracture in the elderly (Wearing and collaborators, 2006).

Concerning the relationship between extreme obesity and mineral density, there were studies that claim that when fat mass is in excess, there may appear a negative correlation between fat mass and bone mineral density.

Thus, Nunez and others performed a study by which they claim that extreme obesity diminishes bone mineral density. They determined mineral bone density in female mice in both the presence and the absence of ovarian hormones and also on post-menopausal women. Also, the percentage of fat mass and the DMO (BMD) were measured in both the ovariectomized and in the non-ovariectomized female mice that had been on a hyper-caloric diet to evolve from slim to extremely obese. Additionally, the percentage of fat mass and the bone mineral density in 37 overweight and extremely obese post-menopausal women was also determined. In mice, the increased levels of adiposity of over 40% of body mass was associated with a low DMO in C57BL/6 ovariectomized female mice. The same
association was noticed in extremely obese post-menopausal females. Thus, extreme obesity of over 40kg/m$^2$ is conducive to the risk of osteoporosis and osteopenia incidence (Nunez and collaborators, 2007).

It is well known that that the obesity by an increased estrogen level also increases the BMD, therefore the authors of this study monitored the leptin in obese mice and in extremely obese menopausal women and suggests that the dramatic increase in leptin levels would influence bone mass.

Other authors assert that once the fat mass is expressed in percentage of the overall body mass, the predictive effect over the bone has dissipated altogether (Jiang and collaborators 2007, Loretzon and collaborators, 2006), or became negative (Hsu and collaborators 2006, Huang and collaborators 2001).

The fat mass presents a positive and very powerfully significant correlation with the BMI, both for the C lot (r = 0.963, p = 0.000), and for the D lot (r = 0.934, p = 0.000), with leptin both for the C lot (r = 0.811, p = 0.000), and for the D lot (r = 0.657, p = 0.000), with adiponectina, the correlation is powerfully significant negative for the fat mass on the C lot (r = -0.623, p = 0.001) and on the D lot (r = -0.553, p = 0.003), with an IGF1 (p = 0.411, p = 0.041) and with testosterone (r = -0.448, p = 0.025) in lot C. We noted that between the T lumbar score and the fat mass there exists a significantly positive correlation in both pre-menopause (r = 0.463, p = 0.009), and post-menopause (r = 0.643, p = 0.000), as well as between the Z lumbar score and the fat mass in lot C (r = 0.491, p = 0.005), and in lot D (r = 0.607, p = 0.000). Therefore, in our study, the fat mass is positively correlated with the DMO, with the leptin and with the adiponectina, in both pre-menopause and post-menopause, data that is similar to that found in literature (Reid and collaborators 1992, Reid and collaborators 1992, Salomone and collaborators 1995).

Lean mass
There are studies in specialized literature in which authors claim that the lean mass would be predictive for the bone mass in pre- (Wang and collaborators, 2005) and post-menopausal (Sahin and collaborators, 2003), as well as in men regardless of age (Loretzon and collaborators, 2007, Peng and collaborators, 2008, Douchi and collaborators, 2003). There was a study carried out in the US by Wang and his collaborators, that examined 921 young women between the age of 20 and 25, of various ethnic groups, 317 out of which were African American women, 154 Asian, 322 Caucasian and 128 Latin American. The lean mass, the fat mass, and the mineral bone density were determined employing the DEXA method, by means of a Lunar osteodensitometer. There has been determined that the lean mass and the fat mass were positively correlated with the bone mineral density in all skeleton sites. In the case where the contribution of the fat mass and that of the lean mass were simultaneously examined, it was determined that these had a positive effect on the bone mass, yet it was noticed that the effect of the fat mass was much lower than the positive effect of the lean mass. In post-menopausal women, the adipose tissue mass would be more important in predicting the bone mass, whereas in pre-menopausal women the lean mass would predict the bone mass (Wang and collaborators, 2005). Other authors claim that the lean mass would be predictive of the bone mass in pre and post menopausal women (Sahin, 2003) as well as in men, regardless of age (Lorentzon and collaborators, 2006, Peng and collaborators, 2008).

Sahin and his collaborators monitored the body composition, the bone mineral density and the circulating leptin levels in Turkish post-menopausal women, also monitoring which of the lean mass and the fat mass are best in predicting the bone mass. Within the study there were included 100 post-menopausal women of the age between 55.1 ± 6.3 years. There were monitored the bone mineral density at the lumbar spine and at the hip level, the body composition, the lean mass, the fat mass, the fat mass percentage, employing X-ray double absorptiometry. The conclusions of the study were that the lean mass was positively correlated with the bone
mineral density in all monitored sites \((r = 0.339 \text{ and } p = 0.00, r = 0.312 \text{ and } p = 0.01, r = 0.523 \text{ and } p = 0.00, r = 0.636 \text{ and } p = 0.00)\), being a much more important predictor for the BMD than the fat mass (Sahin and collaborators, 2003).

Multiple studies were undertaken regarding the lean mass - bone mass correlation in men, of which we will mention only two, one carried out on Chinese men and the other on young Swedish males.

Peng and his collaborators studied 232 Chinese men aged between 20 and 80 and they examined, beside various correlations between adiponectin, resistine, leptin and bone, the lean mass prediction regarding the bone mineral density. The conclusions of the study were that the lean mass was an important factor in predicting the BMD (Peng and collaborators, 2008).

Another major study was undertaken by Lorentzon and his collaborators, who monitored 1068 Swedish men between the ages of 18 and 20, in which they measured the mineral bone density at the hip spine level, as well as the fat mass-lean mass body composition. The overall lean mass was 37.4% versus the fat mass, of only 8.7%. It was perceived that the lean mass exerts a greater impact over the mineral bone density than the fat mass (Lorentzon 2006). When the adipose tissue mass was compared to the total mass, its predictive quality over the bone mass all but disappeared (Yhao and collaborators, 2008) or turned negative (Nunez and collaborators, 2007).

There are significant positive correlations in regard to the lean mass and the BMI as well, for both the C lot \((r = 0.830, p = 0.000)\), and for the D lot \((r = 0.810, p = 0.000)\), between leptin and lean mass, for both the C lot \((r = 0.530, p = 0.000)\), and for the D lot \((r = 0.758, p = 0.000)\). Regarding the adiponectin, the correlation is significantly negative for the C lot \((r = -0.611, p = 0.001)\), as well as for the D lot \((r = -0.389, p = 0.045)\).

Between the IGF1 and the lean mass the correlation is positive and significant \((r = 0.505, p = 0.010)\) for the C lot alone. There exists significant positive correlation between the T lumbar score and the lean mass \((r = 0.630, p = 0.000)\) in pre-menopausal
women, as well as in post-menopausal women ($r = 0.746$, $p = 0.000$), as well as between the Z lumbar score and the lean mass in both the C lot ($r = 0.680$, $p = 0.000$), and the D lot ($r = 0.734$, $p = 0.000$).

Similar to the data in literature (Sahin, 2003), the lean mass is correlated with the DMO in both pre-menopausal and post-menopausal women.

**Physical exercise**

Reid and others suggested the idea that physical exercise might dissociate the relationship between the fat mass and the BMD. They found a positive association between the fat mass and the BMD in sedentary women, yet not in those who were exercising regularly (Reid and collaborators, 1995). Another study undertaken on post-menopausal, both sedentary women and women who exercised, it was noted that the lean mass was correlated to the BMD in those women who exercised regularly (Douchi and collaborators, 2003).

A recent study, also monitored, beside the BMD, the bone mineral content, and the bone geometry at the femoral collar level, observing an increase in femoral strength, especially through bone addition at the femoral cortical surface level (Beck and collaborators, 2011).

By monitoring the relationship between physical exercise and the various parameters from within the C and D lots it was established that there was a moderately significant negative correlation between physical exercise and leptin ($r = -0.526$, $p = 0.007$) on the C lot alone. There's also a weakly significant negative correlation between physical exercise and the fat mass on the D lot alone ($r = -0.339$, $p = 0.050$)(fig. B140). Let it be mentioned, however, that the intensity and the regularity of physical exercised wasn't monitored here at all.

In concordance with data from literature, we found no positive association between physical activity and the DMO, yet we noticed that physical exercise decreased fat mass, especially in post-menopausal women. Throughout the study, however, we didn't have the chance of evaluating the effect of physical exercise on bone resistance.
Conclusions

1. The bone mass is correlated to body weight in Caucasian women, both pre and post menopausal, mainly probably through a direct mass effect, caused by gravitational stress. The increased body mass prevents losing bone mass in post-menopausal women.

2. The various body compartments influence bone mass gain in different ways, including through mass-effect independent mechanisms. Thus, the lean mass tissue acquires a more important predictive role over the bone mass than the adipose tissue mass, or the overall body weight. The lean mass is the best predictor of mineral bone content, regardless of age, weight, or pre-post menopausal status.

3. The adipose tissue may influence the bone structure through its mass, contributing by a mass effect in gaining greater weight, that would consecutively lead to greater bone mass, yet also by its adipokines secretory profile.

4. Leptin is a positive prediction factor for the bone mass in post-menopausal women, regardless of the fat mass $r^2 = 0.596$ or the body weight $r^2 = 0.620$. The bone mineral density is positively correlated with fat mass unit normalized leptin $r^2 = 0.226$.

5. In concordance with literature data, adiponectin is a negative prediction factor of bone mass in pre-menopause alone, significant correlations in post-menopause being non-existent, implying the existence of more complex mechanisms that influence post-menopausal bone mineral density.

6. The apparently paradoxical lack of correlation between sexoid hormones and bone mass could be explained by the fact that, for acquiring a protective role, estrogens would have to exceed a certain level.

7. The important predictive role of lean tissue mass over the bone mass may be explained by a hormonal profile propitious for the collagen matrix development, such as a higher level of IGF1. In our study, the IGF1 correlates positively to the bone mass in pre-menopause women alone, suggesting that the IGF-1 serum level in
younger women may help identify the loss in bone mass and the incidence of osteoporosis in a timely fashion.

8. In concordance with the data found in literature, we did not identify positive associations between physical exercise and the DMO, yet we noticed that physical activity helps decrease the fat mass, especially in post-menopause women.

9. To conclude, the maintaining of an acceptable level of bone mass throughout the post-menopausal period is crucially influenced by the pre-menopausal gains in bone mass, the latter depending on weight, lean mass, the levels of IGF1, and leptin as positive factors, yet also on adiponectin as possible negative prognostic factor.

**Present thesis future outlook**

Osteoporosis represents a serious public health issue, in Romania alone the number of osteoporosis patients being of approx. 1.5 million (IOF), which determined the interest in studying the factors that cause osteoporosis.

The purpose of this study is that of determining the implications that various hormonal factors have upon mineral bone density, the either positive or negative correlation of body weight, adipose tissue or muscular mass with bone mass.

Through complex statistical analysis, studying each marker in both individuals and in correlation to others, we established that mineral bone density is influenced by multiple factors, correlations being extremely complex. Thus it is established that a great body mass is positively correlated to DMO, and we demonstrated that both the fat mass and the lean mass exert a positive effect on the bone mass, the lean tissue mass playing a far more important predictive role than the adipose tissue.

We also proved that certain hormones, such as IGF 1, leptin, adiponectin, influence bone mass in either a positive or a negative fashion.

The data extracted from our study represent sufficiently strong arguments for monitoring osteoporosis patients, attempting to
correct the factors that may cause either gain or preservation of bone mass.

The positive effects of leptin over the bone, proven in both our study and in specialized literature, opens new therapeutic prospects that suggest that one day probably leptin would be used in curing osteoporosis.

Besides, we should stress upon physical exercise that diminishes the risk of fracture, by both improving muscular strength and the reduction in the risk of falling in elderly, as well as increasing bone resistance.

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