Analysis of body composition performed by bioimpedance in obese patients with hypertension

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GRADUATION PAPER

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Contents

Abstract

Introduction Prevalence of obesity and hypertension is increasing worldwide. Obesity and hypertension share many pathophysiological links and cardiovascular outcomes.

Aim The aim of this thesis is to establish the difference in body composition between obese people with and without hypertension

Patients and methods Data of 40 obese patients (body mass index – BMI >30 kg/ m^2) were obtained retrospectively from Department of Endocrinology and Diabetology, Internal Medicine Clinic, University Hospital Centre Zagreb. Patients were divided in two groups; with hypertension (Group 1, 7 men and 13 women) and without hypertension (Group 2, 5 men and 15 women). Secondary causes of obesity were excluded. Control group were healthy non-obese normotensive individuals (Group 3, 6 men and 8 women). Body composition was estimated by bioelectrical impedance analysis (fat percentage, fat mass, muscle mass and visceral fat rating).

Results Comparison of non-obese participants form Group 3 with obese ones from Group 1 and 2 showed that all of parameters of body composition estimated by bioelectrical impedance differ significantly. There was a positive correlation between BMI and fat mass in Group 1 and Group 2 ($r=0.91$ and $r=0.80$ respectively), but obese patients with hypertension had significantly more fat mass ($p=0.01$) and fat percentage ($p= 0.02$) than those without hypertension. Male obese hypertensive patients had more fat mass was found in than females.

Conclusion Obese patients with and without hypertension have different body composition than non-obese normotensive individuals. Obese patients with hypertension have significantly more fat mass which is more prominent in males. Those finding confirm the fact that fat tissue produces bioactive molecules that promote development of obesity-associated hypertension.

Keywords: body composition, bioimpedance, obesity, hypertension

Sažetak

Uvod Prevalencija pretilosti i hipertenzije je sve veća. Pretilost i hipertenzija dijele mnoge patofiziološke poveznice i imaju iste posljedice srčanožilnih bolesti.

Cilj Cilj je utvrditi razliku sastava tijela između pretilih osoba s hipertenzijom i bez nje.

Ispitanici i metode Retrospektivno su analizirani podaci 40 pretilih bolesnika (indeks tjelesne mase - ITM>30 kg/m^2) praćenih na Zavodu za endokrinologiju i dijabetologiju, Klinike interne medicine, Kliničkog bolničkog centra Zagreb. Bolesnici su podijeljeni u dvije skupine; na one s hipertenzijom (Grupa 1, 7 muškaraca i 13 žena) i bez hipertenzije (Grupa 2, 5 muškaraca i 15 žena). Sekundarni uzroci pretilosti su isključeni. Kontrolnu skupinu činili su normotenzivni ispitanici uredne tjelesne mase (Grupa 3, 6 muškaraca i 8 žena). Sastav tijela procijenjen je bioelektričnom impedancijom (udio masti, masa masti, masa mišića i visceralna masnoća).

Rezultati Usporedba ispitanika normalne tjelesne mase iz Grupe 3 s pretilima iz Grupe 1 i 2 pokazala je da se svi parametri sastava tijela procijenjeni bioelektričnom impedancijom statistički značajno razlikuju. Nađena je pozitivna korelacija između ITM-a i mase masti u Grupi 1 i Grupi 2 ($r = 0,91$ i $r = 0,80$), no pretili bolesnici s hipertenzijom imali su značajno višu masu tjelesne masti ($p = 0,01$) i udio masti ($p = 0,02$) od onih bez hipertenzije. U muških pretilih bolesnika s hipertenzijom bilo je više tjelesnih masti nego kod žena.

Zaključak Pretili bolesnici s i bez hipertenzije imaju drugačiji tjelesni sastav od normotenzivnih osoba koje nisu pretile. Pretili bolesnici s hipertenzijom imaju znatno veću masu tjelesne masti koja je izraženija kod muškaraca. Ti nalazi potvrđuju činjenicu da masno tkivo proizvodi bioaktivne molekule koje potiču razvoj hipertenzije povezane s pretilošću.

Keywords: kompozicija tijela, bioimpedancija, pretilost, hipertenzija

Abbreviations

WHO World Health organization

ESH European society for hypertension

ESC European society for cardiology

EASO European Association for the Study of Obesity

RAAS Renin-angiotensin-aldosterone system

SNS Sympathetic nervous system

DEXA Dual-energy X-ray absorptiometry

OGTT Oral glucose tolerance test

TSH Thyroid-stimulating hormone

BM Total body mass

BH Total body height

BMI Body mass index

ANOVA Analysis of variance

SD Standard deviation

1 Introduction

Obesity and hypertension are one of the most widespread noncommunicable diseases whose impact on the society and health has greatly increased in last few decades. Even though previously known as the diseases of the developed societies, these diseases are nowadays present in all population structures and inflict both economically developed and undeveloped countries.

Obesity is defined as excessive accumulation of the body fat. It is a consequence of unusually high imbalance between energy intake and expenditure. Worldwide epidemic of obesity is currently on the rise. In little over 30 years obesity has been increased worldwide by 28%. Rough estimates indicate that there are around 700 million people in the world who are obese. (1) Current situation is getting worse due to fact that all the diseases associated with the obesity are getting more and more prevalent. This is particularly true for multiple cardiovascular diseases which are the leading cause of mortality worldwide (2,3). Hypertension is one of the leading worldwide causes of mortality and morbidity. Hypertension has a known association with the obesity. Obesity and hypertension lead to higher rates of mortality and morbidity than normal-weight normotensive individuals. The relationship between hypertension and obesity is multifactorial; the etiology is complex and it is not well elucidated.

The aim of this thesis is to explore differences in body composition analyzed by bioelectrical impedance analysis between obese patients with and without hypertension and compare the results with healthy non-obese normotensive individuals.

1.2 Obesity

World Health organization (WHO) defined obesity as a state of abnormal and excessive accumulation of fatty tissue in the organism which presents a risk to health. Normal percentage of fatty tissue in females is 20-25% and in males is 15-20% of BM (4). Obesity in females is considered having more than 25% of fatty tissue while in males the cut off value is slightly lower at 20%. It is usually measured through body mass index (BMI), a measure based on individuals height and weight that applies to adult men and women calculated as weight (kg)/height (m^2) and is usually expressed in units of kg/m^2. Even though there are more reliable and precise methods such as bioimpedance, calculation BMI is still the predominant one in general usage (5).

1.2.1 Classification of obesity

There are several different classifications and definitions for obesity, however the most accepted classification is the one from the WHO and it is based on BMI. Current WHO guidelines define normal/healthy BMI in range of 18.5-24.9 kg/m² (6). Everything above 25 kg/m² is considered to be overweight. Obesity is defined as with BMI above 30 kg/m^2 (grade 1 obesity 30-35 kg/m^2, grade 2 obesity 35-40 kg/m^2 and grade 3 as severe or morbid obesity with BMI greater than 40 kg/m^2). Taking into account the location of excess fatty tissue obesity can be divided into the central and peripheral one. In the central type of obesity, also known as an abdominal obesity occurs when there is excessive accumulation of the abdominal fat in the area around the stomach and abdomen to an extent which has a negative impact on health. This type of obesity is associated with significant number of different metabolic and cardiovascular diseases due to excessive amount of the metabolically active adipose tissue located in the visceral part of the abdomen (7). Peripheral or gynoid type of obesity is characterized by accumulation of fatty tissue in lower part of the body, particularly in the gluteal and thigh region. Overall regional division of fatty tissue is determined by gender as well as genetics while it is mediated by the hormones. In females predominates gluteal, gynoid or female type of obesity in which fatty tissue is accumulated in the lower part of the body on the gluteal and thing region (i.e. pear shape) (8). In the male population predominant type is the abdominal obesity with the fatty tissue predominantly accumulated in the abdomen (i.e. apple shape). Moreover, obesity can be divided on the basis of the size and number of fat cells into hypertrophic and hyperplastic obesity. Hypertrophic type is defined by increased overall volume of fatty tissue cells, while hyperplastic is defined by increased number of fatty tissue cells. The waist-hip ratio or waist-to-hip ratio is the ratio of the circumference of the waist to that of the hips. This is calculated as waist measurement divided by hip measurement with

normal values 0.9 or less in men and 0.85 or less for women and is also an indicator of central type of obesity.

1.2.2 Epidemiology of obesity

According to the last data from WHO more than 1.9 billion adults are obese or overweight, of which 650 million are obese. Considering gender differences there is female to male predominance of obesity (11% males and 15 % females) although this data is not universally the same. Worldwide prevalence of obesity nearly tripled between 1975 and 2016. (9). A decade ago, obesity was predominately problem of rich industrial countries whose population has availability of large amounts of relatively cheap, accessible and high caloric food. Nowadays obesity is found even in the undeveloped countries in which predominates diet is rich in fats (10). The worldwide epidemic of obesity has been reported in few but not all regions. The highest noted rate of obesity has been reported in the Pacific Islands while the lowest rates have been reported in Asia. The rates in North American are generally high, while the rates in Africa and Middle Eastern countries are variable (11). In Europe more than half of adult population) is overweight or obese, 51.6% of which 15.9% are obese. In Croatia 57.4% of adults are suffering from being overweight or obese, of which 18.7% are obese (20.8 are male and 16.8% are female) (12).

1.2.3 Pathophysiology and etiology of obesity

As it is the case with other chronic noncommunicable diseases, obesity is a result of a complex interaction between different environmental influences and genetic predisposition to weight gain. Recent research has identified several major single-genes whose effects over time are resulting in severe and early-onset obesity as well as multitude of minor genes with more variable effects on weight, fat distribution and age of onset and severity of obesity (13). However, currently known major and minor genes provide explanation for only a small portion of body weight variations in the population. It is believed that 32 most common genetic variations are responsible for only 1.45% of BMI variations (14). The role of genetics in obesity can't be underestimated in the development of obesity, but its relatively small influence on BMI and dramatic increase in obesity prevalence in last century implies that the environmental, behavioral, psychosocial and cultural factors probably play more important role in the development of the obesity. Obesity appears when the energy intake is too great or energy expenditure is small (or in the worst cases both). All this excess energy is stored in the form of triglycerides in adipose tissue. The primary role of adipocytes is to store excess energy when calories are in excess and to mobilize energy from this triglycerides reservoir when needed (15). Weight gain during adulthood is characterized by hypertrophy of adipocytes. From evolutionary standpoint this previous necessary adaptation for survival is now arguably producing more problems than it solves. Moreover, adipocytes are also active from endocrine point of view secreting different hormones (e.g. leptin) and growth factors (e.g. insulin growth factor 1) that regulate metabolism through feedback mechanism. It is believed that the storage function of adipocytes protects body from fatty acid toxicity. In obese patients with excessive concentration of fatty acids in blood stream there is relatively significant increase in the oxidative stress throughout the body. This mechanism is

particularly stimulated by enhanced sympathetic state which exists in obesity and results in enhanced lipolysis. Fatty acids and their metabolites crate oxidative stress in endoplasmic reticulum and mitochondria both in adipose and non-adipose tissue. This mechanism is active in pathology of liver and pancreas amongst others (16). The excess of fatty acids in blood stream also inhibits lipogenesis and prevents satisfactory clearance of sodium triglycerides levels which then contributes to hypertriglyceridemia preventing adequate clearance of serum triglycerides.

The physiological mechanism in maintaining normal body weight is a complex system composed of central and peripheral systems. Central part is composed of hypothalamus in which the center for hunger is located. There different signals from periphery and brain cortex are unified, processed and sent back in coordinated fashion. Peripheral part is composed of already mentioned adipocytes, digestive system, endocrine system and sympathetic nervous system. Together they form a harmonious unit which informs hypothalamus about the fat content, eating, type of ingested food and many others (17). The main change in recent human history resulted in change in behavior from outgoing individual who actively spends energy to highly sedentary individual. In addition to this change suddenly abundance of relatively cheap, high caloric food has flooded the marked resulting in ever increasing intake of calories per individual on population level.

1.3 Hypertension

Hypertension according to the guidelines of European society for hypertension (ESH) and European society for cardiology (ESC) is defined as chronic illness characterized by permanently increased value of systolic ≥ 140 mmHg and diastolic blood pressure ≥ 90 mmHg (18). It is one of the leading causes of mortality worldwide and one of the major risk factors for stroke, myocardial infarction, heart failure, kidney disease, peripheral vascular disease, cognitive decline and premature death.

1.3.1 Classification of hypertension

Hypertension can be divided into two main types; in 95% of cases the background of hypertension is multi factorial; it is called primary or essential hypertension. It is likely to be consequence of hereditary, environmental and genetic factors (19). In other 5 - 10% of cases it is secondary hypertension; a hypertension with an identifiable underlying primary cause (including endocrine diseases, kidney diseases, side effect of a medication e.t.c).

1.3.2 Epidemiology of hypertension

Worldwide hypertension is estimated to result with 7.5 million deaths, which represents about 12.8% of total deaths. Prevalence of hypertension in adults older than 25 was around 40%. Since 1980 the proportion of world population with hypertension is on decrease, but due to population growth and aging the overall number of people with hypertension rose from 600 million to more than 1 billion (20). Hypertension affects individuals across all income groups. Data show that people in low- and middle-income countries have on average double the mortality risk due to hypertension (21). According to the data from „Croatian Health Statistics Yearbook 2017“ hypertension was identified as the 10th leading cause of death in Croatia resulting in 924 death (1.7%) (22).

1.3.3 Pathophysiology of hypertension

A number of different physiological mechanism play role in maintenance of normotension. Pathology of those complex mechanisms is assumed as a cause of primary hypertension, which is the most common one. Pathognomonic factors responsible for primary hypertension have been extensively studied; those are excess sodium, obesity, the renin-angiotensin-aldosterone system (RAAS) alterations, the stress and sympathetic nervous system (SNS) overactivity, genetics and insulin resistance. Excess sodium intake results with hypertension by increasing intravascular volume and by doing so increases preload and cardiac output. Excess salt intake also influences vascular reactivity and renal function. Data suggest that only a part of the population is susceptible, probably because of different renal defects in sodium excretion (23). It is assumed that renin plays a major role in the pathogenesis of hypertension. In some cases, low renin levels are responsible for hypertension, but in majority of cases hypertension is caused by “inappropriately” normal or

even elevated plasma renin activity levels. Excess of aldosterone mediates most its effect by interaction with the SNS. On the other hand, stress may be activated SNS which will increase vascular constriction and result with hypertension (24). Few different genes and genetic factors have been associated with the development of the primary hypertension. Therefore, it is quite difficult to precisely evaluate relative significance of each of those genes. However available data states that hypertension is twice as common in subjects whose one or both parents suffered from hypertension. Furthermore, epidemiological studies suggest that genetic factors are responsible for 30% of variations in blood pressure amongst different populations (25). Hypertension in obese individuals may arise in large part due to insulin resistance and resultant hyperinsulinemia which occurs due to increased amount of fat tissue. Mechanism included are enhanced renal sodium and water reabsorption, changes in transmembrane electrolyte transport, stimulation of growth factors (especially in vascular smooth muscle), stimulation of SNS, reduced synthesis of prostaglandins, increased secretion of endothelin. This mechanism of insulin resistance might be also the cause of hypertension in non-obese individuals (26). Pathophysiology of obesity and hypertension will be explained in following section.

1.4 Association between obesity and hypertension

Central or android type of obesity is associated with the greater risk for hypertension, type 2 diabetes, wide range of cardiovascular diseases and other elements of metabolic syndrome due to stronger inflammatory action of adipose tissue in visceral area. Inflammatory process itself is linking obesity (particularly central type), insulin resistance and hypertension. Hypertension and obesity are mutually interwoven: factors directing fat pathogenesis are the factors which as well influence development of hypertension. Most hypertensive patients suffer from insulin resistance, while it is almost universally present in patients with hypertension and obesity (27). Insulin stimulates release of nitric oxide using signal pathways of phosphoinositide 3-kinase and phosphorylation of endothelial nitric oxide synthase. In healthy individual ingesting food results with release of insulin and deposition of glucose which leads to vasodilatation of skeletal muscle vasculature. In patients with insulin resistance intracellular activity of insulin is decreased resulting with decreased production of nitric oxide and increased secretion of endotelin-1. Endotelin-1 acts as a vasoconstrictor which is stimulated by insulin activity through mitogen activated protein kinase. Endothelin-1 is inhibited by nitric oxide (28). In insulin resistance many pro inflammatory cytokines are activated (interleukin-6, tumor necrosis factor-α and many others). Lower levels of adiponectin and decreased leptin sensitivity are also result in decreased release of nitric oxide and increased release of endothelin-1 (29). Except leptin mediated effects on appetite and metabolism, leptin can lead to increased sympathetic activity in hypothalamus (ventromedial and dorsomedial part). Insulin increases absorption of sodium in distal nephron with consequential fluid retention, alongside with new distribution of sodium and potassium resulting in increased peripheral vascular resistance. Increased intravascular volume in obese patients increases absolute volume and it is mainly redistributed in cardiopulmonary system.

This are leading hemodynamic changes associated with hypertension and obesity. Moreover, higher sodium concentration stimulates adrenergic activity. Increased sympathetic activity resulting in vasoconstriction is present in obese patients even without hypertension (30). RAAS system also represents an important role in linking pathophysiology of obesity and hypertension. Increased levels of circulating angiotensin in obese individuals can be caused by increased mass of adipose tissue which leads to vasoconstriction and increased blood pressure.

1.5 Body composition analysis

There are multiple methods of body composition analysis. The most popular method is BMI. Distribution of the adiposity is estimated using previously described BMI and adding waist-to-hip ratio. Nowadays in different epidemiological studies the method of waist and height of the body is most commonly used. Most exact method in evaluation of body composition is dual-energy X-ray absorptiometry (DEXA) which provides substantial amount of qualitative data about body composition (31). DEXA works on the principle of two ionizing x-ray beams with different energy levels aimed at whole or part of the body that are registered and processed by computer software. DEXA provides with a detailed snapshot of one's body composition including how the body weight breaks down into fat, bone and lean tissue. While quite useful and reliable it is still not widespread, mostly due to its ionizing nature.

1.5.1 Bioelectrical impedance analysis of body composition

Bioelectrical impedance is popular method used for analysis of body composition. It is widespread, reliable and noninvasive. Bioelectrical impedance measures the electrical signals (composed of very low dose of electricity up to 800 μamp) passing through body adipose tissue, muscle and water. Patient's soles are in contact with metal electrodes found on surface of the balance or attached to the palms. Ranges of different tissues resistance are standardized from previous population laboratorial measurement. Muscle tissue contains substantial amount of water and has low resistivity to electricity. On the other hand, adipose tissue contains small amount of water with high resistance to electricity flow. The data about height, weight, age and sex is imputed into the device and then after computer us processing data about one's adipose tissue dry mass and water content.

2 Hypothesis

Hypothesis of this thesis is that there is difference in body composition analyzed by bioelectric impedance among obese patients with hypertension and obese patients without hypertension.

3 Objectives

The primary goal of this analysis is to establish the differences in body composition between obese patients with hypertension and obese patients without hypertension using bioelectrical impedance analysis.

The secondary goal is to compare specific elements of body composition in obese patients (with hypertension or without hypertension) to body composition of normotensive non - obese subjects.

4 Patients and methods

4.1 Participants

This retrospective study was conducted at the Department of Endocrinology, Internal Clinic, University Hospital Centre Zagreb. The retrospective analysis was approved by Ethic committee of University Hospital Centre Zagreb. Data from 40 obese patients and data form 14 healthy normotensive normal weight participants was analyzed. Inclusion criteria for obese patient Group were BMI above 30 kg/m². Exclusion criteria were secondary cause of obesity (abnormal values of thyroid-stimulating hormone-TSH and cortisol after overnight suppression with 1 mg dexamethasone) and without clinical and/or laboratory suspicion of secondary hypertension (clinical status, normal values of sodium, potassium, calcium, without anamnestic data suggesting pheochromocytoma). The first Group consisted of 20 obese patients with diagnosed hypertension (7 males and 13 females, mean age 44.9 range 25-66). In the second Group there were 20 obese patients (5 males and 15 females mean age 41.5 range 29-65) with normal blood pressure. Healthy normotensive normal weight participants were in the third Group (6 males and 8 females, mean age 35.5 years range 26-58 years). Inclusion criteria for healthy normal weight normotensive Group were adult age (over 18 yrs.), BMI 18-27 kg/m² (for participants with BMI > 25 kg/m² fat percentage were normal for gender and age). Health status of the participants was determined by fasting blood parameters of the total blood count, standard biochemistry tests, TSH, urine chemistry, oral glucose tolerance test (OGTT), 24-h urine protein excretion, and glomerular filtration assessment. No pathology was noted on standard 12-lead electrocardiogram, 24-h blood pressure monitoring and kidney ultrasound. Furthermore, none of the participants in their history suffered from

hypertension, diabetes, kidney disease, myocardial infarction, cerebrovascular incidents or malignancy within the last 5 years.

The data concerning body composition (fat percentage, fat mass and muscle mass) was obtained using bioelectric impedance device Tanita body composition analyzer (model SC-330, Tanita Europe BV, Amsterdam, Netherlands). Other laboratory data were obtained from hospital information system.

Table1: Patients anthropometric characteristics from Group 1 , Group 2 and Group 3. BM body mass, BH body height, BMI body mass index, SD standard deviation

	Group 1 N=20 (males 7, females 13)				Group 2 N=20 (males 5, females 15)				Group 3 N=14 (males 6, females 8)			
	Median	**Min**	**Max**	**SD**	**Median**	**Min**	**Max**	**SD**	**Median**	**Min**	**Max**	**SD**
Age (yrs)	44.90	25.00	66.00	10.96	41.50	26.00	65.00	10.73	35.50	26.00	48.00	7.62
BM (kg)	136.31	91.50	239.90	37.08	116.39	78.00	186.90	27.26	92.14	53.40	150.83	24.16
BH (cm)	171.83	155.00	198.00	12.60	170.58	153.00	189.00	9.66	173.29	162.00	187.00	9.22
BMI (kg/m^2)	45.34	37.12	41.19	6.54	39.75	29.06	52.30	7.18	23.15	18.10	28.40	2.77
Fat (%)	47.40	36.40	55.30	4.63	42.65	28.70	54.60	7.30	22.04	14.00	32.80	6.00
Fat mass (kg)	64.39	43.20	120.40	20.94	49.15	26.50	77.40	13.27	15.30	7.90	23.00	4.61
Muscle mass (kg)	67.20	44.70	117.00	18.66	63.14	43.80	126.90	19.64	54.56	38.10	77.40	11.27

4.2 Methods

Data from 40 obese patients were retrospectively analyzed. Patients attended structured weight loss program at the Obesity Treatment Centre accredited as Croatian Obesity Treatment Referral Centre and Collaborating Centre for Obesity Management of European Association for the Study of Obesity (EASO). 5-day structured educational program included daily consultations with a multidisciplinary healthcare team. The team leads experienced endocrinologist-diabetologist and nurse-educator. It includes nutritionist, physiotherapist, psychiatrist and psychologists. Anthropometric values (height, weight, BMI) as well as body composition measured by bioelectrical impedance analysis (fat mass, muscle mass) and laboratory analysis were estimated during the 5-day program.

Healthy non-obese subjects participated in another study (Natriuretic Effect of GLP-1 in Healthy Non Obese Subjects Followed by Oral Sodium Load: A Randomized, Placebo-controlled, Cross-over Study), approved by the Ethics Committee of University Hospital Centre Zagreb, for which they signed the informed consent.

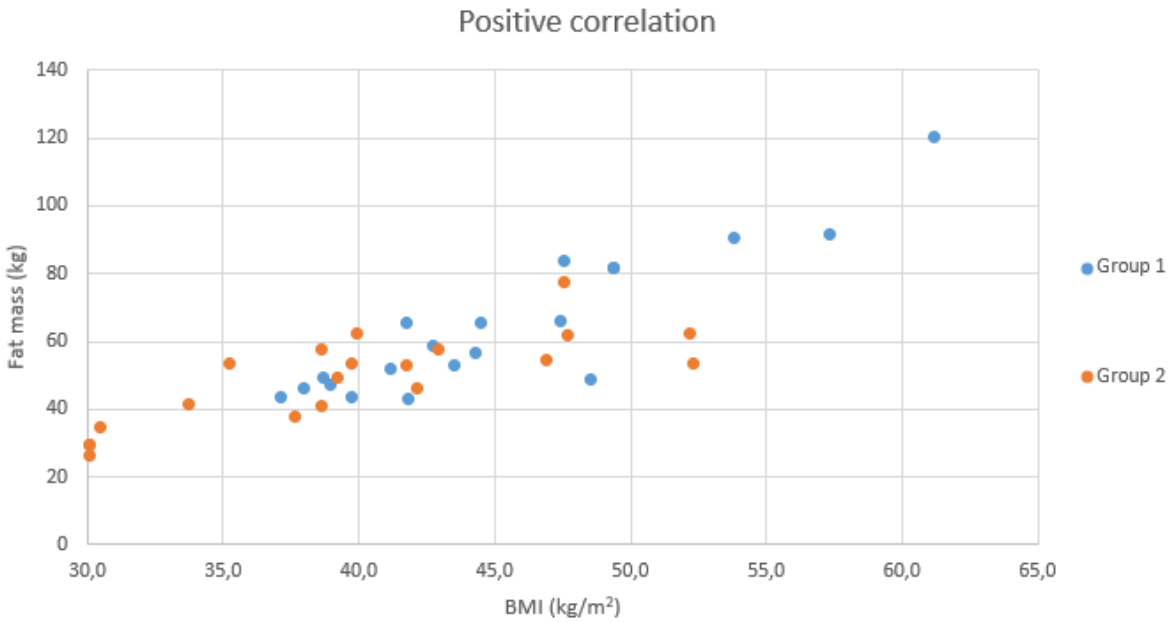
The raw data analysis was performed in Microsoft excel program (Microsoft Excel 2016, Apple, Cupertino, SAD) using descriptive statistics, the two-sample t-test, chi-square test, analysis of variance ANOVA and correlation analysis. Descriptive statistics is used to describe the basic characteristics of the sample mean, standard deviation, minimum and maximum. Statistical analysis was performed with the level of statistical significance set at p= *0.05*

5 Results

Patients included in the study were divided into three separate subgroups (Table 1) on the basis of BMI and hypertension status as previously mentioned. There was same gender distribution in all three groups, the chi-square test did not show any statistical difference among the occurrence of males and females. Obese individuals with hypertension from Group 1 were on average 3.4 years older than obese normotensive patients from Group 2 and 9.4 years older than the healthy Group 3. ANOVA analysis showed significant difference in three groups ($p= 0.03$). However, two sample t-test showed no age difference between Group 1 and Group 2 ($p= 0.33$), so the groups of obese patients were similar age. As expected, there was difference among the groups regarding the BMI, but again two sample t-test showed no difference in BMI between Group 1 and Group 2 ($p= 0.87$), so the groups of obese patients had similar BMI.

There was a positive correlation between BMI and fat mass in Group 1 and Group 2 ($r= 0.91$ and $r= 0.80$ respectively) with stronger correlation among BMI and fat mass on obese hypertensive patients (Picture 1). Fat mass also significantly correlated with the BM in Group 1 and 2 ($r= 0.93$ and $r= 0.69$ retrospectively), again with stronger correlation among BM and fat mass in obese hypertensive patients. Mean difference among fat mass from Group 1 and Group 2 was 15.24 kg (Table 1). Two sample t-test showed statistical difference in fat mass ($p=0.01$) and in fat percentage ($p= 0.02$) among Group 1 and 2.

Picture 1: Positive correlation between fat mass and BMI in a group of obese hypertensive patients (Group 1) and obese normotensive patients (Group 2)



Further subsection analysis of hypertensive patients was performed to see if there is any difference in anthropometric data between obese male and female patients. In Group 1 BM and BH as expected, differed significantly (BM p= 0.00 and BH p= 0.00). Significantly higher muscle mass (p= 0.00) was present in male population with mean difference 27.4 kg. Increased fat mass was found in male population with mean difference 24.84 kg that was statistically different to females from Group 1 (p= 0.02), but the fat percentage was almost the same in males and females (p= 0.93).

In Group 2 statistical analysis showed no is significant difference between anthropometric characteristics between males and females.

Further analysis was done to compare healthy participants from Group 3 with obese patients from Group 1 and 2. As expected, they had significantly lower BMI while compared with Group (p= 0.02) and while comparing with Group 2 (p= 0.03). Mean BMI difference

between Group 1 and 3 was 22.19 kg/m^2 and between Group 2 and 3 were 18.60 kg/m^2. All other parameters concerning body analysis were statistically different. The difference among fat percentage between Group 1 and Group 3 was 25.36% (p= 0.02) and between Group 2 and Group 3 was 17.70% (p= 0.03). Highest mean difference was observed in the measurement of fat mass where obese hypertensive patients from Group 1 had on average had 49.09 kg more of fats than the healthy participants (p=0.00), while the mean difference between Group 2 and 3 was 33.85kg (p= 0.00). Difference in muscle mass was also observed. In comparison of Group 1 and 3 it resulted in mean difference of 15.64 kg (p= 0.02) and comparison of Group 2 and 3 resulted in mean difference of 11.58 kg (p= 0.04).

6 Discussion

While analyzing two statistically similar groups of 40 obese patients with and without hypertension it was shown that obese patients with hypertension have more fat mass, but also higher fat percentage than those without hypertension. It is important to emphasize that secondary cause of obesity was excluded and that there was no clinical and/or laboratory suspicion of secondary hypertension. Analysis showed that Group 1 had more fat mass and higher fat precentage. It implies the metabolic influence of fat on hypertension. These include increased production of bioactive molecules, such as leptin, angiotensinogen, pro-inflammatory cytokines, and reactive oxygen species. Body has no capacity to accommodate excess energy-intake that is leading to fat storage in tissues and insulin resistance with hyperinsulinemia. Such dysfunctional adipose tissue induces activation of the SNS and RAAS together with oxidative stress (32). All of those processes promote the development of obesity-associated hypertension.

Subsection analysis of obese hypertensive patients regarding gender showed that males have more muscle mass, but also more fat mass. It is well known that normal weight males have more muscle mass than females and that normal weight females have higher fat mass than males (33). Such observation colud be atributed to anabolic effect of testosterone. Testosterone has important role in carbohydrate, fat and protein metabolism, with major influence on body fat composition and muscle mass (34). In the group of obese hypertensive patients, interestingly, the percentage of fat in males was also higher. Active endocrine adipose tissue in obese males contributes significantly to the circulating pool of estrogens which results in distribution of adipose tissue and higher fat percentage between. The enzyme aromatase in adipose tissue primarily results in the extra glandular formation of estrogen (35).

Testosterone deficiency is associated with an increased fat mass (in particular central adiposity). In group of normotensive obese patient there was no alerted fat tissue ratio among males and female. This possibly indicates that obese individuals without hypertension have body composition that is more similar to those with normal body weight, even though they are still more excessive than the normal BMI values.

Finally, as expected, statistical analysis preformed to compare obese individuals with non -obese individuals showed statistical difference in all measured parameters beyond BMI (inclusion criteria itself dictates that BMI has to be significantly lower in non-obese group). There was significant difference compared with both obese hypertensive and normotensive patients in all parameters of body composition.

7 Conclusion

- Obese patients with hypertension have more fat mass and higher fat percentage compared to group of obese patients without hypertension with same age and BMI. Since the secondary causes of obesity were excluded, and that there was no clinical and/or laboratory suspicion of secondary hypertension, this observation implies the metabolic influence of hormone active fat on obesity related hypertension.

- Obese hypertensive males have more fat mass than obese hypertensive females which is unusual ratio for normal-weight individuals. This observation is a result of the influence of estrogen excess (adipose tissue in obese males contributes to the circulating pool of estrogens) and testosterone deficiency (associated with an increased fat mass). Contrary, normotensive obese males had less fat tissue than normotensive obese females indicating that they have body composition that is more similar to males with normal body weight.

- Statistical analysis preformed to compare obese individuals with non-obese individuals showed significant difference compared with both obese hypertensive and normotensive patients in all parameters of body composition.

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10 Biography

I was born in on the 22nd of August 1993 in Zagreb. After completing primary and secondary education, in September 2012 I got accepted into the Medical Studies in English at the University of Zagreb. During my education, I deeply improved myself both personally and academically.

I am very interested in internal medicine and I have attended my clinical rotations in the emergency room department to further develop and improve my clinical skills. During my academic education I have attended many meetings and congress in order to extend my medical knowledge and improve my medical skills. I have also worked on my academic improvement by working and publishing three scientific works.

I have been involved with Pathophysiology and History taking and medical examination as student demonstrator which contributed to strengthen my knowledge. Moreover, I founded faculty e-sports team in which I have won third place in the UnisportZG esport leauge while representing medical faculty.