Glasnik Antropološkog društva Srbije / Journal of the Anthropologycal Society of Serbia
Novi Sad, vol. 43, str 440-447, 2008, UDK 572(05), ISSN 1820-7536

EVALUATION OF THE BODY COMPOSITION IN FEMALE CUSHINGS

UDK 572.512:616-056.7

Šubeska Stratrova Slavica, Dimitrovski Čedomir, Todorovska Lidija*, Stefanovska Balabanova Gabriela. Clinic of Endocrinology, diabetes and metabolic disorders, Institute of Physiology and Anthropology*, Medical faculty, Skopje, Macedonia

Obesity in Cushing's syndrome (CS) is extremely visceral. The aim of this study was to determine the degree of obesity and body composition in CS and nonCS patients. Total fat mass (TFM) and peripheral fat mass (PFM), as well as the rest visceral mass (VM) were determined by Mateigka's equations, and their percentages from the total body mass, PFM% and VM% were also determined. Female Cushings (n=33) with BMI (29.66±4.82 kg/m^2) were examined and 66 obese women (O) matched by their BMI (29.56±4.76 kg/m^2), and a control group (C) with normal BMI (22.41±1.81 kg/m^2) was also examined.

CS and O were not significantly different according to their BMI, as well as their TFM, which was 35.59±7.03 kg in O and (36.86±7.76 kg) in CS, but it was significantly lower in C (24.89±5.73 kg). PFM and PFM% were not significantly different between C (17.86±5.89 kg; 28.93±6.39%) and CS (19.27±6.04 kg; 26.19±6.09%), but it was significantly higher in O (27.32±5.86 kg; 35.45±5.43%) compared to C and CS. VM and VM% were not significantly different between C (7.03±2.69kg; 11.83±4.39%) and O (8.27±3.45 kg; 10.96±4.24%), but both of them were significantly lower compared to CS (18.06±4.89 kg; 25.05±6.04%). Conclusion: increase of the TFM in obese women was a result of a preponderant peripheral fat mass increase, but in CS it was a result of an increase of the visceral mass, not peripheral fat mass, confirming significantly increased fat mass accumulation in visceral depots, but not redistribution of the fat mass from the peripheral to visceral parts of the body.

Key words: Cushing, female, body composition, equation of Mateigka.

INTRODUCTION

CS invariably presents with a classical phenotype comprising central adiposity, prominence of dorsal, supraclavicular and temporal fat pads, bruising, abdominal striae, proximal myopathy, and hypertension (Tomlinson, 2002). CS is associated with weight gain and visceral obesity as well as with low fat-free mass (Schafroth et al. 2000; Ueland et al. 2003; Pirlich et al. 2002). There is a great abnormality of regional body composition in patients with CS who exhibit a lower limb lean mass and a greater truncal fat (Burt et al. 2006). For a given body mass index (BMI), mortality is higher in patients with central compared to generalized obesity (Stewart et al. 1999). Effective methods for assessing visceral fat are important to investigate the role of visceral fat for the increased health risks in obesity (Snijder et al. 2002).

The aim of this study was to evaluate body composition in women with CS, to determine fat-free body mass and fat body mass using anthropometry, to compare these findings with non-cushingoid patients, healthy control obese women matched for age, and BMI, and with healthy control group of women with normal BMI, and to validate previous reports of increased visceral fat in female patients with CS. This investigation examined the accuracy of anthropometric equations of Mateigka in estimating body composition, and the usefulness of anthropometry in predicting intra-abdominal fat in obese women.

MATERIALS AND METHODS

Anthropometric measurements were performed for quantitative assessment of the body composition, and body fat distribution in 33 consecutive patients with recently diagnosed CS, before surgical treatment, with BMI (29.66±4.82 kg/m^2), mean age (38.48±10 yr), and where compared to 33 nonobese healthy controls (C) with normal BMI (22.41±1.81 kg/m^2) and mean age (30.7±8.96 yr), as well as with 66 individually BMI and age-matched healthy obese controls (O), with a mean age (35.43±10 yr), and BMI (29.56±4.76 kg/m^2). The diagnosis of CS was clinically obvious in all cases, and was confirmed by objective tests. The obese and no obese controls had a stable weight for at least several months before performing the study. All subjects were weighed in the morning after an overnight fast.

Several skin-fold thicknesses (biceps, forearm, thigh, leg, chest, abdomen), body circumferences (arm, forearm, thigh and leg) and joint diameters (elbow, knee, wrist, ankle), body height (cm), body mass (kg), were measured and were used in Mateigka's equations. Absolute and relative muscular (M,M%), osseous (OS,OS%), total fat (TFM,TFM%) and peripheral fat mass (PFM,PFM%) components of the total corporal, body mass (BM) in all women were calculated by Mateigka's equations as an indirect anthropometric method (Perunović i sur. 1982; Jović i sur. 1982; Radivojević i sur. 1982). Each relative mass M%, OS%, TFM%, PFM% is a % of the absolute mass from the total BM. The rest mass, visceral mass (VM) was determined indirectly, as a difference of all these components M, OS and PFM from the total corporal mass. The rest mass, visceral mass is mainly dependent on the visceral fat mass, because visceral organ mass is almost constant for each BMI. Lean body mass (LBM) was a sum of M and OS mass. TFM was calculated by subtracting LBM from the total BM.

Circumferences (C), diameters (D) and skinfold thicknesses (SF) measures were performed by the author, in the Clinic of Endocrinology from 1990 to 2006 yr. Body C were measured by plastic tape – Hoffmann La Roche. Small bone caliper, based on the sliding branch principle, was used for bone diameter measurements. The SF were measured with Lange skinfold caliper. Equipment was manufactured in California, USA. BMI was calculated as a ratio of (body weight) kilograms (kg)/(m^2) meters (height).

Statistical analysis was performed with statistical program SPSS 11.0, by a linear correlation Pearson and Sperman rang correlation, and for comparison of the mean values was used analysis of variance ANOVA, and nonparametric tests Kruskal Wallis and Mann Whitney – U test of inversion.

RESULTS

Absolute and relative M mass was (26.61±5.05 kg; 37.17±4.38%) in CS, (31.5±6.57 kg; 41.54±5.05 %) in O and (26.1±4.13 kg; 44.34±4.41 %) in C. M was significantly highest in O ($p<0.0001$), but not significantly different between C and CS. M% in CS was significantly lower compared to C and O ($p<0.0001$). Absolute and relative OS mass was (8.43±0.98 kg; 11.82±1.58 %) in CS, (8.78±0.93 kg; 11.77±1.58 %) in O and (8.38±0.99 kg; 14.29±1.33 %) in C. OS was not significantly different between the groups. OS% in CS was not significantly different compared to O, but it was significantly lower compared to C ($p<0.0001$). LBM is a sum of M and OS mass. TFM was calculated by subtracting LBM from the total BM. BM was (72.26±10.7 kg) in CS, (76.07±11.62 kg) in O and (58.83±6.58 kg) in C. Absolute and relative TFM was (36.86±7.76 kg; 51±4.46 %) in CS, (35.59±7.03 kg; 46,41.±6.06 %) in O and (24.89±5.73 kg; 40±5.2 %) in C. TFM in C was significantly lower compared to CS and O ($p<0.0001$), but it was not significantly different between CS and O ($p>0.05$).

PFM and PFM% determined by Mateigka's equation were (19.27±6.04 kg; 26.19±6.09%) in CS, (27.32±5.86 kg; 35.45±5.43%) in O, and (17.86±5.89 kg; 28.93±6.39%) in C. PFM and PFM% were significantly highest in O compared to C and CS ($p<0.0001$), and were not significantly different between C and CS. VM was calculated by subtracting M, OS and PFM from BM. It was (18.06±4.89 kg; 25.05±6.04%) in CS, (8.27±3.45 kg; 10.96±4.24%) in O and (7.03±2.69kg; 11.83±4.39%) in C. VM and VM% were highest in CS compared to C and O ($p<0.0001$), but they were not significantly different between C and O.

DISCUSION

Cushing's syndrome is characterized by primary hypercortisolism as well as profound visceral adiposity and obesity. Visceral (e.g. omental, mesenteric), or intraabdominal fat is the fat depot most highly associated with illness and death from cardiocerebrovascular disease and diabetes (Peeke & Chrousos, 1995). Cardiovascular accidents represent the most important cause of death in patients with CS (Faggiano et al. 2003.)

Most obese individuals, both children and adults, have an increase in LBM as well as fat, the former accounting for as much as 40 percent of the excess weight in some studies. Intentional overfeeding of normal individuals augments LBM as well as fat. Exceptions are those individuals with CS (Forbes & Welle, 1983). Seidell et al. 1989, concluded that a higher BMI is associated with increased central and peripheral fat stores (but not visceral fat) and increased thigh muscle in obese. Also, Pirlich et al. 2002, found in healthy subjects, without hypercortisolism, that weight gain is associated with an increase of fat mass as well as with an increase of fat-free mass, but in CS this relationship was disturbed. In CS patients and weight-matched controls, body weight and total body fat were significantly higher than in no obese controls. In our study also, body weight as well as total body fat were significantly higher in CS patients and age, BMI-matched obese patients when compared to C, and higher TFM% in CS compared to O was result of a reduced M% in CS. Arm muscle area was significantly lower in patients with CS when compared with weight-matched obese patients ($p<0.05$), indicating a loss of skeletal muscle mass (Pirlich et al. 2002).

Clinical observation confirms that glucocorticoids have a considerable impact on body composition and body fat distribution which leads to visceral fat accumulation and a decrease in muscle mass in limbs (Robaczyk et al. 2003). Patients with anorexia nervosa had a fivefold decrease in subcutaneous fat and only a twofold decrease in intraabdominal fat compared with the values for the volunteers. Patients with CS had less than a twofold increase in subcutaneous fat and greater than a fivefold increase in intraabdominal fat compared with values for the healthy subjects (Mayo-Smith et al. 1989).

In the study of Garrapa et al. 2001, women with CS were overweight and total body fat was significantly higher in CS than in C women. Abdominal fat was significantly higher in CS compared to C women, as well as in our study, in which CS patients had mean BMI borderline value, some of them were overweight, and some were obese.

Enzi in 1986 found in CS patients that the ratio between subcutaneous (sc) and visceral fat areas (S:V ratio) at the abdominal level was significantly lower than in controls matched for age, sex, and BMI. Visceral to total adipose tissue (AT) area ratio was 0.34 in women with Cushing's syndrome, as compared with 0.14 in healthy women (Mayo Smith et al. 1989). In CS, seven out of nine patients showed visceral type and V/S ratio positively correlated with cortisol levels (Yoshida, 1991). Rockall et al. 2003, demonstrated an increase in visceral fat distribution in both male and female patients with CS, with a significant increase in the V:S ratio in CS patients when compared with non-cushingoid controls. There was no difference in the V:S ratio between male and female patients with CS.

Wajchenberg et al. 1995, used CT scaning for measurement of the sc fat area and intraabdominal visceral fat area, in women with CS and compared with those in obese women and those in no obese women. The visceral fat area at the abdominal region was significantly different in the three study groups, being greater in CS patients and decreasing progressively to its lowest value in the no obese subjects. The same was observed in the sc region, but no significance was noticed between CS and obese subjects. The visceral fat area to the sc fat area ratio was significantly higher in CS patients than in the other subjects. However, there was no significant difference between obese and normal weight subjects. The total lean tissue mass was slightly reduced in CS compared to that in the obese subjects due to a significant decrease in the muscle of the legs and arms. The body mineral and bone calcium contents were slightly reduced in CS compared to those in the obese controls. Obese subjects had more fat and lean tissue than their normal weight counterparts, but the CS patients, with the same total fat mass as obese individuals, presented total lean tissue and its fractions, including body mineral and bone calcium contents, similar to those in no obese subjects. Our CS patients had lower M mass and M% compared to O, not significantly different OS% and TFM, but significantly higher TFM%. Higher TFM% in CS was a result of lower M%, because of significantly lower M mass compared to O. These study enabled conclusions that our CS patients had not significantly different M and OS mass, compared to C, but M% and OS% were significantly lower in CS compared to C as a result of a TFM and TFM% increase in CS. CS patients with the same total fat mass as obese individuals presented total lean tissue, similar to those in no obese controls.

The study of Burt et al. 2006, concluded that there is a greater abnormality of regional body composition in patients with CS who exhibit a lower limb lean mass and a greater truncal fat. He found that mean percentage FM was significantly higher by 30% in CS than in normal subjects. LBM was significantly lower by 15% in CS. In CS, the proportion of lean tissue in the limbs was 12% less than in normal. Truncal fat represented a greater proportion of total FM in CS than in normal subjects.

In the study of Pirlich et al. 2002, measurements performed before and 6 months after successful pituitary surgery demonstrated significant loss of body weight (-11%) and body fat (-33%) of initial values, arm muscle area remained constant and did not increase. Ueland et al. 2003, concluded that treatment significantly changes body composition in CS patients by decreasing fat mass, especially in the truncal region, without major effects on lean body mass.

In the study of Schafroth et al. 2000, twenty-three consecutive patients with recently diagnosed CS were systematically evaluated before surgical treatment and compared to 23 age-, sex- and BMI-matched healthy controls without any underlying endocrine or metabolic disorder. Total body composition was measured by dual-energy X-ray absorptiometry. Lean tissue mass was decreased in the legs in CS, but only significantly so in women. In the arms, no differences between patients and controls were observed in lean tissue mass. In a subgroup of 12 patients with CS, truncal fat mass was significantly elevated when compared to obese controls, whereas total fat mass was insignificantly higher in patients with CS, similar as in our study.

Loon et al. 1994, have used a multiscan CT technique to study total and regional volumes of AT and muscle before and after treatment of patients with CS. When expressed as a percentage of initial depot volumes, the reductions were unevenly distributed. AT of viscera and head+neck were reduced by 34% to 36%, subcutaneous trunk by 26%, and AT of arms and legs by 18% and 8%, respectively. Although total skeletal muscle plus skin was not changed, muscle of arms was reduced by 0.3±0.2 L. Except for leg AT, the reductions of all regional AT depots (arms, head+neck, subcutaneous trunk, viscera) were significant when expressed in litters. Body weight was reduced by 10.2 ± 8.1 kg. The total AT was reduced by 23% ±11%. AT was reduced by 8.2±6.1 kg, skeletal muscle plus skin by 1.3±1.7 kg (NS), and visceral organs by 0.6±1.0 kg (NS). Loon's study confirmed our data that visceral mass is dependent on the visceral fat mass, because visceral organs mass is not changed significantly in CS patients. VM increase in CS is dependent on visceral fat mass increase. That gives importance to Mateigka's equation as a very precise indirect method for determining the visceral fat mass, especially important in comparison of weight or BMI matched different groups of patients. There was no significant difference of TFM in CS compared to O in our study, and its significant higher value in O and CS compared to C was a result of significant VM increase in CS, and significant PFM increase in O. Significant higher TFM in CS compared to C was a result of significant increase of VM in CS, because there was not significantly higher PFM in CS compared to C.VM and VM% were significantly higher in CS compared to O and C.

Anthropometry is a simple reliable method for quantifying body size and proportions by measuring body length, width, circumference, and skinfold thickness included in equations to predict body fat percent (Wang et al. 2000). Recent studies indicate that not only total body fat, but also regional fat and skeletal muscle, can be predicted from anthropometrics. Anthropometric examinations are used not only for quantitative assessment of the degree of obesity but also to define the body fat distribution, and to determine the best anthropometric predictors of abdominal type of obesity.

Anthropometric prediction equations that use a combination of circumferences and bony diameters are recommended for older adults, as well as obese men and women (Heyward, 1998). The study of the relationship between anthropometry and visceral adipose tissue (VAT) is of great interest because VAT is associated with many risk factors for noncommunicable diseases and anthropometry is easy to perform in clinical practice (Brambilla et al. 2006). Anthropometry as an easy, low-cost and noninvasive method enables distinguishing CS from obese suspected for CS.

This study discovered that the increase of the total fat mass in obese women was a result of a preponderant peripheral fat mass increase, but in CS it was a result of an increase of the rest mass, visceral mass, not peripheral fat mass, confirming fat mass accumulation in visceral depots, but not redistribution of the fat mass from the peripheral to visceral parts of the body. Anthropometric examination enabled a very important conclusion that Cushing's are characterized with significant accumulation of visceral fat.

REFERENCES:

Brambilla P, Bedogni G, Moreno LA, Goran MI, Gutin B, Fox KR, Peters DM, Barbeau P, De Simone M, Pietrobelli A. Cross validation of anthropometry against magnetic resonance imaging for the assessment of visceral and subcutaneous adipose tissue in children. Int J Obes (Lond). 2006; 30(1):23-30.

Burt MG, Gibney J, Ho KK. Characterization of the metabolic phenotypes of Cushing's syndrome and growth hormone deficiency: a study of body composition and energy metabolism. Clin Endocrinol (Oxf). 2006; 64(4):436-43.

Enzi G, Gasparo M, Biondetti PR, Fiore D, Semisa M, Zurlo F. Subcutaneous and visceral fat distribution according to sex, age, and overweight, evaluated by computed tomography. Am J Clin Nutr. 1986; 44(6):739-46.

Faggiano A, Pivonello R, Spiezia S, De Martino MC, Filippella M, Di Somma C, Lombardi G, Colao A. Cardiovascular risk factors and common carotid artery caliber and stiffness in patients with Cushing's disease during active disease and 1 year after disease remission. J Clin Endocrinol Metab. 2003; 88(6):2527-33.

Forbes GB, Welle SL. Lean body mass in obesity. Int J Obes. 1983; 7(2):99-107.

Garrapa GG, Pantanetti P, Arnaldi G, Mantero F, Faloia E. Body composition and metabolic features in women with adrenal incidentaloma or Cushing's syndrome. J Clin Endocrinol Metab. 2001; 86(11):5301-6.

Heyward VH. Practical body composition assessment for children, adults, and older adults. Int J Sport Nutr. 1998; 8(3):285-307.

Jović D, Perunović D, Radivojević Lj. Određivanje vrednosti masne komponente telesne mase – metoda po Mateigka. ŠMO-SMJ. 1982; XIX (7-9): 199-204.

Lonn L, Kvist H, Ernest I, Sjostrom L. Changes in body composition and adipose tissue distribution after treatment of women with Cushing's syndrome. Metabolism. 1994; 43(12):1517-22.

Mayo-Smith W, Hayes CW, Biller BM, Klibanski A, Rosenthal H, Rosenthal DI. Body fat distribution measured with CT: correlations in healthy subjects, patients with anorexia nervosa, and patients with Cushing syndrome. Radiology. 1989; 170(2):515-8.

Peeke PM, Chrousos GP. Hypercortisolism and obesity. Ann N Y Acad Sci. 1995; 771:665-76.

Perunović D, Jović D, Radivojević Lj. Mišićna komponenta telesne mase – njen znaćaj i određivanje primenom modifikovane metode po Mateigka. ŠMO-SMJ. 1982; XIX (7-9): 205-209.

Pirlich M, Biering H, Gerl H, Ventz M, Schmidt B, Ertl S, Lochs H. Loss of body cell mass in Cushing's syndrome: effect of treatment. J Clin Endocrinol Metab. 2002; 87(3):1078-84.

Radivojević Lj, Jović D, Perunović D. Utvrđivanje apsolutne i relativne mase koštanog tkiva metodom po Mateigka. ŠMO-SMJ. 1982; XIX (7-9): 194-198.

Robaczyk M, Krzyzanowiska-Swiniarska B, Andrysiak-Mamos E, Kulig G, Pilarska K. [Plasma leptin levels in relation to body composition and body fat distribution in patients with Cushing's syndrome]. Pol Arch Med Wewn. 2003; 110(5):1299-308.

Rockall AG, Sohaib SA, Evans D, Kaltsas G, Isidori AM, Monson JP, Besser GM, Grossman AB, Reznek RH. Computed tomography assessment of fat distribution in male and female patients with Cushing's syndrome. Eur J Endocrinol. 2003; 149(6):561-7 .

Schafroth U, Godang K, Ueland T, Berg JP, Bollerslev J. Leptin levels in relation to body composition and insulin concentration in patients with endogenous Cushing's syndrome compared to controls matched for body mass index. J Endocrinol Invest. 2000; 23(6):349-55.

Seidell JC, Bjorntorp P, Sjostrom L, Sannerstedt R, Krotkiewski M, Kvist H. Regional distribution of muscle and fat mass in men--new insight into the risk of abdominal obesity using computed tomography. Int J Obes. 1989; 13(3):289-303.

Snijder MB, Visser M, Dekker JM, Seidell JC, Fuerst T, Tylavsky F, Cauley J, Lang T, Nevitt M, Harris TB. The prediction of visceral fat by dual-energy X-ray absorptiometry in the elderly: a comparison with computed tomography and anthropometry. Int J Obes Relat Metab Disord. 2002; 26(7):984-93.

Stewart PM, Boulton A, Kumar S, Clark PM, Shackleton CH. Cortisol metabolism in human obesity: impaired cortisone-->cortisol conversion in subjects with central adiposity. J Clin Endocrinol Metab. 1999; 84(3):1022-7.

Tomlinson JW, Draper N, Mackie J, Johnson AP, Holder G, Wood P, Stewart PM. Absence of Cushingoid phenotype in a patient with Cushing's disease due to defective cortisone to cortisol conversion. J Clin Endocrinol Metab. 2002; 87(1):57-62

Ueland T, Kristo C, Godang K, Aukrust P, Bollerslev J. Interleukin-1 receptor antagonist is associated with fat distribution in endogenous Cushing's syndrome: a longitudinal study. J Clin Endocrinol Metab. 2003; 88(4):1492-6.

Wajchenberg BL, Bosco A, Marone MM, Levin S, Rocha M, Lerorio AC, Nery M, Goldman J, Liberman B. Estimation of body fat and lean tissue distribution by dual energy X-ray absorptiometry and abdominal body fat evaluation by computed tomography in Cushing's disease. J Clin Endocrinol Metab. 1995; 80(9):2791-4.

Wang J, Thornton JC, Kolesnik S, Pierson RN. Anthropometry in body composition. An overview. Ann N Y Acad Sci. 2000; 904:317-26

Yoshida S, Inadera H, Ishikawa Y, Shinomiya M, Shirai K, Saito Y. Endocrine disorders and body fat distribution. Int J Obes. 1991; 15 Suppl 2:37-40.

TELESNA KOMPOZICIJA KOD ŽENA SA KUŠING SINDROMOM

Šubeska Stratrova Slavica, Dimitrovski Čedomir, Todorovska Lidija*, Stefanovska Balabanova Gabriela
Clinic of Endocrinology, diabetes and metabolic disorders
Institute of Physiology and Anthropology*
Medical faculty, Skoplje, Makedonija

Gojaznost kod osoba sa Kušing sindromom (engl.CS) je ekstremno visceralna. Cilj ovog istraživanja je da se utvrdi stepen gojaznosti i telesna kompozicija kod osoba sa sindromom CS i kod osoba nez sindroma bez-CS. Totalna masna komponenta (engl.TFM) i periferna masna komponenta (engl.PFM), kao i ostatak visceralne masti (engl.VM) su određeni metodom po jednačini Mateigke, a takođe je određen i njihov procenat u totalnoj telesnoj masi, PFM% i VM%. Ispitivanje je obuhvatilo žene sa sindromom Kušing (n= 33) sa BMI (29.66±4.82kg/m^2), i 66 gojaznih žena koje su izabrane po BMI (29.56±4.76kg/m^2) kao i kontrolnu grupu (engl.C) koja je imala normalni BMI (22.41±1.81kg/m^2).

CS i O se nisu značajno razlikovali u BMI, kao i u TFM koji je iznosio 35.59±7.03kg kod O i (36.86±7.76kg) kod CS, ali je značajno niži kod C (24.89±5.73kg). PFM i PFM% se nisu značajno razlikovali između C (17.86±5.89kg; 28.93±6.39%) i CS (19.27±6.04kg; 26.19±6.09%) ali su značajno viši kod O (27.32±5.86kg; 35.45±5.43%) u poređenju sa C i CS. VM i VM% se nisu značajno razlikovali između C (7.03±2.69kg; 11.83±4.39%) i O (8.27±3.45kg; 10.96±4.24%) ali su oba značajno niža u poređenju sa CS (18.06±4.89kg; 25.05±6.04%). Zaključak: Povećanje TFM kod gojaznih žena rezultat je pretežnog povećanja periferne masne komponente, ali je kod CS to rezultat povećanja visceralne masti a ne periferne masne komponente potvrđujući tako značajno povećanje masne komponente u visceralnim depoima ali ne i redistribuciju masne komponente od perifernih do visceralnih delova tela.

Ključne reči: Kušing, žene, telesna kompozicija, jednačina po Mateigki.