ПРОЦЕНА НА ТЕЛЕСНИОТ СОСТАВ И ТЕЛЕСНАТА МАСНА ДИСТРИБУЦИЈА КАЈ ЖЕНИ СО КУШИНГ СО АПСОРПЦИОМЕТРИЈА СО ДВОЈНО ЕНЕРГЕТСКИ X - ЗРАЦИ (DXA)

DUAL-ENERGY X - RAY ABSORPTIOMETRY (DXA) ASSESSMENT OF BODY COMPOSITION AND BODY FAT DISTRIBUTION IN CUSHING'S WOMEN

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Abstract

Introduction. Body composition and body fat distribution show difference in women with Cushing's syndrome (CS) compared to healthy control women (C) with almost equal body mass index (BMI) ($28.89 \pm 3.53 \text{ kg/m}^2$ vs. $29.39 \pm 4.04 \text{ kg/m}^2$) and they were compared with DXA.

Methods. Total and regional fat mass (FM), FM%, tissue mass (TM), TM%, android FM (A), gynoid FM (G), lean body mass (LBM), bone mineral density (BMD) and content (BMC) were determined as well as their relationships in 10 CS and 10 C women.

Results. Regional FM, FM%, TM and TM% values were not different between CS and C except for arm TM % ($45.06 \pm 3.1\%$ vs. $40.23 \pm 6.29\%$) ($p < 0.043$). Arms+legs/trunk TM and FM ratio were significantly lower in CS compared to C ($p < 0.0001$). Arms/A (1.1 ± 0.12), legs/A (3 ± 0.41) and legs/trunk TM ratios (0.52 ± 0.07) were significantly lower in CS compared to C (1.3 ± 0.13) ($p < 0.002$), (4.29 ± 0.67) ($p < 0.0001$) and (0.69 ± 0.09) ($p < 0.0001$). Legs/A (2.57 ± 0.73), legs/trunk (0.48 ± 0.13) and arms+legs/trunk FM ratio (0.66 ± 0.14) in CS were significantly lower compared to C [4.2 ± 1.16 ; 0.71 ± 0.12 ($p < 0.001$) and 0.89 ± 0.14 ($p < 0.002$)]. A/G TM (0.67 ± 0.1) and A/G FM ratio (0.72 ± 0.2) in CS were significantly higher compared to C (0.48 ± 0.05) ($p < 0.0001$) and (0.46 ± 0.09) ($p < 0.001$). Legs LBM in CS $10.8 \pm 1.95 \text{ kg}$ was lower compared to C $12.7 \pm 2.1 \text{ kg}$ ($p < 0.046$). Only spine BMD value in CS ($0.89 \pm 0.09 \text{ kg/cm}^2$) was lower compared to C ($0.94 \pm 0.12 \text{ kg/cm}^2$) ($p < 0.017$).

Conclusion. Central to peripheral regional TM, FM and LBM ratios differentiated significantly and precisely patients with CS and C and confirmed extreme central obesity in CS.

Key words: DXA, body composition, body fat distribution, Cushing's syndrome

Апстракт

Вовед. Телесниот состав и телесната дистрибуција покажуваат разлика кај жени со Кушингов синдром (КС) во споредба со здрави контролни жени (К) со речиси еднаков индекс на телесна маса (ИТМ) ($28,89 \pm 3,53 \text{ kg/m}^2$ vs. $29,39 \pm 4,04 \text{ kg/m}^2$) и тие беа споредени со DXA.

Методи. Вкупната и регионална масна маса (ММ), ММ%, ткивната маса (ТМ), ТМ%, андроидната ММ (А), гиноидната ММ (Г), основната маса (ОМ), коскениот минерален дензитет (КМД) и коскената минерална содржина (КМС) беа одредени и нивниот сооднос кај 10 жени со КС и 10 К.

Резултати. Вредностите на регионалната ММ, ММ%, ТМ и ТМ% не се разликуваа меѓу КС и К освен рака/ТМ% ($45,06 \pm 3,1\%$ vs. $40,23 \pm 6,29\%$) ($p < 0,043$). Рака+нога/труп ТМ и ММ количниците беа значајно пониски кај КС во споредба со К ($p < 0,0001$). Раце/А ($1,1 \pm 0,12$), нозе/А ($3 \pm 0,41$) и нозе/труп количниците на ТМ ($0,52 \pm 0,07$) беа значајно пониски кај КС во споредба со К ($1,3 \pm 0,13$) ($p < 0,002$), ($4,29 \pm 0,67$) ($p < 0,0001$) и ($0,69 \pm 0,09$) ($p < 0,0001$). Количниците нозе/А ($2,57 \pm 0,73$), нозе/труп ($0,48 \pm 0,13$) и раце+нозе/труп ММ ($0,66 \pm 0,14$) кај КС беа значајно помали во споредба со К [$4,2 \pm 1,16$; $0,71 \pm 0,12$ ($p < 0,001$) и $0,89 \pm 0,14$ ($p < 0,002$)]. А/Г ТМ ($0,67 \pm 0,1$) и А/Г ММ ($0,72 \pm 0,2$) количникот кај КС беа значајно поголеми во споредба со К ($0,48 \pm 0,05$) ($p < 0,0001$) и ($0,46 \pm 0,09$) ($p < 0,001$). Нозе ОМ кај КС $10,8 \pm 1,95 \text{ kg}$ беше пониска во споредба со К $12,7 \pm 2,1 \text{ kg}$ ($p < 0,046$). Само спиналниот КМД кај КС ($0,89 \pm 0,09 \text{ kg/cm}^2$) беше помал во споредба со К ($0,94 \pm 0,12 \text{ kg/cm}^2$) ($p < 0,017$).

Заклучок. Количниците на централните со периферните регионални ТМ, ММ и ОМ ги диференцираат значајно и прецизно пациентите со КС и К и ја потврдија екстремната централна дебелина кај КС.

Клучни зборови: DXA, телесен состав, телесна

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Introduction

Cushing's syndrome is associated with weight gain and visceral obesity [1]. Increased central fat mass is characteristic of active CS. Marked osteopenia in the lumbar spine and femoral neck is present in most patients with active CS [2]. As many as 50% of patients with CS suffer from osteoporosis [3,4].

Obesity and central body fat distribution are known risk factors for cardiovascular and metabolic diseases. Thus, there is an increased interest in the evaluation of various methods for assessing body composition and body fat distribution. DXA measurements of fat distribution may be useful in studies related to obesity-associated disease risk [5]. DXA method determines total body fat mass and FM%, bone mass and lean body mass, and separately their regional values for the arms, legs, head and trunk (which includes ribs, pelvis, thoracic spine, and lumbar spine) [6]. DXA determines total and regional body composition. Body composition is the ratio of LBM to fat body mass. Using DXA to determine the proportion of LBM (muscle) versus total body fat is a valuable clinical tool in the management of long-term health and fitness [7]. DXA is considered to be a gold standard for assessment of bone health and body composition, because of its reliability, precision, and the fact that it is based on a three-compartment model [8,9]. Published studies have shown a good correlation between central abdominal fat by DXA and visceral fat by computed tomography (CT) [10] or magnetic resonance imaging (MRI) [11-15].

The aim of this study was to evaluate the differences of the body composition and fat distribution as measured by DXA in women with CS with confirmed abdominal obesity in comparison with healthy control women matched for age, menopausal status, and BMI.

Material and methods

DXA examination was performed in two groups of women: 1st group with confirmed Cushing's syndrome (CS) (n=10) and 2nd group of control healthy women (C) (n=10), matched according to their mean age (40.32±11.25yr.) in CS and (41.91±12.85 yr.) in C as well as their BMI (28.89±3.53kg/m² vs. 29.39±4.04kg/m²) and menopausal status. All examinees were premenopausal. CS had not received any treatment at the time of assessment. All had typical signs and symptoms of CS. Anthropometric, hormonal, and metabolic parameters confirmed CS diagnosis. C had a stable weight for at least several months before being included in the study. Women with CS and C were overweight. Anthropometric measurements of waist circumference, waist-thigh ratio (WTR) and

waist-hip ratio (WHR) were performed and their mean values showed central fat distribution in CS patients.

Table 1. Waist circumference, WTR and WHR in CS and C

	Waist circumference (cm)	WTR	WHR
CS	105±14.78	1.86±0.33	1.11±0.17
C	93.44±10.2	1.45±0.11	0.88±0.07

CS-Cushing's syndrome; C-Control women;

WTR-waist-to-thigh ratio; WHR-waist-to-hip ratio

Body height was measured by a wall stadiometer in barefoot subjects with head in horizontal Frankfurt plane to the nearest 0.1 cm. Body weight was measured by a digital scale while wearing light clothing and it was estimated for each subject in kilograms (kg). BMI was calculated with the following formula: weight (kg)/height (m²). Anthropometric and DXA measurements were performed by the same medical doctor. To obtain WHR, the waist circumference was measured at the midway between the lateral lower ribs and the iliac crests while the subject was standing, after a moderate expiration, and the hip circumference was measured at the widest part over the greater trochanters according to the World Health Organization criteria. Waist and hip circumferences were recorded to the nearest millimetre, and the average of two measurements was used for analysis. Thigh circumference was measured at the highest level of the lower limb.

DXA assessment was performed with DXA System Lunar DPX-NT, which uses encore 10 Windows-XP Professional OS computer. The entire body of each subject was scanned. During DXA scan, the subject was in a supine position while the x-ray scanner performed a series of transverse scans, measured at 1-cm intervals from the top of the head to the bottom of the toes. The DXA machine was calibrated daily in accordance with the manufacturer's guidelines to ensure adequate quality control. The system enables simultaneous assessment of total and regional body composition and fat distribution. A standard whole body DXA examination included total body and three regional measurements of trunk (chest, abdomen and pelvis), arms and legs to analyze body composition according to a three-compartment model: FM, LBM, BMC. Total and regional BMD was expressed in g/cm² and BMC values were expressed in grams (g). BMD and BMC of the lumbar vertebral spine (L2-L4) and proximal femur were also measured.

Total and regional FM and FM% were determined. Truncal FM (TFM), gynoid FM (G) were measured as well as central abdominal fat content; android fat mass (A) was measured from the upper border of L2 to the lower border of L4 (standard software option). Central obesity index (COIt) was calculated as a ratio of the android to gynoid tissue fat mass %, COIt=A/GFMt%; central obesity (CO) index was calculated as a ratio of

android FM% to gynoid FM% ($CO=A/GFM\%$); android FM/gynoid FM ($A/G\ FM$) ratio and android to gynoid TM ($A/G\ TM$) were also determined.

DXA assessment of the TM and TM percentage (TM%) was performed. TM is consisted of FM and bone (mineral) free LBM. TM and LBM values were expressed in kilograms (kg).

Statistical analyses were performed using the statistical software program SPSS for Windows, version 14.0. Each parameter was presented as mean $\pm$ standard deviation (SD). Differences between the groups were tested by unpaired *t*-test. Two-tailed *P* values <0.05 were considered to be statistically significant.

Results

Arms, legs, trunk, A, G and total values of TM as well as TM% were not significantly different between the two groups. Only arm TM% was higher in CS compared to C ($p<0.043$). The results are shown in Table 2.

Table 2. Total and regional TM, TM% and TM ratios of different body compartments

	Cushing	Control	P
Tissue mass (g)			
Arms	7300 $\pm$ 1302	7420 $\pm$ 1431	NS
Legs	20100 $\pm$ 5394	24200 $\pm$ 3852	NS
Trunk	38200 $\pm$ 7735	35500 $\pm$ 6103	NS
Android	6670 $\pm$ 1451	5750 $\pm$ 1197	NS
Gynoid	10300 $\pm$ 2881	11800 $\pm$ 1655	NS
Total	69200 $\pm$ 14235	70800 $\pm$ 10845	NS
Tissue mass (%)			
Arms	45.06 $\pm$ 3.1	40.23 $\pm$ 6.29	0.043
Legs	45.18 $\pm$ 5.63	47.23 $\pm$ 5.67	NS
Trunk	50.15 $\pm$ 5.04	46.26 $\pm$ 4.72	NS
Android	54.14 $\pm$ 6.34	49.29 $\pm$ 6.31	NS
Gynoid	50.76 $\pm$ 4.64	52.57 $\pm$ 4.28	NS
Total	46.9 $\pm$ 3.64	44.76 $\pm$ 4.66	NS
Tissue mass (gr) ratios			
(arm+leg)/trunk	0.715 $\pm$ 0.08	0.897 $\pm$ 0.09	0.0001
Legs/trunk	0.52 $\pm$ 0.07	0.69 $\pm$ 0.09	0.0001
Android/gynoid	0.67 $\pm$ 0.1	0.48 $\pm$ 0.05	0.0001
Arms/android	1.1 $\pm$ 0.12	1.3 $\pm$ 0.13	0.002
Legs/android	3 $\pm$ 0.41	4.29 $\pm$ 0.67	0.0001
Tissue fat mass (%) ratios			
Android/gynoid (COIt)	1.072 $\pm$ 0.15	0.94 $\pm$ 0.11	0.036

COIt-central obesity index *t*

Arms plus legs to trunk TM ratio was significantly lower in CS compared to C ($p<0.0001$). Arms to android TM ratio was significantly lower in CS compared to C ($p<0.002$). Legs to android as well as legs to trunk TM ratio was significantly lower in CS compared to C ($p<0.0001$). Android to gynoid TM ratio was significantly higher in CS patients ($p<0.0001$). Android to gynoid tissue fat mass % ratio was higher in CS ($p<0.036$).

Arms, legs, trunk, android, gynoid and total FM and FM% were not significantly different between CS and C except for arms fat mass%, which was higher in CS

Table 3. Total and regional FM, FM% and FM ratios of different body compartments

	Cushing	Control	P
Fat mass (g)			
Arms	3300 $\pm$ 680	3020 $\pm$ 852	NS
Legs	9300 $\pm$ 3610	11500 $\pm$ 2544	NS
Trunk	19300 $\pm$ 5362	16600 $\pm$ 3714	NS
Android	3640 $\pm$ 1088	2880 $\pm$ 817	NS
Gynoid	5300 $\pm$ 1924	6230 $\pm$ 1092	NS
Total	32800 $\pm$ 9098	31900 $\pm$ 6520	NS
Fat mass (%)			
Arms	43.28 $\pm$ 3.07	38.68 $\pm$ 6.16	0.049
Legs	43.33 $\pm$ 5.56	45.61 $\pm$ 5.55	NS
Trunk	49.4 $\pm$ 5.04	45.31 $\pm$ 4.61	NS
Android	53.81 $\pm$ 6.35	48.88 $\pm$ 6.32	NS
Gynoid	49.67 $\pm$ 4.64	51.54 $\pm$ 4.23	NS
Total	45.49 $\pm$ 3.65	43.28 $\pm$ 4.53	NS
Fat mass ratios			
Legs/trunk	0.48 $\pm$ 0.13	0.71 $\pm$ 0.12	0.001
Legs/android	2.57 $\pm$ 0.73	4.2 $\pm$ 1.16	0.001
Arms+legs/trunk	0.66 $\pm$ 0.14	0.89 $\pm$ 0.14	0.002
Android/Gynoid	0.72 $\pm$ 0.2	0.46 $\pm$ 0.09	0.001
Fat mass % ratio			
Android/Gynoid (CO)	1.09 $\pm$ 0.15	0.95 $\pm$ 0.11	0.032

CO-central obesity

($p<0.049$). Android/gynoid FM ratio was significantly higher in CS compared to C ($p<0.001$). Legs to trunk and legs to android FM ratios were significantly lower in CS compared to C ($p<0.001$), as well as the arm plus legs sum to trunk FM ratio ($p<0.002$). Mean arm FM value in CS was 113% of its value in C.

Table 4. Total and regional LBM and LBM ratios of different body compartments in CS and C

	Cushing	Control	P
Lean mass (g)			
Arms	4000 $\pm$ 701	4400 $\pm$ 771	NS
Legs	10800 $\pm$ 1948	12700 $\pm$ 2059	0.046
Trunk	18900 $\pm$ 3009	18900 $\pm$ 2818	NS
Android	3020 $\pm$ 554	2870 $\pm$ 434	NS
Gynoid	4960 $\pm$ 1013	5590 $\pm$ 828	NS
Total	36400 $\pm$ 5655	38900 $\pm$ 5551	NS
Lean body mass ratios			
legs/trunk	0.57 $\pm$ 0.05	0.67 $\pm$ 0.07	0.002
arms+legs/trunk	0.78 $\pm$ 0.07	0.91 $\pm$ 0.09	0.004

Arms lean mass was lower but not significantly different between CS and C as well as other regional LBM measurements except for leg LBM, which was significantly lower in CS ($p<0.046$). Legs to trunk lean mass was significantly lower in CS compared to C ($p<0.002$), as well as the sum of arms and legs to trunk lean mass ratio ($p<0.004$). Mean arm lean mass value in CS was 91% of its value in C.

Trunk BMC value in CS (586 $\pm$ 102 gr) was significantly lower compared to C (746 $\pm$ 164 gr) ($p<0.017$). Spine BMD values differed between CS (0.93 $\pm$ 0.11g/cm²) and C (1.07 $\pm$ 0.15g/cm²) significantly ($p<0.041$). Other values were not significantly different.

Table 5. Total and regional BMD and BMC in CS and C

	Cushing	Control	P
Bone mineral density (g/cm²)			
Arms	0.78±0.07	0.82±0.11	NS
Legs	1.15±0.12	1.14±0.12	NS
Trunk	0.89±0.09	0.94±0.12	NS
Pelvis	1.09±0.13	1.13±0.14	NS
Spine	0.93±0.11	1.07±0.15	0.041
Total	1.09±0.12	1.13±0.12	NS
Bone mineral content (g)			
Arms	298±50.07	302±57.13	NS
Legs	841±189	860±159	NS
Trunk	586±102	746±164	0.017
Andorid	41.5±8.82	46.5±6.42	NS
Gynoid	221±44.92	231±49	NS
Total	2150±414	2400±437	NS

Discussion

Obesity is a multi-factorial chronic disease characterized with an accumulation of excess fat sufficient to harm health. In addition to general obesity, the distribution of body fat is independently associated with the metabolic syndrome. Body composition is simply the ratio of LBM (structural and functional elements in cells, body water, muscle, bone, heart, liver, kidneys, etc.) to fat body (essential and storage) mass. The study of body composition attempts to partition and quantify body weight or mass into its basic components. Naturally, the objective for optimum health is to minimize body fat and maximize lean mass [16].

Measurements of body composition and body fat distribution have provided a research tool to study the metabolic effects of aging, obesity, and various diseases such as CS [17]. The core abnormality of CS is extreme central (abdominal) obesity. Central body fat distribution is correlated with age, gender and sex hormones [18-21]. Body composition, including fat mass, body fat distribution and muscle mass, gradually change with aging, even if the body weight and BMI remain unchanged. LBM decreases significantly, while fat mass increases and is preferentially stored in abdominal tissues [22,23]. Postmenopausal (postM) women have significantly more fat, a more central fat distribution, and less lean tissue mass than preM women [17,24-26]. BMI of 30 or higher usually indicates excess body fat. In a previous study, in 2011 Shubeska S. discovered with DXA that BMI increase in healthy women was associated with a more pronounced abdominal, visceral fat distribution [27].

Android obesity, which is predominantly visceral, intra-abdominal, is more predictive of adipose-related comorbidities than gynecoid obesity, which has a relatively peripheral (gluteal) distribution. Evaluation of body fat depots, which when increased are closely associated with the insulin-resistance syndrome, is important for the management and prevention of its associated complications. A recent study has suggested that central fat

distribution measured with DXA is a useful marker of insulin sensitivity in healthy subjects, and that a simple measurement of total (visceral plus anterior and posterior subcutaneous fat) abdominal fat mass is highly predictive of health risks and may be as valuable as measuring intra-abdominal fat depots [28,29].

There is a growing evidence that intra-abdominal adipose tissue (IAAT), rather than total body fat, is a risk factor for metabolic conditions associated with obesity. For this reason the evaluation of IAAT is clinically important [30,31]. Chronic hypercortisolemia due to Cushing's disease (CD) results in abnormal adipose tissue (AT) distribution. Because of that, effective methods for assessing visceral fat are important to investigate its role for the increased health risks in obesity [26,32,33].

The most accurate anatomical methods of intra-abdominal fat measurement are CT and MRI [34-37]. Although imaging techniques such as CT and MRI provide accurate and precise assessment of visceral adiposity, they require technical skill to operate, they are expensive, impractical for routine clinical use and, in the case of CT, deliver unacceptable levels of radiation exposure [38,39,34].

DXA is a sensitive technique of body composition assessment, which measures whole and segmental body fat and LBM. It is a relatively new method for reliable and direct measurements of body mass in its three basic components: total body BMC, mineral free lean tissue mass, and fat [40,41]. DXA is a good alternative to CT for predicting total abdominal fat in the elderly population [42]. This method allows us to determine more accurately the degree of obesity of a particular patient as well as body fat distribution [8,17].

DXA is used to quantify abdominal fat mass [6]. DXA cannot determine visceral fat, but it can measure central abdominal fat. Central abdominal fat measured by DXA includes the visceral fat at this region plus anterior and posterior subcutaneous (sc) fat [24,43,44], and it highly correlates with intra-abdominal (visceral) fat measured by CT [10,40,45,46] or MRI [9-12,40,45,47-49]. A strong correlation exists between DXA and CT values for total abdominal fat [42].

CS is characterized by abdominal obesity and enlarged abdominal fat cells, with adipose tissue lipoprotein lipase activity elevated 2-3 times than in normal women and low lipolytic capacity. CS is associated with an increase in the size of intra-abdominal fat stores compared with sc fat, and it is well-known that the accumulation of visceral fat rather than sc fat is more frequently associated with premature death from cardiovascular disease. Patients with CS had less than a twofold increase in sc fat and greater than a fivefold increase in intra-abdominal fat compared with values in healthy subjects. These findings suggest that fat in different body compartments responds differently to disease processes and that DXA can be used to measure these changes [50,51].

A reduction of the total AT volume and a redistribution of AT from visceral to peripheral depots were found

using a multiscan CT technique after normalization of the hypercortisolic state in women with CS [52].

The first study concerning the measurements of body composition in CS using DXA was published by Wajchenberg BL [53]. Body composition determined by DXA and the abdominal visceral fat component determined by CT scanning were examined in women with CD and compared with those in obese women with the same anthropometric parameters and those in non-obese women. Patients with CS had no increase in total body fat or the trunk region (android) component, but had a higher intra-abdominal fat area compared to the obese subjects. The total lean tissue mass (determined with DXA) 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 reduced amounts of fat and lean tissue masses in the arms were the most significant findings in hypercortisolism. The body mineral and bone calcium contents were slightly reduced in CS compared to those in the obese controls [53].

In our study total and arms TM were not significantly lower in CS compared to C. Only arms TM% was significantly higher ($p<0.043$) in CS compared to C, but total TM% was not significantly higher. Significantly higher arm TM% is a result of significantly higher arm FM% ($p<0.049$) which is a result of not significantly higher arm FM in CS (mean 113% of C) and not significantly lower arm lean mass (mean 91% of C). Trunk and android TM and TM% were not significantly higher in CS compared to C. Legs and gynoid TM and TM% were not significantly lower in CS compared to C. Not significantly lower leg TM and TM% in CS is a result of significantly lower leg lean mass ($p<0.046$) and not significantly lower FM and FM%. Total, trunk and android FM and FM%, and arms FM were not significantly higher, but arms FM% was significantly higher ($p<0.049$) in CS compared to C. Legs and gynoid FM and FM% were not significantly lower.

Chronic hypercortisolemia due to CD results in abnormal AT distribution. CD patients had higher visceral to total AT (VAT/TAT) ratios ($p<0.01$) and lower subcutaneous SAT to total TAT ratios ($p<0.05$) compared to controls in the study of Geer EB *et al.* in 2010 [19]. Mass of the skeletal muscle was less but intermuscular AT was not different. These findings on whole-body MRI have implications for understanding the role of cortisol in the abnormal AT distribution and metabolic risk seen in patients exposed to chronic excess glucocorticoids [54]. Body fat distribution is simply determined with DXA by the relationship of the regional (segmental) fat compartments. The relationship of the predominantly visceral, android abdominal fat TM and the gynoid, peripheral fat tissue mass is an indicator of the abdominal (central) obesity [27]. In our study A/G FM ratio differentiated the two groups CS and C with higher significance ($p<0.001$) as well as A/G TM ratio ($p<0.0001$) in comparison to COIt (android to gynoid tissue fat mass % ratio) ($p<0.036$)

and CO (android to gynoid FM% ratio) ($p<0.032$). A/G/FM ratio and A/G TM ratio are more reliable indexes of central obesity compared to COIt and CO. A/G TM ratio differs CS and C with the highest sensitivity. DXA machine gives automatically the COIt value. This shows that it is not enough precise and A/G TM and A/G FM have to be calculated in order to differentiate CS patients more precisely.

Gabriella *et al.* in 2001 [29] evaluated body composition and fat distribution measured by DXA in women with CS compared with healthy C women matched for age, menopausal status, and BMI. Because the mean values of BMI indicated that CS were overweight, C were selected also to be overweight so that the differences in body composition between patients and controls would not be due to different amounts of adiposity. WHR and waist circumference mean values showed that CS and adrenal incidentalomas (AI) had a central fat distribution. This suggests that the increase of fat mass in CS and AI may be more influenced by the disease than by the estrogenic status. Total fat mass, trunk and arms fat mass percentages were significantly higher in CS than in C. Abdominal fat and its percentage were significantly higher in CS than in AI and C women, suggesting that glucocorticoids play a pivotal role in the pathogenesis of central obesity [43]. Leg fat masses were not significantly different between the groups. Total, trunk, and arms fat mass was significantly increased in CS vs. C [29].

In our study arms, legs, trunk, android, gynoid and total fat mass and fat mass percentages were not significantly different between CS and C except for arms fat mass % ($p<0.049$). Legs/trunk and legs/android FM showed a significant difference ($p<0.001$), which was a result of significantly lower leg lean mass in CS compared to C, and not significantly lower FM. Legs/trunk TM ratio differentiates CS from C more precisely in comparison to arms+legs/trunk FM. The ratio of the not significantly lower peripheral parts of the body and not significantly higher central parts of the body legs/trunk FM and arms+legs/trunk FM showed significantly lower value in CS, differentiated the two groups of patients, and also confirmed central body fat distribution in CS in our study.

Burt MG *et al.* in 2006 [55] investigated the impact of CS and GHD on whole and regional body composition and energy metabolism and assessed LBM, FM and regional body composition by DXA. Mean percentage FM was significantly greater by 30% in CS and LBM was significantly lower by 15% in CS ($p=0.002$) than in normal subjects. In CS, the proportion of lean tissue in the limbs was 12% less than in normal ($p=0.001$). Truncal fat represented a greater proportion of total FM in CS ($52.5\pm1.8\%$ vs. $46.9\pm1.3\%$, $p=0.014$) than in normal subjects. It was concluded that FM was higher and LBM lower in both CS and GHD. However, 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 [55].

In our study the ratio of the sum of significantly lower legs lean mass ($p<0.046$) and not significantly lower arms lean mass in CS to not significantly higher trunk lean mass in CS was significantly lower in CS compared to C ($p<0.004$). The ratio of significantly lower legs lean mass ($p<0.046$) in CS to not significantly higher trunk lean mass in CS was significantly lower in CS compared to C ($p<0.002$). Legs/trunk lean mass ratio is a better predictor compared to arms+legs/trunk lean mass ratio in differentiation of CS and C. Legs/trunk lean mass ratio differentiated better CS from C than arms+legs/trunk lean mass ratio.

In a study of Schafröth U including a subgroup of 12 patients, truncal fat mass was significantly elevated when compared to obese controls (19.2 kg vs. 14.7 kg, $p<0.01$, and 42% vs. 36% in percentage of truncal body tissue ($p<0.05$), whereas total fat mass was insignificantly increased [1].

Lean body mass and body fat mass were estimated in 12 patients with Cushing's disease before treatment. By a comparison with the results in simple obesity, it was concluded that the total body fat mass generally was increased in patients with CD [56].

Climacteric changes rather than the aging process are relevant for prediction of body weight and fat distribution, especially for perimenopausal and PostM women, who show a shift to a central, android fat distribution [57]. Examinees in our study were not different according to their BMI and age to avoid their influence on BMD and body fat distribution. CS and controls were all preM and the differences in body composition are not due to estrogenic status.

DXA scanning was primarily developed for the diagnosis of osteoporosis and was initially applied to studies of the clinically important sites of the lumbar spine, femoral neck, and forearm. As a result, DXA has been extended to allow the study of the total skeleton and its regional parts [58].

BMD reduction is both age- and sex-related [59]. Thinner women have lower BMD, especially at weight-bearing sites such as the hip and the spine. PostM women are characterized with significantly lower BMC and BMD.

Endogenous CS causes osteoporosis and marked increases in total body fat with the classical central pattern of deposition [60]. Osteoporosis is a major feature of CS and the most common complication of CS and fragility fractures may be the first sign of the disease. Among several variables examined by multiple logistic regression, the etiology of CS (adrenal vs. pituitary origin) was a significant factor affecting the prevalence of osteoporosis [4]. Prevalence of osteoporosis in patients with CS is influenced by its etiology. A factor associated with pituitary CS, such as adrenal androgen, may protect these patients from glucocorticoid-induced osteoporosis [61,62]. Bone dimension and BMC of the entire skeleton are found to be decreased in endogenous CS. As judged by

biochemical markers of bone remodeling, this is caused by decreased bone formation and an increased bone resorption [63,64]. Marked osteopenia was present in most patients with active CS that was also found in our study on lumbar spine. Our study confirmed significantly lower trunk BMC value in CS compared to C ($p<0.017$), also spine BMD values in CS were significantly lower compared to C ($p<0.041$). Other BMC and BMD values were not significantly different.

By comparing z-scores of reduced BMD in CS patients, spinal trabecular BMD was found to be the most severely affected. Moreover, these data suggested a site and tissue specificity of the effect of glucocorticoid excess on bone mass [65].

Comparison between groups showed that preM C women had significantly higher BMC and lower abdominal and trunk fat masses than preM CS. BMC was significantly decreased in CS vs. C.

It is well-established that chronic excess of glucocorticoids has negative effects on bone and collagen turnover, and that secondary osteoporosis is a known clinical complication of endogenous CS. CS is a well-recognized cause of bone loss [66]. Although many previous studies have shown decreased BMD in the lumbar spine and proximal femur of patients with endogenous CS, so far, the data estimating BMD in their peripheral skeleton are sparse. It was found that BMD in the forearm was reduced only in postM women with newly diagnosed endogenous CS, while BUA in the heel is unaffected in both pre- and postM patients [64,67,68]. BMD was significantly reduced at all sites, except in cortical forearm, in CS patients compared to controls. Compared to matched control subjects, female eumenorrheic CS patients have reduced osteoblastic function, increased bone resorption, and reduced BMD, and the severity of these abnormalities is statistically related to the severity of disease activity, as indicated by urinary free cortisol [65].

Conclusions

Body composition was performed in our study in CS patients and C matched for age, menopausal status, and BMI. Classical central pattern of fat deposition and osteopenia on lumbar spine were present in patients with active CS. Total and regional FM, TM, LBM did not differentiate CS and C significantly and determination of their relationships had to be done. The ratio of the not significantly higher central (abdominal) and not significantly lower peripheral gynoid (gluteal) parts of the body, android/gynoid FM values, showed significantly higher values in CS and differentiated precisely the two groups of patients, CS and C, and confirmed central body fat distribution in CS. DXA machine gives automatically calculated COIt value. This study showed that COIt value is not enough precise and A/G TM and A/G FM have

to be calculated in order to differentiate CS patients more precisely. A/G TM ratio differentiates the best CS and C.

Conflict of interest statement. None declared.

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