# DIAGNOSTIC CENTRAL OBESITY INDEXES CUT – OFF POINT VALUES DETERMINED WITH DUAL-ENERGY X-RAY ABSORPTIOMETRY IN CUSHING'S AND OBESE WOMEN

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# ABSTRACT

**Aim**: The aim of this study was to develop quantiative criteria for defining visceral obesity and to establish dual-energy X-ray absorptiometric (DXA) diagnostic cut-off points (CP) for normal and abnormal values of the central obesity indexes (COI) that best differentiate extreme visceral obesity in Cushing's syndrome (CS) from non CS obese and non obese women.

**Material and Methods**:  $\text{COI}_{1-4}$  values calculated as a ratio of android to gynoid tissue mass, fat mass and their % were determined in 4 groups, each consisting of 18 women: 1<sup>st</sup> group of CS, 2<sup>nd</sup> group of obese women (O<sub>1</sub>) not different according to their age and BMI from CS, 3<sup>rd</sup> group of obese women (O<sub>2</sub>) with BMI of  $35 \pm 1.2$  kg and 4<sup>th</sup> group of non obese healthy women (C) with normal BMI. Diagnostic accuracy (DG) of CP values of COI<sub>1m-4m</sub> indexes of abdominal obesity and CP values of COI<sub>1m-4m</sub> indexes of normal body fat distribution (BFD) was determined.

**Results**:  $\text{COI}_{1.4}$  indexes values were highly significantly different among the 4 examined groups and were significantly highest in CS patients and lowest in group C (p < 0.0001).  $\text{COI}_{1m-4m}$  CP values differentiated extreme visceral, abdominal obesity in CS with highest DG as well as  $\text{COI}_{1n-4n}$  CP values differentiated normal BFD in group C.  $\text{COI}_{1m}$  CP of 0.55 best differentiated CS from O<sub>1</sub> for DG of 100%.  $\text{COI}_{2n}$  of 0.38 best differentiated C from CS and O<sub>2</sub> for highest DG of 100% compared to O<sub>1</sub> because of the significantly higher BMI and  $\text{COI}_{1n-4n}$  values in O<sub>2</sub> that were associated with more pronounced abdominal obesity and highly significantly positive correlation with BMI.

**Conclusions**: DXA cut-off point values of indexes  $\text{COI}_{1\text{m}-4\text{m}}$  and  $\text{COI}_{1\text{n}-4\text{n}}$  were established as diagnostic indexes and criteria useful in discovering extreme abdominal and normal BFD.  $\text{COI}_{1\text{m}}$  CP value of 0.55 was discovered as a diagnostic criterion of extreme abdominal obesity and  $\text{COI}_{2\text{n}}$  of 0.38 as a diagnostic criterion of normal BFD that excluded abdominal obesity. The other indexes  $\text{COI}_{1\text{m}-4\text{m}}$  and  $\text{COI}_{1\text{n}-4\text{m}}$  CP values had also high DG in discovering abdominal and normal body fat distribution.

Keywords: DXA, abdominal obesity, central obesity indexes, cut-off point values

# INTRODUCTION

Metabolic syndrome (MS) is defined as a complex of interrelated risk factors, including obesity (particularly central obesity), impaired fasting glucose, hypertension, elevated serum triglycerides (TG), and low high density-lipoprotein cholesterol (HDL-C). Insulin resistance is considered to be the factor linking these different metabolic abnormalities [1]. MS may also indicate the presence of Cushing's syndrome (CS). Almost all patients with CS are obese or overweight, and have abdominal, visceral adiposity in about 95% of the patients. Many of the CS patients also have glucose metabolism abnormalities, impaired glucose tolerance or diabetes, hypertension, elevated TG levels and low HDL-C. Almost two thirds of CS patients fulfill at least three criteria for MS [2].

Similarities between the MS and CS, and reversibility of the features of CS, suggest that cortisol may contribute to the pathophysiology of both conditions. Emerging data suggest that patients with MS show hyperactivity of the hypothalamic-pituitary-adrenal (HPA) axis, which leads to a state of "functional hypercortisolism" [3, 4]. This abnormality could be central in origin, due to hypersecretion of CRF or ACTH; alternatively, it could represent an adaptive phenomenon secondary to a state of functional cortisol resistance [5].

Android obesity in CS and in non CS abdominal obese with the MS, which is predominantly visceral, intra-abdominal, is more predictive of adipose-related comorbidities than gynecoid obesity, which has a relatively peripheral (gluteal) distribution [6, 7]. Effective methods for assessing abdominal, visceral fat are important to investigate its role for the increased health risks in obesity [8]. For this reason the evaluation of body composition and body fat distribution (BFD) is clinically important. DXA is used to quantify abdominal fat mass and enables precise, accurate body composition and BFD assessment and it can be used in determination of COI values. The limitation of DXA derived body composition is that there are currently no universally accepted reference ranges for body composition based on DXA results. Also, to date CP values of COI have not been provided in order to precisely confirm abdominal obesity in CS and non CS obese [9].

The aim of this study was to develop a set of normative standards, reference ranges with determination of the CP values of DXA indexes of central, abdominal obesity as a ratio of android to gynoid fat and tissue mass and their percentages that best differentiate CS and  $O_1$  and confirm central abdominal obesity, and to determine their normal CP values that best differentiate group C from CS,  $O_1$  and  $O_2$  and exclude abdominal obesity.

#### **MATERIAL AND METHODS**

This transversal study was organized and realized at the University Clinic of Endocrinology, Diabetes and Metabolic Disorders, Faculty of Medicine, "Ss Cyril and Methodius" University of Skopje. DXA assessment of body composition and BFD was performed in four groups of women, each consisting of 18 subjects: 1st group of Cushing's syndrome (CS), with clinically confirmed CS with Body Mass Index (BMI)  $(30.25 \pm 5.64)$ kg/m<sup>2</sup>) and age of  $43.58 \pm 13.58$  years, 2<sup>nd</sup> group of obese women O<sub>1</sub>, matched with CS according to their BMI (29.8  $\pm$  4.08 kg/m<sup>2</sup>) and age (40.4  $\pm$ 12.05 years),  $3^{rd}$  group of obese women O<sub>2</sub> with BMI  $(35 \pm 1.2 \text{ kg/m}^2)$  and age of  $(45 \pm 8 \text{ years})$ , and the 4<sup>th</sup> group C of healthy women with normal BMI (21.59  $\pm$  1.35 kg/m<sup>2</sup>) and age (40.09  $\pm$  12.72 years). All examined women were not different according to their age. BMI in C was significantly lower compared to CS, O<sub>1</sub> and O<sub>2</sub>. BMI was significantly lower in group  $\dot{O}_1$  compared to  $O_2$  (p < 0.0001). CS had not received any treatment at the time of the assessment and had typical signs and symptoms of CS including extreme central obesity. Anthropometric, DXA, hormonal and metabolic parameters confirmed CS diagnosis. Written informed consent was obtained from all patients before commencement of the study.

Body weight was measured to the nearest 0.1 kg using a calibrated digital weighing scale, with subjects minimally clothed in light-weight underwear. Standing height was measured to the nearest 0.1 cm with the shoes removed and the head in the Frankfort plane using a standard stadiometer. BMI was calculated as the patient's weight in kilograms divided by the height in meters squared.

DXA assessment in this study was performed with DXA System Lunar DPX-NT, which uses enCore Windows-XP Professional OS computer calibrated daily according to the standard procedures for maintenance and use as recommended by the manufacturer. For body composi-

tion measurements the entire body of each subject was scanned. During DXA scan, subjects were positioned following the standard manufacturer's protocols in 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. Android (A) and gynoid (G) region were automatically determined as defined by manufacturers instruction as well as A and G tissue and fat mass and their percenatages. Four indexes of central obesity were determined: central obesity index one  $(COI_1)$  as a ratio of A to G tissue mass  $COI_1 = At/Gt$ ;  $COI_2$  as a ratio of A to G fat mass COI, = Af/Gf, COI, as a ratio of A and G tissue % fat  $OI_3 = At\%/Gt\%$  fat and  $OI_4$  as a ratio of A to G fat % COI<sub>4</sub> = Af%/ Gf%. CP values of DXA indexes of central, abdominal obesity  $\text{COI}_{1\text{m}}$ ,  $\text{COI}_{2\text{m}}$ ,  $\text{COI}_{3\text{m}}$  and  $\text{COI}_{4\text{m}}$  were determined to best differentiate CS with confirmed abdominal obesity from O<sub>1</sub>, healthy control women matched for age, menopausal status, and BMI. Also, CP values of DXA indexes of normal body composition and fat distribution  $\text{COI}_{1n}$ ,  $\text{COI}_{2n}$ ,  $\text{COI}_{3n}$  and  $\text{COI}_{4n}$  that best differentiate CS and C as well as  $O_1$  and  $O_2$  from C and exclude abdominal obesity were determined.

Cut-off point values were determined for all four DXA indexes and their sensitivity (S), specificity (SP), positive and negative predictive value (PPV and NPV) and diagnostic accuracy (DG) were evaluated in the following way:

• Sensitivity (true positive rate) is the probability that a test result – extreme visceral obesity will be positive when the disease CS is present.

• Specificity (true negative rate) is the probability that a test result will be negative; there is no extreme central body fat distribution when the disease is not present in C and O.

• Positive predictive value (PPV): the proportion of those with a positive test result (extreme central body fat distribution) who actually have a disease (CS). • Negative predictive value (NPV): the proportion of those with a negative test result (without extreme central obesity) who do not have a disease (C and O).

• Diagnostic accuracy (effectiveness) was expressed as a proportion of correctly classified subjects (true positive rate + true negative rate) among all subjects.

Statistical analyses were performed using statistical software program SPSS for Windows, version 19.0. Variables were presented as means  $\pm$  standard deviations (SD). P values <0.05 were considered to be statistically significant. For normally distributed variables, parametric tests were used for analysis. Differences among the groups were evaluated by performing an analysis of variance (ANOVA) for normally distributed parameters. Correlation coefficients were determined by Pearson's product moment.

#### RESULTS

COI indexes values determined during body composition assessment in total body scans, were highly significantly different among the 4 examined groups and they were highly significantly highest in CS and lowest in group C compared to all other groups (p < 0.0001). COI, was significantly higher in  $O_2$  compared to  $O_1$  (p < 0.0001). COI<sub>2</sub> was significantly higher in  $O_2$  compared to  $O_1$  (p < 0.001) and it was highly significantly different between the other groups (p < 0.0001). COI<sub>3</sub> and  $COI_4$  were significantly higher in  $O_2$  compared to  $O_1$ , (p < 0.017) and (p < 0.018) respectively. COI<sub>1</sub> and COI<sub>2</sub> were significantly higher in CS compared to  $O_1$  (p<0.0001). COI<sub>3</sub> and COI<sub>4</sub> were significantly higher in CS compared to  $O_1$ , (p < (0.009) and (p < 0.007) respectively.

 $COI_1$  correlated highly significantly positively with  $COI_2$  as well as  $COI_3$  and  $COI_4$ 

**Table 1.** Significance of the difference between  $COI_p$ ,  $COI_s$ ,  $COI_s$  and  $COI_4$  values in CS, O and C

Variable	CS	01	02	С	P-value
COI	0.68±0.09	0.46±0.53	$0.55 {\pm} 0.06$	0.38±0.04	0.0001
COL	0.76±0.16	$0.42{\pm}0.09$	$0.55 {\pm} 0.08$	$0.25 {\pm} 0.07$	0.0001
COL	1.07±0.15	0.88±0.12	$0.99 {\pm} 0.07$	0.64±0.15	0.0001
COL	1.12±0.14	0.91±0.12	$1\pm0.07$	0.65±0.15	0.0001
CS – Cushing's Syndrome;		O – obese	e; C – no	C – non obese	

CS – Cushing's Syndrome; O – obese; COI<sub>1</sub> = At/Gt (android/gynoid tissue mass ratio)

 $COI_{2} = Af/Gf$  (and roid/gynoid fat mass ratio)

 $COI_3 = At\%/Gt\%$  fat (android/gynoid tissue % fat ratio)

 $COI_4^3 = Af\%/Gf\%$  (android/gynoid fat % ratio)

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between them (p<0.0001).  $\text{COI}_2$  values in all groups correlated highly significantly positively with  $\text{COI}_1$ ,  $\text{COI}_3$  and  $\text{COI}_4$  values (p<0.0001).  $\text{COI}_1$  values in group  $O_2$  and C correlated significantly positively with  $\text{COI}_3$  and  $\text{COI}_4$  values (p<0.018; p<0.01), and also correlated positively in C (p<0.01; p<0.01).  $\text{COI}_3$  and  $\text{COI}_4$  did not correlate in groups CS and  $O_1$  (p>0.05). BMI correlated highly significantly positively with all COI indexes (p<0.0001).

Cut off point values of COI indexes of central, abdominal obesity  $\text{COI}_{1\text{m}}$  of 0.55 and the values of  $\text{COI}_{2\text{m}}$  of 0.52,  $\text{COI}_{3\text{m}}$  of 0.9 and  $\text{COI}_{4\text{m}}$  of 1.11 that best differentiated extreme central, abdominal, visceral body fat distribution in CS women from group O<sub>1</sub> were determined. COI<sub>1</sub> cut off point value of 0.55 best of all indexes differentiated CS and O<sub>1</sub> for S, Sp, PPV, NPV and DG for 100%. COI<sub>2</sub> coI<sub>3</sub> and COI<sub>4</sub> differentiated CS from O<sub>1</sub> with DG of 94.44%, 70% and 80.56% respectively. Results shown in table 2.

**Table 2.** *S*, *SP*, *PPV*, *NPV* and *DG* of  $COI_{1m}$ ,  $COI_{2m}$ ,  $COI_{3m}$  and  $COI_{4m}$  cut-off point values in differentiation of CS and  $O_1$ 

Variables	COI <sub>1m</sub> 0.55	$\mathrm{COI}_{\mathrm{2m}}0.52$	$\mathrm{COI}_{3\mathrm{m}}0.9$	COI <sub>4m</sub> 1.11	
Sensitivity (%)	100	100	90	61.11	
Specificity (%)	100	88.9	50	100	
PPV (%)	100	90	64.29	100	
NPV (%)	100	100	83.33	72	
DG (%)	100	94.44	70	80.56	

Cut-off point values of DXA indexes of normal body composition and fat distribution  $\text{COI}_{1n}$ ,  $\text{COI}_{2n}$ ,  $\text{COI}_{3n}$  and  $\text{COI}_{4n}$  were determined.  $\text{COI}_{2n}$  cut off point value of 0.38 best differentiated CS and C for S, Sp, PPV, NPV and DG for 100%.  $\text{COI}_{1n}$  value of 0.42 and  $\text{COI}_{4n}$  value of 0.9 differentiated CS and C for DG of 97.22%.  $\text{COI}_{3n}$  value of 0.82 differentiated CS and C for DG of 97.26%.

Cut off point value  $\text{COI}_{2n}$  of 0.38 best differentiated C and O<sub>2</sub> for S, Sp, PPV, NPV and DG for 100%, but differentiated C from O<sub>1</sub> with lower DG of 80.56. Also, cut off point value  $\text{COI}_{3n}$  of 0.82 and  $\text{COI}_{4n}$  value of 0.9 differentiated C from O<sub>2</sub> for DG of 94.44%, but differentiated C from O<sub>1</sub> with lower DG of 83.33% and 80.56% respectively.  $\text{COI}_{1n}$  of 0.42 differentiated C from O<sub>2</sub> with DG of 91.67% but differentiated C from O<sub>1</sub> for DG of 86.11%.

#### DISCUSSION

Obesity is a complex and multifactorial chronic disease originating from a genetic and environmental or behavioral interchange, caused by an imbalance between energy intake and expenditure [10, 11]. Obese subjects have higher percentage of fat mass from the total body mass compared to non obese and differ not only according to the degree of excess fat which they store, but also in the regional distribution of the fat within the body [11, 12]. MS is associated with abdominal obesity, blood lipid disorders, inflammation, insulin resistance, full-blown di-

**Table 3.** *S*, *SP*, *PPV*, *NPV* and *DG* of  $COI_{1n}$ ,  $COI_{2n}$ ,  $COI_{3n}$  and  $COI_{4n}$  cut-off point values in differentiation of CS and C

	CS -C						
Variable	COI <sub>10</sub> 0.42	COI <sub>20</sub> 0.38	COI <sub>3n</sub> 0.82	$COI_{4n} 0.9$			
Sensitivity (%)	100	100	100	100			
Specificity (%)	94.44	100	88.89	94.44			
PPV (%)	94.74	100	83.33	94.44			
NPV (%)	100	100	100	100			
DG (%)	97.22	100	92.86	97.22			

**Table 4.** *S*, *SP*, *PPV*, *NPV* and *DG* of  $COI_{1n}$ ,  $COI_{2n}$ ,  $COI_{3n}$  and  $COI_{4n}$  cut-off point values in differentiation of  $O_1$  and  $O_2$ , with C

Variable	COI <sub>10</sub> 0.42		COI <sub>2</sub> 0.38		COI <sub>20</sub> 0.82		COI <sub>40</sub> 0.9	
	O <sub>1</sub> -C	O <sub>2</sub> -C	0 <sub>1</sub> -C	<sup>—</sup> O <sub>2</sub> -C	0,-C	<sup>5</sup> O <sub>2</sub> -C	0 <sub>1</sub> -C	
Sensitivity (%)	88.89	100	61.11	100	77.78	100	66.67	94.44
Specificity (%)	83.33	83.33	100	100	88.89	88.89	94.44	94.44
PPV (%)	84.21	85.71	100	100	87.5	90	92.31	94.44
NPV (%)	88.24	100	72	100	80	88.89	73.91	94.74
DG (%)	86.11	91.67	80.56	100	83.33	94.44	80.56	94.44

abetes, and increased risk of developing cardiovascular disease, increased predisposition to cancers. CS have profound body composition changes, including increased central, visceral adiposity and decreased lean mass that is especially strongly linked to cardiovascular and metabolic risks [13]. Measurements of body composition and BFD have provided a research tool to study the metabolic effects of aging, obesity, and various diseases such as CS [14].

CS patients had a higher intra-abdominal fat area compared to obese subjects with the same anthropometric parameters, higher visceral to total and visceral to subcutaneous adipose tissue (AT) ratios on CT scan, especially in female CS. These data demonstrated that increased visceral BFD in both female and male patients with CS may increase the risk of the MS in that group of patients [15, 16, 17]. The impact of CS on whole and regional body composition and energy metabolism was assessed by DXA in Burt's study who showed that mean percentage fat mass was significantly greater by 30% in CS. Lean body mass was significantly lower by 15% in CS, and the proportion of lean tissue in the limbs was 12% less than normal [18]. Patients with CS had less than a twofold increase in subcutaneous fat and greater than a fivefold increase in intra-abdominal fat compared with values in healthy subjects. These findings suggested that fat in different body compartments responded differently to disease processes and that CT can be used to measure these changes. Effective treatment of hypercortisolism improved each of the five MS components and dramatically improved body composition abnormalities [19]. From the alterations in body composition observed after normalization of a hypercortisolic state, it was concluded that cortisol in CS directly or indirectly increased the total mass of AT and redistributed AT from peripheral to visceral depots as the same as body AT distribution in non CS obese before weight loss [15, 20]. Body composition and fat distribution measured by DXA were evaluated in women with CS and were compared with healthy control women matched for age, menopausal status, and BMI and discovered that trunk fat mass percentage was significantly higher in CS and leg fat mass was not significantly different between the two groups [21, 22]. It is well established that the location of excess body fat is more important than the total quantity of adipose tissue when predicting the cardiometabolic consequences of obesity. There is

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 [22]. Accurate quantitative assessment of the visceral adiposity is essential in the evaluation of potential risk for the development of serious medical illnesses. As visceral obesity is associated with poor prognosis, metabolic disturbances and degree of pathology in several chronic diseases, it is of great importance to identify methods that quantify AT accurately and can specifically depict visceral from total adipose tissue. Effective methods for assessing visceral fat are important to investigate the role of visceral fat for the increased health risks in obesity [9, 23]. At present, reliable imaging techniques for measuring visceral, abdominal adiposity include magnetic resonance imaging (MRI) and computed tomography (CT), which directly measure IAAT, allowing for quantification of several fat depots. CT may give better discrimination between fat and other tissues but MRI has the advantage that it does not expose subjects to ionising radiation. However, both methods are costly, time-consuming, inconvenient to apply, and often unavailable for clinical and research purposes [16, 17, 22].

DXA method is the gold standard for assessment of bone health and body composition that provides accurate, comprehensive, precise measurements of total body fat percentage, along with segmental BFD in regions such as arms, legs, android (waist) and gynoid (hips) [24,25]. DXA measures three of the principal components of the body: fat mass, lean soft-tissue mass, and the bone mineral content [26, 27, 28]. Physicians today use DXA for body composition assessment because it accurately shows exactly where fat is distributed throughout the body. DXA, which has emerged as a method for assessing regional and whole body soft tissue composition is less invasive, less expensive and more accessible than CT, and involves only minimal exposure to ionizing radiation [6, 27, 29]. Agreement between DXA and whole-body CT fat mass has been found to be very high as well with correlations of 0.99. Measurement of IAAF by MRI, was highly correlated to the central abdominal fat measured by DXA [29]. In obese women, it was found that DXA could predict IAAT [21, 25] and the V/S tissue ratio may provide a better index of the cardiometabolic impact of body fat

composition than absolute quantification of each deposit independently [30, 31].

The necessity for precise and clinically expedient measures for quantifying visceral AT is evident. However, it is also essential to develop quantitative criteria for defining visceral obesity relative to the metabolic disturbances, and it is important to establish diagnostic CP for normal and abnormal values. To date, these criteria have not been clearly defined in any modality [9, 30]. There is no consensus in the literature for a diagnostic CP for visceral obesity that would indicate increased cardiovascular risk; this is partially because of limitations in performing CT scans on a large scale. Also, there are no diagnostic CP for abdominal, visceral obesity for DXA relations of central to peripheral body fat compartments. DXA is "gold standard" that can help improvement of equations for more accurate clinical assessment of lean and fat body mass [29, 30, 32, 33]. DXA continues to be used as the reference standard for whole body composition analysis in research studies. A single DXA measure, especially of fat mass and its percentage in different body regions would not be used in the medical management of the patients, particularly in MS and all consecutive complications.

The intention of this study was to discover normal and abnormal body composition with DXA indexes of the relationships of the changed different body compartments characteristic for the MS. Reference values of some DXA indexes for normal and pathologic body composition are needed to be performed that will be useful for all populations of patients at different ages.

Shubeska [6] evaluated the differences of the body composition and BFD as measured by DXA in women with CS with confirmed extreme abdominal, visceral obesity in comparison with healthy obese control women matched for age, menopausal status, and BMI [34, 35]. It was discovered that total and regional fat mass, tissue mass, lean body mass values did not differentiate CS and O significantly and concluded that determination of the relationships of their regional values had to be done. It was shown with DXA scans of the entire body that the ratios of the not significantly different central (abdominal) and peripheral regional parts of the body, significantly and precisely differentiated the patients with CS and non CS obese, and confirmed extreme central BFD in CS. DXA enabled determination of BFD as well as central obesity index, which

is an indicator of central, abdominal obesity, and was calculated as a ratio of A to G tissue percent fat. The objective of this study was to develop prediction equations for estimating visceral adiposity measured by DXA and to establish CP values to define visceral adiposity as well as normal BFD. Four indexes of central obesity COI<sub>1</sub> were determined in order to best differentiate CS and  $O_1$  and to confirm visceral, abdominal obesity in CS and also to best differentiate CS and C as well as  $O_1$  and  $O_2$  from C in order to discover normal body fat distribution in C and exclude abdominal obesity. COI<sub>1-4</sub> values were highly significantly different among the 4 groups and were significantly highest in CS patients, confirming extreme visceral obesity in CS and were lowest in group C indicating normal BFD.

Highly significantly higher values of COL and COI, and their percentage ratios COI, and  $COI_4$  in CS compared to  $O_1$  and  $O_2$  as well as C indicated predomination of android to gyoid tissue and fat mass and their percentages from the total tissue and fat mass in CS. Also, significantly higher values of these DXA indexes in group O<sub>2</sub> with significantly higher BMI compared to group  $O_1$  that was matched with CS with their BMI and age, indicated positive association between BMI increase and central, abdominal visceral BFD. Significantly positive correlation among  $COI_1$  and  $COI_2$  as well as  $COI_3$  and  $COI_4$ showed that tissue mass increase was associated with fat mass increase as well as their percentages from the total body mass. Also, BMI highly significantly positive correlation with all COI in a group of non CS women (C,  $O_1$  and  $O_2$ ) confirmed that BMI increase is associated with increase of indexes of abdominal, visceral obesity indicating increased abdominal BFD. BMI correlation with COI also confirmed BMI increase positive association with BFD increase. Shubeska in 2009 discovered with DXA that BMI increase in healthy women was associated with a more pronounced abdominal BFD, associated with higher obesity degree [36], indicating substantially higher risk for development of metabolic and cardiovascular complications especially in postmenopausal women [20, 21, 26, 34, 35, 37].

CP values of DXA indexes of central, abdominal obesity  $\text{COI}_{1\text{m}}$  of 0.55,  $\text{COI}_{2\text{m}}$  of 0.52,  $\text{COI}_{3\text{m}}$  of 0.9 and  $\text{COI}_{4\text{m}}$  of 1.11 differentiated with highest DG extreme central, abdominal, visceral body fat distribution in CS women in comparison to group  $O_1$  and they also could be used in discovering central, abdominal body fat distribution in non CS obese women with MS that are associated with increased risk of MS complications. COI<sub>1m</sub> cut off point value of 0.55 best differentiated CS and O<sub>1</sub> with highest DG of 100%. CP values of DXA indexes of normal body composition and BFD COI<sub>1n-4n</sub>, differentiated with highest DG CS from group C with normal BMI and normal BFD. COI<sub>2n</sub> cut off point value of 0.38 best differentiated CS and C for highest DG of 100%. CP values of DXA indexes of normal body composition and BFD COI<sub>1n</sub>

were determined that best differentiated with highest DG group C from group  $O_1$  and  $O_2$  with significantly higher BMI than group C.  $COI_{2n}$  cut off point value of 0.38, differentiated C from  $O_2$ for DG of 100%. CP values of DXA indexes of normal body composition and BFD  $COI_{1n-4n}$  differentiated C and  $O_2$  with higher DG compared to  $O_1$  as a result of a significantly higher BMI in  $O_2$  compared to  $O_1$  and they enabled more precise distinction of normal COI<sub>n</sub> values.

### CONCLUSION

This study discovered DXA diagnostic criteria of visceral, abdominal obesity and normal body composition and body fat distribution. COI indexes ratios values of central to peripheral parts of the body, android to gynoid tissue and fat mass and their percentages  $COI_{1m}$  CP value of 0.55 and  $COI_{2m}$  value of 0.52 were discovered as DXA diagnostic indexes of visceral, abdominal obesity that best differentiated CS from group  $O_1$  as a consequence of the hyrepercortisolism that enabled significant differentiation between the two groups.

COI indexes ratios were significantly lowest in group C compared to all other groups, showing normal and excluding abdominal BFD. Cut-off point values of DXA indexes of normal body composition and BFD COI<sub>1n-4n</sub>, differentiated with high DG CS from group C, but  $COI_{2n}$  cut off point value of 0.38 differentiated them with the highest DG of 100% and it can be used as the best DXA diagnostic index of normal body composition and BFD. That was also confirmed in the differentiation of groups C and O<sub>2</sub>. CP values of DXA indexes of normal body composition and BFD  $COI_{1n-4n}$  differentiated group C and  $O_2$  compared to  $O_1$  with higher DG. Significantly higher BMI values in  $O_2$  compared to  $O_2$  associated with significantly higher COI

to  $O_1$  associated with significantly higher  $OI_{1n}$ indexes values confirmed the association of higher degree of obesity with more central, abdominal, visceral BFD in obese women that was also confirmed with highly significantly positive correlation of BMI with all COI indexes in a non CS group consisted of groups C,  $O_1$  and  $O_2$ . CP value of DXA index of normal body composition and BFD COI<sub>2n</sub> of 0.38 differentiated group C from  $O_2$  for DG of 100% and it was confirmed that it could be used as diagnostic criterion of normal BFD.

Determination of DXA COI indexes CP values of abdominal, visceral obesity is very important to discover obese women with visceral obesity, which is the main characteristic of the MS that is associated with higher cardiometabolic risks and increased risk of other MS complications. It can be concluded that DXA COI indexes were confirmed as useful diagnostic parameters in discovering abdominal BFD and they could be used as useful diagnostic criteria of the MS.

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#### Резиме

# ПРЕСЕЧНИ ТОЧКИ НА ДИЈАГНОСТИЧКИ ИНДЕКСИ НА ЦЕНТРАЛНА ДЕБЕЛИНА ОДРЕДЕНИ СО АПСОРПЦИОМЕТРИЈА СО ДВОЈНОЕНЕРГЕТСКИ Х-ЗРАЦИ КАЈ КУШИНЗИ И КАЈ ДЕБЕЛИ ЖЕНИ

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Цел: Целта на оваа студија беше да се развијат квантитативни критериуми за дефинирање на висцерална дебелина и да се воспостават, со абсорпциометрија со двојноенергетски Х-зраци (DXA,) дијагностички пресечни точки (CP) на нормалните и на абнормалните вредности на индексите на централна дебелина (COI), кои најдобро ја диференцираат екстремната висцерална дебелина кај Кушинговиот синдром (CS) од жени што се дебели без CS и недебели жени.

**Материјал и методи:** Вредностите на COI<sub>1-4</sub> пресметани како однос на андроидната и гиноидната ткивна маса, масна маса и нивните % беа одредени во 4 групи, секоја составена од 18 жени: прва група CS; втора група дебели жени (O<sub>1</sub>), кои не се разликуваа според нивната возраст и BMI со CS; трета група дебели жени (O<sub>2</sub>) со BMI 35 ± 1,2 kg и четврта група на недебели здрави жени (C) со нормален BMI. Дијагностичката точност (DG) беше одредена на пресечните точки (CP) на  $COI_{1m-4m}$  индексите на абдоминалната дебелина и на  $COI_{1n-4n}$  индексите на нормална телесна масна дистрибуција (BFD).

**Резултати:** Вредностите на индексите COI<sub>1.4</sub> беа високо сигнификантно различни меѓу четирите испитани групи и беа сигнификантно највисоки кај пациенти со CS и најниски во групата C. COI<sub>1m,4m</sub> CP вредностите ја диференцираа екстремната висцерална, абдоминална дебелина кај CS со највисока DG, исто како и COI<sub>1n,4m</sub> CP вредностите, кои ја диференцираа нормалната BFD од групата C. COI<sub>1m</sub> CP од 0,55 најдобро ги диференцираше CS од O<sub>1</sub> за DG од 100 %. COI<sub>2n</sub> од 0,38 најдобро ги диференцираше C од CS и O<sub>2</sub> за најголема DG од 100% во споредба со O<sub>1</sub> поради значително повисоките вредности на BMI и COI<sub>1n,4m</sub> во O<sub>2</sub>, кои беа поврзани со поизразена абдоминална дебелина кај дебелина и високо сигнификантна позитивна корелација со BMI.

Заклучок: Вредностите на DXA-пресечните точки на индексите COI<sub>1m-4m</sub> и COI<sub>1n-4n</sub> беа утврдени како дијагностички индекси и критериуми корисни за откривање на екстремно абдоминална и нормална BFD. COI<sub>1m</sub> CP вредноста од 0,55 беше докажана како дијагностички критериум на екстремна абдоминална дебелина и COI<sub>2n</sub> од 0,38 како дијагностички критериум на нормална BFD што ја исклучи абдоминалната дебелина. Другите вредности на CP на индексите COI<sub>1m-4m</sub> и COI<sub>1n-4m</sub> исто така имаа висока DG во откривање на абдоминалната и нормалната телесна дистрибуција на масти.

Клучни зборови: DXA, абдоминална дебелина, индекси на централна дебелина, пресечни точки