ISSN 2545 – 4439
ISSN 1857 - 923X

INTERNATIONAL JOURNAL

Institute of Knowledge Management

KNOWLEDGE

Vol. 34. 4.
Scientific Papers

MEDICAL SCIENCES AND HEALTH

KIJ Vol. 34 No. 4 pp. 767 - 1164 Skopje, 2019

KNOWLEDGE

INTERNATIONAL JOURNAL

SCIENTIFIC PAPERS
VOL. 34.4

Promoted in Kavala, Greece
2019

INSTITUTE OF KNOWLEDGE MANAGEMENT
SKOPJE

KNOWLEDGE

International Journal Scientific papers Vol. 34.4

Print: GRAFOPROM – Bitola

Editor: IKM – Skopje

Editor in chief
Robert Dimitrovski, PhD

KNOWLEDGE - International Journal Scientific Papers Vol. 34.4

ISSN 1857-923X (for e-version)
ISSN 2545 – 4439 (for printed version)

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KNOWLEDGE – International Journal
Vol.34.4
September, 2019

ESTIMATED CENTRAL OBESITY INDEX – WORTHWHILE SCREENING TEST PROCEDURE OF ABDOMINAL OBESITY

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Abstract: Central obesity index (COI) is an indicator of central, abdominal obesity, which is the main characteristic of the metabolic syndrome. Dual-energy x-ray absorptiometric (DXA) assessment of the body fat distribution was performed through the COI values determined with a scan of the entire body in comparison to estimated COI values (eCOI) on spine and hip performed scans. COI was determined as a ratio of android (A) tissue percent fat (A-Tf%) and gynoid (G)-Tf% (COI=A/G-Tf%) as well as eCOI=eA/eG-Tf% in 3 groups of women: 1st group of women with Cushing's syndrome (CS) (n=14), 2nd group of obese (O) women (n=21), 3rd group of non obese healthy women (C) (n=22). The examinees were not different according to their age, which was 44.32±13.83 years in the 1st group, 43.33±12.58 years in the 2nd group and 42.56±14.67 years in the 3rd group, as well as according to their BMI, which was 30.02±5.02 kg/m^2 in CS, 29.66±4.88 kg/m^2 in O, but it was in normal range 21.76±1.43 kg/m^2 in non obese control group of healthy women.
The values of eA, eG and eA/eG were not significantly different compared to the correspondent values A-Tf%, G-Tf% and A/G-Tf% in all examined groups ($p>0.05$). The values of eA and A-Tf% in CS were significantly higher compared to O ($P<0.05$), as well as compared to C and O+C and in O compared to C ($p<0.0001$). COI value (1.05±0.15) and eCOI (1.04±0.1) in CS were significantly higher compared to O ($p<0.006$ and $p<0.008$) and highly significantly higher compared to C, O+C and in O compared to C ($p<0.0001$). Estimated values eA, eG and eA/eG correlated highly significantly positively with the correspondent values A-Tf%, G-Tf% and A/G-Tf% ($p<0.0001$) and COI values correlated highly significantly with eCOI, eA and A-Tf% ($p<0.0001$) and not significantly with G-Tf% and eG ($p>0.05$) in O confirming COI positive association with central, abdominal fat distribution.
Conclusion: DXA indexes COI and eCOI discovered extreme central body fat distribution in CS women, differentiated them significantly and precisely from C and CO, and could be used as diagnostic DXA indexes of extreme central, abdominal obesity in CS and non CS abdominal obese women in DXA body composition and fat distribution assessment. Determination of eCOI is reliable, more practical and faster, with lower radiation and is more acceptable compared to COI, and it can be a routine screening procedure for body composition and body fat distribution assessment, during regular spine and hip scans for osteoporotic risk assessment instead of COI body fat distribution determination with total body composition measured scans which are used in scientific studies and are not necessary to be performed in clinical body fat distribution examinations.
Keywords: DXA, body fat distribution, central obesity index, Cushing's syndrome, obese.

INTRODUCTION

Obesity and abdominal, central body fat distribution are known risk factors for cardiovascular and metabolic diseases. Excess abdominal fat is referred to as android obesity and it is an important, independent risk factor for disease. Android obesity in CS and in non CS abdominal obese with the metabolic syndrome, which is predominantly visceral, intra-abdominal, is more predictive of adipose-related comorbidities than gynecoid obesity, which has a relatively peripheral (gluteal) distribution (Shubeska-Stratrova, Dimitrovski, Todorovska, & Stefanovska Balabanova, 2008; WHO, 2016).
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 (Shubeska-Stratrova, 2010; Hunter & Nagy, 2002; Ulbrich, Nanz, Leinhard, Marcon & Fischer, 2018). Because of that, effective methods for assessing visceral fat are important to investigate its role for the increased health risks in obesity (Snijder et al, 2002). There is an increased interest in the evaluation of various methods for assessment of body composition and fat distribution (Kim, Yoo, Kim, & Lee, 2007; Borga et al, 2018). Shubeska-Stratrova, Dimitrovski, Todorovska, and Stefanovska Balabanova (2008) discovered with DXA that BMI increase in healthy women was associated with a more pronounced abdominal body fat distribution, indicating substantially higher risk for development of metabolic and cardiovascular complications (Shubeska-Stratrova, 2009; Brownbill & Ilich, 2005; Snijder et al, 2002).

Shubeska-Stratrova, Markovik, and Petrovski (2015), showed with DXA scans of the entire body that the ratios of insignificantly different central and peripheral regional parts of the body, precisely differentiated the patients with CS and non CS obese, and confirmed central body fat distribution in CS (Shubeska Stratrova & Todorovska, 2017a; Shubeska-Stratrova, Todorovska, Efremovska, & Gligorovska, 2017b; Jebb,1997). In that study, DXA enabled determination of body fat distribution as well as central obesity index COI, which is an indicator of central, abdominal obesity, and was calculated as a ratio of the android to gynoid tissue percent fat. COI differentiated significantly CS from suspect obese and it could be used as a screening test procedure and diagnostic criterion of extreme central, abdominal obesity in CS and in non CS. To date, the standard spine and hip DXA scans of an estimated android and gynoid tissue percent fat, have not been used to determine their ratio in order to investigate it as a screening diagnostic test procedure of central, abdominal obesity.

The aim of this study was DXA assessment of the body composition and body fat distribution in women with CS with confirmed abdominal obesity in comparison to healthy control women matched for age, menopausal status, and BMI as well as with healthy women with normal BMI in order to determine COI values with a scan of the entire body as well as estimated COI values (eCOI) with a spine and hip scans, and to estimate their relationship in three examined groups.

MATERIALS AND METHODS

This transversal study was organized and realized at the University Clinic of Endocrinology, Diabetes and Metabolic Disorders, University „Ss Cyril and Methodius", Medical Faculty in Skopje. DXA assessment of the body fat distribution was performed in 3 groups of women: 1st group of Cushing's syndrome (CS), with confirmed CS with BMI (30.02±5.02 kg/m^2) and age of 44.32±13.83 yr. (n=14), 2nd group of obese women (n=21), matched with CS according to their BMI (29.66±4.88 kg/m^2) and age (43.33±12.58 yr.) and the 3rd group (n=22) of healthy women with normal BMI (21.76±1.43 kg/m^2) and age (42.56±14.67 yr.). 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. O and C had a stable weight for at least several months before being included in the study. All investigated women gave a personal permission to be included in this study and have been treated according to the Declaration of Helsinki. The data of the examined women are shown in table 1.

Table 1. Age, body weight, body height and BMI in CS, O and C

	Age	body weight	body height	BMI
CS	44.32±13.83	76.91±14.86	162.35±6.44	30.02±5.02
O	43.33±12.58	76.15±13.26	160.28±5.51	29.66±4.88
C	42.56±14.67	57.41±6.12	162.31±7.53	21.76±1.43
mean	43.25±13.5	68.83±14.63	161.58±6.55	26.58±5.53
P	NS	0.0001	NS	0.0001
P_1	NS	NS	NS	NS
P_2	NS	0.0001	NS	0.0001
P_3	NS	0.0001	NS	0.0001

CS – Cushing's syndrome women O – Obese women C – Control healthy non obese women
P – significance of the difference between the groups CS, O, C
P_1 – significance of the difference between the groups CS and O
P_2 – significance of the difference between the groups CS and C
P_3 – significance of the difference between the groups O and C

Body height was measured by a wall stadiometer in barefoot subjects with a 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 (m^2).

DXA assessment in this study was performed with DXA System Lunar DPX-NT, which uses enCore Windows-XP Professional OS computer. For body composition measurements the entire body of each subject was scanned. During DXA scan, the subjects were 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 enabled simultaneous assessment of total and regional body composition and fat distribution. Central obesity index (COI) values were determined during body composition assessment in total body scans as a ratio of android (A)

tissue percent (%) fat (A-Tf%) and gynoid (G) Tf% (G-Tf%), COI= A/G-Tf%. Using the scan tissue data from standard spine and hip scans an estimate of the Android/Gynoid Tfat% was performed and eA-Tf% and eG-Tf% values of the lumbar vertebral spine (L_2-L_4) and proximal femur were also determined and eCOI=eA/eG-Tf% was calculated. Correlation and the difference between eCOI values in the spine and hip scans and COI values in total body scans were compared among the three examined groups of women.

Statistical analyses were performed using statistical software program SPSS for Windows, version 19.0. Variables were presented as means ± standard deviations (SD). P values <0.05 were considered to be statistically significant. 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

DXA assessment of the body fat distribution was performed through the COI (A/G-Tfat%) values determined as a ratio of android to gynoid tissue percent fat with a scan of the entire body as well as estimated COI values eCOI (eA/eG-Tfat%) determined with spine and hip performed scans in 3 groups of examined women. The data are shown in table 2.

Table 2. Significance of the difference between A, G and A/G estimated values and the correspondent Tfat% values determined with total body DXA scans in all examined groups

	eA	A-Tfat%	eG	G-Tfat%	eA/eG	A/G-Tfat%	N	P_1	P_2	P_3
CS	**52.86±5.69**	**53.26±6.89**	**50.89±3.31**	**51.11±4.09**	**1.04±0.097**	**1.05±0.15**	**14**	**0.871**	**0.876**	**0.891**
O	**48.33±6.72**	**47.61±6.42**	**51.07±3.85**	**52.64±3.78**	**0.945±0.103**	**0.91±0.12**	**21**	**0.723**	**0.19**	**0.263**
C	**30.99±7.01**	**30.55±8.67**	**42.35±5.31**	**45.53±5.6**	**0.725±0.097**	**0.67±0.15**	**22**	**0.857**	**0.061**	**0.141**
O+C	**39.46±11.09**	**38.88±11.47**	**46.61±6.37**	**49±5.95**	**0.83±0.15**	**0.78±0.18**	**43**	**0.814**	**0.076**	**0.176**

P1 - significance of the difference in CS, O, C and O+C between eA and their A-Tfat% value
P2 - significance of the difference in CS, O, C and O+C between eG and G-Tfat% value
P3 - significance of the difference in CS, O, C and O+C between eA/eG and their A/G-Tfat% value
CS – Cushing's syndrome women; O – Obese women; C – Control healthy non obese women
O+C – obese women + control non obese healthy women

The values of eA, eG and eA/eG were not significantly different compared to the correspondent values A-Tfat%, G-Tfat% and A/G-Tfat% in all examined groups (p>0.05). Estimated values eA, eG and eA/eG correlated highly significantly positively with the correspondent values A-Tfat%, G-Tfat% and A/G-Tfat% (p<0.0001).

Table 3. Significance of the difference between A, G and A/G estimated values and the correspondent Tfat% values determined with total body DXA scans between the examined groups

	eA	A-Tfat%	eG	G-Tfat%	eA/eG (eCOI)	A/G-Tfat% (COI)
CS	**52.86±5.69**	**53.26±6.89**	**50.89±3.31**	**51.11±4.09**	**1.04±0.097**	**1.05±0.15**
O	**48.33±6.72**	**47.61±6.42**	**51.07±3.85**	**52.64±3.78**	**0.9451±0.1026**	**0.91±0.12**
C	**30.99±7.01**	**30.55±8.67**	**42.35±5.31**	**45.53±5.6**	**0.7246±0.09734**	**0.67±0.15**
O+C	**39.46±11.09**	**38.88±11.47**	**46.61±6.37**	**49±5.95**	**0.83±0.15**	**0.78±0.18**
P_1	**0.05**	**0.033**	**0.902**	**0.342**	**0.008**	**0.006**
P_2	**0.0001**	**0.0001**	**0.0001**	**0.001**	**0.0001**	**0.0001**
P_3	**0.0001**	**0.0001**	**0.0001**	**0.0001**	**0.0001**	**0.0001**
P_4	**0.0001**	**0.0001**	**0.002**	**0.148**	**0.0001**	**0.0001**

Significance of the difference between eA, eG, eA/eG and the correspondent values A-Tfat%, G-Tfat% and A/G-Tfat%: P_1 – in CS and O. P_2 – in CS and C. P_3 – in O and C. P_4 – in CS and O+C.
CS – Cushing's syndrome women; O – Obese women; C – Control healthy women; O+C – obese women + control healthy women; COI – central obesity index; eCOI - estimated central obesity index

The values of eA and A-Tfat% in CS were significantly higher compared to O (P_1<0.05), as well as CS compared to C and O+C and in O compared to C ($P_{2,3,4}$<0.0001). The values of eG and G-Tfat% were not significantly higher in CS compared to O (P_1>0.05), but they were significantly higher compared to C and in O compared to C

($P_{2,3}$<0.0001). A/G-Tfat% (COI) value 1.05±0.15 and eA/eG (eCOI) value 1.04±0.1 in CS were significantly higher compared to O (P_1<0.006 and P_1<0.008) and highly significantly higher compared to C, O+C and in O compared to C ($P_{2,3,4}$<0.0001). COI correlated highly significantly with eCOI, eA and A-Tfat% (p<0.0001), but not significantly with G-Tfat% and eG (P>0.05) in O, confirming COI positive association with central, abdominal Tfat%, and abdominal fat distribution.

DISCUSSION

Obesity is a medical condition in which excess body fat has accumulated to an extent that it may have a negative effect on health (WHO, 2016). Obese subjects have higher percentage of FM from the total body mass compared to non obese (Snijder et al, 2002). In addition to general obesity, the distribution of body fat is independently associated with the metabolic syndrome. There is a growing evidence that intra-abdominal adipose tissue, rather than total body fat, is a risk factor for metabolic conditions associated with obesity (Neeland, et al. 2015; Shubeska-Stratrova, & Janicevic Ivanovska, 2019). For this reason the evaluation of intra-abdominal adipose tissue is clinically important.

Cushing's syndrome is associated with weight gain and extreme central, visceral, abdominal obesity. Increased central fat mass is characteristic of active CS. In Jebb's study (Jebb, 1997) Cushing disease patients had higher visceral versus total adipose tissue ratios, suggesting that glucocorticoids play a pivotal role in the pathogenesis of central obesity (Schafroth, Godang, Ueland, Berg, & Bollerslev, 2000). The first study concerning the measurements of body composition in CS using DXA and CT was published by Wajchenberg et al (1995). Patients with CS had no increase in total body fat or the trunk region, but had a higher intra-abdominal fat area compared to obese subjects (Lonn, Kvist, Ernest, & Sjostrom, 1994). 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 suggest that fat in different body compartments responds differently to disease processes and that DXA can be used to measure these changes (Mayo-Smith et al, 1989; Rebuffe-Scrive, Krotkiewski, Elfersson & Bjorntorp, 1988). Burt, Gibney, and Ho (2006) concluded that fat mass was higher and lean body mass was lower in CS. Garrapa, Pantanetti, Arnaldi, Mantero, and Faloia (2001) evaluated body composition and fat distribution measured by DXA in women with CS compared with healthy control (C) women matched for age, menopausal status, and BMI and discovered that trunk fat mass percentage was significantly higher in CS compared to C and leg fat mass was not significantly different between the groups. DXA is used to quantify abdominal fat mass (Lear, Birmingham, Chockalingam & Humphries, 2006; McCormack, Meendering, Specker, & Binkley, 2016; Choi, Seo, Lee, & Chung, 2015). DXA method determines absolute (kg) and relative (%) total, bone, lean and fat body mass and separately their regional values on arms, legs, head and trunk (Brownbill & Ilich, 2005; Lear, Birmingham, Chockalingam & Humphries, 2006). DXA enables precise, accurate body composition and body fat distribution assessment and determines central obesity index (COI) values. 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 (Hunter & Nagy, 2002; Salamone, Fuerst, & Visser, 2000). It's a very reliable method and its results are extremely repeatable; in addition, the method is safe and presents little burden to the subject. Published studies have shown a good correlation between central abdominal fat by DXA and visceral fat by computed tomography or magnetic resonance imaging (Neeland, Grundy, Li, Adams-Huet, & Vega, 2016).

Shubeska-Stratrova, Dimitrovski, Todorovska, and Stefanovska Balabanova (2008) evaluated the differences of the body composition and fat distribution as measured by DXA in women with CS with confirmed extreme abdominal, visceral obesity in comparison with healthy control women (CO) matched for age, menopausal status, and BMI. That study discovered that total and regional fat mass, tissue mass, lean body mass (LBM) values did not differentiate CS and O significantly and concluded that determination of the relationships of their regional values had to be done. Shubeska-Stratrova, Markovik, and Petrovski (2015) showed 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 body fat distribution in CS (Hunter & Nagy, 2002). DXA indexes of central, abdominal obesity A/G, trunk/total, legs/trunk and android/legs TM and FM ratios discovered extreme central body fat distribution in CS, differentiated them significantly from healthy women with normal BMI and obese with the same BMI as CS, and were discovered as DXA indexes, indicators of abdominal, central obesity that should be used as DXA indexes of extreme central, abdominal obesity in CS and in non CS obese women (Shubeska-Stratrova, & Todorovska, 2017a; Shubeska-Stratrova, Todorovska, Efremovska, & Gligorovska, 2017b). COI was discovered as a useful method for assessing body fat distribution which is in a positive relation with abdominal (central) obesity, and the metabolic syndrome. It was concluded that CS patients were discovered as gold standard of extreme central, visceral, abdominal body fat distribution (Schafroth, Godang,

Ueland, Berg, & Bollerslev, 2000), and that these DXA indexes of extreme central, abdominal body fat distribution in CS could also be used as a gold standard for abdominal obesity in non CS.

In this study DXA assessment of the body fat distribution was performed through the COI values determined with a scan of the entire body as a ratio of android to gynoid tissue percent fat as well as estimated COI values eCOI determined with spine and hip performed scans in 3 groups of examined women CS, O and C. The values of eA, eG and eA/eG were not significantly different compared to the correspondent values A-Tfat%, G-Tfat% and A/G-Tfat% in all examined groups ($p>0.05$), and correlated highly significantly positively with them ($p<0.0001$), which confirmed their realibility. The values of eA and A-Tf% in CS were significantly higher compared to O ($P_1<0.05$), as well as CS compared to C and O+C and in O compared to C ($P_{2,3,4}<0.0001$). The values of eG and G-Tf% were not significantly higher in CS compared to O ($P_1>0.05$), but they were significantly higher compared to C and CO+C and in O compared to C ($P_{2,3}<0.0001$). A/G-Tf% (COI) value 1.05±0.15 and eA/eG (eCOI) value 1.04±0.1 in CS were significantly higher compared to O ($P_1<0.006$ and $P_1<0.008$) and highly significantly higher compared to C, O+C and in O compared to C ($P_{2,3,4}<0.0001$). COI correlated highly significantly with eCOI, eA and A-Tf% ($p<0.0001$), but not significantly with G-Tf% and eG ($P>0.05$) in O, confirming COI positive association with central, abdominal Tf%, and abdominal fat distribution. Estimated values eA, eG and eA/eG correlated highly significantly positively with the correspondent values A-Tf%, G-Tf% and A/G-Tf% ($p<0.0001$).

COI is an indicator of central, abdominal obesity, which is the main characteristic of the metabolic syndrome. This study established that eCOI measurements were reliable and comparable to measured COI values. Determination of eCOI was more practical, faster, with lower radiation and is more acceptable; moreover spine and hip bone mineral content were determined at the same time. Body composition measurements are used in scientific studies and are not necessary to be done in body fat distribution examination. It indicated the need of eCOI values determination during regular spine and hip DXA measurements for body fat distribution assessment instead of body composition examination for COI body fat distribution determination, which should not be performed. High significance of the COI and eCOI correlation with android tissue percent fat and its estimated value was detected in comparison with the correspondent gynoid values, confirming COI positive association with central, abdominal fat and tissue mass, and abdominal fat distribution. COI and eCOI DXA indexes of central body fat distribution in CS have to be diagnostic screening test procedure of extreme central, visceral, abdominal fat distribution in different types of obesity (non CS).

CONCLUSION

DXA indexes COI and eCOI discovered extreme central body fat distribution in CS women, differentiated them significantly and precisely from C and CO, and could be used as diagnostic DXA indexes of extreme central, abdominal obesity in CS and non CS abdominal obese women in DXA body composition and fat distribution assessment. Determination of eCOI values can be a routine screening test procedure for body composition and body fat distribution assessment, during regular spine and hip scans for osteoporotic risk assessment.

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