

UDK 37

ISSN 2545 – 4439

ISSN 1857 - 923X

INTERNATIONAL JOURNAL

Institute of Knowledge Management

KNOWLEDGE



Scientific Papers

Vol. 35. 4.

MEDICAL SCIENCES AND HEALTH



KIJ

Vol. **35**

No. **4**

pp. **1061 - 1398**

Skopje, **2019**

Global Impact & Quality Factor

1.322 (2016)

<http://globalimpactfactor.com/knowledge-international-journal/>

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INTERNATIONAL JOURNAL

**SCIENTIFIC PAPERS
VOL. 35.4**

*Promoted in Bansko, Bulgaria
2019*

**INSTITUTE OF KNOWLEDGE MANAGEMENT
SKOPJE**



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Print: GRAFOPROM – Bitola

Editor: IKM – Skopje

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KNOWLEDGE - International Journal Scientific Papers Vol. 35.4

ISSN 1857-923X (for e-version)

ISSN 2545 – 4439 (for printed version)

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LIPID PROFILE CHANGES RELATIONS TO BODY FAT DISTRIBUTION CHANGES DETERMINED WITH DUAL-ENERGY X-RAY ABSORPTIOMETRY DURING THE WEIGHT LOSS

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Abstract: Obesity and central body fat distribution are known risk factors for cardiovascular and metabolic diseases. Dual-energy x-ray absorptiometry (DXA) enables precise, accurate body composition and body fat distribution assessment and it measures and monitors body composition changes in obese patients undergoing weight loss. Obesity is associated with dyslipidemic profile. Low HDL-C levels are frequently associated with raised levels of plasma triglycerides and increased risk of cardiovascular disease and TG/HDL-C ratio may be a better predictor of insulin resistance and cardiovascular disease. LDL-C is one of the major culprits in the development of atherosclerotic heart disease and reduction of LDL-C levels is the primary target of therapy.

The effect of weight loss on body fat distribution was examined through android, legs and android/legs tissue and fat mass ratios indexes of central, abdominal obesity determined by DXA and their relationship with lipid profile changes. The following parameters were determined before and after weight loss: body mass index (BMI), body weight (BW), android (A) and legs (L) tissue mass (TM) and fat mass (FM), their % with DXA, their ratios, indexes of abdominal fat distribution A/L-TM and TM% and A/L-FM and FM%, as well as lipid profile: total cholesterol (C), triglycerides (TG), HDL-C, LDL-C, LDL/HDL-C, C/HDL-C and TG/HDL-C.

BW of 62.96 ± 1.2 kg and BMI value of 28.98 ± 0.78 kg/m² before the weight loss lowered to 49.96 ± 1.3 kg ($p < 0.012$), and normal BMI 22.81 ± 0.62 kg/m² ($p < 0.012$). A-TMf% value decrease from $50.41 \pm 1.7\%$ to $29.55 \pm 1.34\%$ after weight loss was significant ($p < 0.006$) and A-FM% $49.92 \pm 1.2\%$ decrease to $29.25 \pm 1.34\%$ was also highly significant ($p < 0.005$). A-TM 5.43 ± 0.71 kg and A-FM 2.74 ± 0.71 kg lowered to 3.76 ± 0.25 kg and 1.11 ± 0.12 kg after weight loss ($p < 0.05$). L-TMf% $50.31 \pm 1.7\%$ lowered to $35.2 \pm 2.12\%$ ($p < 0.018$) and L-TM 19.69 ± 0.71 kg lowered to 16.15 ± 0.55 kg ($p < 0.033$). L-FM% $48.51 \pm 1.14\%$ lowered to $33.8 \pm 1.98\%$ ($p < 0.009$) and L-FM 9.89 ± 0.64 kg lowered to 5.68 ± 0.16 kg ($p < 0.0002$). A/L-TMf% value decrease from $1.01 \pm 0.07\%$ to $0.84 \pm 0.014\%$ and A/L-FM% value decrease from 1.03 ± 0.04 to 0.87 ± 0.07 were also significant ($p < 0.05$).

TG values decrease from 1.21 ± 0.01 mmol/l to 0.83 ± 0.07 mmol/l was significant ($p < 0.002$) and C values decrease from 6.5 ± 0.01 mmol/l to 5.43 ± 0.37 mmol/l was also significant ($p < 0.05$). LDL-C values 4.3 ± 0.1 mmol/l lowered to 3.39 ± 0.34 mmol/l ($p < 0.026$) and TG/HDL-C ratio 0.73 ± 0.01 lowered to 0.52 ± 0.03 ($p < 0.011$).

This study showed that A-TMf% and A-FM% lowered highly significantly, indicating significant FM% reduction in android, abdominal TM. Atherogenic lipids TG, C and LDL-C and atherogenic index TG/HDL-C ratio lowered significantly. Also, it was confirmed that DXA indexes of central, abdominal obesity A/L-TM% and A/L-FM% were increased in overweight subjects before the weight loss and lowered highly significantly after the weight loss and increased A/L TM and A/L FM values lowered to normal values, indicating that normal BMI and BW reached after the weight loss were associated with normalized body fat distribution, and significant reduction of the atherogenic lipid profile indicating reduced atherogenic risk.

Keywords: DXA, abdominal obesity, weight loss, lipid profile.

1. INTRODUCTION

Central obesity can be an early warning sign of a condition called metabolic syndrome. The core abnormality of Metabolic Syndrome is increased body weight, and particularly central, abdominal obesity as well as dyslipidemia. Dyslipidemic profile and increased C/HDL-C, LDL/HDL-C and TG/HDL-C ratios values are especially important components and indicators of cardiovascular risk. Their predictive value is greater than the isolated parameters. Obesity is associated with dyslipidemic profile with low HDL-C levels, and high triglycerides and total cholesterol levels as independent predictors of coronary heart disease (Kyle, Dhurandhar, & Allison, 2016). Obesity and 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, which is associated with increased risk for cardiovascular disease.

Shubeska, (2011) discovered with DXA that BMI increase in healthy women was associated with a more pronounced abdominal body fat distribution (Shubeska, 2009), indicating substantially higher risk for development of metabolic and cardiovascular complications. DXA also measures and monitors body composition changes in obese patients undergoing weight loss (Shubeska, & Janicevic Ivanovska, 2019b). It monitors how much fat was lost in different body compartments. Some relationship ratios between central (android, abdominal) regional tissue and FM to peripheral gynoid regional parts of the body in patients with Cushing's syndrome (CS) were discovered as diagnostic criteria of visceral, abdominal obesity in patients with CS (Shubeska, Markovik Temelkova, & Petrovski, 2015; Shubeska, & Todorovska, 2017a; Shubeska, Spasovski, & Velikj Stefanovska, 2019a).

The assessment of abdominal fat accumulation, especially in postmenopausal (postM) women, is an important screening tool for the prevention of the obesity associated health complications (Shubeska-Stratrova, 2010). DXA measurements of fat distribution are very useful in studies related to obesity-associated disease risk.

The aim of this study was to investigate body composition and body fat distribution in postmenopausal women with DXA parameters android FM and TM as well as legs FM and TM and their %, and DXA indexes of central, abdominal obesity, A/L-TM, A/L-FM, A/L-TMf% and A/L-FM% ratios as well as lipid values and atherogenic indexes and their changes after weight loss with consequent normal BMI. It was important to discover weight loss influence on body fat distribution and lipid metabolism.

2. MATERIAL AND METHODS

The examinees were three postmenopausal women with mean BMI $28.98 \pm 0.78 \text{ kg/m}^2$, and BW $62.96 \pm 1.2 \text{ kg}$ that lowered to normal values of $22.81 \pm 0.62 \text{ kg/m}^2$ and $49.96 \pm 1.3 \text{ kg}$ ($p < 0.012$). BMI and BW were determined before and after weight loss, as well as android (A) and legs (L) fat mass (FM) and its percentage (FM%), tissue mass (TM) and TM fat percentage (TMf%) and the changes of the DXA indexes of abdominal body fat distribution A/L-FM and A/L-FM%, A/L-TM and A/L-TMf%.

Total cholesterol (C), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), LDL/HDL-C, TC/HDL-C and TG/HDL-C were also determined.

Body height was measured by a wall stadiometer in barefoot subjects with head in a horizontal Frankfurt plane to the nearest 0.1 cm. BW was measured by a digital scale while wearing light clothing and it was estimated in kilograms (kg). BMI was calculated with the following formula: weight (kg)/height (m^2). DXA assessment was performed with DXA System Lunar DPX-NT, which uses encore 10.x Windows-XP Professional OS computers. The entire body of the subject was scanned. During the 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 enabled simultaneous assessment of total and regional body composition and body fat distribution.

Statistical analyses were performed using the statistical software program SPSS for Windows, version 19. The qualitative series were processed by determining the coefficient of relations, proportions, and rates, and were shown as absolute and relative numbers. Quantitative series were analyzed with measures of central tendency (average, median), as well as with dispersion measures (standard deviation, standard error). Lipid values before and after the weight loss were tested by T-test for dependant samples and the Dependant means differences test was used to examine DXA parameters. The differences between the percentages were tested with Percentage difference test. P values < 0.05 were considered to be statistically significant.

3. RESULTS

Table 1. A/L-TM, A/L-TMf%, A/L-FM and A/L-FM% values before and after weight loss

Parameters	Before weight lost	After weight lost	P*
Android/Legs TM	0.28 ± 0.04	0.23 ± 0.02	t-difference: 1,936; df-t: 1,7; p= 0,209
Android/Legs TMf%	1.01 ± 0.07	0.84 ± 0.014	t-difference: 4,125; df-t: 1,5; p= 0,05*
Android/Legs FM	0.28 ± 0.05	0.19 ± 0.021	t-difference: 2,874; df-t: 1,6; p= 0,108
Android/Legs FM%	1.03 ± 0.04	0.87 ± 0.07	t-difference: 3,437; df-t: 1,9; p= 0,05*

TM - tissue mass FM - fat mass TMf% - tissue mass fat percent FM% - fat mass percent

*dependant means differences test significant for $p < 0,05$

A/L-FM% and A/L-TMf% lowered significantly ($p<0.05$), indicating significant FM% reduction in android, abdominal TM.

Table 2. Android TM and TMf%, legsTM and TMf%, android FM and FM%, legs FM and FM%, before and after weight loss

Parameters	Before weight lost	After weight lost	P*
Android TMf%	50.41±1.7	29.55±1.34	t-difference=16,723; df-t: 2,8; p=0,006*
Legs TMf%	50.31±1.7	35.2±2.12	t-difference=9,625; df-t: 2,9; p=0,018*
Android TM	5.43±0.71	3.76±0.25	t-difference=3,843; df-t: 1,6; p=0,05*
Legs TM	19.69±0.71	16.15±0.55	t-difference: 6,827; df-t: 2,8; p= 0,033*
Android FM%	49.92±1.2	29.25±1.34	t-difference: 19,903; df-t: 3,3; p= 0,005*
Legs FM%	48.51±1.14	33.8±1.98	t-difference: 11,144; df-t: 1,9; p= 0,009*
Android FM	2.74±0.71	1.11±0.12	t-difference: 3,921; df-t: 1,5; p= 0,05*
Legs FM	9.89±0.64	5.68±0.16	t-difference: 63,564; df-t: 1,5; p= 0.0002*

*dependant means differences test significant for $p<0, 05$

TM - tissue mass FM - fat mass TMf% - tissue mass fat percent FM% - fat mass percent

Android and legs TMf% lowered significantly ($p<0.006$; $p<0.018$) as well as android and legs FM% ($p<0.005$; $p<0.009$). Android and legs TM lowered significantly ($p<0.05$; $p<0.033$) as well as android and legs FM ($p<0.05$, 0.0002).

Table 3. Lipid levels and atherogenic indexes before and after weight loss

Fat mass	Before weight lost	After weight lost	P*
Triglycerides	1.21±0.01	0.83±0.07	T=15,496; df=2; p=0,002*
Total Cholesterol	6.5±0.01	5.43±0.37	T=4,106; df=2; p=0,05*
HDL cholesterol	1.64±0.01	1.58±0.06	T=0,209; df=2; p=0,853
LDL cholesterol	4.3±0.1	3.39±0.34	T=6,065; df=2; p=0,026*
LDL-C/HDL-C	2.58±0.07	2.15±0.24	T=3,005; df=2; p=0,095
TC/HDL-C	3.94±0.05	3.44±0.3	T=2,087; df=2; p=0,172
TG/HDL-C	0.73±0.01	0.52±0.03	T=9,827; df=2; p=0,011*

* T-test for dependant samples significant for $p<0, 05$

TG values lowered significantly ($p<0.002$) as well as C ($p<0.05$), LDL-C ($p<0.026$) and TG/HDL-C ($p<0.011$).

4. 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). Very recently, the World Obesity Federation argued that ‘obesity was considered as a chronic, relapsing, progressive, disease process’ that requires intervention (Bray, Kim, & Wilding, 2017). The main characteristic of the metabolic syndrome is increased body weight, and particularly central, abdominal obesity as well as dyslipidemia (Matsuzawa, 2014; Sharma, Campbell, & Scherer, 2017). People with metabolic syndrome have elevated blood pressure, high triglycerides, low levels of HDL cholesterol and insulin resistance (Lesser et al, 2015). This combination of factors creates an especially high risk for stroke, coronary artery disease, cardiovascular disease-related mortality and type 2 diabetes. Obese subjects have higher percentage of FM from the total body mass compared to non obese.

Menopause is a high-risk time for weight gain. PostMP women have significantly more fat, a more central fat distribution, and less lean tissue mass than premenopausal women (Svendsen, Hassager, & Christiansen, 1995; Shubaska, 2010; Lesser et al, 2015). Menopause-related central body fat accumulation potentially contributes to the increased incidence of disease observed in postMP, compared with preMP women (Garaulet, Pérez-Llamas, Baraza, Garcia-Prieto, & Fardy, 2002). The subjects in this study were postmenopausal.

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. 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). DXA body composition and fat

distribution assessment may be useful in studies related to obesity-associated risks (Kamel et al, 1999; Brownbill, & Ilich, 2005). DXA enable precise, accurate body composition and body fat distribution assessment. In a previous study, Shubeska, (2011) discovered with DXA that BMI increase in healthy women was associated with a more pronounced abdominal, visceral fat distribution. Also, BMI reduction, the quantity of fat loss, body composition and body fat distribution changes are monitored with DXA in obese patients undergoing weight loss. It monitors how much fat was lost during weight loss. 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. 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 (Haarbo, Gotfredsen, Hassager, & Christiansen, 1991; Jensen, Kanaley, Reed, & Sheedy, 1995). Trunk FM increase is a result of dominant android, abdominal FM increase indicating increased risk for metabolic complications (Shubeska, Todorovska, Efremovska, & Gligorovska, 2017b). Body fat distribution is simply determined with DXA by the relationship of the regional (segmental) fat compartments. The relationship of the predominantly central, android, abdominal fat mass and tissue mass and the gynoid (peripheral FM and TM) is an indicator of the central, abdominal obesity (Shubeska et al, 2019a). DXA is fast becoming the new gold standard because it provides a higher degree of precision in only one measurement and has the ability to show exactly where fat is distributed throughout the body. 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.

It was found that low weight, independent of menopausal status, leads to the typical gynoid pattern of fat distribution while excess weight and obesity result in an android pattern of distribution in pre- and postMP women (Kamel et al, 1999). By measuring body composition, a person's health status can be more accurately assessed and the effects of both dietary and physical activity programs better directed. Since a scale measures "body weight", which includes fat, muscles, bones and organs, it can't specifically tell how much fat had been lost (Wallner, Luschnigg, Schnedl, Lahousen, & Sudi, 2004; Shubeska, Dimitrovski, Todorovska, & Stefanovska Balabanova, 2008), and the only way to measure actual fat loss is to measure "body composition", not body weight in weight loss programs. Total body analysis with DXA is the ideal way for the serious athlete, the person monitoring or beginning a program of exercise or weight loss, or anyone curious or concerned about their health to receive a quick, painless, accurate and confidential assessment of their body's composition. Also, measurements of body composition and body fat distribution with DXA have provided a research tool to study the metabolic effects of aging, obesity, and various wasting conditions. Changes in body composition during weight loss programs might have a significant effect on long-term results and sensitive DXA indexes of abdominal, central obesity are needed, because of lack of normal reference data, which is an issue that is currently being addressed.

CS patients are a discovered gold standard of extreme central, visceral, abdominal body fat distribution. DXA indexes of central, abdominal body fat distribution in Cushing's (CS) could also be used as a gold standard for abdominal obesity in non CS. Shubeska, 2015, showed that the ratios of insignificantly different central and peripheral regional parts of the body and DXA indexes A/L-TM and A/L-FM ratios and android/legs TMf% and FM% ratios precisely differentiated the patients with CS and non CS obese, and confirmed central body fat distribution in CS (Hendel, Gotfredsen, & Andersen, 1996; Brownbill, & Ilich, 2005; Shubeska et al, 2008). DXA indexes of central body fat distribution in CS could also be a gold standard and diagnostic criterion of extreme central, abdominal fat distribution in different types of obesity (non CS). Cut-off points of the following indexes confirmed extreme central, abdominal obesity: A/L-TM ratio higher than 0.27 and A/L-FM ratio higher than 0.26 (Brownbill, & Ilich, 2005; Shubeska Stratrova et al, 2015). Normal cut-off point values were also discovered, A/L-TM value lower than 0.24 and A/L-FM value lower than 0.25, and they differentiated CS patients and C with normal BMI and body fat distribution with sensitivity, specificity, positive and negative predictive and diagnostic value of 100%.

In this study, mean A/L-TM ratio value of 0.28 before the weight loss was higher than normal cut-off point value of 0.24, which confirmed abdominal body mass distribution, and it reduced to normal mean value of 0.23 indicating normal body fat distribution. Also, mean A/L-FM ratio value of 0.28 was higher than normal cut-off point value of 0.25 which also confirmed abdominal body fat mass distribution, and it reduced after weight loss to normal mean value of 0.19 indicating normal body fat distribution. A/L-TMf% and A/L-FM% also lowered significantly after the weight loss ($p < 0.05$). Significant reduction in these indexes of central obesity after the weight loss confirmed reduction of abdominal obesity and normalized body fat distribution. (Shubeska Stratrova et al, 2015; Shubeska, & Todorovska, 2017a; Shubeska et al, 2017b; Shubeska et al, 2019a).

Significant increase in total cholesterol concentration, and specifically LDL cholesterol (an atherogenic lipid marker), and reduced HDL cholesterol concentration are correlated with numerous risk factors, including the components of the metabolic syndrome, and probably involve independent risk (Hong, Romm, Reagan, Green, &

Rackley, 1991; Kinosian, Glick, Garland, 1994; Ascaso et al, 2007). Low-density lipoprotein (LDL) cholesterol concentration has been the prime index of cardiovascular disease risk and the main target for therapy.

In an attempt to optimize the predictive capacity of the lipid profile, several lipoprotein ratios or “atherogenic indices” have been defined. These ratios can provide information on risk factors difficult to quantify by routine analyses and could be a better mirror of the metabolic and clinical interactions between lipid fractions. Total/high-density lipoprotein (HDL) cholesterol, TG/HDL-C and LDL/HDL cholesterol ratios are risk indicators with greater predictive value than isolated parameters used independently, particularly LDL. Total cholesterol/HDL ratio is considered a more sensitive and specific index of cardiovascular risk than total cholesterol (Natarajan, Glick, Criqui, Horowitz, & Lipsitz, 2003; Nam, Kannel, & D’Agostino, 2006; Ingelsson et al, 2007; Kishida, Funahashi, Matsuzawa & Shimomura, 2012).

In this study lipid levels in the examined overweight subjects also showed higher risk for development of metabolic complications. Atherogenic index TG/HDL-C reduced significantly ($p < 0.011$). BMI and BW reduction to normal levels was associated with significant decrease of indexes of central body fat distribution android/legs TM and FM to normal values as well as significant reduction of atherogenic lipid indexes indicating reduced atherogenic risk.

5. CONCLUSION

It can be concluded that android/legs TM and FM ratios values before the weight loss confirmed abdominal obesity with dyslipidemic profile indicating higher cardiovascular risk in a DXA examined overweight subjects. BMI, BW, A/L-TM ratio and A/L-FM ratio as well as A/L-TMf% and A/L-FM% changed and significant reduction in these indexes of central obesity to normal levels after the weight loss, confirmed reduced abdominal obesity (abdominal body fat distribution) and consecutive normalized body composition and body fat distribution. This showed that body weight reduction in overweight subjects and especially in obese subjects is important in order to improve body composition and body fat distribution and minimize the cardiometabolic profile and risk. These results confirmed that DXA measurements of body composition and body fat distribution are very useful in studies related to obesity-associated disease risk. A/L-TMf% and A/L-FM% are also useful DXA indexes in body fat distribution assessment. This study confirmed that A/L-TM and A/L-FM indexes are worthwhile, diagnostic procedure parameters of abdominal obesity and obesity associated risks.

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