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Changes in Fasting Plasma Glucose, HbA1c and Triglycerides Are Related to Changes in Body Composition in Patients with Type 2 Diabetes

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ABSTRACT

Objectives: *The objective of this analysis was to evaluate the relationship between the changes in the body composition and the changes in the glycemic control as evaluated by glycemia and glycated hemoglobin (HbA1c) and the lipid metabolism parameters in adults with type 2 diabetes.*

Material and Methods: *This was a retrospective cohort study, in which we collected data from the files of 171 patients with type 2 diabetes. The patients were followed for 6 months. Body composition (visceral fat area [VFA; cm], body fat mass [BFM, kg] and percent body fat [PBF; %] was assessed by bioelectric impedance. Delta parameters were calculated as the value of the parameter at month 0 minus the value of the parameter at month 3 or month 6.*

Outcomes: *All body composition parameters decreased significantly from baseline to month 3 and then to month 6. VFA decreased from 176. 26 cm^2 at baseline to 151.21 cm^2 at month 3 and to 146.64 cm^2 at month 6. PBF decreased from 36.48% to 32.78% at month 3 and to 31.64% at month 6. BFM had a median value of 34.60 kg at baseline and decreased to 29.00 kg at month 3 and 27.95 kg at month 6. At 3 months, delta VAT and delta BFM were correlated with changes in glycemic control and lipid parameters. At 3 months only BFM remained correlated with these parameters.*

Conclusion: *In the population included in this analysis we showed that changes in VFA and BFM were correlated with changes in glycemic control during the 3-month follow-up period and that changes in BFM were correlated with changes in lipid parameters during the entire follow-up.*

Keywords: type 2 diabetes, body composition, glycemic control, triglycerides

INTRODUCTION

Obesity has been recognized as a risk factor for diabetes, hypertension, coronary heart disease, stroke and certain types of cancer (1). According to Institute for Health Metric and Evaluation, between 1980 and 2013 the proportion of overweight or obese adults increased from 28.8% to 36.9% in men, and from 29.8% to 38.0% in women (2). Furthermore, World Health Organization estimated that 38 million deaths that occurred

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in 2012 were due to non-communicable diseases (NCDs) such as cardiovascular diseases (46.2% of NCD deaths), cancers (21.7% of NCD deaths), respiratory diseases (10.7% of NCD deaths) and diabetes (4% of NCD deaths) for which obesity represents a risk factor (1). The central role in this association is played by insulin resistance (3-5) and the abdominal fat tissue (both visceral and subcutaneous one) has been shown to play a greater role in the association of obesity with insulin resistance than the overall fat mass (6-8).

The objective of the analysis presented here was to evaluate the relationship between the changes in the body composition as assessed by bioimpedance and the changes in the glycemic control as evaluated by glycemia and glycated hemoglobin (HbA1c) and the lipid metabolism parameters in adults with type 2 diabetes. ❑

MATERIAL AND METHOD

This was a retrospective cohort study, with data collection from the files of patients with type 2 diabetes who were followed-up in an outpatient clinic from Cluj-Napoca between January 2010 and January 2014. Patients were included in the analysis if they were >18 years old; they had three consecutive visits registered in the files (baseline – the first consultation in the private clinic, at 3 and 6 months); at all visits had complete anthropometric, body composition, and biochemical measurements (glucose metabolism and lipid metabolism) recorded in the files. Pregnant or lactating women and oncological patients were not included in the analysis. The diagnosis of type 2 diabetes was collected from patient files.

Biochemical measurements recorded were fasting plasma glucose (FPG), HbA1c, total cholesterol, HDL-cholesterol, LDL-cholesterol and triglycerides. As per local procedures all these parameters were measured by a fully automated analyzer (Cobas Integra 400 Plus, Roche).

The anthropometric parameters collected from files included age (years) and height (cm) (baseline only), weight (kg) and waist circumference (cm) (for each visit). For each visit the body mass index (BMI) was calculated as weight (kg)/ [height (m)]^2.

Body composition was assessed by bioelectric impedance analysis, using InBody (720) (Biospace, Korea). The device uses an eight-point tetrapolar electrode system method which assesses the resistance to five specific frequencies (1 kHz, 50 kHz, 250 kHz, 500 kHz, and 1000 kHz) and reactance at three specific frequencies (5 kHz, 50 kHz, and 250 kHz) of a small alternate electrical current applied on the body. 30 impedance measurements are performed in order to provide the following information: total body weight, skeletal muscle mass, fat free mass, total body water, protein, body fat percentage, waist-to-hip ratio, BMI, segmental muscle mass showing the difference between each arm and leg, body shape graph, nutritional assessment, fitness score. For the analysis presented here we collected data on visceral fat area (VFA; cm), body fat mass (BFM, kg) and percent body fat (PBF; %).

Statistical analysis

Statistical analysis was performed using SPSS-PC 17.0 (SPSS Inc., Chicago, IL, USA) and Stata 14.0 (StataCorp LP). According to the distribution of variables the data were presented as mean ± standard deviation (SD) for normally-distributed variables, median (1st quartile; 3rd quartile) for variables with abnormal distribution and percentage for categorical variables. For the comparison of the parameters evaluated at baseline, month 3 and month 6 we used *t*-test for the comparison of means and related-samples Friedman's two-way analysis of variance for the comparison of medians. In order to compare the level of change in the evaluated parameters at 3 and 6 months we calculated delta parameters as the value of the parameter at month 0 minus the value of the parameter at month 3 or month 6 and results were compared using the independent samples Mann-Whitney U test. The correlation between delta VFA, delta PBF and delta BFM and the changes in the biochemical parameters, systolic and diastolic blood pressure was evaluated using the nonparametric partial correlation procedure adjusted for age, sex, delta weight, delta BMI and delta waist at 3 or 6 months. For all tests p-value was considered statistically significant if <0.05. ❑

OUTCOMES

We included in this analysis 171 adult patients (84 men and 87 women) with type 2 diabetes and complete anthropometric, body

composition, and biochemical measurements (glucose metabolism and lipid metabolism) measurements recorded in the files.

Participants mean age was 53.47 years and the median duration of diabetes 0.1 years (Table 1). During the 6-month follow-up the weight decreased from 96.05 kg to 89.7 kg ($p<0.001$) and the BMI from 32.20 kg.m^2 to 30.10 kg/m^2 ($p<0.001$). The levels of FPG and HbA1c decreased from baseline to month 3 and further to month 6. FPG decreased from 128 mg/dl to 119.73 mg/dl at month 3 and to 110.00 mg/dl at month 6. HbA1c decreased from 8.12% to 6.41% at month 3 and to 6.31% at month 6. The levels of all parameters describing the lipid metabolism improved from baseline to month 3 ($p<0.001$ for all) and then plateaued until month 6 (triglycerides and HDL-cholesterol) or slightly increased (total cholesterol, LDL-cholesterol and non-HDL cholesterol). For triglycerides, although the p-value for trend showed a non-statistically significant decrease, the values at month 3 and at month 6 were statistically significant lower compared to baseline ($p = 0.043$ for month 3 and $p=0.018$ for month 6). Systolic and diastolic blood pressure showed a trend similar to the one observed for the lipid metabolism parameters. Both decreased significantly from baseline to month 3 (systolic blood pressure from 140 mmHg to 120 mmHg; diastolic blood pressure from 90.00 mmHg to 80 mmHg) and then plateau ed until month 6.

All body composition parameters decreased significantly from baseline to month 3 and then to month 6. VFA decreased from 176. 26 cm^2 at baseline to 151.21 cm^2 at month 3 and to 146.64 cm^2 at month 6. BFM had a median value of 34.60 kg at baseline and decreased to 29.00 kg at month 3 and 27.95 kg at month 6.

The change in parameters between baseline and month 3 and between baseline and month 6 is shown in Figure 1.

The correlation coefficients between the change in the VFA, BFM and the change in the systolic and diastolic blood pressure and the change in the glycemic and lipid metabolism parameters at 3 and 6 months are displayed in Tables 2 and 3. After adjustment for age, sex, diabetes therapy, delta BMI, delta weight and delta waist circumference, delta VAT at 3 months was significantly correlated with delta glycemia, delta HbA1c, delta cholesterol, delta triglycerides, delta LDL-cholesterol, delta HDL-cholesterol and delta non-HDL cholesterol at 3 months. Delta BFM at 3 months was correlated significantly with delta glycemia, delta HbA1c and delta triglycerides, delta LDL-cholesterol, delta HDL-cholesterol and delta non-HDL cholesterol at 3 months. At 6 months, delta VAT was correlated with delta systolic blood pressure and delta diastolic blood pressure at 6 months, delta BFM with delta glycemia, delta HbA1c, delta triglycerides, delta LDL-cholesterol, delta HDL-cholesterol and delta non-HDL cholesterol at 6 months. ❑

CONCLUSION

In this population of men and women with type 2 diabetes, the decrease of VFA and BFM at 3 months was correlated with improved glycemic control as assessed by FPG and HbA1c. At 6 months only the decrease in BFM re-

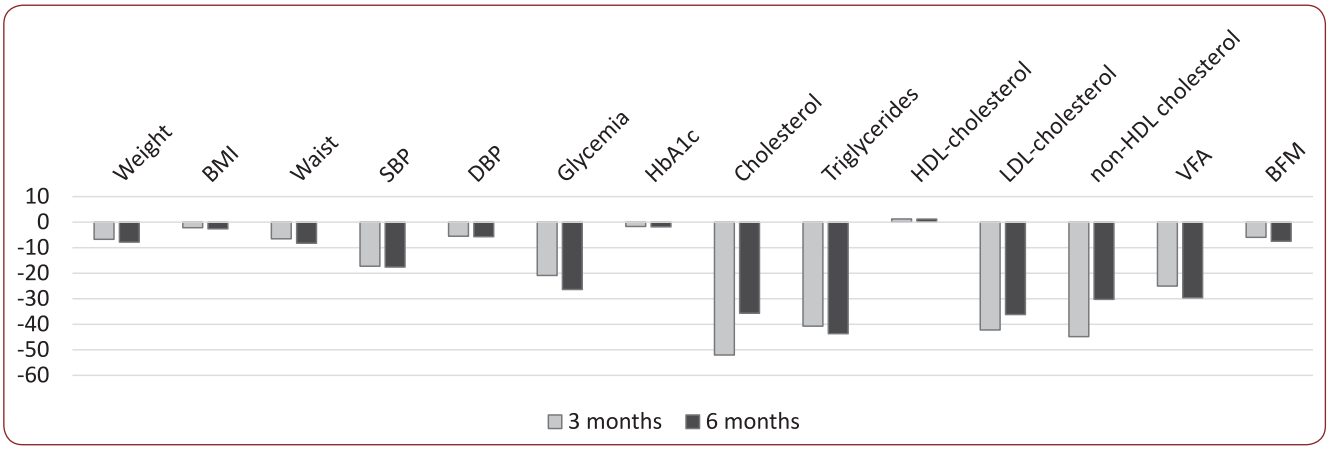

FIGURE 1. Changes in clinical, anthropometric, body composition and metabolic parameters at 3 and 6 months.

BMI, body mass index; VFA, visceral fat area; PBF, percent body fat; BFM, body fat mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin.

Variable	Baseline values	3 months	6 months	P for trend
Age, years	53.47±10.34			
Diabetes duration, years	0.1 (0.0; 5.0)			
Weight, kg	96.05 (84.43; 107.30)	89.60 (80.88; 101.45)	89.75 (80.25; 98.35)	<0.001
BMI, kg/m^2	32.20 (28.85; 36.05)	30.65 (27.38; 33.80)	30.10 (27.30; 33.05)	<0.001
Waist circumference, cm	113.00 (104.00; 120.00)	106.00 (99.75; 114.00)	104.50 (99.00; 113.00)	<0.001
SBP, mmHg	140.00 (130.00; 150.00)	120.00 (110.00; 130.00)	120.00 (110.00; 130.00)	<0.001
DBP, mmHg	90.00 (80.00; 90.00)	80.00 (80.00; 90.00)	80.00 (80.00; 90.00)	<0.001
Glycemia, mg/dl	128.00 (104.86; 146.18)	119.73 (116.91; 122.25)	110.00 (100.00; 117.55)	<0.001
HbA1c, %	8.12±1.60	6.41±0.81	6.31±0.72	<0.001
Cholesterol, mg/dl	200.55 (190.32; 210.22)	155.59 (155.58; 155.61)	177.80 (169.61; 185.31)	<0.001
Triglycerides, mg/dl	119.75 (62.08; 178.95)	109.80 (98.01; 121.24)	109.60 (101.81; 117.03)	0.330
HDL-cholesterol, mg/dl	36.96 (34.21; 39.55)	37.82 (34.40; 41.14)	37.26 (33.27; 41.76)	<0.001
LDL-cholesterol, mg/dl	150.54 (142.52; 157.44)	108.08 (98.54; 116.86)	114.0905 (103.93; 124.54)	<0.001
Non-HDL cholesterol, mg/dl	156.09 (147.28; 164.04)	121.92 (116.39; 127.45)	140.62 (128.07; 152.63)	<0.001
VFA, cm^2	176.26±46.92	151.21±42.18	146.64±42.32	<0.001
BFM, kg	34.60 (27.35; 43.33)	29.00 (22.28; 36.30)	27.95 (20.45; 35.38)	<0.001
Diabetes therapy Metformin Sulfonylurea DPP-4 inhibitors Insulin	 141 (82.5%) 33 (19.4%) 19 (11.1%) 17 (19.9%)			

TABLE 1. Clinical, anthropometric, body composition and metabolic parameters at baseline, 3 and 6 months.

BMI, body mass index; VFA, visceral fat area; BFM, body fat mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin.

mained correlated with parameters of glycemic control. Although of low intensity, these correlations were independent of the changes in BMI and waist circumference.

A large number of research reported an association between obesity and glucose metabolism mediated by its relationship with insulin resistance and impaired insulin secretion. Visceral adipose tissue has been considered the main driver of the insulin resistance, with numerous studies showing that it is an independent risk factor for insulin resistance, glucose intolerance, and cardiovascular risk factors (10,11). The pathogenetic mechanism hypothesized to mediate this association are decreased skeletal muscle glucose uptake due to decreased sensitivity to insulin, lower reesterification of free fatty acids (FFA) and increased lipolysis due to insulin resistance in the visceral and peripheral adipocytes (12-14). Goodpaster et al showed that in obese persons the reduction of visceral adipose tissue following weight loss was the only parameter associated with improved insulin sensitivity (15). Increased VAT accumulation has been also shown to be associated with impaired insulin secretion and this association has been described in both lean and obese persons with various grades of insulin resistance (16-18). In a study enrolling 60 obese women with normal glycemia, impaired fasting glucose and diabetes, Gletsu-Miller et al showed that independent of total adiposity and age, VAT was associated with beta-cell dysfunction as assessed by markers of insulin secretion and that increased VAT was associated with increasing levels of FPG (18). The hypothesized pathogenetic mechanism involved in this association is the lipotoxicity caused by increased free fatty acids release from VAT with consequent oxidative stress induction and beta-cell apoptosis (19).

Although VAT is considered the main contributor to the development of insulin resistance and dysglycemia, the relationship between intra-abdominal fat accumulation and the insulin sensitivity was reported to be non-linear (20). Additionally, clinical investigations have shown that subcutaneous adipose tissue, and especially subcutaneous truncal fat and subcutaneous abdominal fat, may also play a

Variable	Delta VFA 3 months		Delta BFM 3 months	
	Coefficient	P	Coefficient	P
Delta SBP 3 months	--0.178	0.089	-0.187	0.074
Delta DBP 3 months	-0.202	0.054	-0.187	0.074
Delta glycemia 3 months	0.300	0.045	0.209	0.046
Delta HbA1c 3 months	0.265	0.015	0.263	0.016
Delta cholesterol 3 months	0.300	0.045	0.209	0.046
Delta triglycerides 3 months	0.300	0.045	0.209	0.046
Delta HDL-cholesterol 3 months	-0.300	0.045	-0.209	0.046
Delta LDL-cholesterol 3 months	0.300	0.045	0. 209	0.046
Delta non-HDL cholesterol 3 months	0.300	0.045	0.209	0.046

TABLE 2. Correlation coefficients at 3 months, model adjusted for age, sex, diabetes therapy, delta weight, delta body mass index and delta waist at 3 months.

VFA, visceral fat area; BFM, body fat mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin.

Variable	Delta VFA 6 months		Delta BFM 6 months	
	Coefficient	P	Coefficient	P
Delta SBP 6 months	-0.242	0.020	-0.170	0.106
Delta DBP 6 months	-0.244	0.019	-0.175	0.094
Delta glycemia 6 months	0.087	0.410	0.251	0.016
Delta HbA1c 6 months	0.164	0.136	0.293	0.007
Delta cholesterol 6 months	0.077	0.465	0.251	0.016
Delta triglycerides 6 months	0. 077	0.465	0.251	0.016
Delta HDL-cholesterol 6 months	0. 077	0. 465	-0.251	0.016
Delta LDL-cholesterol 6 months	0. 077	0. 465	0.251	0.016
Delta non-HDL cholesterol 6 months	0. 077	0. 465	0.251	0.016

TABLE 3. Correlation coefficients at 6 months, model adjusted for age, sex, diabetes therapy, delta weight, delta body mass index and delta waist at 6 months.

VFA, visceral fat area; BFM, body fat mass; SBP, systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin.

role in the development of insulin resistance (21-24). In our population we observed that both the changes in the VFA and in the parameter describing the body adiposity over all – BFM - at 3 months were correlated with the changes in the glycemic control. We can hypothesize that the correlation between the BFM and the parameters describing glycemic control were mediated through the subcutaneous adipose tissue.

Numerous studies have shown both cross-sectional and prospective association between subcutaneous adipose tissue, VAT and increased level of triglycerides, with VAT being the strongest predictor (8,25,26). In our study we observed a significant correlation, albeit of lower intensity, between the changes in the VFA and the changes in the lipid profiles only at 3 months of follow-up. In our population the changes in the BFM were correlated with the changes in the triglycerides levels both at 3 and at 6 months and the observed relationship was independent of the changes in BMI and waist circumference – the most frequently used measures for the assessment of adiposity. Additionally, in our study changes in BFM were correlated with changes in all other lipid profile parameters included in the analysis both at 3 and at 6 moths. These results are in line with previous reports of this association and showing BFM as being more strongly associated than BMI with serum lipid concentrations (27).

This study has several limitations. The most important one is the retrospective collection of data from patient files and not a prospective study design which have allowed us to establish a causal-effect relationship between the parameters evaluated. Another one is the use of bioelectrical impedance for the evaluation of the body composition analysis instead of DEXA which is considered the golden standard for this evaluation.

In the population included in this analysis we showed that changes in VFA and BFM were correlated with changes in glycemic control during the 3-month follow-up and that changes in BFM were correlated with changes in lipid profile parameters both at 3 and at 6 months. The evaluation of changes in body fat depots by bioelectrical impedance conveys additional

information over changes in standard anthropometric indices including BMI and waist circumference in predicting changes in the glycemic control and lipid levels in patients with type 2 diabetes. Additionally, the assessment of the body composition parameters provides additional information on cardiovascular risk and corroborated with laboratory parameters play an important role in the health state evaluation. Also they allow a better selection of patients who may be candidates for more intensive CV risk reduction interventions.

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