The Effect of VASER Abdominal Liposuction on Metabolic Profile in Overweight Males

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Abstract

The aim of the current study was to examine the liposuction-induced metabolic changes with regard to release of major adipokines and insulin sensitivity in overweight male patients. Seventeen overweight male patients aged 37.15 ± 9.60 years (6 with diabetes type 2, 11 without comorbidities) and 10 age-matched healthy lean controls were enrolled in the study. Using Vibration Amplification of Sound Energy at Resonance System, ultrasound assisted liposuction was applied onto the deep layers of abdominal subcutaneous adipose tissue. The mean volume supranatant fat was 2208 ± 562 ml. To eliminate the confounding effects of postsurgical inflammation and to evaluate delayed metabolic effects, fasting blood was collected on the day of liposuction, within 1 to 2 months and more than 6 months after surgery. Serum leptin, soluble receptor for leptin, adiponectin, insulin, and glucose concentrations were tested and insulin sensitivity was calculated using updated model Homeostasis Model Assessment 2. Both treatment groups (diabetic and nondiabetic patients) experienced similar postsurgical weight reduction with concomitant lowering of body mass index value at 1 to 2 months follow-up, which was sustained after 6 months from surgery. Improvement in insulin sensitivity at 1 to 2 months follow-up was observed (p = .017 and p = .002, for diabetics and nondiabetics, respectively) and this change persisted over the next 4 months. At the same time, no significant changes in adipokines and soluble leptin receptor were found. These data demonstrate that in terms of metabolic consequences, Vibration Amplification of Sound Energy at Resonance abdominal liposuction might have beneficial effects in overweight diabetic and nondiabetic males by improving their insulin sensitivity.

Keywords

liposuction, insulin sensitivity, adiponectin, leptin, overweight males

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Introduction

Being overweight or obese rises the risk for other health problems such as insulin resistance (IR) and impaired glucose tolerance, hypertension, dyslipidemia, or atherosclerosis which are all classified as a components of cardiometabolic syndrome. The prevalence of obesity and cardiometabolic syndrome is high in both genders (Beigh & Jain, 2012); however, men have been underrepresented in weight-related trials. As suggested by Tsai, Lv, Xiao, and Ma (2015), improving overweight and obesity prevalence in men requires increased male participation in weight loss research. Thus, finding any mechanisms that promote better tissue response to insulin activity in men deserves high priority in clinical research. According to the International Society of Aesthetic Plastic Surgery, liposuction is one of the most frequently performed plastic procedures worldwide. Immediate removal of fat excess may lead to metabolic consequences, which have been widely studied in recent years. As suggested by many authors, liposuction could be a viable method not only for aesthetic purposes but also for increasing the efficiency of insulin and improving tissue metabolism, especially when combined with regular

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Creative Commons Non Commercial CC-BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 3.0 License (http://www.creativecommons.org/licenses/by-nc/3.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage). exercise and proper diet (Giugliano et al., 2004; González-Ortiz, Robles-Cervantes, Cárdenas-Camarena, Bustos-Saldańa, & Martínez-Abundis, 2002). Contrary to these results, a number of studies reported no or even diverse effects of liposuction on metabolic profile (Klein et al., 2004; Weber, Buckley, Fried, & Kral, 2000). Conflicting findings about abdominal liposuction and its metabolic effects may result from noncohesive study populations (gender, patients' lifestyle, obese vs. overweight patients, comorbidities, etc.), small number of study participants, different experimental methodologies (follow-up time, different methods measuring insulin sensitivity, etc.) and different types of liposuction procedures. Thus, the current data cannot bring a clear evidence suggesting that liposuction itself results in important metabolic outcomes, and on the other hand, the possibility that liposuction may serve as an additional strategy for rapid restoration of impaired metabolic profile cannot be completely excluded.

The current study was designed to investigate metabolic consequences of ultrasound assisted liposuction (UAL) using a Vibration Amplification of Sound Energy at Resonance (VASER) System that is minimally invasive, selectively destroys fat cells (FC) localized deeply below the superficial subdermal fascia and is the best known alternate to traditional technology. The authors examined whether abdominal liposuction affects insulin sensitivity and adipose tissue derived hormones involved in maintenance of metabolic homeostasis in overweight males. To the authors' knowledge, this is the first report describing the metabolic consequences of VASER abdominal liposuction in males.

Material and Method

Participants

Participant recruitment for the research was carried out between March 2012 and December 2015. Seventeen overweight male patients aged 37.15 ± 9.60 years, who comprised a relatively homogenous study group, participated in the study. Participants were weight-stable in the 3 months preceding the procedure. For the parallel control group (n = 10), normal-weight healthy voluntaries aged 35 ± 6.70 years were recruited. Study participants were in apparently good state of health and underwent prestudy screening by standard physical examination and routine clinical laboratory tests. All patients gave their written consent for participation in the study which was conducted with the approval of the Ethical Committee. The exclusion criteria were based on the presence of any of the following: female sex, obesity, hypertension, hypercholesterolemia, acute cardiovascular event within past 6 months, surgery within past 6 months, acute infection or allergic

reaction within past 4 months, chronic inflammatory disease, neoplasm, renal and/or hepatic failure. Hypertension was recognized according to patient's medical history or when blood pressure averaged from three readings was systolic blood pressure ≥140 mm Hg and/or diastolic pressure \geq 90 mm Hg (Whitworth & World Health Organization, International Society of Hypertension Writing Group, 2003). Six patients had confirmed diabetes type 2. Diabetes was defined, according to American Diabetes Association recommendations, as fasting glucose ≥126 mg/dL and/or glycated hemoglobin (HbA1c) level 6.5% or higher (American Diabetes Association, 2015) and patient's medical history. All of the diabetic patients enrolled in the study (n = 6) presented with relatively well-controlled diabetes type 2 (mean HbA1c level 7.8 \pm 1.1%) on oral agents. Five patients were treated with metformin and one with a combination of metformin and sulfonylureas. No specific supportive lifestyle intervention was implemented after surgery and the patients, as well as controls, based on the classification proposed by Pate et al. (1995) were classified as being moderately active (3-5 MET, approximately 145 minutes/week). The daily exercise, living habits, and nutritional behavior of the controls were similar to the study group.

Liposuction Procedure. Using VASER System, UAL with tumescent local anesthesia technique was applied onto the deep adipose tissue, below the superficial subdermal fascia of the abdominal region. Local anesthesia was combined with IV monitored mild sedation and analgesia (using nonsteroid anti-inflammatory drugs and opioids). Access incisions were 3 mm to 4 mm in length and wetting solution containing lidocaine at the total dose limited to 35 mg/kg and epinephrine was infused. After infiltration of the desired areas, ultrasound probes were used for ultrasound action and low-pressure suction of the liquid fat was performed. The amount of infused tumescent infiltrate was 4200 ± 771 ml. For each 100 ml of tumescent solution infused approximately 70 ml was aspirated, of which the mean volume of supranatant fat was $2208 \pm$ 562 ml. The mean volume of total aspirate including fat, wetting solution, and blood was 2945 ml (range from 2200 ml to 3520 ml).

The surgery was done as an outpatient. Before being discharged all patients were monitored for 2 hours in the recovery room and no surgical complications were observed.

Data Collection

The following anthropometrical measurements were obtained: body weight (BW) and waist circumference (WC; measured at the end of gentle expiration with a plastic tape midway between the lowest rib and the iliac

Variable	Control $(n = 10)$	All patients $(n = 17)$	þ (test)	DP (n = 6)	NDP $(n =)$	þ (test)
Age (years)	35.00 ± 6.70	37.15 ± 9.60	ns	43.00 ± 11.80	31.75 ± 7.29	ns
WC (cm)	80.4 ± 6.4	99.70 ± 4.70	.032 (Student <i>t</i>)	106.11 ± 4.12	95.01 ± 2.28	.047 (Student t)
BW (kg)	78.10 ± 8.11	91.65 ± 11.10	.037 (Student t)	98.83 ± 6.22	87.73 ± 10.90	.048 (Student t)
BMI (kg/m ²)	21.2 ± 2.6	29.16 ± 4.02	.001 (Cohran Cox)	29.98 ± 2.05	29.69 ± 4.08	ns
Insulin (uIU/ml)	13.20 ± 9.98	20.36 ± 10.99	.017 (Cohran Cox)	30.38 ± 12.60	14.89 ± 5.19	.028 (Cohran Cox)
Glucose (mg/dL)	93.34 ± 9.25	118.18 ± 23.16	.000 (Student t)	144.67 ± 12.23	100.74 ± 11.54	.000 (Student t)
%S	59.02 ± 12.21	46.00 ± 21.13	.042 (Student t)	27.07 ± 10.40	56.32 ± 18.71	.003 (Student t)
IR	1.89 ± 0.92	2.77 ± 1.51	.041 (Cohran Cox)	4.20 ± 1.68	1.99 ± 0.70	.022 (Cohran Cox)
Leptin (ng/ml)	2.25 ± 1.64	5.36 ± 2.19	.004 (Student t)	5.31 ± 1.16	4.98 ± 1.94	ns
SLR	27.10 ± 2.01	18.26 ± 3.09	.025 (Student t)	17.07 ± 1.22	18.91 ± 3.70	ns
Adiponectin	4972.57 ± 739.83	6243.52 ± 1739.83	.042 (Student t)	5062.73 ± 640.81	6887.59 ± 1869.86	.037 (Student <i>t</i>)

 Table 1. Descriptive Characteristics of Study Participants.

Note. BW = body weight; BMI = body mass index; S = insulin sensitivity; ns = not significant; IR = insulin resistance; SLR = soluble leptin receptor; DP = diabetic patients; NDP = nondiabetic patients. Data are presented as means ± SD. p < .05 was considered significant.

crest with the participant standing). Body mass index (BMI), defined as weight (kg) divided by the square height (in meters), was calculated at the time of blood samples collection. To eliminate the confounding effects of postsurgical inflammation and to evaluate delayed metabolic effects of liposuction, fasting blood was collected three times: the morning of the surgery (Collection 1-just before surgery), within 1 to 2 months after liposuction (Collection 2), 6 and more months after liposuction (Collection 3). The percentage of hemoglobin A1c (HbA1c) was determined by immunoturbidimetric method. Fasting serum insulin (HI-14K Human Insulin-Specific RIA, Merck) and glucose (hexokinase methodology, Reflotron system) concentrations were measured and insulin sensitivity was calculated using free software updated model Homeostasis Model Assessment2 provided by The University of Oxford Diabetes Trial Unit. Leptin level was assessed using DRG Leptin ELISA Kit (No cat. EIA-2395), soluble receptor for leptin using DRG Leptin Receptor (human) ELISA Kit (No cat. EIA-3527), and adipnectin by DRG Adiponectin ELISA Kit (No cat. EIA-4177).

Statistics

The Student's *t* and Cochran Cox tests were used for calculations of descriptive statistics. The results were quantitative; thus, the variables were described using an arithmetic mean and standard deviation as the numerical data had normal distribution (checked with the Kolmogorov–Smirnov test). The one-way analysis of variance with repeated measures was used to compare one quantitative variable with normal distribution at three points of time. When analysis of variance showed significance, the post hoc Tukey's honestly significant different test was applied to indicate which measurements tested in three time points of the study were significantly different. For data not normally distributed, Friedman's nonparametric test was used for comparison of

repeated measured values over the study period at the three time points, followed by the Dunn's post hoc test to detect differences between each time point. Pearson's linear correlation coefficients were calculated to assess associations between variables with normal distribution. For the variables not normally distributed, the Spearman rank correlation method was used. The level for statistical significance was $p \leq .05$ throughout the study.

Results

Patient baseline data are shown in Table 1. The control group in this study was used to evaluate the baseline validity of tested parameters. According to the World Health Organization (2009), BMI classification guidelines controls were lean and patients were overweight. Compared with controls, patients had higher baseline insulin (p = .017), lower insulin sensitivity %S (p = .042), higher IR (p = .041), higher adiponectin (p = .042), higher leptin (p = .004), and lower soluble leptin receptor (SLR) concentrations (p = .025). Patients and controls were weight-stable in the 3 months preceding the procedure and controls did not show further reduction of BW, BMI, and WC in the 6 months after surgery. Significant differences within the study group were also identified when diabetics versus nondiabetics were compared. The diabetic group was more insulin-resistant, as evidenced by higher IR values (IR above 4.0, p = .022), had greater baseline insulin which was above reference range (Chevenne, Trivin, & Porquet, 1999), and lower adiponectin levels (p = .037). There was no significant difference in leptin and SLR concentration between both treatment groups at study entry. Correlations of BMI, WC, insulin, adiponectin, leptin, and insulin sensitivity %S are presented in Table 2. Insulin sensitivity was negatively correlated with BMI, WC, and insulin concentration in all patients and positively with adiponectin in diabetics. When the estimates between three time points

	BN	11	W	С	Insu	ılin	Adipon	ectin	Lep	tin
	DP	NDP	DP	NDP	DP	NDP	DP	NDP	DP	NDP
WC	-0.120	-0.022								
Insulin	0.382*	0.095	-0.051	0.027						
Adiponectin	-0.101	0.082	-0.187	-0.124	0.066	0.098				
Leptin	0.418*	0.622*	0.395*	0.116	0.368*	0.675*	0.064	0.052		
%S	-0.382*	-0.268*	-0.438*	-0.296*	-0.893*	-0.557*	0.313*	0.095	-0.073	-0.042

Table 2. Baseline Correlations of Body Mass Index (BMI), Waist Circumference (WC), Insulin, Adiponectin, and Leptin, and Insulin Sensitivity (%S) in Overweight Diabetic (DP) and Nondiabetic (NDP) Patients.

*p < .05.

of the study were analyzed (Table 3; also see Table 4.), significant improvement was identified in insulin sensitivity at 1 to 2 months follow-up and this change persisted over the next 4 months in all patients, but not in the controls. The level of glycated hemoglobin (HbA1c) in diabetics declined significantly within the study period, but the decline was significant 6 months after surgery. Both treatment groups experienced postsurgical weight reduction with concomitant lowering of BMI value at 1 to 2 months follow-up, which was sustained after 6 months from surgery. At the same time, no changes in adipokines and SLR were observed.

Discussion

The current study's descriptive data show that in overweight insulin-resistant patients, when compared with insulin-sensitive nondiabetic individuals, serum adiponectin differs and is lower, whereas leptin level is similar. As described by others, higher levels of insulin in insulinresistant patients may down regulate adiponectin secretion (Balsan, Vieira, Oliveira, & Portal, 2015; Mohlig et al., 2002) and, even though correlations do not necessarily imply causation, observed in the current study's diabetics, positive correlation between adiponectin and %S seems to confirm this association. Regarding serum leptin, the current results support previous studies reporting a strong link between leptin and adiposity (Ayina et al., 2016; Considine et al., 1996)-leptin was positively correlated with BMI and both studied groups represented similar BMI, therefore, baseline leptin did not differ between them. The difference, as expected, was significant for both adipokines and insulin when overweight patients were compared with lean controls.

It is evident that abdominal obesity is a primary risk factor for IR and diabetes type 2 (Després, 1993). In this study, %S negatively correlated with BMI, WC, and insulin level. One of the explanatory theories states that increased depots of abdominal fat is linked with IR when subcutaneous adipose tissue (SAT) is overloaded with triacylglycerols and the buffering capacity for lipid storage in adipocytes is decreased (Patel et al., 2013). Consequently, high amounts of free fatty acids are released to the circulation adversely affecting insulin action (Boden, 2001). Although a large body of data links IR with increased depots of visceral adipose tissue (VAT) (D.L. Chen, Liess, et al., 2015; Després, 1993), the importance of the site of abdominal fat accumulation in relation to insulin sensitivity is still a matter of debate. A number of authors suggest that deep layers of SAT are functionally similar to VAT and the amount of deep abdominal SAT is strongly related to IR in a manner nearly identical to that of visceral adiposity (Kelley et al., 2000; Kim et al., 2016). Moreover, individuals with larger adipocytes in SAT may have a lower capacity for further lipid storage, so the subsequent excesses of fat may be stored in VAT, liver, and skeletal muscle, which in turn results in worsening of insulin action and glucose tolerance (Danforth, 2000). In the current study, removal of deep depots of SAT by UAL improved insulin sensitivity in both overweight diabetic and nondiabetic male patients (Figure 1 and Figure 2). The effect was significant after 1 to 2 months of stable BW postliposuction and noted as a substantial and sustained at a later time. Additionally, improvement of insulin sensitivity resulted in better glycaemic control expressed by a significant decline of HbA1c at a third time point of the study in diabetic patients and of six diabetic patients, two reported slight dose reduction of daily oral agents within follow-up. This supports the hypothesis that deep subcutaneous abdominal adipose tissue is associated with IR and the current finding is in accordance with previous reports demonstrating that liposuction modulates insulin sensitivity (Giugliano et al., 2004) with a beneficial effect that may persist over months from surgery (Giese, Bulan, Commons, Spear, & Yanovski, 2001; González-Ortiz et al., 2002). The impact of physical activity cannot be completely excluded. However, the current study's patients reported to be moderately active before surgery and they maintained their activity at the similar level after surgery. No specific supportive exercise program was implemented. Moreover, as reported by

Variable	_	2	Э	þ (test)	l vs. 2	l vs. 3	2 vs. 3	-	2	3	þ (test)
Patients $(n = 17)$									Controls $(n = 10)$		
BW (kg)	91.65 ± 11.10	89.I2 ± I0.43	89.85 ± 11.03	.045 (ANOVA)	ρ = .038 (Tukey's HSD test)	ρ = .042 (Tukey's HSD test)	I	78.I0 ± 8.II	78.65 ± 7.21	78.44 ± 7.75	su
BMI (kg/m ²)	29.16 ± 4.02	28.32 ± 3.95	28.48 ± 4.28	.050 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)		21. ± 2.6	21.6 ± 2.4	21.4 ± 2.2	su
WC (cm)	99.70 ± 4.70	96.57 ± 5.32	96.98 ± 5.84	.032 (Friedman)	φ < .05 (Dunn)	p < .05 (Dunn)	I	80. ± 6.4	80.7 ± 6.6	80.5 ± 7.0	su
Insulin (ulU/ ml)	20.36 ± 10.99	I5.78 ± 7.34	l6.99 ± l0.12	.000 (Friedman)	φ < .05 (Dunn)	þ < .05 (Dunn)	I	13.20 ± 9.98	12.96 ± 9.72	13.12 ± 9.73	su
Glucose (mg/ dL)	 8. 8 ± 23. 6	96.29 ± 25.48	95.8I ± 22.88	.002 (Friedman)	þ < .05 (Dunn)	φ < .05 (Dunn)		93.34 ± 9.25	92.99 ± 9.30	93.40 ± 9.44	su
S%	46.00 ± 21.13	56.65 ± 24.25	56.55 ± 26.03	0.000 (ANOVA)	0.0002 (Tukey's HSD)	0.0002 (Tukey's HSD)	I	59.02 ± 12.21	61.04 ± 11.98	60.04 ± 12.01	su
R	2.77 ± 1.51	2.12 ± 1.06	2.26 ± 1.40	.000 (Friedman)	φ < .05 (Dunn)	p < .05 (Dunn)		I.89 ± 0.92	I.88 ± 0.96	I.85 ± 0.95	su
Leptin (ng/ml)	5.36 ± 2.19	4.98 ± 2.25	5.14 ± 2.47	ns (ANOVA)	I	I	I	2.25 ± 1.64	2.59 ± 1.82	2.61 ± 1.91	su
SLR	18.26 ± 3.09	18.38 ± 2.89	18.53 ± 2.79	ns (ANOVA)	I	I	I	27.10 ± 2.01	27.43 ± 2.32	27.50 ± 2.41	su
Adiponectin	6243.52 ± 1739.83	6800.60 ± 1627.62	6734.49 ± 1906.83	<i>n</i> s (Friedman)			Ι	4972.57 ± 739.83	4899 ± 645.92	5125 ± 880.13	su

Table 3. Effect of VASER Abdominal Liposuction on Metabolic Variables in Male Patients and Controls.

Note. VASER = Vibration Amplification of Sound Energy at Resonance; BW = body weight; BM1 = body mass index; ns = not significant; %S = insulin sensitivity; IR = insulin resistance; SLR = soluble leptin receptor; DP = diabetic patients; NDP = nondiabetic patients; ANOVA = analysis of variance; HSD = honestly significant difference; 1 = variable measured before liposuction; 2 = variable measured 1 to 2 months after liposuction; 3 = variable measured at least 6 months after liposuction. Data are presented as means ± 5D.

Variable	_	2	з	þ (test)	l vs. 2	l vs. 3	2 vs. 3
DP (n = 6)							
BVV (kg)	98.83 ± 6.22	96.02 ± 5.23	96.13 ± 5.56	.038 (ANOVA)	p = .032 (Tukey's HSD)	p = .038 (Tukey's HSD)	Ι
BMI (kg/m2)	29.98 ± 2.05	28.77 ± 3.21	28.84 ± 3.68	.050 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)	I
VVC (cm)	106.11 ± 4.12	101.75 ± 3.17	102.03 ± 3.34	.050 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)	I
Insulin (uIU/mI)	30.38 ± 12.60	21.13 ± 8.89	24.92 ± 12.34	.000 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)	I
Glucose (mg/dL)	144.67 ± 12.23	100.30 ± 29.85	II3.53 ± 29.99	.045 (ANOVA)	.018 (Tukey's HSD)	.032 (Tukey's HSD)	I
% HbA1c	7.8 ± 1.1	7.2 ± 1.2	6.7 ± 0.8	.050 (ANOVA)	Ι	.042 (Tukey's HSD)	.044 (Tukey's HSD)
%S	27.07 ± 10.40	38.50 11.74	35.53 ± 13.90	(ANOVA) (10.	.017 (Tukey's HSD)	.051 (Tukey's HSD)	i I
R	4.20 ± 1.68	2.93 ± 1.32	3.37 ± 1.81	.000 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)	φ < .05 (Dunn)
Leptin (ng/ml)	5.31 ± 1.16	6.91 ± 1.46	7.31 ± 1.38	SU		·	
SLR	17.07 ± 1.22	17.02 ± 1.260	17.40 ± 1.45	su	I		I
Adiponectin	5062.73 ± 640.81	6326.80 ± 1677.61	5981.07 ± 1763.25	su	I		I
NDP $(n = 11)$							
BVV (kg)	87.73 ± 10.90	85.37 ± 9.96	85.51 ± 10.11	.042 (ANOVA)	.028 (Tukey's HSD)	.030 (Tukey's HSD)	I
BMI (kg/m ²)	29.69 ± 4.08	28.24 ± 4.12	28.56 ± 4.79	.050 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)	I
WC (cm)	95.01 ± 2.28	92.12 ± 2.18	92.38 ± 3.06	.049 (Friedman)	p < .05 (Dunn)	p < .05 (Dunn)	I
Insulin (uIU/mI)	14.89 ± 5.19	12.87 ± 4.50	12.67 ± 4.69	.004 (ANOVA)	.013 (Tukey's HSD)	.006 (Tukey's HSD)	Ι
Glucose (mg/dL)	100.74 ± 11.54	87.84 ± 13.56	86.15 ± 9.84	.050 (ANOVA)	.006 (Tukey's HSD)	.018 (Tukey's HSD)	Ι
%S	56.32 ± 18.71	66.55 ± 23.80	68.01 ± 24.04	.002 (ANOVA)	.007 (Tukey's HSD)	.003 (Tukey's HSD)	Ι
R	1.99 ± 0.70	1.68 ± 0.56	I .66 ± 0.59	(ANOVA) 100.	.005 (Tukey's HSD)	.002 (Tukey's HSD)	Ι
Leptin (ng/ml)	4.98 ± 1.94	3.93 ± 1.89	3.95 ± 2.11	su	I		Ι
SLR	18.91 ± 3.70	19.12 ± 3.29	19.15 ± 3.19	su	I		Ι
Adiponectin	6887.59 ± 1869.86	7059.04 ± 1619.64	7145.45 ± 1933.05	su	I	I	I
	L F						

Table 4. Effect of VASER Abdominal Liposuction on Metabolic Variables in Diabetic (DP) and Nondiabetic (NDP) Patients.



Figure 1. Insulin sensitivity (%S) changes in overweight diabetic male patients undergoing VASER abdominal liposuction. Note. VASER = Vibration Amplification of Sound Energy at Resonance; I = variable measured before surgery; 2 = variable measured I to 2 months after surgery; 3 = variable measured at least 6 months after liposuction. *Statistically different comparing 1 versus 2. **Statistically different comparing 1 versus 3.



Figure 2. Insulin sensitivity (%S) changes in overweight nondiabetic male patients undergoing VASER abdominal liposuction. Note. VASER = Vibration Amplification of Sound Energy at Resonance; I = variable measured before surgery; 2 = variable measured I to 2 months after surgery; 3 = variable measured at least 6 months after liposuction.

*Statistically different comparing I versus 2. **Statistically different comparing I versus 3.

others (Kriketos et al., 2004; Miyatake et al., 2004), regular exercise increases secretion of adiponectin and reduces secretion of leptin. In the current study, comparing pre- and postoperative periods, no significant changes in these adipokines were noted.

Leptin, a modulator of energy intake and expenditure, is produced primarily by adipose tissue. White adipose tissue presents as the major site of its synthesis and leptin mRNA levels have been found to be higher in SAT than in VAT. Moreover, only subcutaneous leptin production correlates with its circulating levels (Van Harmelen et al., 1998). It has been postulated that liposuction, by decreasing adiposity, could possibly restore leptin level from high to normal and initiate metabolic changes normalizing its peripheral signaling pathways. This phenomenon was noted in the populations of obese patients with at least second class of obesity (BMI > 35) when higher baseline leptin level is often related to leptin resistance (Busetto et al., 2008; Klein et al., 2004). High total leptin level is associated with low SLR concentration in obese patients, as an adaptive response in order to increase the availability of active (free) leptin, and leptin appears to reciprocally regulate its own binding protein (Chan et al., 2002). In the current study's overweight population, both leptin and SLR concentrations did not change but the improvement of insulin sensitivity was significant and sustained over 6 months from surgery. A number of data demonstrate stimulatory effect of insulin on leptin secretion and leptin gene expression in adipocytes (Z. L. Chen, Shao, et al., 2015; Wabitsch et al., 1996). Although the exact mechanisms are not yet fully understood, this stimulation is unlikely to be due to a direct effect of insulin per se, but it seems to be secondary to the effect of insulin to stimulate glucose uptake and metabolism in adipocytes (Mueller et al., 1998). Thus, the authors dispose toward the following hypothesis: An improvement in insulin sensitivity with concomitant increase in glucose transport might possibly affect leptin secretion, preventing it from dropping due to the removal of excess fat in overweight males. Another possibility is that after liposuction, the endocrine white adipose tissue activity in nonobese male population is kept at the level to maintain body's response to almost unaltered energy balance, since the current study's patients did not show further reduction of body mass in the 6 months after surgery. The latter explanation could also refer to postoperative adiponectin in this experiment. Contrary to the studies describing that diminished resistance to insulin is associated with significant increase in adiponectin concentration (Fasshauer, Klein, Neumann, Eszlinger, & Paschke, 2002), the authors have found an uncoupling between changes in insulin sensitivity and adiponectin levels after VASER abdominal liposuction in overweight males. As shown by others, reduction in FC size that occurs in response to dietary

and/or exercise intervention corresponds to changes in circulating adipokines (increased adiponectin and decreased leptin; Bahceci et al., 2007; Varady, Tussing, Bhutani, & Braunschweig 2009). Removal of subcutaneous fat by liposuction is a procedure that lowers the number of FC, not their size, whereas hypertrophy of FC is inversely correlated with serum adiponectin (Hoffstedt, Arvidsson, Sjölin, Wåhlén, & Arner, 2004; Meyer, Ciaraldi, Henry, Wittgrove, & Phillips, 2013) and positively with expression of leptin (Jernås et al., 2006). Even though the current study cannot clearly determine the reason why liposuction did not change adipokine levels, it seems to be logical that the type of intervention, which was different than exercise and/or diet, must play a role.

Several limitations of the current study need to be acknowledged. First, although the study group was homogenous (overweight male patients, similar lifestyle, and nutritional habits), the authors admit that their observations are restricted to a relatively small number of study participants, so any interpretation should be made with caution. Second, the authors understand that the interplay among insulin, leptin, and adiponectin is a matter of complex processes and it is possible that unmeasured parameters, for example, body fat distribution and activity using imaging techniques, blood lipid profile, or metabolic rate, may account for the changes observed. Last, although the authors report improvement in insulin sensitivity and no change in fasting adipokines, the study was not designed to establish causality between these findings. However, the authors believe that the results may serve as a good starting point for the next experiments evaluating mechanistic insights to investigate this process in detail.

In summary, the main finding of the present study is that in overweight male patients, VASER liposuction removing deep depots of SAT changes insulin level and improves insulin sensitivity. Both overweight diabetic and overweight nondiabetic males may benefit from this surgical procedure.

Declaration of Conflicting Interests

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References

American Diabetes Association. (2015). Classification and diagnosis of diabetes. *Diabetes Care*, 38(Suppl. 1), S8-S16. doi:10.2337/dc15-S005

- Ayina, C. N., Noubiap, J. J., Etoundi Ngoa, L. S., Boudou, P., Gautier, J. F., Mengnjo, M., . . . Sobngwi, E. (2016). Association of serum leptin and adiponectin with anthropomorphic indices of obesity, blood lipids and insulin resistance in a Sub-Saharan African population. *Lipids in Health* and Disease, 15, 96. doi:10.1186/s12944-016-0264-x
- Bahceci, M., Gokalp, D., Bahceci, S., Tuzcu, A., Atmaca, S., & Arikan, S. (2007). The correlation between adiposity and adiponectin, tumor necrosis factor alpha, interleukin-6 and high sensitivity C-reactive protein levels: Is adipocyte size associated with inflammation in adults? *Journal of Endocrinological Investigation*, 30, 210-214. doi:10.1007/ BF03347427
- Balsan, G. A., Vieira, J. L., Oliveira, A. M., & Portal, V. L. (2015). Relationship between adiponectin, obesity and insulin resistance. *Revista da Associação Médica Brasileira*, 61(1), 72-80. doi:10.1590/1806-9282.61.01.072
- Beigh, S. H., & Jain, S. (2012). Prevalence of metabolic syndrome and gender differences. *Bioinformation*, 8, 613-616. doi:10.6026/97320630008613
- Boden, G. (2001). Free fatty acids: The link between obesity and insulin resistance. *Endocrine Practice*, 7, 44-51. doi:10.4158/EP.7.1.44
- Busetto, L., Bassetto, F., Zocchi, M., Zuliani, F., Nolli, M. L., Pigozzo, S., . . . Enzi, G. (2008). The effects of the surgical removal of subcutaneous adipose tissue on energy expenditure and adipocytokine concentrations in obese women. *Nutrition, Metabolism and Cardiovascular Diseases, 18*, 112-120. doi:10.1016/j.numecd.2006.09.009
- Chan, J. L., Blüher, S., Yiannakouris, N., Suchard, M. A., Kratzsch, J., & Mantzoros, C. S. (2002). Regulation of circulating soluble leptin receptor levels by gender, adiposity, sex steroids, and leptin: Observational and interventional studies in humans. *Diabetes*, 51, 2105-2112. doi:10.2337/ diabetes.51.7.2105
- Chen, D. L., Liess, C., Poljak, A., Xu, A., Zhang, J., Thoma, C., Trenell, M., . . . Greenfield, J. R. (2015). Phenotypic characterization of insulin-resistant and insulin-sensitive obesity. *Journal of Clinical Endocrinology & Metabolism*, 100, 4082-4091. doi:10.1210/jc.2015-2712
- Chen, Z. L., Shao, W. J., Xu, F., Liu, L., Lin, B. S., Wei, X. H., . . . Jin, T. R. (2015). Acute Wnt pathway activation positively regulates leptin gene expression in mature adipocytes. *Cellular Signalling*, 27, 587-597. doi:10.1016/j. cellsig.2014.12.012
- Chevenne, D., Trivin, F., & Porquet, D. (1999). Insulin assays and reference values. *Diabetes & Metabolism*, 25, 459-476.
- Considine, R. V., Sinha, M. K., Heiman, M. L., Kriauciunas, A., Stephens, T. W., Nyce, M. R., ... Bauer, T. L. (1996). Serum immunoreactive-leptin concentrations in normal-weight and obese humans. *New England Journal of Medicine*, 334, 292-295. doi:10.1056/NEJM199606063342314
- Danforth, E., Jr. (2000). Failure of adipocyte differentiation causes type II diabetes mellitus? *Nature Genetics*, 26, 13. doi:10.1038/79111
- Després, J. P. (1993). Abdominal obesity as important component of insulin-resistance syndrome. *Nutrition*, 9, 452-459.
- Fasshauer, M., Klein, J., Neumann, S., Eszlinger, M., & Paschke, R. (2002). Hormonal regulation of adiponectin

gene expression in 3T3-L1 adipocytes. *Biochemical and Biophysical Research Communications*, 290, 1084-1089. doi:10.1006/bbrc.2001.6307

- Giese, S. Y., Bulan, E. J., Commons, G. W., Spear, S. L., & Yanovski, J. A. (2001). Improvements in cardiovascular risk profile with large-volume liposuction: A pilot study. *Plastic and Reconstructive Surgery*, 108, 510-520. doi:10.1097/00006534-200108000-00035
- Giugliano, G., Nicoletti, G., Grella, E., Giugliano, F., Esposito, K., Scuderi, N., & D'Andrea, F. (2004). Effect of liposuction on insulin resistance and vascular inflammatory markers in obese women. *British Journal of Plastic Surgery*, 57, 190-194. doi:10.1016/j.bjps.2003.12.010
- González-Ortiz, M., Robles-Cervantes, J. A., Cárdenas-Camarena, L., Bustos-Saldańa, R., & Martínez-Abundis, E. (2002). The effects of surgically removing subcutaneous fat on the metabolic profile and insulin sensitivity in obese women after large-volume liposuction treatment. *Hormone and Metabolic Research*, 34, 446-449. doi:10.1055/s-2002-33603
- Hoffstedt, J., Arvidsson, E., Sjölin, E., Wåhlén, K., & Arner, P. (2004). Adipose tissue adiponectin production and adiponectin serum concentration in human obesity and insulin resistance. *Journal of Clinical Endocrinology & Metabolism*, 89, 1391-1396. doi:10.1210/jc.2003-031458
- Jernås, M., Palming, J., Sjöholm, K., Jennische, E., Svensson, P. A., Gabrielsson, B. G., . . . Lönn, M. (2006). Separation of human adipocytes by size: Hypertrophic fat cells display distinct gene expression. *FASEB Journal*, 20, 1540-1542. doi:10.1096/fj.05-5678fje
- Kelley, D. E., Thaete, F. L., Troost, F., Huwe, T., & Goodpaster, B. H. (2000). Subdivisions of subcutaneous abdominal adipose tissue and insulin resistance. *American Journal* of *Physiology: Endocrinology and Metabolism*, 278, E941-E948.
- Kim, S. H., Chung, J. H., Song, S. W., Jung, W. S., Lee, Y. A., & Kim, H. N. (2016). Relationship between deep subcutaneous abdominal adipose tissue and metabolic syndrome: A case control study. *Diabetology & Metabolic Syndrome*, *12*(8), 10. doi:10.1186/s13098-016-0127-7
- Klein, S., Fontana, L., Young, V. L., Coggan, A. R., Kilo, C., Patterson, P. W., & Mohammed, B. S. (2004). Absence of an effect of liposuction on insulin action and risk factors for coronary heart disease. *New England Journal of Medicine*, 350, 2549-2557. doi:10.1056/NEJMoa033179
- Kriketos, A. D., Gan, S. K., Poynten, A. M., Furler, S. M., Chisholm, D. J., & Campbell, L. V. (2004). Exercise increases adiponectin levels and insulin sensitivity in humans. *Diabetes Care*, 27, 629-630. doi:10.2337/diacare.27.2.629
- Meyer, L. K., Ciaraldi, T. P., Henry, R. R., Wittgrove, A. C., & Phillips, S. A. (2013). Adipose tissue depot and cell size dependency of adiponectin synthesis and secretion in human obesity. *Adipocyte*, 2, 217-226. doi:10.4161/adip.24953
- Miyatake, N., Takahashi, K., Wada, J., Nishikawa, H., Morishita, A., Suzuki, H., . . . Fujii, M. (2004). Changes in serum leptin concentrations in overweight Japanese men after exercise. *Diabetes Obesity and Metabolism*, 6, 332-337. doi:10.1111/j.1462-8902.2004.00351.x

- Mohlig, M., Wegewitz, U., Osterhoff, M., Isken, F., Ristow, M., Pfeiffer, A. F., & Spranger, J. (2002). Insulin decreases human adiponectin plasma levels. *Hormone and Metabolic Research*, 34, 655-658. doi:10.1055/s-2002-38248
- Mueller, W. M., Gregoire, F. M., Stanhope, K. L., Mobbs, C. V., Mizuno, T. M., Warden, C. H., . . . Havel, P. J. (1998). Evidence that glucose metabolism regulates leptin secretion from cultured rat adipocytes. *Endocrinology*, *139*, 551-558. doi:10.1210/en.139.2.551
- Pate, R. R., Pratt, M., Blair, S. N., Haskell, W. L., Macera, C. A., Bouchard, C., . . . Wilmore, J. H. (1995). Physical activity and public health: A recommendation from the Centers for Disease Control and Prevention and the American College of Sports Medicine. *Journal of the American Medical Association*, 273, 402-407. doi:10.1001/ jama.1995.03520290054029
- Patel, P., & Abate, N. (2013). Role of subcutaneous adipose tissue in the pathogenesis of insulin resistance. *Journal of Obesity*, 4, 489187. doi:10.1155/2013/489187
- Tsai, S. A., Lv, N., Xiao, L., & Ma, J. (2015). Gender differences in weight-related attitudes and behaviors among overweight and obese adults in the United States. *American Journal of Men's Health*, 10, 389-398. doi:10.1177/ 1557988314567223
- Van Harmelen, V., Reynisdottir, S., Erikkson, P., Thorne, A., Hoffstedt, J., Lönnqvist, F., & Arner, P. (1998). Leptin

secretion from subcutaneous and visceral adipose tissue in women. *Diabetes*, 47, 913-917. doi:10.2337/diabetes.47.6.913

- Varady, K. A., Tussing, L., Bhutani, S., & Braunschweig, C. L. (2009). Degree of weight loss required to improve adipokine concentrations and decrease fat cell size in severely obese women. *Metabolism*, 58, 1096-1101. doi:10.1016/j. metabol.2009.04.010
- Wabitsch, M., Jensen, P. B., Blum, W. F., Christoffersen, C. T., Englaro, P., Heinze, E., . . . Hauner, H. (1996). Insulin and cortisol promote leptin production in cultured human fat cells. *Diabetes*, 45, 1435-1438. doi:10.2337/diabetes.45.10.1435
- Weber, R. V., Buckley, M. C., Fried, S. K., & Kral, J. G. (2000). Subcutaneous lipectomy causes a metabolic syndrome in hamsters. *American Journal of Physiology: Regulatory, Integrative and Comparative Physiology*, 279, R936-R943.
- Whitworth, J. A., & World Health Organization, International Society of Hypertension Writing Group. (2003). 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *Journal of Hypertension*, 21, 1983-1992. doi:10.1097/01.hjh.0000084751.37215.d2
- World Health Organization. (2009). Global database on body mass index. Retrieved from http://apps.who.int/bmi/index. jsp?introPage=intro_3.html