

Effect of Large-Volume Abdominal Liposuction on Serum Adiponectin Level and its Metabolic Consequences in Obese Women

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ABSTRACT

Liposuction is one of the most common elective surgical procedures in the US and is supposed to be on the increase. There are no reported studies specifically addressing the metabolic sequelae of liposuction in obesity. Adiponectin is a novel adipocytokine that has been thoroughly investigated for its potential insulin sensitizing properties. We undertook the present study to assess the effects of large volume abdominal liposuction on serum adiponectin level and its impact on insulin resistance in obese women. Forty female subjects were submitted for the study. Eleven obese women who had normal glucose tolerance (BMI, 37.1±3.4), nine obese women who had type 2 diabetes (BMI, 39.9±5.6) and twenty healthy premenopausal age-matched normal weight (BMI <25) women were taken as control. In obese women, insulin sensitivity, as measured by the Homeostasis Model Assessment (HOMA = Fasting plasma glucose x fasting serum insulin divided by 25), as well as serum adiponectin, were significantly lower, as compared with non-obese women ($p < 0.01$), indicating insulin resistance. All obese women were submitted to a single large volume liposuction (tumescent technique): The mean aspirate volume was 5.5 liters (range 4.6-6.7). After 12 weeks of stable body weight post-liposuction, diabetic obese women were less insulin resistant ($p < 0.05$) and had increased serum levels of adiponectin ($p < 0.01$). There was a significant correlation between the amount of fat aspirate and changes in HOMA ($r = -0.28$, $p < 0.05$) and adiponectin ($r = 0.34$, $p < 0.01$). Our study demonstrated that liposuction is safe and is associated with amelioration of metabolic consequences of obesity which may help obese subjects to reduce their insulin resistance.

INTRODUCTION

Abdominal obesity, manifested by increased waist circumference, increased abdominal subcutaneous fat and increased visceral fat, is associated with insulin resistance and other metabolic risk factors [1]. Although both the abdominal subcutaneous fat mass and the visceral fat mass are associated with insulin resistance, it is not known whether one or both of these fat depots are actually involved in the pathogenesis of insulin resistance or whether they are simply associated with the metabolic complications of obesity [2].

Adiponectin, an adipose tissue-specific plasma protein, was recently revealed to have a potential role in many of the obesity associated metabolic disorders such as vascular disorders, dyslipidemia and glucose intolerance. Its plasma levels are significantly lower in obese human subjects with type 2 diabetes mellitus. Therefore, it may provide a biological link between obesity and obesity-related disorders especially insulin resistance and hence type 2 diabetes, against which it may confer protection [3].

Although diet-induced weight loss improves the metabolic complications of abdominal obesity, however successful long-term weight management is difficult to achieve and the majority of obese persons who lose weight by implementing lifestyle changes regain their lost weight over time [3,4]. Frustration with the efficacy of current obesity therapies has led to increased interest in alternative approaches. Recently, it has been suggested that liposuction, which can remove large amounts of body fat, is a potential treatment for the metabolic complications of obesity [5,6,7].

Liposuction, also known as lipoplasty or suction-assisted lipectomy, is the most common aesthetic surgical procedure performed in the United States; nearly 400,000 procedures are performed annually [8]. Recent advances in liposuction techniques now make it possible to remove considerable amounts of subcutaneous adipose tissue [9]. Therefore, abdominal liposuction provides a unique opportunity to evaluate the importance of subcutaneous abdominal fat in the pathogenesis of insulin resistance in persons with abdominal obesity. However, the metabolic effects of liposuction are unclear because the results of studies have varied [5,6,7,10,11].

The interpretation of data from such studies is confounded by lifestyle and weight changes that occurred among the subjects after liposuction was performed, by variations in the volume of adipose tissue removed and the site of its removal, by differences in the methods used to assess insulin sensitivity and by differences in the subjects' baseline weight and insulin sensitivity. Therefore, the purpose of the present study was to determine the effect of large-volume abdominal liposuction on serum adiponectin and insulin sensitivity. Obese women with normal glucose tolerance and those with type 2 diabetes were studied to assess the potential beneficial effects of liposuction in persons with moderate or severe insulin resistance.

MATERIAL AND METHODS

Subjects:

We studied eleven obese women (BMI, 37.1 ± 3.4) who had normal oral glucose tolerance but moderate insulin resistance [mean (\pm SD) age, 44 ± 3 years] and nine obese women (BMI, 39.9 ± 5.6) who had type 2 diabetes and more severe insulin resistance (age, 51 ± 3 years). All obese subjects included had abdominal obesity (waist circumference, more than 100cm). Twenty healthy age-matched (age, 47 ± 3 years) lean (BMI, 22.3 ± 2.1) women were taken as a control group. The women with type 2 diabetes were being treated with a combination of two or three oral hypoglycemic medications without any extrinsic insulin supplementation. All chronic medical illnesses that would hinder surgical intervention as well as any endocrinal disorders other than type 2 diabetes were considered as exclusion criteria. They were consecutive eligible patients who were scheduled to undergo large-volume liposuction and were enrolled between November 2006 and March 2008. Before surgery, subjects had completed a comprehensive medical evaluation, which included a history and physical examination, electrocardiography, standard blood and urine tests. All the subjects had had a stable weight (with fluctuations of not more than 2 percent of the body weight) for at least two months and had been sedentary (exercising for less than one hour per week) for at least six months before entering the study. Each subject provided written informed consent before participating.

Sampling:

All participants were subjected to the assessment of fasting glucose, insulin and adiponectin levels. Blood samples were taken once from lean controls and twice from liposuction candidates; 48-hours pre-operatively and 10 to 12 weeks post-operatively. The 10-to-12-week delay was intended

to eliminate the confounding effects of postsurgical inflammation on our study end points. Serum was separated by centrifugation within 30 minutes after collection and stored at -70°C until final analyses were performed. Plasma glucose concentrations were determined enzymatically (Roche/Hitachi 911 Analyzer, Roche Diagnostics). Enzyme-linked immunosorbent assay kits were used to measure insulin and adiponectin levels. In obese women, insulin sensitivity, was measured by the Homeostasis Model Assessment (HOMA = fasting plasma glucose \times fasting serum insulin divided by 25).

Liposuction:

Each obese subject underwent large-volume tumescent liposuction, defined as the removal of more than 4 liters of aspirate [12], which primarily addressed superficial and deep subcutaneous abdominal fat. In addition, smaller amounts of fat were removed from the arms, flanks, hips, or thighs in six subjects without diabetes and in five subjects with diabetes. The mean volume of aspirated fat was 5.2 ± 1.3 liters in subjects with normal oral glucose tolerance and 6.1 ± 1.8 liters in those with type 2 diabetes. Subjects were instructed to resume their normal lifestyle after the initial recovery period and to weigh themselves weekly at home, maintaining their usual food intake and physical activity in order to maintain a stable body weight. No serious complications occurred in any subject and all were able to return to their usual lifestyle within 10 days after liposuction. For each of the nine subjects with type 2 diabetes, hypoglycemic medications were regulated by the subject's physician. Re-evaluation of BMI and waist circumference was undertaken 10-12 weeks post-operatively.

Statistical analysis:

Base line data of control subjects and those of obese non-diabetic and obese diabetic subjects were analyzed with SPSS11 software using paired *t*-test and repeated measure ANOVA. In obese subjects, a two-way analysis of variance with repeated measures was used to compare the effects of liposuction on body composition, basal adiponectin level and insulin resistance. All reported *p* values were two-sided and a *p* value of 0.05 or less was considered to indicate statistical significance. Pearson's correlation co-efficient was done between the amount of fat aspirate and changes in all studied parameters and also between changes in HOMA and adiponectin levels.

RESULTS

Concerning baseline data, there was statistically significant difference in BMI, waist circumference,

HOMA and serum adiponectin levels between the control group and both obese groups. There was also a statistically significant difference in HOMA and serum adiponectin levels between obese non-diabetics and obese diabetics. However, there was no statistically significant difference in BMI and waist circumference between obese non-diabetics compared to obese diabetics (Table 1).

Regarding the impact of large volume liposuction on body mass composition in both obese groups (non-diabetic and diabetic), there was significant reduction in BMI and waist circumference (10 to 12 weeks after surgery) in comparison to baseline values of each group (48 hours before surgery) (Tables 2,3; Fig. 1). Data analysis revealed that liposuction has resulted in significant decrease

in insulin resistance; as indicated by HOMA with concomitant elevation of serum adiponectin levels in obese diabetics. However, there were no significant changes in HOMA values or serum adiponectin levels in obese non-diabetics after liposuction (Figs. 2,3).

Our correlation studies proved a significant correlation between the amount of fat aspirate and changes in body weight ($r=-0.32, p<0.01$), waist circumference ($r=-0.22, p<0.05$), HOMA ($r=-0.28, p<0.05$) and serum adiponectin levels ($r=0.34, p<0.01$) in both obese groups; non-diabetic and diabetic. Moreover, we demonstrated that serum adiponectin levels were inversely correlated with insulin resistance as measured by HOMA ($r=-0.31, p<0.01$).

Table (1): Baseline parameters of different studied groups.

Parameter	Control	Obese Non-Diabetic	Obese Diabetic	ANOVA
BMI (kg/m ²)	22.3±2.1 b,c	37.1±2.4 ^a	39.9±5.6 ^a	<0.01
Weight (kg)	62.4±4.7 b,c	100.2±9.5 ^a	106.5±14.7 ^a	<0.01
Waist Circumference (cm)	91±5 b,c	108±13 ^a	119±10 ^a	<0.01
Plasma Glucose (mg/dL)	83±4 ^c	90±6 ^c	121±39 ^{a,b}	<0.01
Plasma Insulin (µIU/mL)	8.2±5.4 b,c	11.0±8.1 ^{a,c}	15.1±7.6 ^{a,b}	<0.05
HOMA	26.6±7.2 b,c	39.6±9.2 ^{a,c}	76.7±14.3 ^{a,b}	<0.01
Adiponectin (ng/mL)	8.1±3.4 b,c	5.0±2.2 ^{a,c}	4.3±2.3 ^{a,b}	<0.01

BMI: Body Mass Index (the weight in kilograms divided by the square of the height in meters).

HOMA: Homeostasis Model Assessment.

a: Denotes significant difference between the mean of the group and the corresponding mean of the control group; $p<0.05$.

b: Denotes significant difference between the mean of the group and the corresponding mean of the obese non-diabetic group; $p<0.05$.

c: Denotes significant difference between the mean of the group and the corresponding mean of the obese diabetic group; $p<0.05$.

Reference Ranges:

Fasting Plasma Glucose: 70-110 mg/dL.

Fasting Plasma Insulin: 2-25 µU/mL.

Table (2): Effects of liposuction on parameters of obese non-diabetic subjects.

Parameter	Before Liposuction	After Liposuction	<i>p</i> Value
BMI (kg/m ²)	37.1±2.4	32.7±2.7	<0.01
Weight (kg)	100.2±9.5	93.7±10.6	<0.05
Waist Circumference (cm)	108±13	94±9	<0.01
Plasma Glucose (mg/dL)	90±6	89±4	0.33
Plasma Insulin (µIU/mL)	11.0±8.1	9.4±5.9	0.41
HOMA	39.6±9.2	33.5±8.3	0.13
Adiponectin (ng/mL)	5.8±2.2	6.1±2.2	0.23

Table (3): Effects of liposuction on parameters of obese diabetic subjects.

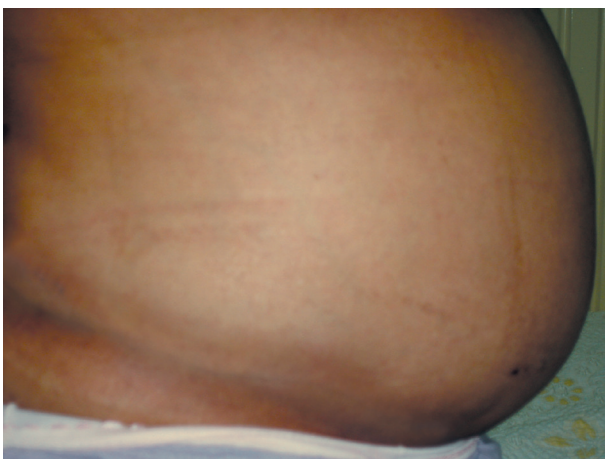
Parameter	Before Liposuction	After Liposuction	<i>p</i> Value
BMI (kg/m ²)	39.9±5.6	35.6±5.1	<0.01
Weight (kg)	106.5±14.7	98.6±13.0	<0.01
Waist Circumference (cm)	119±10	107±9	<0.05
Plasma Glucose (mg/dL)	127±41	121±39	0.84
Plasma Insulin (µIU/mL)	15.1±7.6	12.9±7.9	0.44
HOMA	76.7±14.3	62.4±11.7	<0.05
Adiponectin (ng/mL)	4.1±2.3	5.3±2.2	<0.05



(A)



(B)



(C)

Fig. (1): A: Marked abdominal obesity. B: Aspirate of tumescent large-volume liposuction. C: 12-weeks postoperative outcome.

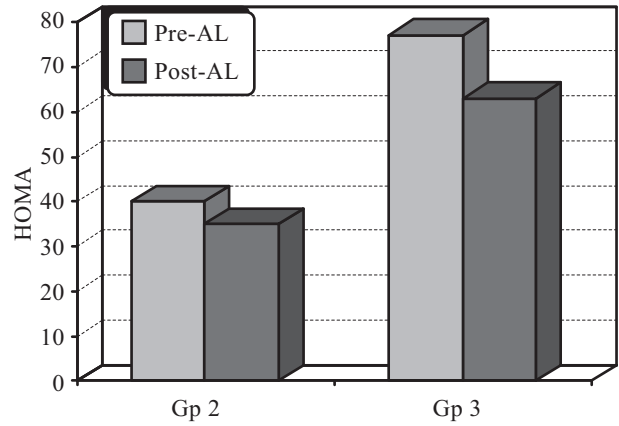


Fig. (2): HOMA values pre- and post-abdominal liposuction (AL) in both obese groups.
Gp 2: Obese non-diabetic, $p=0.13$ (non-significant increase)
Gp 3: Obese diabetic, $p<0.05$ (significant increase).

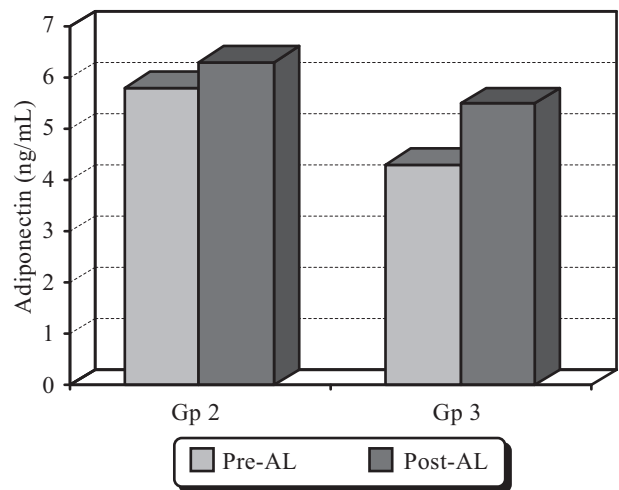


Fig. (3): Adiponectin levels pre- and post-abdominal liposuction (AL) in both obese groups.
Gp 2: Obese non-diabetic, $p=0.23$ (non-significant increase).
Gp 3: Obese diabetic, $p<0.05$ (significant increase).

DISCUSSION

Abdominal fat (both visceral and subcutaneous) accumulation is associated with an increased risk of developing insulin resistance. The latter stands as the basis upon which diabetes, hypertension and atherogenic dyslipidemia tend to build up. Hence, abdominal liposuction (AL) could theoretically hold metabolic benefits [4,5,6,7]. Adiponectin, the adipose tissue cytokine, has been shown in many previous reports to mediate insulin resistance in obese subjects [13]. Therefore, we undertook the present study to assess the effects of large-volume

abdominal liposuction on serum adiponectin levels and insulin sensitivity in obese women who had either moderate insulin resistance and normal glucose tolerance or more severe insulin resistance and type 2 diabetes. Weight stability was carefully maintained before and after liposuction to eliminate the confounding effects of changes in energy balance on the study end points.

Our baseline data showed that, compared to lean subjects, both obese groups (diabetics and non-diabetics) had significant insulin resistance as evidenced by higher HOMA value together with significant low serum adiponectin. In addition, there was significantly higher insulin resistance and lower adiponectin levels in the obese diabetic group in comparison to the obese non-diabetic group. Also, adiponectin levels were inversely correlated with insulin resistance in both obese subjects. These findings strongly confirm what has been stated in previous studies as concerns the involvement of adiponectin in insulin resistance and thereby the development of type 2 diabetes in obese individuals [14,15,16]. A proposed hypothesis stated that reduced adiponectin levels were caused by interactions of genetic factors such as single nucleotide polymorphisms (SNPs) in the adiponectin gene itself and environmental factors causing obesity such as a high fat (HF) diet [14]. Reduced adiponectin actions could also result from down-regulation of adiponectin receptors linked to obesity. These reductions of adiponectin actions may play a crucial causal role in the development of insulin resistance, type 2 diabetes, metabolic syndrome and atherosclerosis [16].

After liposuction, data analysis revealed that the aspiration of large amounts of subcutaneous abdominal adipose tissue resulted in a considerable decrease in body weight and thus BMI as well as waist circumference in both obese groups (non-diabetic and diabetic). In obese non-diabetics, although post-operative results showed decrease in insulin resistance and elevation of serum adiponectin levels, yet the changes were statistically insignificant as compared to baseline data. In contrast, post-operative data of obese diabetics demonstrated statistically significant changes in both insulin resistance and adiponectin levels. Moreover, the amount of fat removed by liposuction in our subjects was proportional to the changes achieved in body weight, waist circumference, insulin resistance and serum adiponectin levels. Our findings come in accordance with previous reports demonstrating that after 12 weeks of stable body weight post-liposuction, obese women turned

to be less insulin resistant and had increased serum levels of adiponectin. These studies also emphasized a significant correlation between the amount of fat aspirate and changes in HOMA and adiponectin levels [17].

In the present study, the amount of fat removed by liposuction was equivalent to the weight loss achieved by optimal behavioral and pharmacologic treatments [3]. A total weight loss of approximately 12 percent of body weight would be required to achieve the fat loss resulting from liposuction, because about 75 percent of the decrease in body-mass that occurs by dieting is due to loss of body fat [18]. This amount of weight loss usually results in marked improvement in the metabolic abnormalities associated with obesity and improves insulin sensitivity [19], blood pressure [20] and concentrations of serum lipids [21] and circulating markers of inflammation [22]. Therefore, it is not striking that the amount of fat loss achieved by liposuction in our diabetic and non-diabetic subjects did improve these metabolic variables. The increase in plasma adiponectin despite the reduction of the only tissue of its own synthesis suggests that the expression of adiponectin is under feedback inhibition in obesity [23]. This has been further explained by Engl and colleagues who stated that profound weight loss was associated with an increase in total adiponectin, which was mainly and consistently caused by increases in moderate molecular weight (MMW) adiponectin. These changes result in a shift from low molecular weight (LMW) to MMW and high molecular weight (HMW) adiponectin isoforms, which may be related to improvements in both anthropometric and metabolic parameters [15]. Moreover, Faraj and co-workers suggested that preoperative adiponectin concentrations may be predictive of the extent of weight loss and changes in adiponectin are predictive of improved insulin action in patients experiencing active weight loss [16].

In contrast to the previous views; the results of Klein et al., in 2004 showed that removing a large amount of abdominal subcutaneous fat by liposuction did not significantly affect the levels of serum adiponectin as well as other circulating mediators of inflammation that are probably involved in the development of insulin resistance [24]. Their results suggest that induction of a negative energy balance, not simply a decrease in the mass of adipose tissue, is critical for achieving the metabolic benefits of weight loss [25]. They added that even small amounts of weight loss induced by a negative energy balance affect many variables pertaining

to body-fat composition and lipid metabolism that probably contribute to the metabolic abnormalities associated with obesity [26-29]. These findings implicate that negative energy balance influences adipocyte and monocyte activation and thereby gene expression that encodes for adiponectin and other related adipocytokines [24]. Moreover, several studies emphasized the fact that weight loss decreases visceral fat mass [30], intramyocellular fat [31], intrahepatic fat [32], fat-cell size [33] and the rate of release of fatty acids from adipose tissue [34]. In contrast, liposuction removes subcutaneous abdominal fat and reduces the total number of body fat cells, without altering visceral fat mass [35], the size of the remaining fat cells, intramyocellular fat, or intrahepatic fat [10].

However, our results and those of many other reporters [4,5,6,7,17,36,37], strongly implicate that weight reduction through large volume abdominal liposuction has undoubted influences on insulin resistance and other metabolic sequelae of obesity. This signifies that surgical removal of subcutaneous adipose tissue, though it does not entail alteration of energy balance or visceral fat integrity, yet by virtue of significant reduction of fat cell mass, it can achieve comparable metabolic impacts to that of other conventional weight-reducing therapeutic modalities. Adipose tissue is now recognized as an important endocrine organ that produces several bioactive proteins, including leptin, adiponectin, interleukin-6 and tumor necrosis factor- α . These cytokines are collectively responsible for insulin resistance by impairing insulin signaling, stimulating lipolysis and fatty acid release, increasing hepatic synthesis of C-reactive protein, and increasing systemic inflammation [38,39,40], whereas the production of adiponectin by adipose tissue can improve insulin sensitivity and inhibit vascular inflammation [41,42]. Fat loss achieved by conventional obesity treatments decreases the plasma concentrations of C-reactive protein, interleukin-6 and tumor necrosis factor- α [43,44] and increases the concentration of adiponectin [23]. Similarly, liposuction in our study did significantly change the plasma concentrations of adiponectin and thereby insulin resistance and glucose intolerance.

In conclusion, the results of the present study demonstrate that large-volume abdominal liposuction should, by itself, be considered a clinical therapy for obesity and its metabolic sequelae. Aspiration of large amounts of subcutaneous abdominal fat in women with abdominal obesity, besides having cosmetic benefits, does significantly improve insulin sensitivity through altering serum

levels of adiponectin and probably other obesity markers. Therefore, the procedure is safe and could successfully help obese subjects to reduce their potential metabolic risks.

Summary:

Obesity is a disabling disease which has gained greater attention worldwide. It significantly increases the risk for other diseases such as insulin independent diabetes mellitus also known as diabetes type 2. The most common surgical procedure for obesity is liposuction. It is traditionally performed either as small-volume liposuction or large-volume liposuction, the majority being small-volume liposuction procedures. Large-volume liposuction has been clinically shown to improve insulin sensitivity in obese patients thus reducing their risk of developing type 2 diabetes, or beneficially improving their already manifest glucose intolerance. In this paper, evidence is presented to support the hypothesis that liposuction, through altering serum level of adiponectin, could eventually disrupt the pathway that brings about insulin insensitivity in obese women. Therefore, it is proposed that using liposuction in the overall treatment of obesity could lead to an improvement in insulin sensitivity and thus greatly ameliorate the quality of life of the obese patient.

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