



Effect of Reduction Mammoplasty on Insulin and Lipid Metabolism in the Postoperative Third month: Compensatory Hip Enlargement

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Abstract

Backgrounds The positive effects of reduction mammoplasty on metabolic profile have been shown in a limited number of studies. This study objective to reveal the effects of reduction mammoplasty on metabolic profile and anthropometric measurements.

Subjects and Method The study was prospectively conducted on 42 patients who were operated between April 2019 and March 2020. Fasting plasma glucose, fasting plasma insulin, total cholesterol, triglyceride, high-density lipoprotein and low-density lipoprotein cholesterol, HgA1c, homeostasis model assessment scores, adiponectin, leptin, and resistin levels were evaluated. In addition, age, height, weight, body mass index; breast, chest, waist, hip circumference; waist-hip ratio, and bilateral breast resection tissue weights were recorded. Data and blood samples were collected one hour before the operation, 6 and 12 weeks after the operation.

Result The patients' mean age was 43.14 ± 10.24 , and their average height was 159.42 ± 4.96 cm. The excised bilateral dermo fatty tissue weight was 1435.85 ± 721.16 g. At the postoperative 40th day a decrease in leptin ($p = 0.001$), resistin ($p = 0.008$), glucose ($p = 0.021$) and insulin resistance values ($p = 0.013$) stated. There was an increase in

adiponectin ($p < 0.001$) and HDL ($p = 0.013$) levels at the postoperative 40th day. In the postoperative third month, these data returned to the previous levels that were measured before operations. However, an increase in hip circumference ($p = 0.034$) and a decrease in waist-hip ratio ($p < 0.001$) was detected in third month. Also, there was no difference in body mass index and weight compared to pre-operation.

Conclusion After reduction mammoplasty, compensatory fat growth in the hip area, an increase in the hip circumference, and a decrease in the waist-hip ratio were observed in the postoperative third month.

Level of Evidence This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Reduction mammoplasty · Hip circumference · Waist-hip ratio

Introduction

Breast hypertrophy is an important clinical problem that causes neck and back pain, intertrigo underneath the breast folds, and restricts physical activities [1]. It can also be seen as a source of embarrassment by patients. This situation may lead to taking kyphotic posture to hide the breasts and psychological distress [2]. For these reasons, breast reduction surgery is among the procedures frequently performed by plastic surgeons. In 2018, breast reduction surgery was performed on approximately 84.600 patients in the USA [3].

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Breast reduction provides a decrease in pains and an increase in physical activities [4]. Also, it provides a postural improvement resulting from a significant improvement in spinal angles such as cervical lordosis, thoracic kyphosis, and lumbar lordosis [5]. With the removal of excess breast tissue, chest wall compliance and ventilation increase, and respiratory function tests improve [6]. Besides all this physical improvement, breast reduction also improves body image and sexual functions [7, 8].

In addition to its lipid storage function, adipose tissue secretes many adipokines such as adiponectin, leptin, resistin, and proinflammatory cytokines. With these features, adipose tissue exhibits autocrine, paracrine, and endocrine effects. In this way, it plays a vital role in energy metabolism, insulin sensitivity, and inflammatory response [9]. Adiponectin increases glucose uptake and fatty acid oxidation; besides increased steatosis decreases adiponectin expression [10]. Leptin has a major role in the regulation of body weight, and its plasma level depends on the amount of subcutaneous adipose tissue [11]. On the other hand, resistin plays a major role in insulin resistance, inflammation, and more specifically vascular damage [12].

It is known that non-visceral upper body adipose tissue contributes to the metabolic complications of obesity [13]. Approximately 60% of breast tissue consists of adipose tissue. The presence of macromastia in adolescence is a predisposing factor for the development of type 2 diabetes mellitus in middle-aged individuals [14]. These data suggest that breast tissue may affect lipid and insulin metabolism. However, its effects on metabolic profile have been referred to in a limited number of studies [15–17]. This study aimed to reveal the effects of reduction mammoplasty on metabolic profile and anthropometric measurements.

Subjects and Method

This prospective self-controlled clinical trial was conducted on patients diagnosed of bilateral macromastia with clinical examination (back pain, neck pain, intertrigo around the breasts, bra strap marks). The study started after the approval of the local ethics committee and was conducted in accordance with the Helsinki Declaration (05.03.2019/2292). Informed consent was obtained from all patients. Non-smoker, non-pregnant patients who did not have any disease (such as diabetes, cardiovascular disease, thyroid dysfunction) and who did not have any prescription drug use and had a fixed weight in the last six months were included in the study. Patients who received medical or surgical treatment due to a new clinical diagnosis were excluded from the study. Patients under 40 years of age were evaluated with breast ultrasound, patients

over 40 years of age were evaluated with mammography (mammogram) in the preoperative period. All imaging studies were reviewed by experienced radiologists, and patients with no risk of breast cancer were operated. In addition, patients with wound infection, pedicle or skin necrosis, and wound healing problems in the postoperative period were excluded from the study. Also, it was strictly advised not to change the preoperative diet regimen and to postpone the exercise programs until the data collection process was completed. Between April 2019 and March 2020, 52 patients underwent reduction mammoplasty. The study was conducted on 42 patients who met the inclusion criteria and did not change their preoperative diet and exercise regimen. 6 of 10 patients who were excluded from the study did not come to postoperative controls (due to the Covid-19 pandemic). Three patients were excluded from the study because of postoperative wound detachment, and one patient because of hematoma. The data were obtained from the results of blood taken, and anthropometric measurements were done one hour before the operation, 40 ± 2 days and 90 ± 2 days postoperatively.

Laboratory Analysis

Blood collection procedures were carried out through venous vessels. Blood was drawn in the morning after 12 hours of fasting. Blood was drawn into a 2 mL empty biochemistry tube to measure fasting plasma glucose, fasting plasma insulin, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol (LDL) levels. Venous blood was collected in 1 mL tube with anticoagulant for HgA1c measurement (preoperatively and at the third month postoperatively). Blood samples were studied in the biochemistry laboratory on the day of collection. Insulin sensitivity was calculated using the homeostasis model assessment index (HOMA-IR, plasma glucose level \times (plasma insulin level)/22.5), and a value greater than 2.5 was accepted as insulin resistance [18].

In order to measure adiponectin, leptin, and resistin values, 2 mL of venous blood was drawn into an empty biochemistry tube. Tubes were centrifuged at 3000 rpm for 10 minutes. Serum parts separated to the Eppendorf tubes and stored at -20°C . Hemolyzed samples were excluded from the study. After the sample collection was completed, the serums were brought to room temperature to be studied. Adiponectin, leptin, and resistin were measured by enzyme-linked immunosorbent assay after 60 minutes of incubation at 37°C (Human adiponectin, leptin, resistin ELISA kit, Bioassay Technology Laboratory, Shanghai, China). The assay was performed according to the manufacturer's instructions manual. The intra-assay and inter-assay coefficients of variation for adiponectin, leptin and

resistin were 4.8–5.1% and 6.5–7.2%, 5.1–6.8% and 5.4–6.9%, 5.2–7.4% and 6.1–7.4% consecutively.

Demographic Data and Anthropometric Measurements

Anthropometric measurements were made with an inelastic tape measure after 12 hours of the fasting period, at the end of expiration, and in a standing position. Data were age, height, weight, body mass index (BMI: weight/the square of height), breast circumference (measured at the level of the nipple), chest circumference (measured at the level of the inframammary fold), waist circumference (measured at the level of the transverse umbilical line), hip circumference (measured at the level of the intertrochanteric line), waist-hip ratio (WHR) and bilaterally resected breast tissue weight.

Surgical and Postoperative Procedures

All patients were operated on under general anesthesia. The preferred technique was superomedial pedicle inverted-T pattern reduction mammoplasty. Excised tissues were sent for histopathological examination. Surgical vacuum drains were removed when drainage fluid was below 25 mL per 24 hours. Patients were discharged with 500 mg first-generation cephalosporin twice a day for five days. Trunk elevation was recommended for two weeks after the surgery, and a compression bra was applied for the 1st month.

Statistical Analysis

SPSS software for Windows (version 26.0; IBM Corporation, Armonk, New York, USA) was used for statistical analysis. Data were defined as the frequency and percentage for categorical variables, the mean and standard deviation for numerical variables. Kolmogorov-Smirnov test was used for normality analysis. When the number of dependent groups was more than two, the repeated-measures ANOVA test and the Friedman test were used for analysis. Paired t test and Wilcoxon rank-sum test were used to compare the two dependent groups. The relationship between the excised dermo fatty tissue and data differences was evaluated using Pearson's correlation test and Spearman's rho test. The statistical significance level was accepted as $p < 0.05$.

Results

The average age of the patients was 43.14 ± 10.24 years, and the average height of the patients was 159.42 ± 4.96 cm. The bilaterally excised dermo fatty tissue weight was 1435.85 ± 721.16 g.

The data obtained from blood results and anthropometric measurements are presented in Table 1. Total cholesterol, triglyceride, LDL, HgA1c levels, chest and waist circumferences were not affected by reduction mammoplasty operation considering 40th day and third-month results postoperatively.

Although reduction mammoplasty operation ensured improvement in metabolic profile on the 40th day postoperatively, this effect was not continued in the third month. Mean serum levels of adiponectin increased on the 40th day compared to the preoperative period (3.26 ± 5.49 , $p < 0.001$), though it was similar to the preoperative period at the third month (0.07 ± 6.07 , $p = 0.731$). Mean leptin levels were decreased on the 40th day (-1.88 ± 3.57 , $p = 0.001$), but again it was similar to the preoperative period at the third month (-0.47 ± 3.85 , $p = 0.730$). Resistin levels decreased like leptin on the 40th day (-0.61 ± 2.46 , $p = 0.008$) and returned to their previous levels at the third month (0.34 ± 3.01 , $p = 0.788$). At the 40th day postoperatively, an increase in HDL levels (3.92 ± 9.85 , $p = 0.013$) a decrease in glucose (-0.10 ± 0.81 , $p = 0.021$), plasma insulin (-2.08 ± 5.92 , $p = 0.024$) and insulin resistance (HOMA-IR; -0.58 ± 1.47 , $p = 0.013$) values were stated compared to the preoperative period. These values returned to their preoperative levels at the third month postoperatively (Table 2).

The net effect of reduction mammoplasty was clearer on anthropometric measurements. Bodyweight (-1.52 ± 1.83 , $p < 0.001$) and BMI (-0.60 ± 0.72 , $p < 0.001$) decreased on the 40th day after surgery, nevertheless both of them returned to their previous rates in the third-month measurements. Breast circumference decreased as expected on 40th day (-3.76 ± 5.09 , $p < 0.001$) and at third-month measurements (-4.35 ± 4.48 , $p < 0.001$). Hip circumference gradually increased at 40th day and third-month measurements (2.90 ± 4.69 , $p < 0.001$). Waist-hip ratio decreased on the 40th day (-0.02 ± 0.07 , $p = 0.034$) and at the third month measurements (-0.04 ± 0.08 , $p < 0.001$). (Table 3).

There is a positive correlation between excised dermo fatty tissue weight and breast circumference at the third month postoperatively ($r = 0.515$, $p < 0.001$). Furthermore, excised dermo fatty tissue weight has positive correlation with waist-hip ratio ($r = 0.321$, $p = 0.038$) and negative correlation with hip circumference ($r = -0.345$, $p = 0.027$) (Table 4).

Discussion

In this study, serum adiponectin, leptin, resistin levels, and plasma lipid profile were studied to evaluate the effect of reduction mammoplasty on lipid metabolism. In order to

Table 1 Metabolic parameters and demographic data in preoperative, postoperative 40th day, and postoperative third month.

	Preoperative Mean±SD	Postoperative 40. Day Mean±SD	Postoperative 3. Month Mean±SD	P
Adiponectin, µg/mL	16.47±9.87	19.74±10.95	16.55±10.16	0.004^a
Leptin, ng/mL	13.20±6.52	11.31±5.24	12.72±6.69	0.009^a
Resistin, ng/mL	1.25±0.73	1.19±0.81	1.29±0.81	0.023^a
Total cholesterol, mg/dL	218.92±39.07	218.00±39.39	218.90±39.53	0.662 ^b
Triglycerides, mg/dL	105.09±51.97	102.21±26.16	106.90±34.54	0.765 ^a
LDL, mg/dL	143.28±30.56	142.09±33.18	142.09±35.74	0.940 ^b
HDL, mg/dL	53.71±10.47	57.64±11.80	54.97±8.68	0.009^b
Glucose, mmol/L	5.32±0.67	5.28±0.66	5.23±0.71	0.645^b
Insulin, µU/mL	11.08±4.77	9.00±3.58	10.92±4.40	0.041^a
HOMA-IR* score	2.66±1.32	2.07±0.85	2.55±1.13	0.049^a
HgA1c (%)	5.45±0.48	-	5.47±0.65	0.609 ^c
Weight, kg	75.85±10.98	74.33±10.46	75.11±11.86	<0.001^a
BMI, kg/m ²	29.86±4.28	29.26±4.05	29.58±4.64	<0.001^b
Breast circumference, cm	107.30±8.32	103.54±8.50	102.92±7.83	<0.001^b
Chest circumference, cm	95.38±7.95	95.45±8.30	94.83±9.91	0.594 ^b
Waist circumference, cm	104.09±9.58	102.47±10.89	102.33±8.47	0.170 ^b
Hip circumference, cm	107.52±8.79	108.76±9.68	110.42±8.04	0.001^b
Waist-hip ratio	0.96±0.05	0.94±0.08	0.92±0.06	0.016^b

The bold symbols indicate statistical significance $p < 0.05$

^aThe repeated-measures ANOVA test.

^bFriedman test.

^cWilcoxon rank-sum test.

*Homeostasis model assessment scores.

Table 2 Differences and statistical relationship of postoperative and preoperative blood values.

	Postoperative 40. day-Preoperative		Postoperative 3. month-Preoperative	
	Difference Mean±SD	p	Difference Mean ± SD	p
Adiponectin, µg/mL	3.26±5.49	<0.001 ^a	0.07±6.07	0.731 ^a
Leptin, ng/mL	- 1.88±3.57	0.001 ^a	- 0.47±3.85	0.730 ^a
Resistin, ng/mL	- 0.61±2.46	0.008 ^a	0.34±3.01	0.788 ^a
HDL, mg/dL	3.92±9.85	0.013 ^b	1.2±6.98	0.249 ^b
Glucose, mmol/L	- 0.10±0.81	0.021 ^b	- 0.86±0.78	0.053 ^b
Insulin, µU/mL	- 2.08±5.92	0.024 ^a	- 0.15±6.28	0.896 ^a
HOMA-IR score*	- 0.58±1.47	0.013 ^a	- 0.10±1.65	0.676 ^a

^aPaired t test.

^bWilcoxon rank-sum test.

*Homeostasis model assessment scores.

evaluate their effects on insulin metabolism, plasma glucose and insulin levels were measured, and insulin resistance was calculated. Also, anthropometric measurements were taken to evaluate body fat distribution. The preoperative data were compared with the postoperative 40th and 90th days data.

Uzun et al. performed reduction mammoplasty on 42 obese patients (BMI, 33.94 ± 2.39). They resected an average of 1954.43 ± 505.81 g of dermo fatty tissue. They

demonstrated a decrease in BMI, leptin level, and insulin resistance in the postoperative second month [16]. Vanci et al. performed reduction mammoplasty on 27 patients who were borderline obese (BMI, 30.5±6.86) and resected an average of 1732.2±796.65 g of dermo fatty tissue from these patients. They determined an increase in adiponectin and HDL levels and a decrease in glucose levels on the postoperative 40th day. In the same study, they did not state any change in BMI and WHR [17]. In this study,

Table 3 Differences and statistical relationship of postoperative and preoperative anthropometric values.

	Postoperative 40. day-Preoperative		Postoperative 3. month-Preoperative	
	Difference Mean \pm SD	<i>p</i>	Difference Mean \pm SD	<i>p</i>
Weight, kg	- 1.52 \pm 1.83	<0.001^a	- 0.73 \pm 4.81	0.130 ^a
BMI, kg/m ²	- 0.60 \pm 0.72	<0.001^b	- 0.28 \pm 1.90	0.141 ^b
Breast circumference, cm	- 3.76 \pm 5.09	<0.001^b	- 4.35 \pm 4.68	<0.001^b
Hip circumference, cm	1.23 \pm 4.77	0.101 ^b	2.90 \pm 4.69	<0.001^b
Waist-hip ratio, cm	- 0.02 \pm 0.07	0.034^b	- 0.04 \pm 0.08	<0.004^b

The bold symbols indicate statistical significance $p < 0.05$

^aPaired t test.

^bWilcoxon rank-sum test.

Table 4 Association between fat removed and data that preoperative and postoperative difference.

	Postoperative 40. day - Preoperative Difference		Postoperative 3. month - Preoperative Difference	
	<i>r</i>	<i>p</i>	<i>r</i>	<i>p</i>
Adiponectin	0.140	0.376 ^b	0.227	0.148 ^b
Leptin	0.028	0.860 ^a	0.167	0.292 ^a
Resistin	- 0.023	0.886 ^a	0.140	0.378 ^a
Triglycerides	0.070	0.657 ^b	0.023	0.887 ^a
HDL	0.251	0.109 ^b	0.237	0.080 ^b
Glucose	0.477	0.001^b	0.52	0.744 ^b
Insulin	- 0.087	0.583 ^b	-0.006	0.969 ^b
HOMA-IR* score	0.085	0.592 ^b	-0.078	0.622 ^a
Weight	0.175	0.267 ^a	-0.287	0.066 ^a
BMI	0.154	0.330 ^b	-0.191	0.225 ^b
Breast circumference	0.405	0.008^b	0.515	<0.001^b
Waist circumference	0.047	0.766 ^b	0.056	0.856 ^b
Hip circumference	- 0.110	0.490 ^b	-0.345	0.027^a
Waist-hip ratio	0.116	0.464 ^b	0.321	0.038^b

The bold symbols indicate statistical significance $p < 0.05$

^aSpearman's rho test.

^bPearson's correlation test.

*Homeostasis model assessment scores

removal of breast tissue by reduction mammoplasty provided metabolic improvement on the 40th day postoperatively. The decrease in leptin, resistin, glucose values, and insulin resistance, and increase in adiponectin and HDL levels was stated. Unlike these studies, metabolic improvements were not detected in our study in the third-month controls.

In the early period after reduction mammoplasty, weight loss and improvement in BMI were observed due to the removal of dermo fatty tissue. However, when evaluated for a long period of time, many studies have shown that reduction mammoplasty did not improve weight and BMI. Rinomota et al. reported that patients who underwent abdominoplasty ($n = 16$) and reduction mammoplasty ($n = 17$) gained weight at the 18th month after surgery.

They also stated that lipectomy had limited effects on weight loss [19]. Singh et al. observed patients who underwent breast reduction for two years. It was found out during the follow-up that the operation caused weight loss in the group of patients who thought that the operation was motivating for weight loss and weight increase in the group of patients who thought it would not be motivating [20]. Sarıcı et al. stated no significant difference in weight and BMI of the 62 patients who underwent reduction mammoplasty in the postoperative third month [14]. In our study, a decrease in BMI and weight loss was detected on the postoperative 40th day. However, it was determined that reduction mammoplasty did not reduce weight and BMI in the third month.

For many years, it was believed that in humans, the number of adipocytes was stable. Therefore, the human body was reacting to weight gain and loss by changing adipocyte cell size rather than cell number [21]. Recent studies have proven that the adipocyte turnover rate varies between 10 and 100% [22, 23]. In 2001, Mauer et al. applied lipectomy to different regions in ground squirrels and showed that adipocyte levels were restored in areas where lipectomy was not performed [24]. In humans, breast enlargement after abdominal liposuction due to compensatory adipose tissue growth has been pointed out in many studies [25–27].

Tchoukalova et al. have performed a study on 28 healthy adult volunteers. They stated that the increase in subcutaneous fatty tissue occurred in 2 months with overfeeding. Abdominal and upper body adipocytes reacted to overfeeding with hypertrophy, besides lower body adipocytes reacted with hyperplasia. Hyperplasia in lower body fatty tissue may contribute to the prevention of fatty tissue accumulation in the upper body. Also, hyperplasia of lower body adipocytes may prevent lipid accumulation in visceral organs [28]. In this study, there is a statistically significant negative correlation between excised dermo fat tissue amount and hip circumference in the postoperative third month. Measurements have shown that body fat distribution has changed, and lower body subcutaneous fatty tissue has increased. These findings have given rise to thought that reduction mammoplasty has caused compensatory hip enlargement in postoperative third month.

In this study, to maximize the effect of reduction mammoplasty on fat metabolism, it was suggested that patients should not change their diet regimen and physical activity after the operation. During the short 40-day time interval, the patients' physiology is recovering from surgery and not just responding to the reduction in breast fat/parenchyma. The patient's physiology responds to the assault of surgery itself: Anesthetic response, trauma response, pain, and wound healing. Therefore, the observed metabolic parameters and anthropometric values cannot be attributed to fat reduction alone. Although approximately 1500 g of dermo fat tissue was removed from the patients, there was no change in BMI and weight in the postoperative third month. The most important factor that explains this situation seems to be the compensation of the upper body fat mass, which is surgically removed, with the hip region fat mass. Also, we think that the decrease in breast circumference on the 90th day compared to the 40th day is due to the regression of edema secondary to the operation. Changes in body fat distribution after lipectomy are not a new finding. However, the most important finding that distinguishes this study from other studies is that it is shown that the distribution of fat after breast reduction is shaped in the direction of the lower body.

It is known that central obesity increases insulin resistance and its related complications. In the meta-analysis in which approximately 83 thousand patients were evaluated, greater WHR showing central obesity was associated with cardiovascular disease and associated mortality. In the same study, BMI, which is an indicator of global obesity, was not associated with cardiovascular disease [29]. Increased hip circumference, especially in women, has protective effects against obesity-related coronary artery disease and cardiovascular disease [30, 31]. In addition, large hip and thigh circumferences reduce the risk of type 2 diabetes regardless of age, BMI, and waist circumference [32]. The results of this study suggest that reduction mammoplasty increases hip circumference and decreases WHR. Consequently, reduction mammoplasty may reduce the risk of cardiovascular disease and type 2 diabetes.

This study has some limitations. Although compensatory hip enlargement after reduction mammoplasty has not been demonstrated previously, larger sample size and longer follow-up periods will strengthen the data. Patients included in the study were healthy adults. If the studies were conducted in morbid obese or diabetic patients, possible direct positive effects of reduction mammoplasty could have been revealed. Plus, body fat distribution was defined by anthropometric measurements. Although there is a strong correlation between anthropometric measurements and dual-energy X-ray absorptiometry and computed tomography, obtaining more quantitative data with the latter two methods will increase the level of evidence of the study [33]. Finally, it could have been an important input in this study to demonstrate the effect of reduction mammoplasty on feminine hormones (estrogen, progesterone, prolactin, follicular stimulating, and luteinizing hormone) and the reduction of risks associated with a possible decrease in their levels. However, these hormone levels change in the premenopausal and postmenopausal periods, and in premenopausal patients, the duration of blood collection varies according to ovulation and menstrual cycle. We thought that the inclusion of these hormones in the study would decrease the continuity of the study as it would increase the number of visits and blood draws, and statistical power would decrease with increasing the groups. We also did not have enough funds to study feminine hormones. Therefore, we have considered evaluating feminine hormones in a separate study.

Conclusion

Although there was no metabolic and biochemical improvement after reduction mammoplasty in the postoperative third month, body fat distribution has changed.

Compensatory fatty tissue growth in the hip area increased hip circumference and decreased the WHR.

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Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval “All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.” The study started after the approval of the local ethics committee (05.03.2019/2292).

Informed Consent Informed consent was obtained from all patients involved.

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