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## Histopathological findings obtained from reduction mammoplasty specimens

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**Background/aim:** Reduction mammoplasty is a common surgical procedure. We report the incidence of nonproliferative and proliferative breast lesions in breast reduction specimens from a single institution over a 6-year period.

**Materials and methods:** The histopathology reports of all patients were analyzed. The clinical and histopathological findings of the patients were recorded.

**Results:** Between 2004 and 2010, 106 patients underwent breast reduction. Fifty-six patients (52.8%) had proliferative breast lesions, 84 patients (79.2%) had nonproliferative lesions, 8 patients (7.5%) had columnar cell lesions without atypia, 61 patients (57.5%) had columnar cell lesions with atypia, 5 patients (4.7%) had atypical ductal hyperplasia, and 6 patients (5.6%) had lobular carcinoma in situ. No invasive breast cancer was identified.

**Conclusion:** In Turkey, there is limited evidence regarding the role of histopathological analysis in reduction mammoplasty. Moreover, none of the previous studies determined columnar cell lesion rates in reduction mammoplasty patients. The detection of significantly elevated columnar cell lesions, with or without atypia, especially in patients under the age of 40, increases the importance of screening tests, especially in Turkey, which has a high incidence of breast cancer in early ages, and addresses the need to starting screening tests early in these patients.

**Key words:** Reduction mammoplasty, breast reduction, histopathology

### 1. Introduction

Reduction mammoplasty is one of the most commonly performed procedures of plastic surgery. The main physical complaints, secondary to macromastia, include pain in the back, stomach, shoulders, arms, neck, and breasts, and headache, itching, rash, other forms of dermatitis under the breasts, and various paresthesias (1–5). Reduction mammoplasty surgery can also be performed for cosmetic reasons as well as symptomatic causes. In addition to achieving a reduction in the breast volume, breast reduction surgery also enables histopathological investigation of the resected breast tissue, thereby detecting any potential malignant and premalignant lesions, even if the patient does not have any complaints (1,3).

Even if only a few specimens are randomly selected and examined among the specimens sent for pathological investigation, a large spectrum of lesions from benign to proliferative lesions, and even malignant ones, can be detected. This trial was designed to retrospectively review the histopathological diagnoses of reduction

mammoplasty specimens and to determine the incidence of breast lesions in asymptomatic females.

### 2. Materials and methods

We reviewed 106 reduction mammoplasty specimens sent to the Hacettepe University Medical Faculty Pathology Department between 2004 and 2010. We observed that some cases had 2 or more diagnoses. The patients had no symptoms other than macromastia and its associated symptoms. They had applied for cosmetic and reconstructive correction of breast deformities, mostly due to breast hypertrophy.

The cases were classified according to age, mean weight of the specimen, number of tissue sections investigated, and pathological findings. The pathological findings were categorized based on the Cancer Committee of the College of American Pathologists consensus established in 1998 (Table 1) (5). The only exception was columnar lesions, which were diagnosed and classified according to Collins and Schnitt (6).

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**Table 1.** The relative risks of invasive breast carcinoma according to the 1998 Consensus of Cancer Committee of the College of American Pathologists (5).

Risk
No increased risk/nonproliferative lesions
Adenosis (other than sclerosing adenosis)
Ductal ectasia
Fibroadenoma without complex features
Fibrosis
Mastitis
Ordinary cysts
Simple apocrine metaplasia
Squamous metaplasia
Slightly increased risk/proliferative lesions (1.5–2.0 times)
Fibroadenoma with complex features
Moderate or florid hyperplasia
Sclerosing adenosis
Solitary papilloma without coexisting atypical hyperplasia
Moderately increased risk (4.0–5.0 times)
Atypical ductal hyperplasia
Atypical lobular hyperplasia
Markedly increased risk (8.0–10.0 times)
Ductal carcinoma in situ
Lobular carcinoma in situ

### 2.1. Statistical analysis

SPSS 20.0 for Windows was used to analyze the data. Percentage distribution and frequency of data were given. Data found to be abnormally distributed were analyzed using the Mann–Whitney U test. Differences were accepted as being significant at  $P < 0.05$ .

### 3. Results

Six of the reduction mammoplasty specimens sent between 2004 and 2010 were unilateral while 100 were bilateral. The ages ranged between 18 and 64 years, with a mean age of  $39.2 \pm 12.3$  (Table 2).

The weight of the breast specimens ranged between 60 and 2730 g. While the weight of the specimens was not reported for 4 patients of <40 years of age, it ranged between 60 g and 1900 g with a mean weight of 587.1 g. As for the patients of  $\geq 40$  years of age, the weight was not reported in 2 cases; the weights ranged between 90 g

**Table 2.** Age distribution of women who underwent reduction mammoplasty.

Age distribution	Number	%
<40 years of age	52	49.05
$\geq 40$ years of age	54	50.94

and 2685 g, with a mean weight of 782.2 g. A statistically significant difference was observed between age groups in terms of average weight ( $P < 0.05$ ). The average weight of the group above 40 years of age was significantly higher compared with the group under 40 years.

The number of paraffin blocks obtained from the specimens ranged between 4 and 23 in patients below 40 years of age, with a mean block number of 10.5. As for patients of  $\geq 40$  years of age, the number of blocks ranged between 1 and 46, with a mean block number of 11.0. No statistically significant difference was observed between age groups in regard to sum of blocks ( $P > 0.05$ ). Although not statistically significant, the sum of blocks was found to be higher in patients aged 40 years and older.

Pathological findings were detected in 94.3% of the specimens. Pathologic findings are summarized in Table 3.

The review revealed that 2 of the 6 patients with lobular carcinoma in situ had received reduction mammoplasty surgery due to breast asymmetry while 4 underwent surgery for cosmetic reasons. All patients with lobular carcinoma in situ were above 40 years of age. Seventy-nine patients had nonproliferative breast lesions (37 patients of <40 years, 42 of  $\geq 40$  years), 56 had lesions mildly increasing the risk of breast carcinoma (18 patients of <40 years, 38 of  $\geq 40$  years), 5 had lesions moderately increasing the risk of breast carcinoma (1 patient of <40 years, 4 of  $\geq 40$  years), and 6 had lesions markedly increasing the breast carcinoma (Table 3).

There were 6 cases of reduction mammoplasty (5.7%) without any pathological findings detected, of which 4 patients were under 40 years of age.

### 4. Discussion

Reduction mammoplasty is one of the most frequently performed operations on the female breast, both worldwide and in Turkey. Bilateral reduction mammoplasty is mostly performed due to symptomatic macromastia, while unilateral reduction mammoplasty is performed commonly for correcting the congenital asymmetry or asymmetry secondary to surgical operations (7).

Puossion and Verchere were the first authors to describe reduction mammoplasty. This procedure became increasingly popular in the past several decades in treating breast hyperplasia and hypertrophy, and the associated symptoms of neck, shoulder, and back pain; shoulder furrowing; intertrigo beneath the breast; and ulnar nerve paresthesias from traction on the ulnar nerve. In approximately 95% of the patients treated, reduction mammoplasty has been shown to relieve symptoms (8).

A similar age distribution was observed in our study population of patients undergoing reduction mammoplasty compared with previous published studies. The literature showed an average patient age of 35.8 years, which in our study was 39.5 years.

**Table 3.** The distribution of the histopathological diagnoses of the breast reduction specimens

Histopathological diagnosis	n	<40 years of age (%)	≥40 years of age (%)
LCIS	6	-	6 (11.1%)
ADH	5	1 (1.9%)	4 (7.4%)
Ductal epithelial hyperplasia	40	15 (28.8%)	25 (46.3%)
Atypical columnar cell lesions	61	22 (42.3%)	39 (72.2%)
Sclerosing adenosis	15	3 (5.8%)	12 (22.2%)
Complex apocrine metaplasia	28	8 (15.4)	20 (37.0%)
Blunt duct adenosis	52	24 (46.2%)	28 (51.9%)
Intraductal papilloma	1	-	1 (1.9%)
Fibrocystic disease	76	36 (69.2%)	40 (74.1%)
Columnar cell lesions without atypia	8	2 (3.8%)	6 (11.1%)
Fibroadenoma	8	4 (7.7%)	4 (7.4%)
Radial scar	1	-	1 (1.9%)

The weight of the breast specimens varied between 60 and 2730 g. In the patients of <40 years of age, the mean weight was 587.1 g, while in those of ≥40 years, it was 782.2 g. A statistically significant difference was observed between age groups in terms of average weight ( $P < 0.05$ ). The average specimen weight of the group above 40 years of age was significantly higher compared with the group under 40 years.

While reduction mammoplasty specimens are referred to pathology departments for investigation, there is currently no standard procedure for assessing these specimens, with the number of macroscopic samples varying between the centers. Both Bondeson et al. and Ambaye et al. reported that careful macroscopic sampling and minimal microscopic investigation involving 1 or 2 blocks is sufficient in patients under 30 years of age, while they recommended assessment via multiple samplings, even in the absence of macroscopic findings, for patients of ≥40 years of age (7,9).

In order to allow the pathologist to determine the histological characteristics and location of any lesions noted, the breast reduction specimens should be handled with care and labeled and oriented in a standard fashion. Cook et al. showed that microscopic examination of macroscopically normal breast tissue from breast reduction specimens may provide important pathological findings (4). Karabela-Bouropoulou et al. demonstrated that routine sampling of all solid parts of each breast specimen is warranted in all women over 40 years of age (10). In our center, we perform standard macroscopic evaluations, which we also use for evaluation of nonneoplastic adjacent

parenchyma of mastectomy and lumpectomy specimens. We first slice specimens at 0.5-cm intervals. Next, besides observation of the cut surface of each slice, we also palpate them. All solid and firm areas detected by observation or palpation are sampled. In our study group, while the median number of blocks was 10.5 for patients of <40 years of age, it was 11.1 for patients of ≥40 years. No statistically significant difference was observed between age groups in regard to the sum of blocks ( $P > 0.05$ ). Although not statistically significant, the sum of blocks was found to be higher in patients aged 40 years and older.

In our trial, we aimed to assess the distribution of breast lesions in women without breast masses. We observed that breast pathologies were common, even in asymptomatic patients. We detected no pathological findings in only 6 of the 106 cases (5.6%). All of the studies to date in which histopathologic examinations were evaluated in reduction mammoplasty cases revealed a wide spectrum of nonpathologic findings (Table 3). In a retrospective trial by Pitanguy et al. on 2488 cases, normal breast parenchyma was detected at a rate of 3.7% ( $n = 91$ ) (11). In contrast, Clark et al. reported that histologic evaluation of breast reduction specimens revealed normal breast tissue in 41.8% ( $n = 235$ ), and this group was of <40 years of age (3). Bondeson et al. reported only 29% ( $n = 58$ ) of normal breast tissue in their sample (9). Furthermore, the definition of normal breast tissue is controversial and dependent on multiple factors, including histopathological appearance, age, and hormonal effects. In general, normal breast tissue is described as having an absence of morphological changes in the glandular and ductal elements and in the fibro-connective tissue (11).

In our series, the most common lesions were fibrocystic changes (71.6%), as seen in other studies. While the clinical rate of fibrocystic changes in breast tissue was reported to be 60% in postmortem trials, this rate was detected to be 34% in breast biopsies (12). In a trial by Ayhan et al. performed on 149 cases, fibrocystic changes were detected in nearly half of the cases (46.8%) (1). This rate suggests that fibrocystic changes frequently accompany breast hypertrophy. These patients are considered to have no increased risk of breast cancer (Table 1).

In our trial, lesions associated with a mildly increased carcinoma risk were identified in 52.8% (n = 56) of cases; while 16 of these patients were of <40 years of age, 40 were of  $\geq 40$  years of age. The proportion of patients with mildly increased carcinoma risk increased with age. This rate was 9.3% (n = 52) in study of Ishag et al. (2), while in study of Samdanci et al. it was 72.1% (n = 197) (5).

In the current study, we observed 8 cases of columnar cell lesion without atypia. Two (3.8%) of these patients were of <40 years of age, while 6 (11.1%) were of  $\geq 40$  years of age. Atypical columnar cell lesions (as shown in Figure 1a) were identified in 61 cases. Twenty-two (42.3%) of these patients were of <40 years of age, while 39 (72.2%) were of  $\geq 40$  years of age. In the literature, we could not find any information regarding the incidence of columnar cell lesion in breast reduction specimens.

In 5 patients (4.7%), atypical ductal hyperplasia (ADH; as shown in Figure 1b), which is an indicator of moderately increased carcinoma risk, was observed (1 patient of <40 years of age, 4 of  $\geq 40$  years of age). ADH presents a relative risk factor of 4–5. An invasive carcinoma will develop in a mean period of 8.3 years in 4%–22% of women who are carriers of ADH. Ishag et al. and Kakagia et al. detected the rates of atypical lesions [ADH + atypical lobular hyperplasia (ALH)] as 1.4% and 1.6% and the rates of in situ lesions [ductal carcinoma in situ/lobular carcinoma in situ (DCIS/LCIS)] as 0.2% and 0.3%, respectively (2,13). To date, the reported rate of ADH/ALH varies between 0.7% and 4.4% in different trials (2–4,7). Freedman et al. noted malignancy (invasive carcinoma + DCIS) in 6 out of 700 patients (0.86%) and high-risk lesions (ADH + ALH

+ LCIS) in 31 of the patients (4.4%) (14). Our incidence of ADH is slightly higher compared with previous reports. However, Horo et al. assessed 145 reduction mammoplasties and reported borderline lesions (ADH) in 12 (15.6%) of the patients (15).

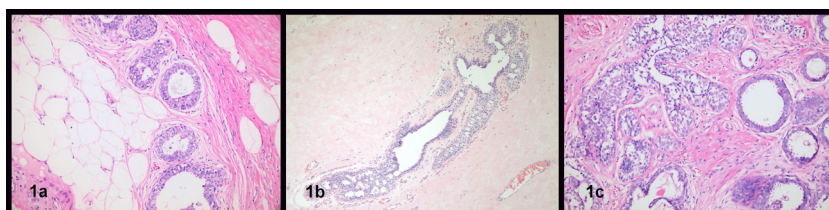
While no DCIS or occult invasive carcinoma was detected, lobular carcinoma in situ (as shown in Figure 1c) was observed in 6 patients (5.6%) in our series. In the literature, when we looked at the category of carcinoma, some authors reported invasive carcinoma only (1), while others also included DCIS and LCIS (2,4,7). Most trials have not made this distinction clear. This situation leads to differences in the rate.

Bondeson et al. detected lobular carcinoma in situ in 8% of cases over 40 years of age (9). In our trial, we detected a lobular carcinoma in situ rate of 11.1% (6 of 54 cases) for patients of  $\geq 40$  years of age, and this rate is higher than that reported by Bondeson et al. We did not detect lobular carcinoma in situ in patients younger than 40 years.

For the first time, Snyderman and Lizardo detected breast carcinoma in 19 cases (0.038%) in their trial where they investigated 5008 breast reduction specimens in 1960 (16). Recently, an increase was reported in the breast cancer incidence of reduction mammoplasty specimens from asymptomatic women. While this rate ranged between 0.006% and 0.6% according to different authors, some authors reported a 2% incidence (1–5,11,13,17–23). For a comparison of histopathological findings on all breast reduction specimens in the literature covering the years 1985–2012, see Table 4.

This variability in the incidence of breast abnormality is likely attributable to tissue sampling methods, differences in sample numbers, differences in histological classification criteria, selected patient population, age distribution, and the number of patients selected.

In Turkey, breast cancer makes up a quarter of all cancers in women and is the most common type of cancer in women. Each year, 30,000 women develop breast cancer in Turkey. Therefore, today in Turkey, besides an increased incidence of breast cancer and high-risk breast diseases in



**Figure 1.** a) Atypical columnar cell lesions [hematoxylin and eosin (HE), 200 $\times$ ], b) atypical ductal hyperplasia (HE, 100 $\times$ ), c) lobular carcinoma in situ (HE, 200 $\times$ ) in a reduction mammoplasty specimen.

**Table 4.** Studies regarding histopathologic findings in breast reduction specimens.

Reference	Year	No. of patients	Normal tissue (%)	Benign breast lesion (%)	DCIS/LCIS (%)	Cancer (%)
Bondeson et al. (9)	1985	200	-	21 (10.5%)	7 (3.5%)	0 (0)
Cruz et al. (18)	1989	100	-	96 (96)	0 (0)	0 (0)
Karabela-Bouropoulou et al. (10)	1994	55	0 (0)	55 (100)	0 (0)	0 (0)
Ayhan et al. (1)	2002	149	58 (45.01%)	-	-	2 (0.68%)
Ishag et al. (2)	2003	560	-	447 (69%)	1 (0.2%)	3 (0.5%)
Blansfield et al. (8)	2003	182	163 (89%)	19 (10%)	1 (0.5%)	-
Colwell et al. (19)	2004	800	-	-	3 (0.4%)	3 (0.4%)
Cook et al. (4)	2004	1289	-	1258 (97.6%)	4 (0.3%)	1 (0.1%)
Kakagia et al. (13)	2005	314	-	133 (43%)	1 (0.3%)	2 (0.6%)
Viana et al. (20)	2005	274	-	260 (95%)	1 (0.3%)/1 (0.3%)	1 (0.3%)
Pitanguy et al. (11)	2005	2488	91 (3.7%)	2389 (92%)	1 (0.04%)	7 (0.3%)
Dotto et al. (21)	2008	516	-	119 (23%)	1 (0.2%)/17 (3%)	1 (0.2%)
Clark et al. (3)	2009	562	235 (41.8%)	296 (52.7%)	1.1%/0.7%	-
Ambaye et al. (7)	2009	202	-	177 (87.6%)	3 (1.48%)	2 (0.99%)
Mazhar et al. (22)	2010	1588	-	-	1 (0.06%)	5 (0.31%)
Horo et al. (15)	2011	145	35 (45.5%)	30 (38.9%)	-	-
Şamdancı et al. (5)	2011	273	44 (16.1%)	197 (56%)	1 (0.3%)	-
Rajabian et al. (23)	2012	350	233	108	-	4 (2.28%)
Freedman et al. (14)	2012	700	-	-	4/8	2

patients of  $\geq 40$  years of age, the breast cancer frequency among women of  $< 40$  years old was reported as 20%, which is very high compared to Western countries (24). The Ministry of Health in Turkey recommends routine mammography screening every 2 years for women starting at the age 40 (between the ages of 40 and 69) (<http://thsk.saglik.gov.tr/2013-10-01-11-00-51/halk-sagligina-yonelik-bilgiler/424-meme-kaner-tarama-standartlari.html>).

Routine cancer detection procedures (i.e. mammography, ultrasonography, magnetic resonance imaging) should also be recommended in reduction mammoplasty candidates who are younger than 35 years with no family history of breast cancer. Our study showed that histopathological evaluation of clinically and macroscopically normal breast tissues from reduction mammoplasty specimens in all age groups may provide important pathological findings.

We want to emphasize that columnar cell lesions of the breast were commonly encountered in our study population (3.8% in  $< 40$  years of age, 11.1% in  $\geq 40$  years of age with columnar cell lesion without atypia; 42.3% in  $< 40$  years of age, 72.2% in  $\geq 40$  years with columnar cell lesion with atypia). In retrospective studies, the presence of columnar cell lesions with or without atypia was found to be associated with a very low risk for subsequent breast cancer, with a relative risk of 1.5 times normal (25). Nevertheless, we think that importance should be attached to scanning tests for patients below the age of 40 as well, because atypical columnar cell lesions were observed below 40 years of age at a high rate of 42.3%, and they need careful evaluation to exclude breast cancer.

In conclusion, it should be remembered that the supporting data for the relationship of columnar cell lesions and subsequent breast cancer are limited, and additional long-term follow-up studies are needed.

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