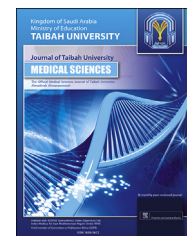




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Original Article

## Prerequisites for histopathological evaluation of reduction mammoplasty specimens: Recommendations based on an audit in a tertiary care hospital



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### المخلص

**أهداف البحث:** إيجاد توصيات للشروط المسبقة لتقييم عينات أنسجة عمليات تصغير الثدي التجميلي بناء على التدقيق في مستشفى رعاية ثالثة في المملكة العربية السعودية.

**طرق البحث:** أجريت دراسة استيعابية لتقييم جميع عينات تصغير الثدي التجميلي التي وردت إلى قسم علم الأمراض التشريحي في مستشفى الرعاية الثالثة. وروجعت السجلات الطبية للعمر، والتاريخ العائلي لسرطان الثدي، وسبب إجراء العملية الجراحية والتقييم الشعاعي. كما روجعت تقارير عينات الأنسجة بحثاً عن عدد كتل العينات والتشخيص. وتم وضع بروتوكول بشروط مسبقة استناداً إلى أوجه القصور والمعوقات الملحوظة في هذا التقييم.

**النتائج:** تم استلام ٢٦ حالة من عينات تصغير الثدي التجميلي، كانت منها ٢ فقط (٧.٦٩٪) عينات من الذكور. تراوح عمر المرضى من ٢٦ إلى ٥٠ عاماً. كما تم التوصل إلى أسباب العملية الجراحية في جميع الحالات (١٠٠٪)، وكان تضخم الثدي أكثر الأسباب انتشاراً. بينما كانت المعلومات عن التاريخ العائلي لسرطان الثدي والأدلة الشعاعية مفقودة أو لم تقدم في جميع الحالات. وكان عدد قطع الأنسجة التي فحصت مجهرياً أقل من ٤ في ١٧ (٧٣.٩١٪) حالة، و٨-٥ قطع في ٥ (١٩.٢٣٪) و٨-١٢ قطعة في ٤ حالات (١٥.٣٨٪). ومثل تليف الثدي الكيسي النتيجة الأكثر انتشاراً في الفحص المخبري، كما تم ملاحظته لدى ١٢ (٤٦.١٥٪) من المرضى. ولم يجر التصوير الشعاعي للعينات لأي حالة.

**الاستنتاجات:** هناك حاجة لتقسيم الحالات إلى عالية، متوسطة أو منخفضة الخطورة بالنسبة لسرطان الثدي استناداً إلى التاريخ العائلي لسرطان الثدي، والتقييم السريري والشعاعي. ويجب توجيه الحالات العالية الخطورة، بتحديد الأطراف وأخذ العينات بطريقة واسعة. وينبغي إجراء التصوير الشعاعي للعينات للمرضى الأصغر سناً، حينما لا ينصح بالتصوير الشعاعي للثدي.

**الكلمات المفتاحية:** تليف الثدي الكيسي؛ علم الأمراض التشريحي؛ عمليات تصغير الثدي التجميلي؛ عينة التصوير الشعاعي؛ سرطان الثدي

### Abstract

**Objective:** To recommend prerequisites for the histopathological evaluation of reduction mammoplasty (RM) specimens based on an audit in a tertiary care hospital.

**Methods:** All reduction mammoplasty specimens received at department of pathology, in a tertiary care hospital over a 3 years period were re-evaluated retrospectively. Medical records were checked for age, family history of breast cancer, indication for surgery and radiological evaluation. Pathology reports were reviewed for number of blocks sampled and diagnosis. A pre-requisites protocol was developed based upon deficiencies and impediments noted.

**Results:** We received a total of 26 cases of reduction mammoplasty. Only 2 (7.69%) specimens were from males. The age of the patients ranged from 26 to 50 years. Indication for surgery was provided in all (100%) of cases, with macromastia being most prevalent indication. Family history of breast carcinoma and radiological evidence was absent or not provided in all cases. The number of blocks prepared were in range of <4 in 17 (73.91%), 5–8 blocks in 5 (19.23%) and 8–12 blocks in 4 cases (15.38%). The main histopathological finding was fibrocystic change. (n = 12, 46.15%). Specimen radiography was not conducted in any case.

**Conclusion:** There is a need to stratify RM cases as high, moderate and low risk of breast cancer based on family history of breast carcinoma, clinical and radiological evaluation. The high risk cases should be oriented, with

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margins inked and extensive sampling done. Specimen radiography should be carried out in younger patients in which mammography is not recommended.

**Keywords:** Breast cancer; Fibrocystic disease; Histopathology; Reduction mammoplasty; Specimen radiography

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## Introduction

Reduction mammoplasty (RM) is a common surgical procedure used for cosmetic reasons, symptomatic macromastia, or correction of asymmetry. RM produces a variable amount of tissue that is submitted for histopathological evaluation, with only a small number of random sections usually being sampled. Most cases turn out to be benign, but rarely, occult breast carcinomas have been documented.<sup>1,2</sup>

In 2002, the Royal College of Pathologists circulated a document, labelled as “Histopathology of limited or no clinical value”, to all pathologists in the UK.<sup>3</sup> This document included a list of the specimens for which histological examination was of doubtful or limited significance, thereby making little or no contribution to patient care. This document primarily aimed to redirect the focus of pathologists to specimens that are clinically and diagnostically more apt and relevant. Breast reduction mammoplasty was considered to be a specimen needing little histopathological concentration. As the percentage of incidental carcinoma is very low, no consensus currently exists regarding benefits of a detailed and thorough pathological examination.<sup>4</sup> Sections from macroscopically abnormal areas are justified, but the value of random histology appears minimal.<sup>1</sup>

Based on the low incidence of pathologically or clinically important lesions in RM specimens in the last decade, surgeons have started to consider not sending RM specimens for pathological examination if radiology reveals nothing suspicious for patients.<sup>5</sup> In addition, cost-effectiveness for histopathological evaluation of RM could also be considered to be a limiting factor. In the United States, in 2007, nearly 220,000 RM were performed, and it was calculated that the total cost to the health care system for these pathological examinations was \$25 million annually.<sup>6,7</sup>

The above mentioned trends are currently being debated and are changing as a result. Occult carcinomas have been reported in RM specimens, and this finding justifies a highly detailed histopathological evaluation for all RM specimens.<sup>5</sup> Absolute reliance on radiological diagnosis is also not a preferred modality; for example, Amichetti et al. revealed that mammographically and ultrasonographically non-suspicious breasts might yield clinically important histopathological lesions that can alter patient management.<sup>8</sup> Increased incidence of breast cancer in patients of macromastia suggest that this incidence may be a factor predisposing patients to breast cancer. Therefore, surgeons

should undertake a preoperative screening consisting of a recommended triple breast evaluation; a detailed patient history, specifically any personal or family history of breast cancer; a clinical examination; and imaging by either a mammogram or breast ultrasound.<sup>9</sup>

In our centre, all breast reduction samples are routinely sent to the histopathology laboratory where microscopic examination is conducted, regardless of the macroscopic picture or radiological findings. To the best of our knowledge, no study to date has been undertaken to validate this approach. In the current study, we conducted an audit of reduction mammoplasty specimens received in the last three years in order to evaluate the current submission and diagnostic practice with the aim of developing a proper pre-requisites protocol.

## Materials and Methods

This retrospective study was conducted at the Department of Pathology, King Fahd Hospital of the University of Dammam after the mandatory approvals. An audit and re-evaluation of RM specimens received from 1st January 2012 to 30th December 2014 was conducted.

The inclusion criteria were all RM specimens received during the period under review (3 years) for whom hospital record of patient, complete set of paraffin blocks, and histopathology diagnosis were available. Any specimen that did not fulfil the above criteria was excluded from the study.

Age, sex, indication for surgery, family history of breast cancer, and radiological evaluation before surgery were checked in the medical record of each patient. The number of blocks sampled and macroscopic findings were recorded from the pathology reports. A proforma-cum-checklist was prepared to note age, gender, family history, pre-op mammographic findings, indication for surgery, any specific findings noted at the time of surgery, number of blocks, initial reported diagnosis, diagnosis at re-evaluation, any discrepancy between the two diagnoses, and specific detailed microscopic findings. Three categories of cases were developed based on the number of paraffin blocks made at the time of grossing. These categories were designated as Category-I: <4 blocks, Category-II: 5–8 blocks, and Category-III: 8–12 blocks.

The re-evaluation was independently made by two members of the team (AA & MAS). A detailed microscopic report and final diagnosis were made and recorded separately. The results of both the pathologists were later compared. In case the results did not match, a third member (AMN) also re-evaluated the case, and the results were discussed until a consensus was reached.

The microscopic diagnosis for each case was classified into one of four categories<sup>5</sup>:

- (1) Normal or benign breast disease.
- (2) Lesions of uncertain malignant potential, including atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), intraductal papilloma, and lobular carcinoma in situ (LCIS).
- (3) Ductal carcinoma in situ (DCIS) or microinvasive carcinoma.

#### (4) Invasive carcinoma.

The current protocol for breast reduction specimens received at our laboratory for histopathological examination involves the specimen being sliced and examined macroscopically. If no lesion is grossly identified, an average of two to three random blocks of breast tissue are taken from each breast. If a macroscopic lesion is present, sampling is concentrated on its vicinity, with selection of an appropriate number of blocks being considered necessary by the pathologist. A macroscopic abnormality is defined as the presence of a discrete mass, cysts, or calcification. Fibrosis is not included in this definition. If an important microscopic finding is identified, further tissue blocks are taken. In most cases, the specimens are received as multiple fragments and are not oriented.

#### Statistical analysis

The collected data were entered in the SPSS-19 statistical software package. Data were expressed using descriptive statistics in the form of number and percentages for qualitative variables. Mean  $\pm$  standard deviation (SD) was calculated for quantitative variables.

Based on the findings of audit and histopathological re-evaluation, a prerequisites protocol for RM specimens was proposed.

#### Results

We received a total of 27 cases of reduction mammoplasty specimens in three years. One case was excluded as it lacked complete patient records and was also autolyzed. Out of the final 26 cases of RM evaluated, most of the cases were female (24/26). The age of the patients ranged from 26 to 50 years with a mean age of  $33.33 \pm 9.17$  years. The numbers of blocks for these cases were in the range of <4 in 17 cases (73.91%), 5–8 blocks in 5 cases (19.23%) and 8–12 blocks in 4 cases (15.38%). All cases (100%) had either normal or benign breast disease. Normal breast tissue was observed in eight cases (30.77%), and benign breast disease was observed in 18 cases (69.23%). The benign breast diseases identified were lipomatous hyperplasia in two cases (7.69%), fibrocystic changes in 12 cases (46.15%), mammary duct ectasia in one case (3.85%), and marked foreign body granulomatous reaction in one case (3.85%). In the latter, the patient had a history of scar tissue removal from a previous mammoplasty. The two males (7.69%) had gynaecomastia. The spectrum of fibrocystic changes consisted mainly of non-proliferative changes in seven cases (58.33%), while proliferative changes were observed in five cases (46.67%). The proliferative changes comprised mild to florid epithelial ductal epithelial hyperplasia of the usual type, sclerosing adenosis, and focal columnar cell change. There were no lesions of uncertain malignant potential, ductal carcinoma in-situ, or microinvasive or invasive carcinoma.

The parameters recorded are presented in Table 1. The percentages of main histopathological lesions in RM specimens are presented in Figure 1, and surgical indication for RM is presented in Table 2.

#### Discussion

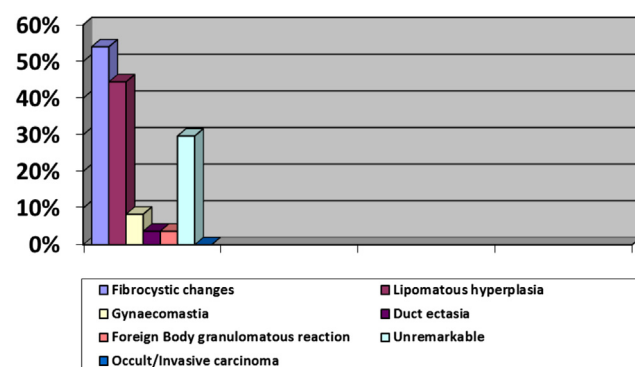
Breast tissues from RM procedures are commonly encountered specimens in surgical pathology; however, no well-defined guidelines are available for pathological examination of these specimens. Only a small number of reports are available in the literature discussing histological findings in RMs. The complete absence of any pre-malignant or malignant lesions in these specimens in our study, as well as the trend of implementing specimen radiography for gross specimens, are the major issues to discuss.

In 1960, Snyderman and Lizardo reported a study on the detection of malignant neoplasms in routine breast plastic operations, including RM procedures. Of 5008 RM cases, 19 breast carcinomas were discovered pre-operatively by physical examination, intra-operatively by frozen section, and post-operatively by routine histopathological evaluation.<sup>10</sup> In 1998, Jansen and colleagues<sup>11</sup> reported an incidence of occult invasive breast carcinoma in 0.16% of 2576 specimens. Bondeson and colleagues reported seven cases (8%) of lobular carcinoma in situ (LCIS) in patients older than 40 years.<sup>12</sup> In our set of cases, out of the total of 26 cases, only three patients were above the age of 40 years. The microscopic findings comprised fibrocystic changes in

**Table 1: Parameters recorded in all reduction mammoplasty specimens.**

Parameters recorded	Data available (% of cases)
Age of the patient	n = 26 (100%)
Gender	n = 26 (100%)
Indication of surgery	n = 26 (100%)
Any specific findings noted at the time of surgery	N.A
Family history	N.A
Radiological diagnosis	N.A
Initial reported diagnosis	n = 26 (100%)
Diagnosis at re-evaluation	n = 26 (100%)
Any discrepancy between the two reported diagnosis	None
Number of blocks prepared per case.	(<) 4, 5–8 and 8–12

N.A = Not available.



**Figure 1: Percentages of histopathological lesions in reduction mammoplasty specimens (n = 26).**

**Table 2: Age-wise indication for reduction mammoplasty (n = 26).**

Indication for RM	Age < 35 No. (%)	Age ≥ 35 No. (%)
Macromastia	9 (34.62%)	14 (53.85%)
Developmental asymmetry	0	2 (7.69%)
Post procedure	0	1 (3.85%)
Total	9 (34.62%)	17 (65.38%)

two cases and mild epithelial proliferation of the usual type in one along with lipomatous hyperplasia. In the same study mentioned above, Bondenson et al found no pathological abnormalities in all patients younger than 30 years. Based on the large amount of material generated by RM specimens and minimal incidences of pathologically and clinically serious lesions, the authors challenged the concept of extensive sampling of all tissues. The authors concluded that in patients younger than 30 years, careful gross examination with or without minimal microscopic examination (1 or 2 blocks) is adequate. Extensive microscopic examination was recommended for specimens from women older than 40 years, even in the absence of grossly evident lesions.<sup>12</sup> However, the definition of extensive sampling has not been delineated to date. In the cases described in this study, no suspicious areas were detected grossly or microscopically, i.e., all were found to be benign, and the number of blocks in the majority of cases (73.91%) was less than four per case. The question remains whether this extent of sampling was sufficient to detect occult pre-malignant lesion, and determining a precise definition of parameters for grossing such samples is warranted.

In our set of cases, there was a complete absence of incidental carcinoma, despite the high prevalence rate of breast cancer in Saudi women, which accounts for 27.4% of all diagnosed female cancers in the year 2010.<sup>13</sup> This discrepancy could be attributed to our small sample size compared to the studies documented above. Alternatively, the cause might be attributed to missing a carcinoma by not taking extensive sampling and not incorporating radiological sampling parameters, as protocols for sampling such specimens are not well-delineated to date.

A cut-off age limit of 35 years was made for indication for surgery and radiological findings because mammographic evaluation is recommended after 35 years, and risk of carcinoma and associated surgeries also change with increasing age.<sup>14,15</sup>

Standard use of preoperative mammography is controversial in patients considering RM. In a study conducted between 2001 and 2005, screening mammography was performed before reduction mammoplasty. Sixteen percent of the patients were observed to have abnormal pre-operative mammographic results, which all were determined to be false positive.<sup>16</sup> Mammography is rarely used by surgeons, as depicted in a multi-institutional analysis conducted in UK and Ireland; the authors found that 72% of clinicians never performed a pre-operative mammogram, 28% of clinicians only do a mammogram once before the operation, and only one surgeon did a mammogram before, as well as 6 months after, the operation.<sup>17</sup> Similarly, no

mammography was performed preoperatively in the cases in this study. Ishag et al. demonstrated that patients undergoing RM need to be stratified in three risk groups: (1) 'high-risk persons' are those with a family history of breast cancer, BRCA1 or BRCA2 mutations, or a personal history of previous radiation to the chest or cancer syndromes; (2) 'intermediate-risk persons' are those with family history of breast cancer; and (3) 'low-risk persons' are those under 30 years of age with no family history of breast cancer. These researchers recommended that specimen processing with orientation of margins and inking of margins needs to be conducted in high-risk patients.<sup>18</sup> In addition, a stratified group for mammographic evaluation also needs to be formulated. Mammography screening is associated with a 19% overall reduction of breast cancer mortality but may also cause harm. For a 40 or 50-year-old woman undergoing 10 years of annual mammograms, the cumulative risk of a false-positive result is approximately 61%. The benefits of mammographic screening can be increased by personalizing it, i.e., the decision would be based on each "patient's risk profiles and preferences".<sup>19</sup>

Although one out of every eight women has a risk of developing breast cancer, the reported incidence of breast carcinoma detection in RM materials is rather low. Specimen radiography, which is used for breast biopsies, has not been used for the assessment of breast reduction materials. Ozsmen et al<sup>20</sup> studied the applicability of specimen radiography and its potential benefits in the detection of breast pathologies in RM materials, especially malignancies. Forty patients scheduled for RM were included. In all cases, an inferior pedicle reduction technique was preferred, and the radiographs of the resected breast tissues were taken immediately. The radiographs were evaluated for any possible pathological appearance and all abnormal findings were marked. For histopathological evaluation, in addition to the random sampling by the pathologist, any marked areas were also microscopically examined. In two cases, fibrocystic changes were observed in radiographs, and the same results were obtained by histological examination. No false negative mammograms were observed. Specimen radiography, which is applicable for breast reduction materials, is an easy and cheap method and does not cause any patient discomfort. The radiographs of RM materials are useful to provide guidance to the pathologist during tissue sampling for microscopic examination, especially when large amounts of breast tissue are excised.

In our study, the primary indication for surgery was macromastia in 12 cases, developmental asymmetry in two cases, and post-procedure in one case. It is debatable whether these indications justify undergoing a major operative procedure with its inherent surgical complications. Macromastia, or breast hypertrophy and asymmetry, is a highly common finding and a frequent cause of reduction mammoplasty all over the world.<sup>21</sup> One school of thought considers undergoing surgery for symmetry to be irrelevant as they advocate that asymmetry is "the normal", there is no perfect symmetry in the human body, and searching for it is basically a sign of psychological and psychiatric disorders. For evaluation of the extent of surgical complications associated with RM, one study has



**Table 3: Proposed prerequisites and histopathology evaluation protocol for reduction mammoplasty.**History

Age	<35	<input type="checkbox"/>	>35	<input type="checkbox"/>
Gender	Female	<input type="checkbox"/>	Male	<input type="checkbox"/>
Family History	Positive	<input type="checkbox"/>	Negative	<input type="checkbox"/>
Ultrasonography				
Mammography				

Laboratory protocol

- If age is <35, any gender, and all other are negative in the history above  
Routine 2-4 blocks per case, random sampling
- If age is > 35 and gender is female and family history of breast cancer and radiology suspicious.  
Orientation of the specimen with inking of margins more than 12 blocks per specimen.
- Specimen radiography to be included in all specimens in which pre-op mammography is not performed in category b.

documented a prospective evaluation of wound complications in two hundred eighty-six reduction procedures. Fifty-two patients underwent reduction mammoplasty for macromastia, and 101 did so for macromastia with breast cancer. The wound complications were divided into minor and major complications. Seroma, hematoma, surgical site infection, delayed wound healing, and minor wound dehiscence were included in the minor complication group. Severe complications were necrosis of nipple—areola complex and major incisional wound dehiscence.<sup>22</sup> RM may be limited for overweight and obese women for fear of complications.<sup>23</sup> Correlation between obesity and deficient wound healing has long been established.<sup>24</sup> However, the results of these studies suggest that RM is a safe cosmetic procedure in all patients, and obesity does not increase the complication risk.

Based on the audit, our results, and a discussion, we prepared a prerequisites protocol that is outlined in Table 3.

## Conclusions

Reduction mammoplasty is a common surgical procedure used for cosmetic reasons, symptomatic macromastia, or correction of asymmetry. This procedure produces a variable amount of tissue that is submitted for histopathological evaluation, with only several random sections usually being sampled. Most of the cases are determined to be benign, but rarely, occult breast carcinomas have been documented; this finding justifies a highly detailed and thorough histopathological evaluation for all RM specimens. There was no incidental carcinoma detected in our study, which has an inherent limitation of a notably small sample size. However, in all cases of RM, the surgeons should undertake a preoperative screening, consisting of a recommended triple breast evaluation; taking a detailed patient history, specifically any personal or family history of breast cancer; a clinical examination; and imaging by either a mammogram or breast ultrasound.

## Recommendations

There is a need to stratify RM cases as high-, moderate-, and low-risk of breast cancer based on the family history of breast carcinoma and clinical and radiological evaluation. The high-risk cases should undergo a detailed gross examination with precise orientation, inking of margins, and extensive sampling. In addition, specimen radiography should be performed in younger patients for whom mammography is not recommended.

## Conflicts of interest

The authors have no conflict of interest to declare.

## Authors' contributions

AA conceived and designed the study, as well as collecting, organizing, and interpreting the data. AA, DMT, MAS, AMN, AAS, HAK, and MMH provided research materials, wrote initial and final drafts of the article, and provided logistical support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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