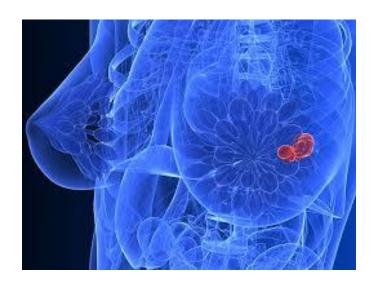


Breast-conserving surgery. Analysis of reduction mammoplasty



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ABSTRACT

- -BACKGROUND: Aiming to achieve better cosmetic results, techniques coming from aesthetic surgery have been applied to cancer treatment, giving birth to the so called "oncoplastic breast-conserving surgery". Reduction mammoplasty (called therapeutic mammoplasty when is used to treat cancer) is one of this techniques.
- -OBJECTIVE: Evaluating the outcomes obtained in patients with breast cancer treated with therapeutic mammoplasty at the Breast Unit of the Hospital Universitario Marqués de Valdecilla (HUMV, Santander, Spain) between 2005 and 2016. We were especially interested in the rates of positive surgical margins, complications and local recurrences. We wanted to know if complications had delayed the start of adjuvant treatment.
- -PATIENTS AND METHODS: We performed an observational study in a group of 68 patients undergoing therapeutic mammoplasty in HUMV between 2005 and 2016. Data of all patients were collected prospectively. We compiled data referring the characteristics of the patients and the tumor, the surgery, the adjuvant treatment and the long-term outcomes (follow-up). We performed data statistical analysis.
- -RESULTS: Mean age of the patients was 57 years (SD: 8). Median follow-up was 56 months. Positive margins rate was 16,18 %. 11 patients (16,18 %) had early complications. The number of local recurrences to date was 0 (0%). We didn't found differences in the delay of adjuvant treatment between complicated and non-complicated patients.
- -CONCLUSIONS: The outcomes of reduction mammoplasty in HUMV are similar to those published in scientific papers to date, with good results referring surgical margins, recurrences and complications. Complications didn't delay the start of adjuvant therapies in our series.

Keywords: breast cancer, breast-conserving surgery, oncoplastic surgery, reduction mammoplasty

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1. Introduction

According to the data compiled by the IARC (International Agency for Research on Cancer) breast cancer is the second type of cancer most frequent around the world and, by far, the most common among women, with an estimated 1,67 million new cases diagnosed in 2012, which means the 25 % of cancers diagnosed in female population¹. It's the main cause of death by cancer in women.

In Spain, the number of female breast cancers diagnosed in 2014 it's estimated to be 26.354. In December 2012, prevalence of cases diagnosed in Spain was 516,2/100.000 women per 5 years².

Age is the main risk factor in breast cancer, given incidence increases after age 35. Other risk factors are early menarche, delaying of first pregnancy, late menopause, family background, hormone replacement therapy, obesity and alcohol intake.

Treatment of breast cancer is multidisciplinary. There are several therapies available: surgery, chemotherapy, radiotherapy, hormonotherapy... Close teamwork is essential to choose the ideal treatment and apply it in the best way in each patient.

Surgical treatment of breast cancer

Surgery plays a key role in treatment. There are two zones where surgical intervention is needed: the breast and the axilla.

In the breast, complete removal of malignant tissue is required.

In the axilla, staging the nodal status is essential for planning. For this purpose, the surgeon searches and takes out the sentinel node: the lymph node where the lymph coming from the breast drains firstly. This node is analyzed to establish if it's invaded by tumor tissue, which will determine the subsequent procedures.

Regarding the surgical interventions performed in the breast, we can talk about two types of surgery: mastectomy and breast-conserving surgery.

1.1 Mastectomy

Mastectomy is a surgical intervention that consists of the complete removal of the mammary gland.

1.2 Breast-conserving surgery

The term "breast-conserving surgery" refers to the interventions where the surgeon only removes the tumor and some healthy tissue around it (security margins).

The rest of the mammary gland is conserved. After the surgery, the treatment it's completed with radiotherapy.

<u>Surgical margins:</u> Surgical margins are defined as the distance between the tumor cells and the ink-marked border of the surgical piece. During long time, it's been a discussion about the optimal size of margins in breast-conserving surgery.

A meta-analysis³ published in 2014 has showed that, in stages I and II of breast cancer treated with breast-conserving surgery plus radiotherapy, appropriate margins are those where the ink doesn't touch the tumor (the so-called ink-free margins), regardless of the distance between the ink and the tumor.

Nowadays, conservative treatment, combined with radiotherapy, is the choice in the majority of women with breast cancer in early stages, because the aesthetic outcomes are better and the 5 year survival-rate doesn't show differences with mastectomy outcomes^{4,5}.

However, despite breast-conserving surgery has better aesthetic results than mastectomy, several studies^{6,7} have shown that between 20 % and 30 % of women subjected to conservative treatment aren't satisfied with the aesthetic outcome, judging it as mediocre or poor. Besides, all patients, even those who are satisfied, notice a certain degree of asymmetry after surgery.

Aiming to improve these results, the tumor-removal techniques were combined with aesthetic surgery techniques, giving birth to a new discipline: oncoplastic surgery.

1.3 Oncoplastic breast-conserving surgery

Oncoplastic breast-conserving surgery is defined as the use of aesthetic surgery techniques in conserving treatment of breast cancer. This type of surgery includes the complete removal of tumor tissues with appropriate surgical margins, preserving the rest of the mammary gland and using local or regional tissues to immediately reconstruct the defect caused by the extirpation of the tumor. After that, the treatment is completed with radiotherapy.

Oncoplastic surgery offers several advantages when compared with traditional breast-conserving surgery: studies have shown that long-term survival rates are as good as those obtained with conserving surgery⁸ and that aesthetic outcomes and patients' degree of satisfaction is better^{9,10.} Furthermore, it has been noticed that oncoplastic surgery techniques have lower re-intervention rates when compared with

conventional surgery⁹ and that they allow wider resections because, with the tissue remodeling, the surgeon can repair larger defects.

In the other hand, tissue remodeling could complicate management in case of positive surgical margins, which could be a disadvantage. However, it has been proved that positive margins rate is lower when employing oncoplastic techniques¹¹, so there are few patients where this problem appears.

Besides showing oncologic and aesthetic outcomes, the studies published have disclosed which is the best way to perform oncoplastic surgery. So, most papers emphasize that it's better to perform tumor resection and mammary reconstruction at the same time, giving radiotherapy after that (because it has been demonstrated that irradiation before reconstruction leads to worse outcomes)¹².

It's also possible to perform an additional intervention in the contralateral breast, in order to correct the asymmetry resulting from the surgery. This symmetry-providing surgery can be done at the same time or afterwards and, besides improving the aesthetic outcome, it allows to explore the contralateral breast searching for hidden tumors.

There are many oncoplastic techniques, which can be sort in two groups:

- Volume displacement techniques, in which the breast is reconstructed employing the mammary tissue which has been left after the extirpation of the tumor. Reduction mammoplasty, the technique studied in this paper, is a volume displacement technique.
- Volume replacement techniques, in which the breast is reconstructed employing tissues from other parts of the body. The surgeon employs flaps to mobilize those tissues.

The choice of one or another technique depends on several factors, as location of the tumor, its size, the tumor volume/breast volume ratio or the ptosis degree.

1.4 Breast-conserving surgery with reduction mammoplasty technique.

Reduction mammoplasty is an aesthetic surgery technique that originally was employed to reduce the breast volume in women with macromastia. It has been adapted to treat breast cancer. Some authors use the term "therapeutic mammoplasty" to name the combination of reduction mammoplasty and radiotherapy in breast cancer treatment, using the term "reduction mammoplasty" in those cases in which this technique is employed in patients who don't have cancer.

Therapeutic mammoplasty is a very versatile technique. It allows the removal of tumors in almost every quadrant of the breast.

In every case, it includes the design of a skin incision pattern and a pedicle that allows to move the areola-nipple complex. The tissue which will be removed must be marked. It must include the tumor with security margins. Once the incision is done, the resection of the demarcated zone is performed, followed by the displacement of the remaining mammary tissue to fill the defect resulting from the tumor extirpation. Then, the pedicle employed to fill the defect is stitched up in the adequate position. Afterwards, the excessive skin it's removed and the cutaneous incision is closed. It's not always necessary to remove the skin situated over the tumor, but some centers include it in the usual protocol. The placement of "clips" in the tumor bed it's important to mark the zone to apply radiotherapy afterwards.

Therapeutic mammoplasty is a technique specially useful in patients with large breast volume (macromastia). Conservative treatment in big breasts used to be challenging, because the adverse effects of radiotherapy, such as fibrosis or retraction, are more frequent in this type of breasts, due to the need of higher doses of radiation and the trouble to provide an uniform dose in the whole breast. Because of that, the long-term aesthetic outcomes were usually poor, with asymmetry and distortions. The use of therapeutic mammoplasty in these patients has proved to be an effective and safe option. It allows to reduce the breast volume, easing the administration of radiotherapy and cutting down its adverse effects¹³. Furthermore, we mustn't forget that macromastia is a symptomatic condition which lows life-quality. Therapeutic mammoplasty improves the quality of life of these patients.

1.4.1 Pedicles

When planning a therapeutic mammoplasty, it's necessary to design a pedicle (or several, because it's possible to use more than one pedicle in the same intervention). The pedicle allows the displacement of the nipple-areola complex (if it's going to be preserved) maintaining its viability or, what it's the same, assuring an adequate vascular supply.

So, during the surgery, the nipple-areola complex, with the rest of tissues that compose the pedicle, is set aside while the tumor is removed. Then, the defect created by the tumor extirpation is filled with these tissues and the nipple-areola complex is put in the correct place.

There's a great variety of pedicles, which are named depending on the direction of its base (zone of the pedicle where the blood vessels enter and that is kept connected to the rest of the breast tissue). The choice of the pedicle depends on several factors, as the tumor location, the surgeon's experience or the adverse effects that could happen. It must be designed trying to assure that the vascular supply (to avoid necrosis) and sensibility of the nipple are as good as possible.

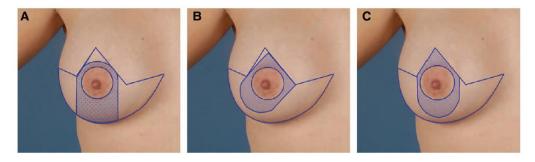


Figure 1. A) Inferior pedicle B) Superomedial pedicle C) Superior Pedicle. All of them with a Wise or inverted-T skin-incision pattern ¹⁴

Some of the pedicles used most frequently are:

- Superior pedicle: The base of the pedicle looks at the upper zone of the breast. It's employed in tumors located in its lower zone, usually when the amount of tissue that will be removed is not very large (less than 1,000 grams). It's main disadvantage is the higher risk for sensory loss of the nipple-areola complex.
- Inferior pedicle: The most used. The base of the pedicle looks at the lower zone of the breast. It's employed when the tumor is located over the nipple, in the outer quadrants or in the lower-inner quadrant. It provides very good results in large resections, with good vascular supply and low rates of sensory loss. The higher incidence of pseudoptosis (fall of the mammary gland under the mammary fold, while the nipple keeps over it).
- Medial pedicle: The base of the pedicle looks at the sternum. It can be used in resections over 1,500 grams, with good sensibility outcomes.
- Lateral pedicel: The base looks at the outer zone of the breast. It has good sensibility outcomes, but the aesthetic results are not optimal, so it isn't used very often.
- Central mound: The skin and sub-cutaneous tissues around the nipple are dissected, leaving a "mound" in the center that names the technique. The breast tissue it's removed and replaced around this mound. The vascular supply is excellent and the sensibility outcomes are good too.



Figure 2. Pre-operative marking of a superomediar pedicle (colour brown, blue border). The tumor (green) is located in the lower-inner quadrant ¹⁵

Skin-Incision patterns

Besides designing the pedicle, it's also necessary to design a skin-incision pattern. The choice of the pattern depends on factors as the breast morphology, the need of removing the skin over the tumor and the surgical access to the tumor. There are several patterns:

Wise pattern or inverted-T pattern: The most used, especially when associated with an inferior pedicle, although it can be used with most of the pedicles. It allows a wide access to mammary tissues and it's very versatile, so it can be used to remove tumors either in the upper or the lower zone of the breast. It's a good option in larger resections, when the skin-quality is bad or in breasts with severe ptosis. Besides, lots of surgeons think Wise patterns is a technique relatively easy to be taught and learned and that its outcomes are more predictable. It's main disadvantage is the high scar burden. The term "inverted-T" refers the appearance of the scar once the surgery is finished.

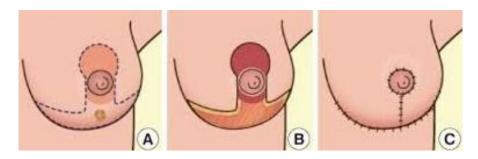


Figure 3. Wise pattern 16



Figure 4. Pre-operative marking of a Wise pattern (left). At the right, the post-operative result, with the characteristic inverted-T scar 17

 Vertical pattern: It's used in surgeries where the volume removed is lower, especially in breasts with moderate ptosis. It's employed mostly in tumors located in the intersection of lower quadrants.

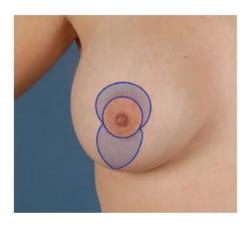


Figure 5. Vertical pattern 14

- L pattern: Resembles Wise pattern, but without its medial branch.
- J pattern: Very useful in tumors located in the lower outer quadrant.
 Resembles the vertical pattern, but the incision under the nipple deflects to the outer zone of the breast.

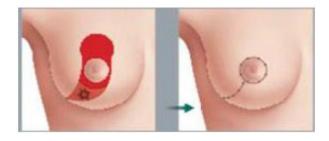


Figura 6. J pattern 18

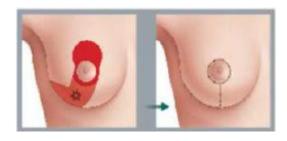


Figure 7. L pattern ¹⁸

1.4.3 Versatility of reduction mammoplasty

One of the main advantages of the use of reduction mammoplasty in breast cancer treatment is the great versatility of this technique. As shown in the previous sections, the variety of pedicles and skin-incision patterns makes reduction mammoplasty suitable for the removal of tumors located in any quadrant of the breast, with low morbidity and good aesthetic outcomes¹⁹.

1.4.4 Disadvantages and complications

Although it has a lot of advantages, using reduction mammoplasty to treat breast tumors also has some disadvantages: it takes more time, it requests more resources and, if the two breast are operated, both of them could suffer complications. The main complications that can occur in this surgery are:

- Nipple sensory loss.
- Necrosis of nipple-areola complex
- Bleeding/hematoma
- Infection
- Seroma
- Pathologic scar
- Wound dehiscence (T-union in Wise pattern)
- Skin necrosis

When this technique was initially applied, surgeons were worried that, being a more complex technique, it could have a higher rate of complications, causing a higher number of re-interventions or a delay in the adjuvant treatment that could affect badly the cancer treatment (because of the loss of therapeutic opportunity). However, several studies¹³ have shown that the complication rate is low and that the complications are usually minor, so there is a low rate of patients whose adjuvant treatment is delayed until the resolution of the surgery issues.

1.5 Therapeutic mammoplasty. Recent publications

We wanted to know the actual situation of therapeutic mammoplasty and the outcomes that have been published in the last years. For that, we performed a search in Pubmed in February 2016. The key words were "oncoplastic", "oncoplastic breast surgery", "reduction mammoplasty", "reduction mammoplasty outcomes" and "therapeutic mammoplasty". We selected the papers published between the years 2010 and 2016.

We were interested in the following aspects: sample size, median follow-up, rate of positive surgical margins, early complications rate, delay in adjuvant therapies, rate of simultaneous interventions in the contralateral breast and local recurrence rate.

The following chart shows the information compiled from the analyzed articles²⁴⁻⁴⁹:

| | | Follow-up | Positive | Early complications | Delay adjuvant | Symmetrization | |
|--------------------|------|-----------|-------------|---------------------|----------------|----------------|----------------------|
| | n | (months) | margins (%) | (%) | therapies (%) | (%) | Local recurrence (%) |
| Fitoussi et al. | 540 | 49 | 18,9 | 11,48 | 1,9 | 46,1 | 6,8 |
| Song et al. | 28 | 32 | 32,14 | * | * | 100 | 3,57 |
| Munhoz et al. | 106 | 47 | * | 22,6 | * | * | * |
| Chang et al. | 79 | 39 | 18,9 | 14,1 | * | * | 2,3 |
| Currie et al. | 20 | 34 | 5,9 | 25 | * | * | 0 |
| Denewer et al. | 50 | 20 | 0 | 16 | * | 100 | 0 |
| Gulcelik et al. | 106 | 33 | 10,3 | * | * | 100 | 0,9 |
| Schaverien et al. | 48 | * | 2,1 | 39,6 | 2,1 | 87,5 | 0 |
| Grubnik et al. | 251 | 50 | * | 3,2 | * | 88,4 | 4 |
| Semprini et al. | 489 | 60 | * | 20 | | * | 0,6 |
| Romics et al. | 99 | 27 | 14,1 | * | * | * | 2 |
| Rose et al. | 73 | 26 | 13,9 | 12 | 6 | 74 | 1,4 |
| Peled et al. | 37 | 33 | * | 18,9 | * | * | * |
| Kaviani et al. | 258 | 26 | 4,7 | 10,8 | 1,2 | 6,9 | 2,9 |
| Paulinelli et al. | 17 | 28 | 0 | 29,4 | * | * | 0 |
| Acosta et al. | 52 | 12 | * | 5,7 | * | 51,9 | * |
| Imahiyerobo et al. | 64 | 34,6 | * | 16,1 | * | * | 7,9 |
| Emiroglu et al. | 82 | 121 | 3,7 | 12,2 | 4,9 | 100 | 8,7 |
| Colombo et al. | 25 | * | 12 | 12 | * | 73,9 | * |
| Bamford et al. | 68 | * | 4,4 | * | 1,5 | * | 0 |
| Roshdy et al. | 30 | 20 | 0,03 | 23,3 | * | 46,7 | 0 |
| Maguire et al. | 79 | 34 | 0 | 18 | * | 100 | 0 |
| Rezai et al. | 1035 | 62 | 11,4 | * | * | 1,9 | 4 |
| Egro et al. | 117 | 46,1 | * | 24 | * | 0 | * |
| Clough et al. | 272 | * | 11,9 | * | * | * | * |
| Ettinger et al. | 22 | * | 0 | 54,2 | 0 | 100 | * |
| Piper et al. | 1324 | 20-73 | * | * | * | * | 3,1 |
| Kabir et al. | 65 | 72 | 16,1 | * | * | * | 2 |

Chart 1. Series of cases of therapeutic mammoplasty published between 2010 and 2016.

So, regarding the parameters mentioned previously, the outcomes in the papers published between 2010 and 2016 vary within the following figures:

-Sample size: 20-1,324 patients. Most of the studies have samples between 20 and 100 patients.

-Median follow-up: 20-121 months

-Positive margins rate: 0-32 %

-Early complications rate: 3-40 %

-Patients with delayed adjuvant therapy (rate): 0-6 %

-Symmetrization rate: 0-100 %

-Local recurrence rate: 0-8,7 %

2. Objective

The objective of this study is to evaluate the outcomes obtained in patients with breast cancer treated with therapeutic mammoplasty at the Breast Unit of the Hospital Universitario Marqués de Valdecilla (HUMV, Santander, Spain) between 2005 and 2016.

We were interested in the clinical features of the patients, the details of the surgical intervention, its outcomes and early complications. We were especially interested in establishing if there are significant differences in the time from the surgical intervention to the adjuvant treatment in two groups of patients: those who had early complications and those who hadn't.

3. Patients and methods

We performed an observational study in a group of 68 patients undergoing therapeutic mammoplasty in HUMV between 2005 and 2016. Data of all patients were collected prospectively and compiled in a database using the software IBM SPSS Statistics Version 18.

We entered the following variables:

-Age of the patient (years)

- -Date of diagnosis
- -Date of surgery
- -Menstrual stage (pre/postmenopausal)
- Affected breast (right/left or bilateral)
- -Location of the tumor (four quadrants, its intersections, central position and inframmamary fold).
- -Multifocal: Several tumor foci in the same quadrant or less than 4-5 cm between them (Yes/No).
- -Multicentric: Several tumors in different quadrants or more than 4-5 cm between them (Yes/No).
- -Radiological size of the tumor (mm)
- -Radiological exploration used for measuring (echography/mammography/magnetic resonance)
- -Infiltration ("In situ"/Infiltrating).
- -Histological type (ductal/lobular/mixed/papilar/other)
- -Estrogen receptor (+/-)
- -Progesterone receptor (+/-)
- -HER2 receptor (+/-)
- -Ki67 (%)
- -Neo-adjuvant chemotherapy (Yes/No)
- -Sentinel node biopsy (Yes/No)
- -Lymphadenectomy (Yes/No)
- -Number of lymph nodes studied
- -Number of affected lymph nodes
- -Number of patients with positive nodes
- -Harpoon radio-guided surgery (Yes/No)

- -Pedicle (superior/inferior/bipedicled/superomedial).
- -Intervention in contralateral breast (Yes/No)
- -Pathological size of the tumor (mm).
- -Margins (affected/contact/free/wide-more than 1 cm-)
- -Type of margin affection (infiltrating/in situ/both)
- -Early complications (Yes/No): We included the complications which occurred during the first month after the surgery. Infection, necrosis, dehiscence, mastitis or hematomas that requested drainage were considered as complications.
- -Re-intervention (Yes/No).
- -Adjuvant radiotherapy (Yes/No)
- -Start date of adjuvant treatment.
- -Delay of adjuvant treatment (days).

We also created another database compiling the follow-up data of the patients. We used as reference the date of the last mammography and the state of the cancer on that moment. In this database we included the following variables:

- -Date of diagnosis
- -Date of surgery
- -Date of last mammography
- -State of the patient (live/dead)
- -State of the cancer (illness-free/local recurrence/systemic recurrence/both).

The follow-up time was defined as the time passed since the surgery until the last control mammography.

The statistical analysis of the data was made using Spss. The data related to the delay of the adjuvant treatment in patients with and without emplications were compared with a Student's T test for independent data. The results in which p value was lower than 0,05 (p<0,05) were considered significant.

4. Results

4.1 Characteristics of patients and tumors

The clinical features of the patients and tumor location are summarized in Chart 2.

| Chart 2. Characteristics of the patients. | Tumor location |
|---|----------------|
| N | 68 |
| Age (years) | 57, SD:8 |
| Menstrual status | |
| Pre-menopausal | 13 (19,1 %) |
| Post-menopausal | 55 (81 %) |
| Affected breast | |
| Left | 46 (67,6 %) |
| Right | 22 (32,4 %) |
| Tumor location (quadrant) | |
| Upper outer | 18 (26,5 %) |
| Upper inner | 4 (5,9 %) |
| Central | 12 (17,6 %) |
| Lower outer | 2 (2,9 %) |
| Lower inner | 3 (4,4 %) |
| Intersection upper quadrants | 10 (14,7 %) |
| Intersection lower quadrants | 5 (7,4 %) |
| Intersection outer quadrants | 4 (5,9 %) |
| Intersection inner quadrants | 9 (13,2 %) |
| Inframammary fold | 1 (1,5 %) |
| Multifocal | 15 (22,1 %) |
| Multicentric | 1 (1,5 %) |

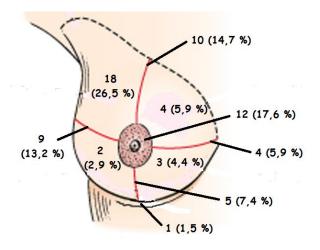


Figure 8. Tumor location

The average size of the tumors, measured with radiological techniques, was of 21 mm (standard deviation: 13 mm). The techniques employed were mammography in 29 patients (42,6 %) and magnetic resonance in 37 (54,4 %).

In 61 (89,7 %) patients the tumor was infiltrating, while in 6 (8,8 %) it was "in situ" and in 1 it was a lymphoma, so the classification as infiltrating or "in situ" was not applied. The histological features of the tumors are summarized in Figure 9.

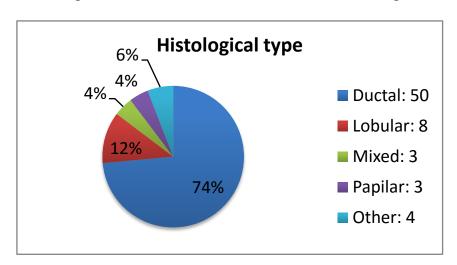


Figure 9. Tumor distribution by histological type

In the category "other" we included two patients with a clear cell carcinoma, another with a mucinous carcinoma and another with a small cell lymphocitic lymphoma.

| | Estrogen receptor | Progesterone receptor | HER2 receptor |
|----------|-------------------|-----------------------|---------------|
| Positive | 52 (76,5 %) | 48 (70, %) | 7 (10,3 %) |
| Negative | 17 (25 %) | 13 (19,1 %) | 50 (73,5 %) |
| Unknown | 3 | 3 | 11 |

Chart 3. Histological features of the tumors

9 patients received neo-adjuvant chemotherapy before the surgery.

4.2 Characteristics of the surgical intervention

In 62 patients (92 %) the intervention was guided with wire-needles placed with radiological control (placed 1 cm aside the radiological margin of the tumor). In the remaining 6 (8 %) wire-needles weren't used. In 44 patients (66,7 %) de number of wire-needles employed was 2 or 3.

In 25 patients (36,8 %) a bipedicled pedicle was used, in 8 (11,8 %) an inferior one, in 3 (4,4 %) a superomedial one and in 1 (1,5 %) a superior one.

26 patients (38,2 %) received surgery in the contralateral breast.

In 60 (88,2 %) patients a sentinel node biopsy was performed. In 10 (14,7 %) a lymphadenectomy was performed: in 7 in the first surgery and in 3 in a second surgery, due to tumor invasion of sentinel node.

14 patients (23 %) had positive nodes.

4.3 Oncologic results

The average pathologic size of the tumor was of 19,5 mm (SD: 13).

11 patients (16,18 %) had positive margins: in 5 of them (7,4 %) the margins were invaded (affected), in 6 (8,8 %) the tumor touched (contact) the borders of the surgical piece). Regarding the type of margin affection, in 6 patients it was infiltrating, in 4 "in situ" and in 1 both.

In the remaining 57 patients (83,82 %) the surgical margins were free.

4.4 Complications

11 patients (16,18 %) had early complications: 4 hematomas, 2 necrosis of the nipple-areola complex, 1 infection (abscess), 1 mastitis and 3 stitch dehiscence (T branch).

9 patients had to undergo a re-intervention: 4 of them because of positive margins (in 3 a mastectomy was performed), 3 to perform a lymphadenectomy because of tumor metastasis in sentinel node and 2 due to complications (hematomas that requested a surgical intervention to be drained).

4.5 Adjuvant treatment

65 patients (94,1 %) received radiotherapy after the surgery. 20 patients (29,4 %) received adjuvant chemotherapy.

| | Neo-ajduvant chemotherapy | Radiotherapy | Adjuvant chemotherapy |
|-----|---------------------------|--------------|-----------------------|
| Yes | 9 | 65 | 20 |
| No | 59 | 3 | 48 |

Chart 4. Adjuvant therapies

The average time between the surgery to the start of adjuvant therapy was of 77 days (SD: 41). In the group of patients without complications it was of 77 days (SD: 43). In the group of patients with complications it was of 78 days (SD: 37).

| | Complicated | Non-complicated |
|---------------------------------------|-------------|-----------------|
| n | 11 | 57 |
| Adjuvant treatment delay (days) | 78 (SD: 37) | 77 (SD:43) |

Chart 5. Delay in complicated vs non-complicated patients

A Student's-T test was performed to establish if the difference between the two groups were significant. Assuming that the variances were equal, we obtained a p value of 0,933 (p>0,05) with a 95 % confidence interval between -31,133 and 29,808 (it includes 0).

In the 11 patients with complications, the individual times of delay were: 34 days; 28 days; 117 days; 83 days; 110 days; 48 days; 59 days; 70 days; 83 days; 153 days; 83 days.

4.6 Follow-up

We include the results of all the patients whose follow-up time was equal or higher than 18 months (29 patients to date).

The median follow-up was of 56 months. 3 patients have died, the other 26 are alive. The 3 patients who died had systemic recurrence of the cancer. The other 26 are illness-free. None of the patients has had local recurrence (0 %).

5. Discussion

Referring the clinical features of the patients and the tumor, there are two remarkable data: the median age of the patients and the tumor location.

The median age of the patient was of 57 years (SD: 8). It's a quite high age, which can be explained because most of the patients come from the early diagnosis programs, that in Cantabria are offered to women older than 50 years. Besides, regarding the breast cancer epidemiology, we see that the risk increases with age and that, according to the National Cancer Institute data²⁰, the median age at the moment of diagnosis is 62 years old (included in our age interval 57 +/- 8).

Regarding the tumor location, the most frequent tumors are those located in the upper outer quadrant, which is the most common location of breast cancer. It's remarkable that central location is the second most frequent in our study, while the recordings of cases that include anatomic location, as the Cancer Research UK ²¹, show

that there are other locations more common than the central one. These results are explained because in centrally located tumors there are few alternatives to mastectomy and therapeutic mammoplasty is one of them. So, it seems logic that in a group of patients undergoing reduction mammoplasty would be a relatively high number of centrally located tumors.

Concerning the surgery and follow-up outcomes, we can see that they are in a similar level as those published in the papers analyzed in the section 1.5. There are some of them that we want to stand out:

- The percentage of patients with positive margins (16,18 %) is in the interval observed in the publications consulted (0-32,14 %)
- The same thing happens with the early complications rate (16,18 % too, while in the studies analyzed it varies between 3,2 and 39,6 %)
- The median follow-up (56 months) is higher than most of the papers reviewed, given that only 4 of the articles read had median follow-ups higher than 50 months.
- The rate of local recurrences is especially good. In our series we haven't had any case of local recurrence to date (0 %). The interval in the publications consulted oscillates between 0 and 8,7 %. So, the outcomes in our series are in the best level.

Finally, we will analyze the outcomes referring the differences between the delay of adjuvant treatment in two groups of patients: those who had early complications and those who hadn't. One of the main concerns about oncoplastic surgery (and reduction mammoplasty is an oncoplastic technique) is that, given that the techniques are more complex, they could cause a higher rate of complications which could force the delaying of adjuvant therapies.

In our series, the average time (in days) until the start of adjuvant treatment is slightly higher in the group of patients with complications (78 days, while in the non-complicated group is 77 days). However, the statistical analysis shows that the difference is not significant or, what is the same, it shows that in the sample studied complications don't cause a delay in adjuvant treatment.

Nevertheless, if we pay attention to each patient with complications, we see that, although the median delay is similar to the non-complicated patients, there are two patients in whom the treatment was remarkably delayed (110 and 117 days) and another one where the delay was almost the double of the median (153 days). So, although we hadn't found significant differences between the two groups, it's possible that in the three patients mentioned complications meant a delay in adjuvant treatment and, thus, a loss of therapeutic opportunity.

6. Conclusions

The outcomes of reduction mammoplasty in HUMV are similar to those published in scientific papers to date, with good results referring surgical margins, recurrences and complications. Complications haven't delayed the start of adjuvant therapies in our series.

Annex (I)

Excel versions of the two databases (data and follow-up) are included in the CD-ROM attached. Patients' identification numbers and birth dates have been erased to protect confidentiality.

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