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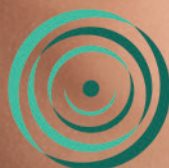
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MASTOLOGY

Mastologia

Cícero Urban^{1*}, Fábio P. Mansani², René Aloisio C. Vieira³, Ruffo Freitas Junior⁴

For the majority of breast specialists, writing is not a priority; therefore, some of them will not write at all during their careers. Although the dictum “publish or perish” is firmly entrenched in academia, most specialists, in daily practice, exhausted by clinical and administrative duties, do not write. However, many young specialists are eager to write, but they do not know how to begin. In the end, writing is an activity performed by only a few.

Nevertheless, there is no progress in a medical specialty without a constant increase in the number and quality of publications. Obviously, publications are not the only key, but they have a direct influence on ascension. Breast specialists need to communicate, and words in a journal are the opportunity to do it for a wider audience. The act of writing is both for pleasure and interest. Few are granted the privilege of inventing something completely new, but all of us are able to evaluate and improve the use of new technologies — an exciting experience.

Mastology was born standing on the shoulders of giants. The former *Revista Brasileira de Mastologia* is a history of success, but it was time to change. The “market” for surgical papers is guided by the impact factor (IF). This is the scientific community score for the prestige of individual journals. It is easy to understand that journals of high IF attract the best manuscripts. While it is very difficult to improve a journal’s IF, it is very easy to lose it due to poor editorial performance, or even worse, not to be quoted due to the journal’s language, as in our case. An article written in English calls the attention of a large audience and recognition among peers. The preeminence of English in medical publishing is a fact. Therefore, for a journal that belongs to the Brazilian Society of Mastology, one of the biggest association of breast specialists in the world, it was necessary to cross the gap and become international.

As Editors, we are aware that crossing the gap and going beyond the border are difficult tasks, even with a great team of editors and international collaborators. Our progress depends greatly on an individual working environment. It is necessary to stimulate the production of good studies. Randomized trials are the first ones in evidence-based medicine, but demographic data, case reports, case series, cohorts, meta-analysis and reviews represent an order of ascending scientific merit too. Then, there is space for everybody with a good and well-structured paper, a good hypothesis and rigorous methodology. As Somerset Maugham said: “There are three rules for writing [...] unfortunately, no one knows what they are.” However, a successful writer has to take the first step, which will then, sooner or later, be natural for each one of us.

We hope that *Mastology*, as an international open-journal, will open the Brazilian and Latin-American mastology research to the world and be an instrument for the education and update of breast specialists.

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BRIEF HISTORY OF THE BRAZILIAN JOURNAL OF MASTOLOGY [REVISTA BRASILEIRA DE MASTOLOGIA]

Breve história da Revista Brasileira de Mastologia

Alfredo Carlos S. D. Barros^{1*}

The Brazilian Society of Mastology (SBM) was founded in 1959 and was later recognized by the Brazilian Medical Association (AMB) and the Medicine Federal Council (CFM) in 1978 and 1989, respectively. In 1982, an analysis of curricular proficiency was conducted to qualify the first specialists and, in 1986, the first contest of the Designation of Mastology Specialist (TEMA) was performed based on evidence.

The *Boletim da SBM* (SBM Bulletin) was edited in the 1980s, which was focused on providing news and small updates. However, an official department of the society to publish research and scientific rationale of national authors was still lacking.

On August 1991, the *Revista Brasileira de Mastologia* (Brazilian Journal of Mastology) was born. It was created by the SBM president at that time, the entrepreneur and idealist Antônio Figueira Filho, with the support of Marconi Luna, the diligent general director. Its first editors were: Antônio Figueira Filho, Henrique M. Salvador Silva and Jairo L. Coelho Jr. There was also a commission of writers comprised of Carlos Henrique Menke, Ezio N. Dias, José A. Ribeiro Filho, José Baptista da Silva Neto and Orlando Silva Telles, besides an editorial board with representatives of many state regionals.

The first edition of the journal included: a presentation – “*A Mastologia no Brasil*” [Mastology in Brazil] by Antônio Figueira Filho; an editorial – “*Câncer de Mama*” [Breast Cancer] by Jorge Marsillac; an original article – “*Ginecomastia: importância do diagnóstico etiológico na orientação do tratamento*” [Gynecomastia: importance of the etiological diagnosis in treatment guidance] by Guido M. C. Magalhães and Harlen T. Merched; three updates – “The current state of breast cancer surgery” by John Hayward, “Câncer da mama masculina” [Male breast cancer] by Ézio N. Dias, “*O seio: uma visão psicanalítica*” [The breast: a psychoanalytical view] by Sônia C. da Silva; a case report – “*Cisticercose da mama*” [Breast Cysticercosis] by Lair B. C. Ribeiro, Hélio Eloy A. Dias and Lygia S. Cunha.

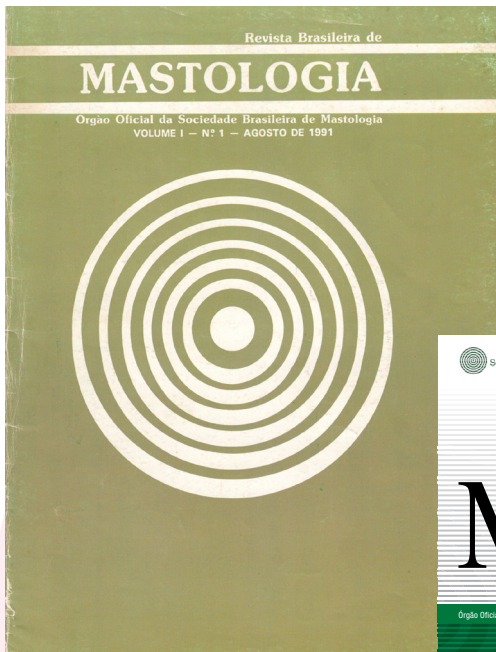
Since its creation, the journal has been published successfully without interruptions. It was first published every four months and then every three months. The effort of its successive editors and members of the editorial boards should be commended. The journal was able to achieve registration in the bibliographic indices Scielo and Lilacs. Recently, the texts started being digitalized and accessed through the Internet, which is a reflex of modernity.

For practical purposes, the journal has accomplished its purposes and achieved distinction and importance. The journal is 26-year-old and mature; therefore, it should face a new phase, with publication of articles in English in order to extend its promotion at an international level.

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TIMELINE OF THE BRAZILIAN JOURNAL OF MASTOLOGY [REVISTA BRASILEIRA DE MASTOLOGIA] EDITORS



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QUALITY OF LIFE IN BREAST CANCER: THE BENEFITS OF PET OWNERSHIP AND PARTICIPATION IN LEISURE ACTIVITIES

Qualidade de vida em câncer de mama: os benefícios da
posse de animais de estimação e participação em atividades de lazer

Monique Binotto^{1*}, Tiago Daltoé², Fernanda Formolo², Patricia Kelly Wilmsen Dalla Santa Spada¹

ABSTRACT

Objective: To evaluate the benefits in the perception of quality of life (QoL) of women with breast cancer related with pet ownership and experiencing leisure activities. **Method:** Cross-sectional study comparing QoL among patients, by applying the WHOQOL-Bref questionnaire. The participants were 272 women diagnosed with breast cancer. **Results:** The pet owners (n=162) had better average of QoL in perceptions of global QoL (72.45 vs. 67.16; p=0.01), and in environmental (67.52 vs. 64.23; p=0.04) and psychological domains (70.29 vs. 66.44; p=0.03) when compared to non-pet owners. Moreover, the patients who reported having leisure activities (n= 214) had better average in perceptions of global QoL (72.43 vs. 62.50; p<0.001), and physical health domain (63.28 vs. 50.92; p<0.001), environmental (68.22 vs. 58.67; p<0.001), psychological (71.01 vs. 60.34; p<0.001) and social relationships (74.73 vs. 65.09; p<0.001) when compared to those who do not have leisure activities. **Conclusion:** Women with breast cancer who are owners of pets and patients who perform leisure activities had better levels of QoL.

KEYWORDS: Quality of life; breast neoplasms; pets; leisure activities; neoplasms.

RESUMO

Objetivo: Avaliar os benefícios na percepção de qualidade de vida (QV) de mulheres portadoras de câncer de mama relacionado à posse de animais de estimação e da vivência de atividade de lazer. **Métodos:** Estudo transversal comparando a QV entre as pacientes, mediante a aplicação do Questionário WHOQOL-Bref. Participaram da pesquisa 272 mulheres diagnosticadas com câncer de mama. **Resultados:** As pacientes tutoras de animais de estimação (n=162) obtiveram melhores médias de QV na percepção de QV global (72,45 vs. 67,16; p=0,01) e nos domínios meio ambiente (67,52 vs. 64,23; p=0,04) e psicológico (70,29 vs. 66,44; p=0,03) quando comparadas as não tutoras de animais de estimação (n=110). Ainda, aquelas que afirmaram realizar atividade de lazer (n=214) obtiveram melhores médias de QV na percepção de QV global (72,43 vs. 62,50; p<0,001) e nos domínios físico (63,28 vs. 50,92; p<0,001), meio ambiente (68,22 vs. 58,67; p<0,001), psicológico (71,01 vs. 60,34; p<0,001) e relações sociais (74,73 vs. 65,09; p<0,001) quando comparadas aquelas que não realizavam tal atividade (n=58). **Conclusão:** Pacientes com câncer de mama tutoras de animais de estimação e pacientes que realizam atividades de lazer tem melhores níveis de QV.

PALAVRAS-CHAVE: Qualidade de vida; neoplasias da mama; animais de estimação; atividades de lazer; neoplasias.

Study carried out at Instituto do Câncer do Hospital Pompéia – Caxias do Sul (RS), Brazil.

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INTRODUCTION

Breast cancer diagnosis is related with consequences for most people who experience it, because of treatments and interventions they have undergone, and these factors can affect the quality of life (QoL) of patients¹. Thus, the QoL is established as an important result in the evaluation of a cancer patient. For the World Health Organization, the term QoL is defined as an individual's perception of his or her life position, in the context of culture, value system in which they live, regarding their goals, expectations, standards and concerns². So, it is understood that several specific factors may change the QoL of a cancer patient, in addition to the tumor itself, such as the patient's ability to cope with the illness and the presence or absence of a supportive environment during the period^{3,4}.

Based on this background, and on the many factors that can cover QoL, it is believed that the QoL of patients with breast cancer can benefit from pet ownership, as well as those benefits are reported in several populations⁵⁻⁷. Similarly, other authors reported that the experience of leisure activities has a positive impact on the QoL of different populations and, therefore, it is believed that these benefits can also be extended to this population of women with breast cancer⁸⁻¹⁰.

According to the Pesquisa Nacional de Saúde 2013 (National Health Research 2013), the population of dogs in Brazilian households was estimated in 52.2 million, comprising an average, 1.8 dogs per household with this animal. One has to consider that 44.3% of Brazilian households have at least one dog, equivalent to 28.9 million households with this animal¹¹. Currently, it is known that owning a dog has become a global phenomenon, so, according to the American Pet Products Association – National Pet Owners Survey, in the United States of America (USA), there are about 54.4 million households that have a dog as a pet, corresponding to 77.8 million pet owners¹².

Regarding pet ownership, it is known that during the last decade it has become widely acceptable that pets and care therapy animals may have positive effects on humans¹³. Thus, it is clear that many psychological benefits may arise directly from the companionship that dogs provide to people, since they are affectionate, demonstrate loyalty and the ability to relieve social isolation⁵.

Regarding leisure activities, studies have shown that such activities help the process of adaptation to new circumstances^{14,15}. Thus, it is believed that leisure contributes with the discovery of personal skills, building meaningful relationships, as well as helping to understand life after a traumatic experience¹⁴. Still, researchers argue that involvement in leisure activities assisted in increasing life satisfaction¹⁵.

Therefore, considering the lack of articles about the impact of pets and leisure activities on the QoL of Brazilian women with breast cancer, this study aims to evaluate the benefits in perception of QoL among women with breast cancer related to pet ownership and leisure activity experience.

METHODS

This study was conducted in Instituto do Câncer do Hospital Pompéia (INCAN), located in the city of Caxias do Sul, state of Rio Grande do Sul, Brazil. This is a cross-sectional study, including 272 women with breast cancer, who attended cancer treatment in the institution. This study was approved by the Research Ethics Committee under CAEE number 23407713.1.0000.5331 and an informed consent was obtained from all individual participants included in the study. All study participants completed a self-administrated QoL questionnaire and a questionnaire developed separately.

The QoL was measured using a WHOQOL-Bref questionnaire, validated in Brazil¹⁶. In this questionnaire, the perception of QoL is measured according to four domains (physical health, environmental, psychological and social relationships) and according to global health perceptions. The results were expressed by scores obtained in each domain of QoL, recorded on a scale of 0-100; higher scores in each domain indicated better QoL.

Epidemiological data were collected from a questionnaire containing variables like age, marital status, schooling, lifestyle, pet ownership and the performance of leisure activities. To ensure greater consistency to the responses, participants were guided as to the merits of the responses of the specific variable, in this case, about pet ownership and the performance of leisure activities. Thus, those participants who had a domestic pet under their responsibility were the only ones considered to be pet owners. As for the performance of leisure activities, Kleiber & Nimrod (2009) defined the term as pleasant activities during the free individual time¹⁷; Pressman et al. (2009) exemplified them as activities in which individuals get involved voluntarily when they are free from work or other responsibilities, and may include sports, hobbies, social activities or setting with nature¹⁸.

Statistical Analysis

Data analysis was performed using the software Statistical Package for Social Sciences (SPSS) 22.0. The normality of the distribution of variables was tested graphically and confirmed by the Shapiro-Wilk test. For the analysis of the variables, the Student t-test was used and a value of $\alpha=0.05$ was adopted.

RESULTS

The mean age of patients at the time of the interview was 58.5(±11.6) years. About marital status, 56% were married, and regarding schooling, 47% had not completed elementary level. In relation to clinical staging, 67% were in stage I or II. In relation to surgical treatment, 50% were submitted to partial or total mastectomy without breast reconstruction. Concerning the family history of cancer (kinship of 1st or 2nd degree), it was present in 72% of the cases. In addition, 75% claimed to be non-smokers, and 80% claimed not to be alcoholic. Comorbidities were present in

66% of patients, and most of them presented with hypertension (32% of the cases).

It was observed that women who claimed to be pet owners (n=162) obtained better average of QoL in perceptions of global QoL (p=0.01) and in the environmental (p=0.04) and psychological (p=0.03) domains when compared to non-pet owners. Table 1 presents the results obtained in the QoL domains of the patients evaluated, comparing the pet owners and the non-pet owners.

Next, it was observed that women who reported performing leisure activities (n=214) obtained better averages of QoL in perceptions of global QoL (p<0.001) and in the physical health

(p<0.001), environmental (p<0.001), psychological (p<0.001), and social relationships (p<0.001) when compared to those who claimed to not perform leisure activities. Table 2 presents the results obtained in the QoL domains of patients evaluated, according the WHOQOL-Bref questionnaire, then compared to patients in the performance of leisure activities.

DISCUSSION

This study shows that pet ownership and the practice of leisure activities have a positive impact on the QoL of patients with breast cancer in several domains. Specifically, it was observed that

Table 1. Quality of life according to pet ownership (n=272).

| WHOQOL-Bref | Pet ownership | N | Average | Standard deviation | Mean Difference | 95% Confidence Interval of the Difference | | P-value |
|----------------------|---------------|-----|---------|--------------------|-----------------|---|-------|---------|
| | | | | | | Lower | Upper | |
| Global* | Yes | 162 | 72.45 | 16.49 | 5.30 | 1.07 | 9.51 | 0.01 |
| | No | 110 | 67.16 | 18.54 | | | | |
| Physical health | Yes | 162 | 61.82 | 18.39 | 2.89 | -1.48 | 7.26 | 0.19 |
| | No | 110 | 58.93 | 17.32 | | | | |
| Environment* | Yes | 162 | 67.52 | 13.02 | 3.28 | 0.10 | 6.46 | 0.04 |
| | No | 110 | 64.23 | 13.14 | | | | |
| Psychological* | Yes | 162 | 70.29 | 14.78 | 3.85 | 0.27 | 7.45 | 0.03 |
| | No | 110 | 66.44 | 14.78 | | | | |
| Social relationships | Yes | 162 | 73.92 | 15.66 | 3.09 | -1.34 | 7.51 | 0.17 |
| | No | 110 | 70.83 | 19.67 | | | | |

*Significant value in Student t-test. Highest average in QoL indicates better quality of life.

Table 2. Quality of life according to practice of leisure activities (n=272).

| WHOQOL-Bref | Leisure activities | N | Average | Standard deviation | Mean Difference | 95% Confidence Interval of the Difference | | P-value |
|-----------------------|--------------------|-----|---------|--------------------|-----------------|---|-------|---------|
| | | | | | | Lower | Upper | |
| Global* | Yes | 214 | 72.43 | 16.05 | 9.93 | 4.96 | 14.90 | <0.001 |
| | No | 58 | 62.50 | 20.41 | | | | |
| Physical health* | Yes | 214 | 63.28 | 16.17 | 12.36 | 6.45 | 18.27 | <0.001 |
| | No | 58 | 50.92 | 20.96 | | | | |
| Environment* | Yes | 214 | 68.22 | 12.14 | 9.55 | 5.89 | 13.21 | <0.001 |
| | No | 58 | 58.67 | 14.07 | | | | |
| Psychological* | Yes | 214 | 71.01 | 13.17 | 10.66 | 5.70 | 15.63 | <0.001 |
| | No | 58 | 60.34 | 17.70 | | | | |
| Social relationships* | Yes | 214 | 74.73 | 16.62 | 9.64 | 4.69 | 14.60 | <0.001 |
| | No | 58 | 65.09 | 18.37 | | | | |

*Significant value in Student t-test. Highest average in QoL indicates better quality of life.

those patients who were pet owners had better average in perceptions of global QoL and in the environmental and psychological domains. Moreover, the practice of leisure activities proved to be beneficial in all QoL domains.

The improvement in the QoL of patients who own pets is in agreement with several studies that affirm that owning a pet results in benefits to the owner⁵⁻⁷. In this context, a study showed that pet owners reported less depression when compared to those without pets⁶. Also, a study with adult patients with chronic schizophrenia concluded that the group that participated in animal-assisted therapy showed more social contact, fewer disease symptoms and better QoL than the control group⁷.

Still, the results of this research show that leisure activities improve the QoL of these patients. Some other authors support these findings, arguing that leisure activities can improve the physical function, promote social interactions and improve health and psychological well-being in adults¹⁸⁻²⁰.

Pets are believed to enhance the feelings of autonomy and self-esteem in their owners⁵. Thus, knowing that the global perceptions of QoL takes into account the judgment each person makes about their QoL by evaluating the facets regarding global QoL and general health perceptions¹⁶, we concluded that living with pets improves the perceptions that these individuals have about their own QoL. We understand that the improvement of the pet owner's self-esteem generated by the pet leads to better health perceptions, in the same way that Orlandi et al. (2007) believe that dog-assisted therapy results in effects on the perceptions of symptoms of cancer patients. The study found that pets have the ability to distract the patient when it comes to some symptoms related to this disease, which improves the health perceptions²¹. This thesis is also supported by Friedmann & Son (2009), who claim that the pet's company reduces the suffering to change the owner's perception, by making the situations seem less stressful²².

Breast cancer affects the QoL and health perception of patients². Thus, the results of this research shows that the practice of leisure activities can be beneficial for perceptions, measured in global QoL, compared to those patients who do not perform this type of activity. These results are in accordance with some authors who believe that greater participation in leisure activities is associated with good perception of QoL and improvements in the health context and general perceptions^{10,20}. This can be explained by the belief that the leisure activities can assist social support and thus mediate the process of stressful perceptions, as well as help the adaptation to possible restrictions caused by conditions or chronic diseases^{23,24}.

It is known that among the facets measured by the environmental domain, there are matters regarding physical safety, security and home environment¹⁶. In this study, it was observed that patients who were pet owners, as well as those participating in leisure activities, had better average of QoL.

In this context, pet ownership can contribute with a sense of security and protection, which is one of the main reasons why people adopt a dog²⁵; so, since this fact is restricted to pet owners, we believe that the improvement of this domain is owed to these factors resulting from the ownership of dogs. In addition, the environment in which the person is inserted can determine their independence and autonomy. Since it can lead to dependence on other people to perform certain activities that the person could perform alone, if he were in a safe environment^{19,26}. Therefore, in a study by Pereira et al. (2006), the environmental domain was the one that mostly contributed with the increasing QoL of the individuals¹⁹. It is believed that the fact of living in a safe environment, for these patients, may be crucial to improve the opportunities of leisure and, consequently, increase the compliance in this type of activity.

Some authors support the thesis that pet ownership generates psychological benefits to people^{5,27}. Accordingly, it was shown that patients who were pet owners obtained better results in the psychological domain of QoL. Therefore, pet ownership is believed to be responsible for psychological benefits in the QoL of this group of patients.

Furthermore, the psychological domain had a positive impact when comparing participating and not participating in leisure activities – the group of people who participated has benefits in QoL. This result is in accordance with that of Argimon et al. (2004), which claims that the performance in cognitive skills is proportionally better when there is involvement in leisure activities. This leads to positive perceptions of life, and, consequently, favors the QoL⁹. In this context, and considering that the population of this study is composed of women with breast cancer, we support Ponde and Santana's (2000) thesis, according to which the participation in leisure activities can help to maintain the mental health of women in adverse conditions⁸ – breast cancer, in this case.

It is a known fact that the social relations domain measures facets regarding personal relations, social support and sexual activity¹⁶, emphasizing interpersonal associations, but not considering other sources of social support, such as pets. Therefore, it is believed that this fact influenced the significance of the domain when evaluating the QoL of pet owners and non-pet owners. On the other hand, when related to leisure activities, it is believed that these activities can mediate the relationship between health and social relations¹⁰, since cancer usually results in the social isolation of the patient²⁸, and therefore sources of social support are necessary to encourage the links of that specific group. Thus, we agree with Santos et al. (2014), who claim that the social activities experienced in leisure allows individuals to have greater social connections, with positive influence on the perceptions of QoL²⁰.

The physical health domain includes facets about pain and discomfort, mobility, energy and fatigue, sleep and rest,

activities of daily living, medication dependency and work ability¹⁶. Thus, considering the limitations caused by cancer, it can establish the relation found in this study. Leisure activities showed significant impact on QoL for patients who reported having leisure time in their daily lives. However, this domain was not significant in the same evaluation for pet owners. So, for the leisure activities, this fact is in accordance with other studies that claim that these moments are associated with physical improvement to health and well-being^{18,29}.

CONCLUSIONS

We emphasized that this is the first article about the impact of pets on the QoL of this specific population. Based on the results

of this study, we conclude that patients with breast cancer who are pet owners and patients performing leisure activities have better QoL. Thus, emphasizing the importance of greater attention to programs that encourage leisure activities and specially the recognition of the benefits of pets to this group of patients, health professional must stimulate this condition because of the positive impacts on QoL.

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CLINICAL, MAMMOGRAPHIC AND HISTOPATHOLOGICAL CORRELATION OF BREAST CANCER IN WOMEN AGED BETWEEN 50 AND 70 YEARS

Correlação clínica, mamográfica e histopatológica do câncer mamário em mulheres com idade entre 50 e 70 anos

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ABSTRACT

Objective: To correlate the clinical, mammographic and histopathological findings of women aged between 50 and 70 years old who were diagnosed with breast cancer and were assisted between 1998 and 2013 at the Mastology Outpatient Clinic of the Center for Full Attention to Women's Health in Universidade Estadual de Campinas (CAISM-Unicamp). **Methods:** This was a cross-sectional and retrospective study, in which the medical records and mammograms of 160 women were analyzed, a sufficient sample size for the statistical analysis. The variables used for comparison were the clinical, mammographic and histopathological findings, analyzed through descriptive and associative statistics. **Results:** Of the 160 cases analyzed, 76.9% were symptomatic, and the main clinical findings included palpable nodule (68.1%) and skin alterations (30%). The prevalent mammographic presentations in asymptomatic women were microcalcifications (48.7%), nodules (43.2%) and architectural distortion (8.1%). Regarding the histological type, 81.3% presented invasive ductal carcinoma (IDC) and 10.7%, ductal carcinoma *in situ* (DCIS). **Conclusion:** The present study showed that there was a predominance of symptomatic women with mammographic presentation of spiculated nodules and histological type of IDC. In the other patients with lesions detected in the screening test, pleomorphic microcalcifications were prevalent as the main finding of DCIS. Diagnostic mammography was the main form of detection of breast cancer, which may represent the lack of access of these women to screening or early detection of malignant lesions. This reveals the need to improve control actions and care protocols of these patients.

KEYWORDS: Breast cancer; women; mammography; histology; diagnosis.

RESUMO

Objetivo: Correlacionar os achados clínicos, mamográficos e histopatológicos de mulheres na faixa etária entre 50 e 70 anos que tiveram diagnóstico de câncer mamário e foram atendidas, entre 1998 e 2013, no Ambulatório de Mastologia do Centro de Atenção Integral à Saúde da Mulher da Universidade Estadual de Campinas (CAISM-Unicamp). **Métodos:** Trata-se de um estudo de corte transversal e retrospectivo, no qual foram analisados os prontuários e as mamografias de 160 mulheres, tamanho amostral suficiente para a análise estatística. As variáveis usadas para comparação foram os achados clínicos, mamográficos e histopatológicos, analisados por meio da estatística descritiva e associativa. **Resultados:** Entre os 160 casos analisados, 76,9% eram sintomáticos e os principais achados clínicos incluíram nódulo palpável (68,1%) e alterações de pele (30%). As apresentações mamográficas prevalentes nas mulheres assintomáticas foram microcalcificações (48,7%), nódulos (43,2%) e distorção arquitetural (8,1%). Com relação ao tipo histológico, 81,3% apresentaram carcinoma ductal invasivo (CDI) e 10,7%, carcinoma ductal *in situ* (CDIS). **Conclusão:** O presente trabalho evidenciou que houve uma predominância de mulheres sintomáticas, com apresentação mamográfica de nódulos espiculados e tipo histológico de CDI. Já nas demais pacientes com lesões detectadas no exame de rastreamento predominaram as microcalcificações pleomórficas como o principal achado do CDIS. A mamografia diagnóstica foi a principal forma de detecção do câncer mamário, podendo representar a falta de acesso dessas mulheres aos exames de rastreamento ou à não detecção precoce das lesões malignas, o que revela a necessidade de melhorar as ações de controle e os protocolos de atendimento dessas pacientes.

PALAVRAS-CHAVE: Câncer mamário; mulheres; mamografia; histologia; diagnóstico.

Study carried out at the Center for Full Attention to Women's Health in Universidade Estadual de Campinas – Campinas (SP), Brazil.

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INTRODUCTION

Worldwide, breast cancer is the leading cause of death among women¹. Studies indicate that women aged more than 50 years are the ones most frequently affected by breast cancer, representing the highest mortality rate due to this disease². In Brazil, in 2016, 57,960 new cases of breast cancer were estimated, with an estimated risk of 56.2 cases per 100,000 women³.

Clinical signs of breast cancer are the bulging or retraction of the skin, including the nipple area, the thickening of the skin, abnormal secretion at the nipple, and palpable breast and/or axillary nodules. In cases in which breast cancer is not detected early, these clinical signs may represent the first perception of an abnormality already at an advanced stage⁴.

For the early detection of breast cancer, mammography is considered a highly effective exam, since it allows the identification of subclinical changes such as microcalcifications (MCs), which may represent the first signs of malignancy⁵. This test should be performed on asymptomatic women at regular intervals⁵. According to recent systematic reviews, the impact of mammographic screening on reducing breast cancer mortality may reach 35%^{6,7}.

The Ministry of Health recommends the annual clinical examination of the breasts, starting at the age of 40, for the early detection of female breast cancer. Mammographic screening should be performed in women aged between 50 and 69 years, with a maximum interval of two years in between the examinations. Finally, the practice of clinical examination of the breasts and annual mammography is recommended starting at the age of 35, for women belonging to population groups at high risk of developing breast cancer⁴.

In recent years, Brazil has been presenting a new demographic pattern generated by the reduction of the population growth rate and the increasing life expectancy, resulting in a significant increase in the number of elderly people⁸. In this context, it is relevant to recognize the specificities of breast neoplasms, as well as in which stage these cancers are being diagnosed in women in the age group between 50 and 70 years. These data, associated with the age group, should be considered as important factors in the choice of the most appropriate treatment and in the health policies for the patients.

Although mammography is the basis of screening, therapeutic decisions and prognostic estimates depend on the histopathological diagnosis, classification and extent of lesions⁹. The most common histological type is invasive ductal carcinoma (IDC), which accounts for 80 to 90% of breast carcinomas¹⁰.

Data from the literature describe higher incidence of ductal carcinoma *in situ* (DCIS) in the mammographic presentations of a cluster of pleomorphic microcalcifications, and higher incidence of IDC in mammographic presentations of irregularly shaped nodules and spiculated margins¹¹.

Although there are several studies that associate the mammographic presentation with the histopathological presentation of breast cancer, there are still few and controversial analyses that relate the clinical, mammographic and histopathological presentation of breast cancer in women in this age group. Authors have already demonstrated that MCs may be present in 90% of DCIS cases and in 40% of IDC cases¹². Therefore, it is important to be fully aware of the characteristics of MCs and their association with the histological type of breast cancer.

In view of this information, the present study correlated clinical, mammographic and histopathological data in women aged between 50 and 70 years who had been diagnosed with breast cancer, and evaluated the most relevant factors in these associations.

METHODS

A cross-sectional and retrospective study was carried out. The medical records and mammograms of 160 women with breast cancer diagnosed in the age group between 50 and 70 years old were studied at the Mastology Outpatient Clinic of CAISM-Unicamp, from 1998 to 2013.

The researchers met the requirements of Resolution 196/1996 regarding the ethical aspects and this research was approved by the Research Commission of CAISM, protocol number 008/2014. No direct procedures were performed with patients, which justifies the request for waiver of the Informed Consent Form.

The variables included in the study were clinical, mammographic and histopathological findings. These data were collected by one of the researchers by the review of medical records. Mammographic exams were analyzed by the physicians at the Image Service of CAISM-Unicamp, all experienced in mammography.

Clinical variables included age (established in full years), presence of palpable nodule, skin changes (including retraction or thickening of the skin), and papillary discharge.

Mammographic variables included the breast density pattern, defined according to the level of replacement of the fibroglandular parenchyma with adipose tissue, being classified into four patterns according to the Breast Imaging Reporting and Data System (BIRADS):

- fat deposition in the breasts (fibroglandular parenchyma almost completely liposubstituted);
- breasts with accentuated liposubstitution (fibroglandular parenchyma dispersed);
- heterogeneously dense breasts (minor replacement with adipose tissue, which may obscure small nodules); and
- extremely dense breasts (extremely dense fibroglandular parenchyma, which reduces the sensitivity of the method)¹³.

The other mammographic variables were the primary and secondary findings¹³. Through the BIRADS system, the former comprise the ones most typically associated with breast cancer. Our study includes as variables the following primary findings:

- nodule;
- microcalcifications; and
- architectural distortion.

Secondary mammographic findings are those that may be associated with the diagnosis of breast cancer, but are considered of importance when identified with primary findings. The most frequent secondary findings that were variables of this study are:

- skin retraction;
- skin thickening; and
- nipple retraction.

Nodules visible on both mammographic incidences were evaluated for shape (round, oval, macrolobulated or irregular), margins (circumscribed, microlobulated, poorly defined or spiculated), size (defined in cm) and association with MCs¹³.

MCs, present in craniocaudal (CC) and mid-lateral oblique (MLO) incidence, were described for morphology (monomorphic, pleomorphic and amorphous) and distribution (grouping, linear, segmental or branched)¹³.

Architectural distortion was present when characterized by fine and radiated spikes converging to a point in both mammographic incidences¹⁴. Histopathological types were classified as IDC, CDIS and others (covering the other histological types of breast cancer)¹⁴.

The sample comprised 160 patients, which is sufficient for the statistical analysis of this research using the method by Nisen and Schwertman, requiring 10 subjects per predictive variable¹⁵. The variables included were:

- age;
- palpable nodule;
- skin changes;
- papillary discharge;
- primary mammographic findings (nodules, microcalcifications and architectural distortion);
- secondary mammographic findings (skin thickening, skin retraction and nipple retraction); and
- histological type (CDIS, IDC and others).

Based on these data, it is estimated that the sample should be composed of at least 130 patients.

The medical records of 160 women assisted consecutively between 1998 and 2013 were selected from a database of the Mastology Section of CAISM. The inclusion criteria were: patients aged between 50 and 70 years, diagnosed with breast cancer and assisted at the Mastology Outpatient Clinic of

CAISM between 1998 and 2013. Cases that did not fit these criteria were excluded.

Data collection sheets especially prepared for this study were used, containing the clinical, mammographic and histopathological information of each patient. The data obtained were typed twice in the Excel software due to quality control, to check for inconsistency in the insertion of information. Later, it was organized and stored in a specific database.

The analysis of the collected data was conducted through descriptive statistics with simple (n) and relative frequencies (%) for the categorical variables, and with the calculations of mean, standard deviation, median and maximum and minimum values for continuous variables. Finally, the association between the categorical variables was verified using the χ^2 or Fisher's exact tests, and the comparison between groups in relation to numerical variables was performed using the Mann-Whitney or Kruskal-Wallis tests. The level of significance was 5%. Data were analyzed using the SAS software, version 9.4.

RESULTS

In total, 160 charts and mammograms of women with breast cancer assisted at the Mastology Outpatient Clinic of CAISM-Unicamp were reviewed. The mean age was 61 years; the mean age of asymptomatic women was 60.8 years, and the mean age of symptomatic women was 60.9, with no significant statistically difference.

The most frequent breast pattern among the women in the study was marked by fat deposition, with prevalence of 81 (50.63%) and mean age of 61 years. Whereas the predominance of women with heterogeneously dense breasts was 39 (24.38%) and mean age of 51 years, the number of women with liposubstituted breasts was 33 (20.63%), with mean age of 64 years. The number of women with dense breasts was 7 (4.38%), and mean age of 59 years.

The prevalence of symptomatic women was 123 (76.9%), and 109 (68.1%) had a palpable nodule, 49 (30.6%) presented skin alterations, and 8 (5%), papillary discharge. Asymptomatic women represented 37 (23.1%) of the patients included in the study.

Among the 49 women with skin changes, 45 (91.8%) had a nodule as a primary mammographic finding, with p-value of 0.0173. The presence of papillary discharge was not significantly associated with the mammographic findings (Table 1).

Regarding the primary mammographic findings, 129 (81%) women presented nodule, 24 (15%) had MCs, and 5, (4%) architectural distortion. The presence of secondary mammographic findings was found in 27 (10.1%) cases.

As to the prevalent characteristics of the nodules presented in 129 women, 79 (61.2%) had irregular shape, and 96 (74.4%) had spiculated margins, with mean size of 2.7 cm (Figures 1 and 2).

Regarding the predominant characteristics of MCs present in 24 women, 16 (66.7%) were pleomorphic, and 8 (33.3) were amorphous. Still on MCs, 13 (54.2%) were grouped.

A predominance of 130 (81.3%) IDC, 17 (10.6%) CDIS and 13 (8.1%) other histological types was found in histopathological findings.

Among the 130 women with IDC, 113 (86.9%) showed a nodule as a primary mammographic finding, with $p < 0.0001$, 89 (78.8%) had spiculated margins, with p -value of 0.0029 (Table 2). Among the 17 women with CDIS, 11 (64.7%) had MCs as the primary mammographic finding, with $p < 0.0001$, and 4 (36.4%) were grouped, with $p < 0.0001$ (Table 3).

DISCUSSION

In Brazil, the Ministry of Health recommends mammography screening in women aged between 50 and 69, but the national program is not organized. Therefore, each state and/or city has been carrying out isolated actions aiming at providing access to mammography screening to as many women as possible⁷. So, even if minor, there was an increase in the number of diagnoses of breast cancer in the initial stages in the last 15 years, and the diagnosis of CDIS presented a growth of 0.2 to 6.2%¹⁶.

However, studies also show great inequality in these numbers depending on the region of Brazil. A recent analysis demonstrated an increase in breast cancer mortality rates in the North and Northeast States, attributed to the patients' poor access to diagnosis, surgery and chemotherapy¹⁷.

Although the number of CDIS diagnoses has increased in the last five years, it is still below the rates observed in the countries of Eastern Europe and the United States, ranging from 11 to 25%. Such level was reached due to population screening programs¹⁷.

Data in the literature also demonstrate great agreement on the efficacy of mammographic screening for early detection and reduction of breast cancer mortality¹⁸.

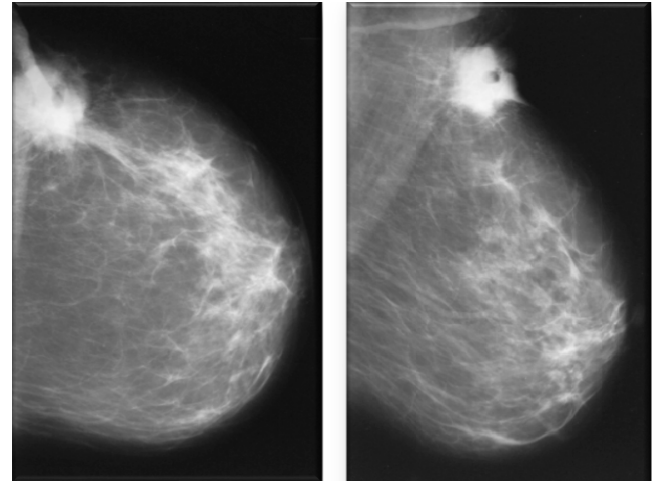


Figure 1. A 61-year-old patient with a palpable nodule in the left breast. In mammography, the patient presented breasts with accentuated liposubstitution, 3.4 cm irregularly shaped nodule and spiculated margins, in the superolateral quadrant of the left breast, with skin retraction and thickening. The anatomopathological study presented invasive ductal carcinoma.

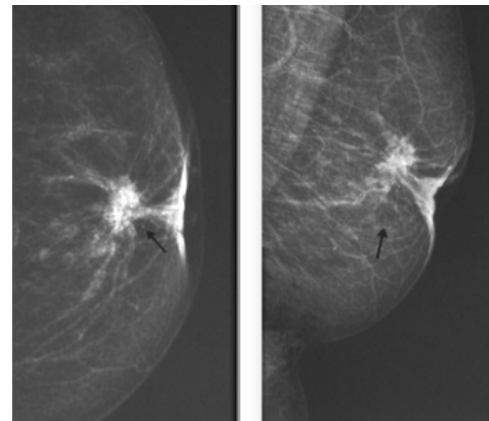


Figure 2. A 62-year-old patient had a palpable nodule in the left breast, skin thickening and nipple retraction. Mammography presents liposubstituted breasts, a 2-cm irregularly shaped nodule, and spiculated margins of retroareolar location in the left breast, associated with microcalcifications. She also presents with nipple retraction, skin retraction and thickening. The anatomopathological study presented invasive ductal carcinoma.

Table 1. Association between mammographic presentation and clinical presentation of breast cancer.

| Variables | Palpable nodule | | | Skin changes | | | Papillary discharge | | |
|-----------------------|-----------------|-----------|---------|--------------|-----------|---------|---------------------|------------|---------|
| | Yes | No | P-Value | Yes | No | P-Value | Yes | No | P-Value |
| | n (%) | n (%) | | n (%) | n (%) | | n (%) | n (%) | |
| Nodule in mammography | | | | | | | | | |
| Yes | 107 (98.2) | 22 (43.1) | <0.0001 | 45 (91.8) | 84 (75.7) | 0.0173 | 8 (100) | 121 (79.6) | 0.3559 |
| No | 2 (1.8) | 29 (56.9) | | 4 (8.2) | 27 (24.3) | | 0 (0) | 31 (20.4) | |
| Microcalcifications | | | | | | | | | |
| Yes | 2 (1.8) | 22 (43.1) | <0.0001 | 1 (2) | 23 (20.7) | 0.0023 | 0 (0) | 24 (15.8) | 0.6072 |
| No | 107 (98.2) | 29 (56.9) | | 48 (98) | 88 (79.3) | | 8 (100) | 128 (84.2) | |

In the present study, the number of CDIS diagnoses was 10.6%, and the frequency of IDC diagnoses was 81.3%, close to those found in other Brazilian studies, which confirms the high number of late diagnoses of this disease¹⁹.

In our study, it was confirmed that breast density suffers modifications due to age, with a gradual replacement of fibroglandular tissue with adipose tissue. Women with liposubstituted breasts had the highest mean age, and women with dense breasts had the lowest mean age. This fact has also been proven in previous analyzes²⁰.

As described in the literature, the extent of mammary neoplasm to the skin may lead to the appearance of secondary mammographic findings (skin retraction and thickening, and nipple retraction), related to high suspicion of malignancy²¹. In the present study, there was low prevalence of secondary mammographic

findings among women with breast cancer, showing that the insufficiency of these findings should not be interpreted as an absence of tumor malignancy²¹.

In this study, only 23.1% (n=37) of the 160 women with breast cancer were diagnosed in the infraclinical stage of the disease, through mammographic screening, indicating the need to increase the access to this diagnostic method.

Our data show that 76.5% of the CDIS cases were asymptomatic, and only 16.2% of the IDC cases were asymptomatic, revealing the greater difficulty in diagnosing the first, in accordance with the literature²². Research indicates that approximately 75 to 95% of CDIS cases are currently diagnosed in asymptomatic women because of the finding of calcifications in mammography, showing the importance of this test in the early diagnosis of breast cancer²².

Regarding the mammographic lesions analyzed, there was predominance of MCs in asymptomatic patients and an expressive number of nodules in those that presented clinical signs and symptoms, confirming the results found by other authors^{23,24}.

Among the symptomatic women, the order of prevalence of clinical signs of breast cancer pointed out by our research corresponded to palpable nodule, skin alterations and papillary discharge, similarly to the information presented by other authors^{25,26}. In our study, we also found strong association between skin changes at the clinical examination and the presence of a nodule on mammography, but this did not occur with papillary discharge, which did not present a significant association with the mammographic findings.

In relation to the most important mammographic characteristics for nodule malignancy, spiculated margins and irregular shape stood out, as shown in the data in the literature²⁷.

With respect to MCs, a greater association of malignancy was observed in the presence of pleomorphic and grouped MCs, whereas amorphous MCs presented low probability of malignancy. Such information was in accordance with results found by other authors²⁸⁻³⁰.

In conclusion, the present study showed there was a prevalence of symptomatic women, with mammographic presentation of spiculated nodules and histological type of IDC. In the patients with lesions detected in the screening test, the pleomorphic and grouped MCs prevailed as the main finding of the CDIS.

Diagnostic mammography was the main form of breast cancer detection. This suggests that the late detection of malignant lesions may be related with the lack of access of these women to the screening tests or to the early mammographic detection of these lesions, revealing the need to improve control actions and care protocols of these patients.

Table 2. Association between mammographic presentation of the nodule and histological presentation of breast cancer.

| Variables | IDC | CDIS | Other | P-value |
|--------------------------|------------|----------|-----------|---------|
| | n (%) | n (%) | n (%) | |
| Nodule | 113 (86.9) | 6 (35.3) | 10 (76.9) | <0.0001 |
| Morphology of the nodule | | | | |
| Round | 16 (14.2) | 1 (16.7) | 3 (30) | 0.2635 |
| Oval | 14 (12.4) | 0 (0) | 2 (20) | |
| Irregular | 71 (62.8) | 5 (83.3) | 3 (30) | |
| Macrolobulated | 12 (10.6) | 0 (0) | 2 (20) | |
| Nodule margin | | | | |
| Spiculated | 89 (78.8) | 4 (66.7) | 3 (30) | 0.0029 |
| Poorly defined | 16 (14.2) | 1 (16.7) | 4 (40) | |
| Microlobulated | 5 (4.4) | 1 (16.7) | 0 (0) | |
| Well defined | 3 (2.6) | 0 (0) | 3 (30) | |

IDC: invasive ductal carcinoma; DCIS: ductal carcinoma *in situ*.

Table 3. Association between mammographic presentation of microcalcifications and histological presentation of breast cancer.

| Variables | IDC | CDIS | Other | P-value |
|-------------------------------------|----------|-----------|----------|---------|
| | n (%) | n (%) | n (%) | |
| Microcalcifications | 10 (7.7) | 11 (64.7) | 3 (23) | <0.0001 |
| Morphology of microcalcifications | | | | |
| Pleomorphic | 8 (80) | 7 (63.6) | 1 (33.3) | 0.3620 |
| Amorphous | 2 (20) | 4 (36.4) | 2 (66.7) | |
| Distribution of microcalcifications | | | | |
| Grouping | 6 (60) | 4 (36.4) | 3 (100) | <0.0001 |
| Linear | 1 (10) | 1 (9) | 0 (0) | |
| Segmental | 2 (20) | 3 (27.3) | 0 (0) | |
| Branched | 1 (10) | 3 (27.3) | 0 (0) | |

IDC: invasive ductal carcinoma; DCIS: ductal carcinoma *in situ*.

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ANALYSIS OF THE ERYTHROCYTE ALLOIMMUNIZATION PROFILE OF WOMEN WITH BREAST CANCER AT THE NATIONAL CANCER INSTITUTE

Análise do perfil de aloimunização eritrocitária de mulheres com câncer de mama do Instituto Nacional do Câncer

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ABSTRACT

Objective: To describe the erythrocyte alloimmunization profile of women diagnosed with breast cancer at the National Cancer Institute, based on a comparison between routine antibody and irregular enzyme techniques. **Methods:** Experimental and prospective study with the application of human antiglobulin techniques and enzymatic technique in the search for irregular antibodies in pre-transfusion tests of women with breast cancer treated at the hemotherapy service of Hospital do Câncer III, between June 2015 and May 2016. The variables were compared using Pearson's χ^2 test or G-test, when indicated. **Results:** 429 cases were included. Of the total, 8 (1.86%) presented positive antibody screening test in routine human antiglobulin technique, while 32 (7.6%) were observed in the enzymatic technique. Significant differences were observed between alloimmunized and non-alloimmunized patients regarding ethnicity, RhD classification, transfusion history and alloantibody incidence time. **Conclusion:** The application of the enzymatic technique is proposed as a routine method in patients with breast cancer, as a way of avoiding transfusion reactions and ineffective phenotype transfusions.

KEYWORDS: Women's health; breast neoplasms; blood group antigens; isoantibodies.

RESUMO

Objetivos: Descrever o perfil de aloimunização eritrocitária de mulheres diagnosticadas com câncer de mama no Instituto Nacional do Câncer a partir da comparação entre as técnicas de pesquisa de anticorpo irregular utilizada em rotina e a técnica enzimática implantada. **Métodos:** Estudo experimental e prospectivo com aplicação das técnicas de antiglobulina humana e técnica enzimática na pesquisa de anticorpos irregulares de testes pré-transfusionais de mulheres com câncer de mama, atendidas no serviço de hemoterapia do Hospital do Câncer III, no período de junho de 2015 a maio de 2016. As variáveis foram comparadas pelo teste do χ^2 de Pearson ou teste G, quando indicado. **Resultados:** Foram incluídos 429 casos. Do total, 8 (1,86%) apresentaram pesquisa de anticorpos irregulares positiva em técnica de antiglobulina humana na rotina, enquanto 32 (7,6%) foram observados na técnica enzimática. Foram observadas diferenças significantes entre aloimunizados e não aloimunizados quanto à etnia, classificação RhD, histórico transfusional e tempo de incidência de aloanticorpo. **Conclusão:** Propomos a aplicação da técnica enzimática como método de rotina em pacientes com câncer de mama, como forma de evitar reações transfusionais e transfusões ineficazes.

PALAVRAS-CHAVE: Saúde da mulher; neoplasias da mama; antígenos de grupos sanguíneos; aloanticorpos.

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INTRODUCTION

Alloimmunization against erythrocyte antigens is an increasingly common problem in oncology patients undergoing transfusion, even in those who are transfused sporadically, such as patients with breast cancer. Since irregular antibodies occur in approximately 0.3–2% of the general population, screening and identification of antibodies are indispensable for proper blood selection for transfusion. Information regarding age, sex, race and clinical, transfusion, and pregnancy histories may provide clues to the identification of these antibodies. The chance of finding irregular antibodies in the serum of receptors increases mainly among females, due to the chance of exposure before pregnancy¹.

The detection of irregular antibodies must be performed with a sensitive technique, capable of detecting antibodies of greater clinical relevance. Failure to detect an alloantibody can lead to acute or late hemolytic transfusion reactions with intensities that may range from mild to severe and further impair the clinical condition of the recipient. Many irregular antibodies disappear over time and may reappear after a new antigenic stimulus. In addition to the low titers, the presence of autoantibody may also mask the presence of alloantibodies of clinical importance².

Hospital do Câncer III (HCIII) mainly serves the female population with a diagnosis of breast cancer. It is a reference for using screening techniques capable of potentiating the identification of antibodies of clinical significance. The set of tests performed before a transfusion is known as pre-transfusion testing. Every transfusion candidate should have a sample of their blood drawn for testing the presence of antigens and antibodies in their red blood cells and serum/plasma, respectively. According to Ordinance No. 158, dated February 4, 2016, from the Brazilian Ministry of Health, mandatory procedures include blood typing for ABO and RhD (Rh blood group D antigen) blood group systems, irregular antibody screening (IAS) and cross-matching³.

Currently, the procedures applied to IAS at HCIII are incubation at 37°C with antiglobulin test (AGT) and gel centrifugation technique. With the current screening technique, the frequency of irregular antibodies is 1.25% out of 2,396 patients assessed in the period between 2011 and 2013. It has been shown that approximately 83% of the irregular antibodies identified in this group of patients may present increased reactivity in an enzymatic medium⁴.

Proteolytic enzymes may enhance the reactivity of some alloantibodies by enzymatic treatment of test red cells. They are especially indicated as an accessory method of identification in cases of antibody mixing, or even in cases of clinically important antibodies but in low titers. Enzyme-treated hemocytes will have the antigens M, N, S, s, Fya and Fyb destroyed and will fail to react with antibodies from the tested serum. On the other hand, Rh, Kell, P, I, Kidd and Lewis blood group antigens will not be destroyed and react more strongly with their antibodies⁵.

As the behavior profile of irregular antibodies is not yet well known in this group of patients, the present study aimed to compare AGT and enzyme techniques, and to describe the alloimmunization profile of breast cancer patients at the HCIII.

METHODS

We performed an experimental and prospective study to analyze erythrocyte alloimmunization in a period of one year (June 2015–May 2016).

The study was carried out at the transfusion center of HCIII, a hospital unit of the Brazilian National Cancer Institute (INCA), located in the city of Rio de Janeiro. Participants in this study included patients with a baseline diagnosis of breast cancer (ICD C50). The inclusion criteria for participation in the study were: female patients treated at chemotherapy, clinical oncology, mastology and surgical centers of the institution. We excluded male patients, female patients who did not continue treatment at the institution and patients suspected of using of anti-D immunoprophylaxis.

We selected peripheral blood samples from included patients for analysis. All samples were submitted to IAS by Liss-AGT and NaCl/enzyme techniques. In cases of positive IAS, we identified the irregular antibody specificity in the corresponding technique.

Positive antibody screening patients were invited to participate in the present study through a formal interview in a suitable environment in order to preserve their privacy. All the patients who accepted to participate in the study signed an informed consent form (ICF). We used a questionnaire to verify alloimmunization profiles and collect sociodemographic and clinical data, which included age, ethnicity (white, black, mulatto and Asian), blood group (A, B, AB and O) and transfusion and pregnancy histories. Pregnancy history was represented by the number of previous pregnancies (zero, one, two or more). Transfusional history was represented by two variables: number of transfusions outside the institution and number of transfusions at the institution (one, two, three or more).

Ordinal and nominal variables were compared by Pearson's χ^2 test, or G-test, when indicated. Statistical analysis was performed using the Bioestat statistical package (version 5.0, 2015). We developed a logistic regression model to identify the variables independently, considering a significance level of 0.10.

This study was approved by the Research Ethics Committee of Hospital das Clínicas, Medical School of Ribeirão Preto (protocol CAAE-41619415.9.0000.5440), under the title *Avaliação da implementação da pesquisa de anticorpos irregulares com hemácias tratadas com enzima nos exames pré-transfusionais de pacientes com neoplasia maligna de mama do Instituto Nacional do Câncer*. All recommendations of good clinical practices were followed in accordance with the Resolution of the Brazilian National Health Council (CNS) nº 466/2012 and the Helsinki Convention.

RESULTS

From June 2015 to May 2016, blood samples were collected from 429 breast cancer patients who were treated at the transfusion center of HCIII, part of the Brazilian National Cancer Institute (INCA). The samples were obtained from pre-transfusion immunohematological tests, of which 112 were transfusion requests and 317, surgical reservations. Of the total, 8 (1.86%) showed positive IAS results by Liss/AGT technique in routine screening. Irregular antibodies specificity identification by Liss/AGT revealed 12 alloantibodies, with anti-D being the most predominant in 5 samples (41.6%), followed by 2 anti-E (16.6), 2 anti-C (16.6%), 1 anti-lea (8.4%), 1 anti-Jka (8.4%) and 1 anti-S (8.4%). All 421 samples that showed a negative IAS result with Liss/AGT underwent complementary testing with papainized red cells, which resulted in 32 positive samples (7.6%). Identification of irregular antibody specificity by enzyme technique revealed 37 antibodies. Anti-E was the most predominant in 13 samples (35%), followed by 9 warm public autoantibodies (24%), 7 anti-Lea antibodies (19%), 4 Anti-D (11%), 1 anti-C (2.75%), 1 anti-Cw (2.75%), 1 anti-K (2.75%) and anti-Dia (2.75%) (Table 1).

The 429 studied patients (40 alloimmunized and 389 non-alloimmunized) were analyzed together as to: age group and ethnicity; ABO/Rh typing; transfusion and pregnancy histories; time between antibody identification by Liss/AGT or enzyme techniques; last pregnancy; and last transfusion.

Regarding age, 147 patients (34.2%) were between 18 and 49, 216 (50.3%) between 50 and 69 and 66 (15.5%) were 70 years or older. Among the alloimmunized patients, 23 (57.5%) aged between 50 and 69 years and 193 (49.6%) non-alloimmunized patients belonged to the same age group. Despite the higher concentration of alloimmunized and non-alloimmunized patients in the intermediate age range (50–69 years), there was no statistically significant difference between the groups (χ^2 ; $p = 0.4314$).

In relation to ethnicity, 192 (44.7%) patients were white, 150 (34.9%) were mulatto, 81 (18.8%) were black and 6 (1.6%) were Asian. Among the alloimmunized patients, 20 (50%) were white, 9 (22.5%) were mulatto, 9 (22.5%) were black and 2 (5%) were Asian, whereas the percentages among non-alloimmunized patients were 44.2%, 36.2%, 18.5% and 1.1%, respectively. Most patients described themselves as white people, with an observed statistically significant difference between the two groups (χ^2 test, $p = 0.0847$) (Table 2).

As for ABO typing, 189 patients (44%) belonged to blood group O; 162 (37.7%) A; 63 (14.7%), B; and 15 (3.6%), AB. The most prevalent blood type among the alloimmunized patients was group O, 19 patients (47.5%), followed by A, 13 patients (32.5%). The most frequent ABO types among non-alloimmunized were also O (43.7%) and A (38.3%), with no statistically significant difference between the two groups (G-test, $p = 0.8779$). As for RhD typing, 382 (89%) were RhD positive and 47 (11%) were RhD negative. The predominance of RhD positive was verified in both groups, with 75% and 90%, respectively. A statistically significant difference was observed between the groups (G-test, $p = 0.0147$) (Table 3).

Of the total studied patients, only 65 (16%) had a history of transfusion. Among the alloimmunized patients, 29 (72.5%) had not received previous transfusions and 11 (27.5%) received transfusions of packed red blood cell at HCIII before the irregular antibody identification by this study. Among the non-alloimmunized patients, 335 (86%) had no transfusion history, determining a statistically significant difference between the two groups (χ^2 test; $p = 0.0398$). Regarding the number of red blood cell transfusions at HCIII, 31 patients (47.7%) received 1-2 transfusions, 22 (33.8%) received 3-4 transfusions, and 12 patients (18.5%) received 5 transfusions or more. Of the total alloimmunized patients, 6 (54.5%) received up to 2 transfusions, 3 (27.3%) received 3–4

Table 1. Percentage Distribution and specificity of erythrocyte alloantibodies, Rio de Janeiro, 2015–2016.

| Alloantibody | INCA's Routine Liss/AGT n (%) | NAEL/ENZYME n (%) | Associated techniques n (%) |
|--------------|----------------------------------|----------------------|--------------------------------|
| Anti-D | 5 (41.6) | 4 (11) | 9 (18.7) |
| Anti-E | 2 (16.6) | 13 (35) | 15 (31.2) |
| Anti-C | 2 (16.6) | 1 (2.75) | 3 (6.2) |
| Anti-cw | 0 (0.0) | 1 (2.75) | 1 (2.12) |
| Anti-K | 0 (0.0) | 1 (2.75) | 1 (2.12) |
| Anti-lea | 1 (8.4) | 7 (19) | 7 (14.6) |
| Anti-Jka | 1 (8.4) | 0 (0.0) | 1 (2.12) |
| Anti-Dia | 0 (0.0) | 1 (2.75) | 1 (2.12) |
| Anti-S | 1 (8.4) | 0 (0.0) | 1 (2.12) |
| Autoantibody | 0 (0.0) | 9 (24.3) | 9 (18.7) |
| Total | 12 (100) | 37 (100) | 48 (100) |

INCA: *Instituto Nacional do Câncer* (Brazilian National Cancer Institute); AGT: antiglobulin test.

transfusions, and 2 (18.2%) received more than 5 transfusions. Among the non-alloimmunized patients, the figures were 46.3, 35.2 and 18.5%, respectively. We observed no statistically significant difference between alloimmunized and non-alloimmunized patients (G-test, $p = 0.8676$). Of the 429 women studied, 387 (90.2%) had a pregnancy history and 42 (9.8%) did not. Of the 40 alloimmunized patients, 37 (92.50%) reported a pregnancy history. Among the non-alloimmunized patients, the vast majority (90%) reported a pregnancy history. There was no statistically significant difference between the two groups (χ^2 test; $p = 0.8162$). Concerning women with a pregnancy history, 76 (17.7%) had only 1 pregnancy and 311 (72.3%) reported having had 2 or more pregnancies. Among the alloimmunized patients, 5 (13.5%) had only 1 pregnancy and 32 (86.5%) had 2 or more pregnancies. Percentage values for non-alloimmunized patients were 20.3 and 79.7%, respectively. There was no statistically significant difference between alloimmunized and non-alloimmunized patients (G test, $p = 0.5128$) (Table 4).

In order to analyze the frequency of irregular antibodies of the 387 women with a pregnancy history, we observed the

time elapsed between the last pregnancy and the first IAS performed in this study. The results showed that 52 (13.4%) ranged from 1-9 years, 82 (21.2%) 10-19 years and 253 (65.4%) 20 years or more. Of the alloimmunized patients, 5 (13.6%) revealed a frequency of up to 9 years, 8 (21.6%) 10-19 years and 24 (64.8%) 20 years or more. Among the non-alloimmunized patients, the values were 13.5%, 21.1% and 65.4%, respectively. In spite of the higher concentration of alloimmunized and non-alloimmunized in the longest frequency (> 20 years), there was no statistically significant difference between the groups (G-test, $p = 0.9973$). We observed the time elapsed between the last transfusion and the first IAS performed in this study in the 60 women with a history of transfusion in order to estimate the incidence of irregular antibodies. Considering that a secondary immune response can occur within a period of up to 72 hours, the selected patients were distributed in margins of higher and lower values than that time. Of the 60 women studied, 51 (85%) showed time greater than 72 hours and only 9 (15%) presented equal and/or inferior time. All alloimmunized patients (100%) had a result superior to 72 hours. Among the

Table 2. Patient distribution according to age and ethnicity, Rio de Janeiro, 2015–2016.

| | Alloimmunized n (%) | Non-alloimmunized n (%) | Chi-square test (χ^2) |
|-------------------|------------------------|----------------------------|---|
| Age group (years) | | | |
| 18–49 | 10 (25) | 137 (35.2) | Contingency = 3x2 $\chi^2 = 1.682$ Degrees of freedom = 2 P = 0.4314 |
| 50–69 | 23 (57.5) | 193 (49.6) | |
| 70 | 7 (17.5) | 59 (15.2) | |
| Total | 40 (100) | 389 (100) | |
| Ethnicity | | | |
| White | 20 (50) | 172 (44.2) | Contingency = 4x2 $\chi^2 = 6.628$ Degrees of freedom = 3 P = 0.0847 |
| Mulatto | 9 (22.5) | 141 (36.2) | |
| Black | 9 (22.5) | 72 (18.5) | |
| Asian | 2 (5) | 4 (1.1) | |
| Total | 40 (100) | 389 (100) | |

Table 3. Patient distribution according to ABO and RhD typing, Rio de Janeiro, 2015–2016.

| | Alloimmunized n (%) | Non-alloimmunized n (%) | G-test |
|------------|------------------------|----------------------------|--|
| ABO typing | | | |
| O | 19 (47.5) | 149 (38.3) | Contingency = 4x2 Degrees of freedom = 3 G test = 0.7119 P = 0.8791 |
| A | 13 (32.5) | 193 (49.6) | |
| B | 6 (15) | 59 (15.2) | |
| AB | 2 (5) | 170 (43.7) | |
| Total | 40 (100) | 389 (100) | |
| RhD typing | | | |
| Positive | 30 (75) | 352 (90) | Contingency = 4x2 Degrees of freedom = 3 G-test = 7.0675 P = 0.0147 |
| Negative | 10 (15) | 37 (10) | |
| Total | 40 (100) | 389 (100) | |

non-alloimmunized patients, the same time was present in 41 (82%) patients. When comparing alloimmunized and non-alloimmunized patients, a statistically significant difference was observed (G-test, $p = 0.0583$) (Table 5).

DISCUSSION

Regarding the age group of individuals with positive IAS, we observed that the highest frequency of alloimmunization was between 50-69 years (57.5%). Our results were similar to that found in Shin⁶, in which alloimmunized cancer patients showed a frequency of 75.4% in the age group over 50 years of age. Our results are inconsistent with those found by Zaman et al.⁷ in their study

on alloimmunization in hematological and oncological patients in India. They observed that only 28% of alloimmunized patients were older than 50 years of age. Mohsin⁸ also presented divergent results from ours. In their study, breast cancer patients accounted for 68% of the analyzed patients and the mean age of the alloimmunized group was 49 years. Despite the low alloimmunization rate in the elderly (≥ 70 years), our study shows that, of all alloimmunized patients, the majority (65.8%) was 50 years of age or older, an index very similar to the control group (64.8%), demonstrating that advanced age could be directly linked to alloantibody titer decay. According to Cozac⁹, some vaccine-related studies have shown that aging weakens B and T lymphocyte response to pathogens, thus shortening the duration of

Table 4. Patient distribution according to transfusion and pregnancy histories, Rio de Janeiro, 2015–2016.

| | Alloimmunized n (%) | Non-alloimmunized n (%) | χ^2 and G-tests |
|------------------------|------------------------|----------------------------|---|
| Transfusion history | | | |
| Yes | 11 (27.5) | 54 (14) | Contingency = 2x2 Degrees of freedom = 1 $\chi^2 = 5.232$ $p = 0.0398$ |
| No | 29 (72.5) | 335 (86) | |
| Total | 40 (100) | 389 (100) | |
| Number of transfusions | | | |
| 1-2 | 6 (54.5) | 25 (46.3) | Contingency = 3x2 Degrees of freedom = 2 G-test = 0.3051 P = 0.8676 |
| 3-4 | 3 (27.3) | 19 (35.2) | |
| 5 or more | 2 (18.2) | 10 (18.5) | |
| Total | 11 (100) | 54 (100) | |
| Pregnancy history | | | |
| Yes | 37 (92.5) | 350 (90) | Contingency = 2x2 Degrees of freedom = 1 $\chi^2 = 0.262$ $p = 0.8162$ |
| No | 3 (7.5) | 39 (10) | |
| Total | 40 (100) | 389 (100) | |
| Number of pregnancies | | | |
| 0 | 3 (7.5) | 39 (10.1) | Contingency = 3x2 Degrees of freedom = 2 G-test = 1.3357 P = 0.5128 |
| 1 | 5 (12.5) | 71 (18.2) | |
| 2 or more | 32 (80) | 279 (71.7) | |
| Total | 40 (100) | 389 (100) | |

Table 5. Patient distribution according to prevalence frequency and alloantibody incidence, Rio de Janeiro, 2015–2016.

| | Alloimmunized n (%) | Non-alloimmunized n (%) | G-test |
|------------------------------|------------------------|----------------------------|--|
| Prevalence frequency (years) | | | |
| 1–9 | 5 (13.6) | 47 (13.5) | Contingency = 3x2 Degrees of freedom = 2 G-test = 0.0054 P = 0.9973 |
| 10–19 | 8 (21.6) | 74 (21.1) | |
| 20 or more | 24 (64.8) | 229 (65.4) | |
| Total | 37 (100) | 350 (100) | |
| Incidence time (hours) | | | |
| Less than 72 | 0 (0.00) | 9 (18) | Contingency = 2x2 Degrees of freedom = 1 G-test = 3.5857 P = 0.0583 |
| 72 or more | 10 (100) | 41 (82) | |
| Total | 10 (100) | 50 (100) | |

immune protection, which should also reflect the persistence of the formed alloantibodies.

In our study, we found a predominance of 50% in alloimmunized Caucasian individuals, with a similar rate in the control group (44.7%) and a statistically significant difference (χ^2 test; $p = 0.0847$). When considering non-Caucasian patients, we observed slightly equivalent rates between alloimmunized (50%) and non-alloimmunized patients (55.8%) and the total number of individuals analyzed (55.3%). With these data, we can infer that erythrocyte alloimmunization occurs from the differences between the erythrocyte phenotypic patterns of the population, whether its exposure is mainly due to pregnancy or from transfusions between donors and recipients. The white predominance in our study over an antigenic exposure of a predominantly brown population in Rio de Janeiro¹⁰ favors erythrocyte alloimmunization.

Among the Brazilian population, the prevalence of the RhD negative phenotype is variable and heterogeneous among the various regions of the country. In our study, the predominance of RhD positive typing was observed in both alloimmunized and non-alloimmunized patients (75 and 90%, respectively). A similar result was observed in a study in Rio de Janeiro, in which the frequency of RhD positive blood donors was 90.2%. The highest proportion of RhD negative women in the alloimmunized group, compared to non-alloimmunized women, falls on the specificity of the irregular antibodies identified in the present study. Based on the assumption that D is considered the most immunogenic of the erythrocyte antigens after the ABO blood group system¹⁰, our study showed anti-D as the main alloantibody identified with AGT.

We observed that 27.5% of the positive IAS patients in our study had a history of transfusion. This result is similar to Alves's findings¹¹, in which 29.41% of the alloimmunized patients had previously received transfusions. In our study, alloimmunized individuals received between 1 and 7 transfusions of red blood cells, with a mean of 3.18 transfusions per patient, which is in agreement with the literature^{6,12}. On the other hand, we observed that the proportion of alloimmunized patients receiving more than 5 transfusions was not statistically significant ($p = 0.8676$) compared to non-alloimmunized patients, since their values were equivalent (18.2 and 18.5%, respectively). The data obtained were expected, since blood transfusion therapy profile of patients with breast cancer is considered non-chronic. A similar result was obtained in a 20-year retrospective multicenter study with alloimmunized, non-chronically transfused patients, in which 80 individuals (57%) were sensitized after receiving an average of 2 red cell units.¹² This result shows that alloimmunization in our study had no correlation with the number of transfusions received at the institution, but with the transfusion history. This finding reinforces a possible prevalence of preformed alloantibodies in this group of cancer patients.

Although nulliparity is indicated as a breast cancer risk among women¹³, our study showed that the vast majority of alloimmunized women had a history of pregnancy (92.5%). Santos¹³ showed a similar result, revealing a frequency of 93.33% of alloimmunized women with a history of pregnancy. Natukunda¹⁴, in turn, revealed that only 62.5% of the women who produced alloantibodies had previous pregnancies. However, in our study, one fact draws a lot of attention. Although there was no statistically significant difference ($p = 0.8135$), this result is exactly the opposite of what was expected, since pregnancies are an important cause of alloimmunization in women^{1,7-10,12,14,15}. Therefore, we consider this a casual result.

In all 4 patients in whom post-transfusion alloimmunization was detected, it was found that the time to alloantibody production varied from 5 days to 1 month, with a mean of 21 days, ranging from the time between the first transfusion of the packed red blood cells and alloimmunization identification. Our results are in agreement with a study cited by Bordin¹², in which alloantibodies were detected with an average of 20 days by AGT. Based on these results, our study considered the period between the last transfusion and the first IAS performed by us as a way of obtaining an estimate of the time interval between transfusion and detection of alloantibodies, with a significant statistical difference. Among the alloimmunized patients, we observed that this time ranged from 5 days to 8 months, whereas in non-alloimmunized patients, the observed time ranged from 1 day to 24 months. In the study carried out by Santos¹³, the time for alloantibody production ranged from 3-97 days, with an average time of 20.88 days. Schonewille¹⁶ observed that 16.8% of the patients became alloimmunized within 14 days after the transfusions and 2.3% produced alloantibodies within a maximum of 3 days, with anti-E as the most common antibody (42.8%). This result is in accordance with our study, in which 2 (50%) of the 4 alloimmunized individuals developed that alloantibody. When we assessed the 22 alloimmunized patients who only had a pregnancy history, we observed that the persistence of alloantibodies ranged from 2-57 years, with an average of 25.4 years. Applying the AGT technique, anti-D was the main alloantibody, detected in 4 patients (18%). With AGT, the persistence ranged from 15-42 years, with an average of 30 years. However, with the enzyme technique, anti-E was the main alloantibody, detected in 8 patients (36%), with persistence ranging from 2-57 years and an average of 23.5 years. These results demonstrate that the enzyme technique can be used in order to detect alloimmunization in a short time after exposure. In the present study, no alloimmunized patient had only a transfusion history.

CONCLUSION

The present study showed a frequency of erythrocyte alloimmunization of 9.32%. Screening was performed in breast cancer

patients with a combination of Liss/AGT and enzyme techniques. Our study also revealed that the application of the enzyme method in the irregular antibody screening routine provided a positivity index up to seven times higher than when only the LISS/AGT method is applied.

Most alloimmunized patients presented with alloantibodies of clinical significance (Rh system). We observed that alloimmunization was not correlated with the number of red blood cell transfusions in the institution, confirming the hypothesis of prior alloimmunization, mainly due to pregnancy and transfusion histories. As previous alloimmunization cannot even be detected in the IAS by Liss/AGT, and once it was observed that

the time to generate alloantibodies would be long (more than 72 hours), our results demonstrated that the enzyme technique can be used to detect alloantibodies in a short time after the exposure to erythrocyte antigens.

Given these facts, we propose the adoption of the enzyme technique as a routine method. We also propose the extension of this project in pre-transfusion testing routines to the other groups of cancer patients. Such a measure will certainly contribute to reducing erythrocyte alloimmunization rates among recipients of packed red blood cells and politransfused patients. Thereby, it would reduce the risk of incompatible phenotype transfusions that could lead to hemolytic transfusion reactions or ineffective transfusions.

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BREAST CANCER IN RIO GRANDE DO NORTE, A RETROSPECTIVE STUDY: EPIDEMIOLOGICAL, CLINICAL AND THERAPEUTIC PROFILE

O câncer de mama no Rio Grande do Norte, um estudo retrospectivo: perfil epidemiológico, clínico e terapêutico

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ABSTRACT

Objective: To analyze the epidemiological, clinical, therapeutic profile of patients with breast cancer assisted at Liga Norte Riograndense Contra o Câncer, in Rio Grande do Norte, between 2011 and 2012. **Method:** This is a descriptive, retrospective, cross-sectional study. Physical records were analyzed to detect sociodemographic, clinical, and therapeutic characteristics of patients. **Results:** 1,176 records related to breast cancer from 2011 and 2012 were assessed. Female gender was predominant, with 99.6% of cases, followed by males, with 0.4% (five cases). The mean age was 55 years, brown ethnicity (63%), married women (51%), with incomplete primary education (27%), living in Natal and Great Natal (57%) with family history in 42% of cases. 64% of patients were coming from the Brazilian Public Health System (SUS). Therapeutic approach comprising surgery, radiotherapy, chemotherapy, and hormone therapy was the most performed (24%), with no evidence of disease after treatment (63%). The level of education did not affect diagnosis in early stages of the disease, and young patients had worse prognosis. **Conclusion:** Determining epidemiological, clinical, and therapeutic profile is a different vision for patients aging less than 40 years, so new breast cancer prevention and screening policies and campaigns are needed for this age group.

KEYWORDS: Epidemiology; breast neoplasms; therapy; diagnosis; medical records.

RESUMO

Objetivo: Analisar o perfil epidemiológico, clínico e terapêutico dos pacientes com neoplasia mamária no Rio Grande do Norte, assistidos na Liga Norte Riograndense Contra o Câncer entre 2011 e 2012. **Métodos:** Trata-se de um estudo transversal retrospectivo descritivo. Realizou-se análise de prontuários físicos para detectar as características sociodemográficas, clínicas e terapêuticas. **Resultados:** Foram analisados 1.176 prontuários com casos de câncer de mama entre 2011 e 2012. Houve predominância do sexo feminino (99,6%), seguido de 0,4% (5 casos) do sexo masculino. A média de idade foi de 55 anos, de etnia parda (63%), mulheres casadas (51%), com ensino fundamental incompleto (27%), residentes em Natal e na Grande Natal (57%), com histórico familiar presente em 42%. Observou-se que 64% eram procedentes do Sistema Único de Saúde (SUS). A conduta terapêutica de cirurgia, radioterapia, quimioterapia e hormonioterapia foi a mais realizada (24%), sem evidência da doença após o tratamento (63%). O grau de escolaridade não interferiu no diagnóstico em estágios iniciais da doença, e pacientes jovens apresentaram pior prognóstico. **Conclusão:** A determinação do perfil epidemiológico, clínico e terapêutico indica uma visão diferenciada para pacientes menores de 40 anos, gerando necessidade de novas políticas e campanhas de prevenção e rastreamento para o câncer de mama nessa faixa etária.

PALAVRAS-CHAVE: Epidemiologia; neoplasias da mama; tratamento; diagnóstico; prontuários.

Study carried out at Hospital Liga Norte Riograndense Contra o Câncer – Natal (RN), Brazil.

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INTRODUCTION

Cancer is a major public health problem in developed and developing countries which accounts for more than 6 million deaths per year and about 12% of all causes of death worldwide¹. Breast cancer is the second most common type of cancer in the world, Brazil included, the most common among women — following skin cancer —, and the leading cause of death by cancer²⁻⁴. The distribution of new cases and deaths related to neoplasm have wide regional differences, with higher rates of incidence and mortality in the South and Southeast regions and lower rates in the North and Northeast regions⁵. Lower level of industrialization in the North and Northeast regions as compared to the South and Southeast regions explain that⁶.

Breast neoplasms affect mainly women in perimenopause⁷. The main risk factors are related to hormonal and reproductive features, age, gender, and family history. They are not common in young women, constituting 5 to 7% of all cases⁸. Among women who develop the disease before the age of 50, the prognosis is worse, since diagnosis is usually made when the patient is symptomatic and, therefore, has already progressed to a more advanced stage^{3,8}. Early diagnosis is related to awareness of the population and health professionals for the signs and symptoms of cancer, thus leading symptomatic people to consultation in health services. Screening means subjecting symptom-free individuals to screening tests to detect cancer or precursor lesions of cancer and to organize referrals for diagnosis confirmation and treatment⁵.

The main strategies for controlling this type of cancer are: primary prevention, with identification and correction of avoidable risk factors; secondary prevention, with early detection and treatment; and tertiary prevention, with rehabilitation and palliative care. Secondary prevention strategies are the only ones able to reduce mortality rates and, for this reason, have been given greater attention at national health services⁹. The level of knowledge of patients increases proportionally to their educational level. Breast self-examination is very important for early diagnosis, which highlights the need for informative and educational projects that respect users' limitations as to schooling⁶.

The guarantee of access to diagnosis method of mammography as a preventive measure for breast cancer to all women from the age of 40 on is given by Federal Law 11,664/2008. It is the method of choice for screening this condition, since it allows early detection of lesions smaller than or equal to one centimeter, which represents a better therapeutic response and healing capacity^{10,11}. Ultrasound has great application in differentiation between cystic and solid tumors. This test brings better results when performed on dense breasts with exuberant glandular tissue,

such as the breasts of young women under 35 years of age¹². Tumor markers are another important test that consists of several substances such as proteins, carbohydrates, lipids, glycoproteins, tumor-specific or associated enzymes when secreted in high concentrations. These markers have contributed greatly with breast cancer predictive diagnosis and prognosis evaluation¹³.

Currently, the therapy for breast neoplasm is performed by a multidisciplinary team, aiming at an integral treatment of the patient. Conducts to be instituted are combinations of conservative or radical surgeries, radiotherapy, chemotherapy or hormone therapy. Thus, the costs of this approach are subordinated to the disease staging upon diagnosis, that is, the more advanced the stage, the more expensive and difficult the treatment¹⁴.

The objective of this study was to describe the epidemiological and clinical features of breast neoplasm in Rio Grande do Norte starting from the analysis of data record from the archive of Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

METHODS

This is a cross-sectional, retrospective, descriptive, hospital-based study. The target population was composed of patients diagnosed with breast cancer, whose data were available in the archive of Liga Norte Riograndense Contra o Câncer. Physical records were analyzed to detect sociodemographic features: gender, age, ethnicity (white, black, yellow, brown), schooling, origin (Natal, Grande Natal — Extremoz, Parnamirim, São Gonçalo do Amarante and Macaíba — and countryside), marital status (single, married, widowed, divorced/separated), family history of breast cancer, alcoholism, smoking, origin of referral. Description of clinical and pathological characteristics was based on previous diagnosis and treatment (without diagnosis and without treatment, with diagnosis and without treatment, with diagnosis and with treatment, and other variations); most important basis for diagnosis, most relevant exams (clinical examination, imaging, exploratory surgery, pathological anatomy, and tumor markers); histology (infiltrating ductal carcinoma, infiltrating lobular carcinoma, mucoid carcinoma, ductal carcinoma in situ, and others); laterality (right, left and bilateral); presence of more than one tumor (yes or no); distant metastases and their locations; clinical stage (0, IIA, IIB, IIIA, IIIB, IIIC, IV); types of treatments received (surgery, chemotherapy, radiotherapy, hormone therapy, bone marrow transplantation, immunotherapy, iodine therapy, and others); correlation with educational level and clinical staging, in order to verify the degree of influence of school level in early or late diagnosis; and total number of deaths and identification of

clinical staging upon obit in patients younger than 50 years, to verify the prognosis in young women.

Initially, 1,176 medical records were selected. The inclusion criteria were patients diagnosed with breast cancer and assisted at participating hospital units, in the mastology service of Liga Norte Riograndense Contra o Câncer, from 2011 to 2012. The analysis of medical records consisted of reading to collect sociodemographic and clinical data between January and April 2016. After that, the variables collected were accounted for in Microsoft Excel. Then, tables and graphs were generated to represent the information.

This study is in compliance with the current principles of the National Health Council (CNS/MS) Resolution 466/12, which addresses research involving human beings, and was approved by the Ethics Committee of Hospital Liga Norte Riograndense Contra o Câncer (CEP/LIGA), protocol 1,184,381.

RESULTS

In total, 1,176 medical records of patients with breast cancer diagnosed between 2011 and 2012 in the mastology service of the Liga Norte Riograndense Contra o Câncer were analyzed, with 569 cases in 2011 and 607 cases in 2012. Predominance of the female gender (99.6%) was found, but 0.4% (5 cases) in males was accounted for. Mean age was 55 years, and the prevalent age range was 41 to 59 years. The most prevailing race/ethnic group was brown (63%), and 40% (464 patients) were patients under 50 years of age with advanced staging (IIIA, IIIB, IIIC or IV, VAT). In 40% of these cases, elementary schooling was incomplete (27%), and 57% were residents of Natal and Grande Natal, being 51% married women. Family history was present in 42% of individuals. As to alcohol consumption and smoking, 52% of patients did not consume alcohol, and 43% were not smokers. Also, 64% of cases were referrals from SUS, with diagnosis and treatment being mostly funded by SUS (53 and 71%, respectively), as shown in Table 1.

As to previous diagnosis and treatment, most patients arrived at the hospital without diagnosis or previous treatment (68%). Considering the laterality of the tumor, there was prevalence of left breast (52%). In addition to the data already shown in Table 1, the occurrence of more than one tumor and metastasis was not prevalent, and the most prevalent site of metastasis was bone (48%). Cancer was predominantly diagnosed in clinical stage I and IIA (18% each). Among the most important bases for the diagnosis — such as clinical research, imaging, cytology, tumor markers, metastasis histology, and histology of primary tumor —, 100% of the cases had diagnosis confirmed by histology of primary tumor. Clinical examination, imaging, and

Table 1. Sociodemographic features of patients with breast cancer assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

| Variables | N | % |
|---------------------------------|-------|-------|
| Age (years) | | |
| >40 | 138 | 12 |
| <40 e >60 | 625 | 53 |
| >60 | 413 | 35 |
| Gender | | |
| Female | 1,172 | 99.6 |
| Male | 5 | 0.4 |
| Ethnicity/Skin color | | |
| White | 333 | 28.00 |
| Black | 90 | 8.00 |
| Yellow | 1 | 0.08 |
| Brown | 735 | 63 |
| Educational level | | |
| None | 107 | 9.0 |
| Incomplete elementary | 313 | 27.0 |
| Complete elementary | 160 | 14.0 |
| High school | 281 | 24.0 |
| Incomplete higher education | 3 | 0.3 |
| Complete higher education | 205 | 17.0 |
| Marital status | | |
| Married | 620 | 51 |
| Single | 305 | 30 |
| Widowed | 166 | 14 |
| Separated | 84 | 7 |
| Origin | | |
| Natal and Grande Natal | 673 | 57 |
| Rio Grande do Norte countryside | 490 | 42 |
| Other States | 13 | 1 |
| Family history of cancer | | |
| Yes | 495 | 42 |
| No | 294 | 25 |
| Alcohol consumption | | |
| Yes | 102 | 9 |
| No | 606 | 52 |
| Formerly | 35 | 3 |
| Smoking habit | | |
| Yes | 117 | 10 |
| No | 505 | 43 |
| Formerly | 198 | 17 |
| Referred from | | |
| SUS | 757 | 64 |
| Others | 419 | 36 |
| Diagnosis funded by | | |
| SUS | 619 | 53 |
| Health insurance | 208 | 18 |
| Privately | 66 | 6 |
| Treatment funded by | | |
| SUS | 839 | 71.0 |
| Health insurance | 272 | 23.0 |
| Privately | 9 | 0.8 |

SUS: Brazilian Public Health System; *Differences in values result from lack of information.

exploratory surgery were the most relevant examinations in 100% of cases. Between 2011 and 2012, 160 deaths occurred, 38% (60) of cases in women younger than 50 years. In 88% of cases, the disease stages were III and IV. Mean age of death occurrences was 38 years, the lowest being 17 years, as shown in Table 2.

The histological types of tumors found are described in Table 3, the most frequent being infiltrating ductal carcinoma (81%).

As for types of treatment, the therapeutic approach comprising surgery, radiotherapy, chemotherapy, and hormone therapy was the most common (24%). After the first treatment, 63% of the patients did not show evidence of the disease. When the option was not to perform the treatment, the reasons were advanced staging (1%) and other reasons not clarified (3%), according to Table 4.

Correlation between educational level and clinical staging was also assessed and the results are shown in Figure 1.

DISCUSSION

The present study showed majority of female patients (99.6%), without losing sight of the five cases in male patients (0.4%). According to Nogueira et al.¹⁵, male breast cancer is uncommon, accounting for about 1% of all breast neoplasms, which corresponds to less than 1% of neoplasms occurring in men, therefore being responsible for less than 0.1% of deaths among them. These data corroborate the results of several studies in the literature^{6,15-17}. Mean age was 55 years, with a prevalent age range from 41 to 59 years (51%). Of the total, 40% were females aged less than 50 years with worse prognosis. This finding is in line with data reported by the National Cancer Institute (INCA) and scientific literature, both having reported rare incidence and worse prognosis in <35-year-old females, becoming progressive in women up to 50 year old^{6,15-18}. Patients were predominantly married (51%). The literature⁶ does not describe this data as a risk factor, but it is worth mentioning for a complete social profile assessment.

As to race/ethnicity, brown skin color was predominant (63%), which corroborates findings by Pinheiro et al.¹⁶, according to which black and brown races are related to higher incidence of breast cancer compared to white-skin people. However, the proportion of cases in white people (28%) was higher than that in black people (8%), making the literature controversial at this point. It is worth noting that the Brazilian population is quite mixed, which makes this variable a limiting factor for the study. The most relevant educational level was incomplete elementary school (27%). The literature¹⁶ describes that the lower the educational level, the lower the chances of diagnosis in early stages, which limits

Table 2. Clinical features of breast cancer cases assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

| Variables | N | % |
|--|-------|-----------|
| Previous diagnosis and treatment | | |
| No previous diagnosis or treatment | 798 | 68 |
| Previous diagnosis without treatment | 135 | 11 |
| Previous diagnosis and treatment | 243 | 21 |
| Laterality | | |
| Left | 612 | 52 |
| Right | 545 | 46 |
| More than one tumor | | |
| Yes | 30 | 3 |
| No | 1,146 | 97 |
| Distant metastasis | | |
| Yes | 115 | 10 |
| No | 1,061 | 90 |
| Metastasis location | | |
| Liver | 17 | 11.0 |
| Bone | 75 | 48.0 |
| Lung | 32 | 20.0 |
| Colorectal | 1 | 0.6 |
| Brain | 31 | 20.0 |
| Pleura | 1 | 0.6 |
| Clinical staging | | |
| 0 | 63 | 5.00 |
| I | 206 | 18.00 |
| IA | 1 | 0.08 |
| II | 2 | 0.20 |
| IIA | 215 | 18.00 |
| IIB | 163 | 14.00 |
| IIIA | 177 | 15.00 |
| IIIB | 122 | 10.00 |
| IIIC | 38 | 3.00 |
| IV | 88 | 8.00 |
| IVA | 1 | 0.08 |
| Deaths | | |
| Breast cancer | 158 | 99.0 |
| Myocardial infarction | 1 | 0.5 |
| Others | 1 | 0.5 |
| Disease staging upon death of patients aged less than 50 years | | 60 deaths |
| II | 7 | 12 |
| III | 31 | 52 |
| IV | 22 | 36 |

*Differences in values result from lack of information.

Table 3. Histology of breast cancer patients assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

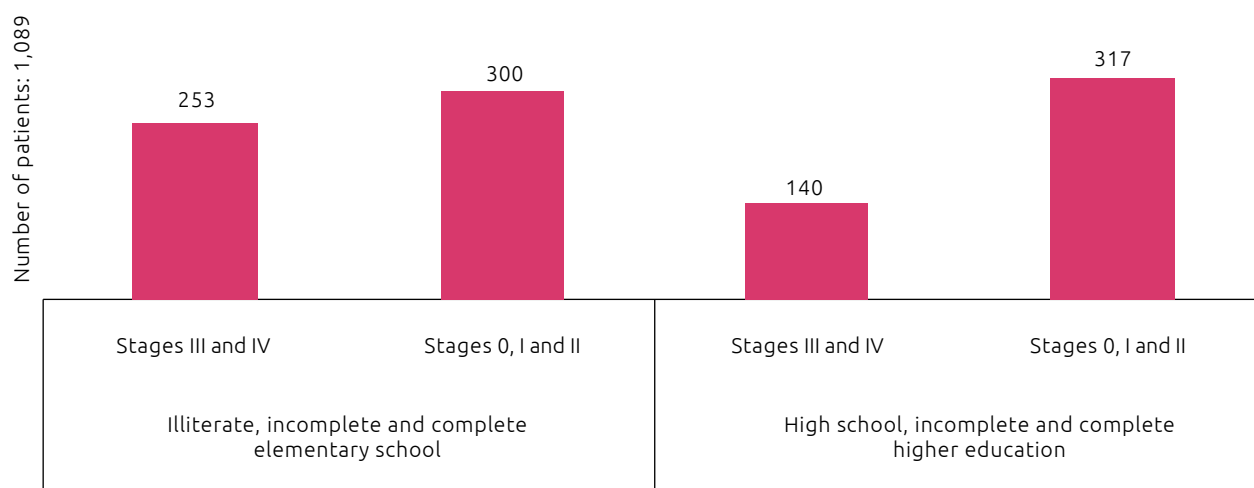
| Histological type | N | % |
|--|-----|-------|
| Infiltrating ductal carcinoma | 955 | 81.00 |
| Leiomyosarcoma | 1 | 0.08 |
| Infiltrating lobular and ductal carcinoma | 2 | 0.20 |
| Apocrine adenocarcinoma | 23 | 2.00 |
| Papillary cystadenocarcinoma | 5 | 0.40 |
| Infiltrating lobular carcinoma | 35 | 3.00 |
| Mucinous carcinoma | 24 | 2.00 |
| Ductal carcinoma <i>in situ</i> | 92 | 8.00 |
| Small-cell carcinoma | 2 | 0.20 |
| Unclassified malignant tumor | 3 | 0.30 |
| Mixed infiltrating ductal carcinoma | 3 | 0.30 |
| Infiltrating papillary adenocarcinoma | 7 | 0.60 |
| Neuroendocrine carcinoma | 1 | 0.08 |
| Metaplastic carcinoma | 5 | 0.40 |
| Diffuse large-cell lymphoma | 2 | 0.20 |
| Apocrine metaplastic adenocarcinoma | 1 | 0.08 |
| Fibroadenoma-originated tumor | 1 | 0.08 |
| Malignant epithelial carcinoma of unknown origin | 4 | 0.30 |
| Mammary Paget's disease | 2 | 0.20 |
| Undifferentiated carcinoma | 1 | 0.08 |
| Microinvasive squamous-cell carcinoma | 1 | 0.08 |
| Papillary carcinoma | 1 | 0.08 |
| Medullary carcinoma | 1 | 0.08 |
| Lobular carcinoma <i>in situ</i> | 3 | 0.30 |
| Hodgkin's lymphoma | 1 | 0.08 |
| Tubular adenocarcinoma | 1 | 0.08 |

*Differences in values result from lack of information.

Table 4. Types of treatment received by patients with breast cancer assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

| Variable | N | % |
|--|-----|-------|
| Type of treatment | | |
| Radiotherapy and hormone therapy | 16 | 1.00 |
| None | 59 | 5.00 |
| Surgery, radiotherapy, and hormone therapy | 37 | 3.00 |
| Surgery | 107 | 9.00 |
| Radiotherapy | 159 | 13.00 |
| Chemotherapy | 48 | 4.00 |
| Hormone therapy | 19 | 2.00 |
| Surgery, radiotherapy, and chemotherapy | 166 | 14.00 |
| Chemotherapy and hormone therapy | 5 | 0.40 |
| Surgery, radiotherapy, chemotherapy, and hormone therapy | 277 | 24.00 |
| Surgery and radiotherapy | 111 | 9.00 |
| Surgery and chemotherapy | 54 | 5.00 |
| Chemotherapy, hormone therapy and radiotherapy | 13 | 1.00 |
| Surgery, chemotherapy, and hormone therapy | 37 | 3.00 |
| Surgery and hormone therapy | 35 | 2.00 |
| Radiotherapy and chemotherapy | 32 | 1.70 |
| Surgery, chemotherapy, hormone therapy, and iodine therapy | 1 | 0.08 |
| Staging after treatment | | |
| No evidence | 740 | 63 |
| Partial remission | 13 | 1 |
| Stable disease | 156 | 13 |
| Progressing disease | 114 | 10 |
| Non-treatment reasons | | |
| Performed elsewhere | 1 | 0.08 |
| Advanced disease | 17 | 1 |
| Others | 33 | 3 |

*Differences in values result from lack of information.

**Figure 1.** Comparison between educational level and clinical staging in breast cancer patients assisted at Liga Norte Riograndense Contra o Câncer in 2011 and 2012.

the implementation of preventive measures. However, in our study, we found a higher proportion of early-stage neoplasia diagnosis in patients with low educational level — 30% of which were diagnosed in initial stages 0, I (including IA) or II (including IIA, IIB) —, and in those with higher schooling level, 31% of which were diagnosed in initial stages 0, I (including IA) or II (including IIA, IIB). These findings differ from those reported in the literature^{6,16,19}.

Family history is an important risk factor for breast cancer, due to mutations of the BCRA1 and BCRA2 genes, passed on from one generation to the next. Our study showed that 42% of patients had family history of breast cancer, which agrees with findings by Pinheiro et al.¹⁶. About 52% of patients reported not drinking alcohol. The consumption of alcoholic beverages is an important risk factor for breast cancer development, that is, the greater the consumption, the greater the chance of having it²⁰. A total of 43% of patients reported not smoking. Most researchers agree that there is no consistent evidence to determine the influence of smoking habit on breast cancer²⁰. Our study found the majority of medical records from Natal and Grande Natal (Extremoz, Parnamirim, São Gonçalo do Amarante, Macaíba) (57%) followed by patients from Rio Grande do Norte countryside (42%), an important finding for demographic characterization.

The number of patients referred by SUS for breast cancer diagnosis and treatment (53 and 71%, respectively) was higher compared to cases referred from private networks or people seeking care by their own (18% for diagnosis and 23% for treatment). In most cases, patients arrived at the hospital undiagnosed or without previous treatment, which is compatible with studies performed by Dugno et al.⁶ and Pinheiro et al.¹⁶. As to tumor characteristics, infiltrating ductal carcinoma was the most frequent histological type, followed by ductal carcinoma *in situ*. Other histological types are less frequent and some are even rare, including mammary Paget's disease, results that agree with those of previous studies^{4,16,21,22}.

Regarding the laterality of the tumor, left breast was prevalent, which reinforces data described in previous studies^{16,21,23}. Analysis data from this study showed that, in most cases, there was not more than one tumor or distant metastasis, finding that meets the scientific literature^{4,16}. Bone was the most common location of distant metastasis (48%), a result that also coincides with previous findings. Previous studies have reported that bone, liver, and lung metastases are the most common ones, as observed in this study²⁴. Clinical staging is established through the TNM system, which groups the size of the tumor (T), the number of lymph nodes involved (N), and presence or absence of metastases (M). In our study, most females had I, IIA and

IIIA staging, which is compatible with data described in the literature¹⁵. Advanced staging (\geq III) was found in younger women and less advanced staging in women aged 50 years or older, results also found by Gnerlich et al.²⁵.

Histology of primary tumor was the most important basis for diagnosis closure in all cases, a result that agrees with reports from the scientific literature²⁶. In most cases, clinical examination, imaging and exploratory surgery were the most relevant search approaches, which is also in agreement with data described by previous studies^{16,27}.

According to our results, there was predominance of surgery associated with radiotherapy, chemotherapy and hormone therapy, followed by combination of surgery, radiotherapy and chemotherapy, with no evidence of disease after treatment. Results of combination therapy differ from data described in the literature, according to which the most common treatment is surgery plus chemotherapy, as mentioned by Pinheiro et al.¹⁶ and Torres et al.²⁸. Such findings corroborate the results obtained by Barros et al.¹⁴. Reasons for absence of treatment included advanced disease, once the approach in such cases is only palliative, as recommended by INCA²⁹.

Identification of staging in cases of death, bringing both years together, showed 38% (60 deaths out of 160 cases) of patients younger than 50 years of age with advanced staging, with prevalence of stages III and IV (88%), and therefore with worse prognosis. These results are similar to data from several studies in the literature^{1,16,21,30}. The greater vulnerability of young women to diagnosis in advanced stages may be explained by the lack of screening actions and difficulty in reading and interpreting mammographic results due to high breast density⁷. Therefore, higher mortality rate and lower disease-free survival in young women are detected when compared to patients aged above 50 years, who have a better prognosis^{12,16}.

Conclusion is that determining epidemiological, clinical, and therapeutic profile in the present study constituted a different view for patients younger than 40 years old, causing the need for new breast cancer prevention and screening policies and campaigns that include this age group. In the population studied, most patients were from Natal and Grande Natal, mean age being 55 years, most of them married, with incomplete elementary school, brown ethnicity, non-alcoholic, non-smokers, and with treatment and diagnosis predominantly funded by SUS. Educational level did not influence early diagnosis. Both low-grade and high-grade patients had prevalence of 0, I (including AI) and II (including IIA, IIB) stages at diagnosis. The largest number of cases was in the left breast, there being no prevalence of more than one tumor or distant metastasis. When metastasis was confirmed, the bone type was more

common. In most cases, clinical staging was I, IIA, and IIIA, approached with surgery, radiotherapy, chemotherapy, and hormone therapy, the latter being the most used treatment. After treatment, there was no evidence of recurrence during follow-up in most patients. As to death occurrences, 38% of cases involved patients aged less than 50 years and with worse prognosis.

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USE OF 125IODINE SEEDS (ROLLIS) FOR INTRA-OPERATIVE LOCALIZATION OF NONPALPABLE BREAST LESIONS: ANALYSIS OF THE IMPLANT OF 338 SEEDS IN 284 PATIENTS

Uso de sementes de iodo-125 (ROLLIS) para localização intraoperatória de lesões impalpáveis da mama: análise do implante de 338 sementes em 284 pacientes

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ABSTRACT

Objective: To analyze the feasibility, efficacy and results of the use of 125Iodine seeds for intra-operative localization of nonpalpable breast lesions. **Method:** Retrospective review of 284 patients, referred by various breast specialist surgeons, with radiologically detected but clinically nonpalpable microcalcifications or nodules, submitted to pre-operative 125Iodine seed implant, between July 2012 and September 2016. A total of 338 seeds were implanted in ordinary radiologic departments, supported by ultrasonography or mammography exams, chosen according to the morphologic aspect of the lesion. Radioguided surgical procedure took place on the same day or few days after the implant of the seeds, with the help of a radiation detector called Gamaprobe, which directs the surgeons towards the radioactive seeds and to the lesion to be resected. **Results:** All implants were performed as outpatient procedures, with patients immediately returning to their daily activities. No complications such as pain, bleeding, infection and haematoma were recorded. Pathologists had no difficulty in preparing the surgical specimens for histopathologic analysis. Surgical safety margins were considered adequate in all pathologic reports, with no need for re-operations. The healing process was not jeopardized by radiation, and the surgeons were pleased with the improvement on intraoperative lesions localizations and shortening on operatory time. Cosmetic results were well accepted by the patients. **Conclusion:** The 125Iodine seed implant is an effective alternative method for intraoperative localization of radiologically detectable and clinically nonpalpable breast lesions.

KEYWORDS: Breast; iodine radioisotopes; breast diseases; diagnostic techniques, radioisotope.

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RESUMO

Objetivo: Avaliar a exequibilidade e a eficácia do método de implante de sementes de ¹²⁵Iodo (ROLLIS) para localização intraoperatória de lesões impalpáveis da mama. **Método:** Trata-se de um estudo retrospectivo, incluindo 284 pacientes com nódulos ou microcalcificações mamárias, visíveis na mamografia e/ou ultrassonografia, porém, clinicamente impalpáveis, submetidas a implantes de sementes de ¹²⁵Iodo, de julho de 2012 a setembro de 2016, sendo implantado um total de 338 sementes. As pacientes foram encaminhadas por diversos mastologistas que executaram cirurgias radioguiadas com auxílio de detector de radiação denominado Gamaprobe, realizadas no mesmo dia do implante ou vários dias após, seguindo a agenda do centro cirúrgico, da equipe médica e a conveniência da paciente. **Resultados:** Os implantes foram realizados em regime ambulatorial, com imediato retorno das pacientes às atividades cotidianas, não sendo registrada qualquer complicação como dor, hemorragia, infecção ou hematoma. Os patologistas não constataram prejuízo no processamento do espécimen cirúrgico. O processo cicatricial se efetuou normalmente, obtendo-se plena satisfação por parte dos cirurgiões, que referiram maior facilidade na localização intraoperatória das lesões e diminuição no tempo operatório. O resultado cosmético também foi beneficiado, sendo bem aceito pelas pacientes. As margens cirúrgicas foram consideradas adequadas em todos os casos, graças à avaliação feita pelo patologista e às ampliações executadas no momento da cirurgia, dispensando re-excisões. **Conclusão:** O implante de sementes de ¹²⁵Iodo (ROLLIS) é uma técnica segura e eficaz para localização intraoperatória de lesões radiologicamente visíveis, porém clinicamente impalpáveis, da mama.

PALAVRAS-CHAVE: Mama; radioisótopos do iodo; doenças mamárias; técnicas de diagnóstico por radioisótopos.

INTRODUCTION

Recent media campaigns and dissemination on the prevention of breast cancer, along with the technological advances in radiology, have considerably increased the diagnosis of radiologically visible, though clinically impalpable, breast lesions referred for surgical excision, becoming a major challenge for surgeons¹.

The most commonly used method for the surgical localization of these lesions, since its creation in 1979, it is the insertion of a metallic wire with an arrow-shaped tip (Kopans Wire) into the lesions, guided by radiological images². Although practiced universally for many years, this technique includes several drawbacks³. Literature studies⁴ show that this method leads to high rates of positive surgical margins, ranging from 20 to 70%, requiring reoperations, with high levels of local recurrence, in cases of malignancy. This is an important factor, since the main objective of any given procedure to locate a lesion is to facilitate a complete surgical excision in a single event, discarding new interventions. Another drawback of the metallic wire is its displacement in the preoperative period or during surgery, with reports of its migration into the pleural cavity⁵, the myocardium⁶, pulmonary hilum⁷, abdominal cavity⁸, in addition to cases of bending and rupture both before and during surgery^{9,10}. Surgeons complain that the tip of the metallic wire is difficult to be felt in palpation during the operative event, impairing the complete excision of the lesion with adequate safety margins¹¹. The insertion point of the wire into the skin is usually located in an area far from the ideal incision position, requiring an extended surgical area in order to identify the wire and for the lesion to be removed¹¹. Another disadvantage of this method is the need to perform

the surgery on the same day of the wire implant, once its exteriorization through the skin requires dressings, immobilization maneuvers, protection and care by the patients. In addition, complications such as pain, bruises and infections are reported in 8 to 10% of cases¹². Due to the many drawbacks mentioned, researchers were encouraged to find another method for intraoperative localization of impalpable breast lesions. Then, there was the idea of using radiation emitted by radioactive isotopes as a guide to surgical targets¹³.

In 1999, Luini et al.¹³ published a new technique called radioguided occult lesion localization (ROLL), using colloidal albumin marked with ^{99m}-technetium as a radiotracer, which, when injected directly into the lesions, under mammography or ultrasonography guidance, allows the localization of nodules and microcalcifications by means of gamma-type radiation emitted by the radioisotope and detected through a device called Gamaprobe. Several subsequent studies demonstrated the advantages of the ROLL technique in comparison to the metallic wire, observing inferior levels of inappropriate surgical margins, reducing the need for re-excisions and reducing the volume of breast parenchyma removed in the operative specimen¹⁴⁻¹⁶. Despite the advantages of this method over the metallic wire, some drawbacks related to difficulties and limitations to its use have been found. The colloidal albumin marked with ^{99m}-technetium is not radiopaque, making it difficult to be visualized in radiological tests, impairing the confirmation of its positioning within the lesions. Also, it has a rather short half-life (six hours), which requires the execution of the surgery on the same day of the implant. Due to its liquid form, its diffusion through neighboring

tissues after being injected is unavoidable, making it rather difficult to perform the surgery by producing ill-defined margins and thus generating insecurity in the surgeon, who is forced to withdraw greater amounts of breast parenchyma, which interferes negatively on the cosmetic result¹⁷.

Due to the inconveniences described, the search for a method with lesser difficulties continued. In 2001, Gray et al.¹⁸ published a new technique using radioactive seeds of 125Iodine (ROLLIS), which, due to its small dimensions, concentrates the radiation within the target lesion (unpalpable lesion), facilitating the surgeon's work, by making it easier to be found through radiation. Subsequent publications¹⁹⁻²¹ demonstrated many advantages to this method, such as reduced occurrence of compromised margins, reduced amounts of breast tissue removed, reduced surgical time due to easier location of the lesion and better cosmetic result, when compared to wire and 99m-technetium^{20,21}. The external capsule of the 125Iodine seed is made of titanium, which, being radiopaque, is easily visible during mammography and ultrasound. This is a very important characteristic, once it allows verifying, at the moment of the implant, the position of the radioactive source within or near the lesion to be resected. Another advantage of 125Iodine is its prolonged half-life (60 days), allowing the surgery to be carried out up to 2 months after the implant, with no need of being performed on the same day or the day after the procedure. This flexibility to schedule the surgery facilitates the organization of the medical team, the surgical center and the patient, providing everyone involved with comfort and tranquility. Another favorable finding for the use of the seed is the absence of displacement and migration of the marker to other areas but the area of interest, despite surgical manipulation and free movements of the patient²².

Due to 125Iodine radioemission, doubts arose regarding the doses absorbed by the patient and by the medical team. According to Pavlicek et al.²³, the maximum dose deposited in the residual breast that received the seed implant is rather low, around 2 cGy, equivalent to the dose of two X-ray incidences of a routine mammography. A survey on the amount of radiation received by the surgical team showed that no one received a dose higher than the environmental level²⁴, proving the absence of risk to the medical staff, to the patient and to the general population.

The ROLLIS technique proved to be easy to learn, intuitive and learning-curve-free, a fact proven by the constant results found during all the years of its execution¹.

MATERIAL

This study was approved by the Ethics Committee of the *Hospital Pró-cardíaco – Esho Empresa de Serviços Hospitalares/Hospital Pró-cardíaco* (HPC), CAAE registration No. 47149315.4.0000.5533. It is a cohort, retrospective, observational study, consisted of

284 patients with impalpable breast lesions, submitted to 125Iodine seed implants.

Indication to the use of seed in this work include radiologically visible, though clinically impalpable lesions, which would be submitted to excisional biopsy for histopathological diagnosis, and lesions which already had a pathological report and would be treated by surgery. Before the implant, patients were given detailed explanations on the method, for full knowledge and authorization for the procedure.

1. Seed:

125Iodine seeds are capsules containing salts of titanium-coated 125Iodine, measuring 5 x 0.8 mm, with a half-life of 59.4 days, low-energy gamma emission (27 keV), acquired through the Institute of Energy and Nuclear Research (*Instituto de Pesquisas Energéticas e Nucleares – IPEN*), loaded with radioactive material ranging between 0,2 and 0,9 mCi, sterilized and handled according to the safety guidelines of the National Nuclear Energy Commission.

125 Iodine seed

The emission of low-energy photon radiation causes the radiobiological effect in neighboring tissues to be of negligible intensity, without harming the histopathological analysis of the surgical specimen nor the healing process. Also, there is no need for sophisticated and expensive radioprotective measures, although it is necessary to adopt the established care for the manipulation of radioactive material.

2. Needle:

The seed are implanted through stainless steel needles, with centimetric marking, echogenic tip and shear bevel, visible during ultrasound and on X-ray films. They measure 20 cm in length and 18 Gauge in diameter and are supplied sterilized, being discarded after use. They have a metallic plunger, which pushes the seed into the lesion. Due to the rigidity of the stainless steel, they easily penetrate the breast tissue, moving toward the predetermined targets without deviations, curves or ruptures, implanting the seed with great precision and little trauma.

Needle and 5 seeds

3. Gamaprobe:

It is the low-energy gamma radiation (27 Kev) detector, measuring the radiation emitted by the 125Iodine seed, consisting of a radiation recording compartment, connected to a sensor through a flexible probe, with suitable weight and dimensions for an easy displacement. The device used is made by Johnson & Johnson, Neoprobe 2000 model, capable of also detecting gamma radiation of 140 Kev emitted by the 99m-technetium phytate, which makes it able to differ the radiation released by the seed from that emitted by the sentinel lymph node, in the same procedure.

METHODS

Implanting the seed

The implant of the seed is carried out in a conventional radiological center, by a radiologist assisted by the radio-oncologist. The choice between mammography and ultrasonography as an auxiliary radiological method is made by the radiologist, based on the morphological characteristics of the lesion. In general, nodular lesions are implanted using ultrasonography, while microcalcifications are best seen during mammography with biplanar or stereotaxic methods. After positioning the patient in the selected device, the asepsis is performed, followed or not by local anesthesia. All cases implanted during ultrasonography are subsequently radiographed in craniocaudal and profile incidences, in order to confirm the perfect positioning of the seed. After the implant, the patient is immediately released and may return to their daily routine activities, discarding special care, dressings or any limitation to their routine.

Surgical procedure

The preoperative procedure is the same of any surgical breast intervention, planned conventionally, and may be performed on the same day of the implant or up to 60 days after it, to the convenience of the medical team, the surgical center and the patient, without any urgency or pressure on any of the parties involved. The surgical center is chosen by the surgeon and has no need for sophisticated radioprotection equipment. The surgery is radioguided by the Gamaprobe sensor, which shows the position of seed and lesion by emission of a sound signal directly proportional in intensity to the amount of radiation detected. Based on this information, the surgeon defines the position and type of incision, guiding the dissection to the seed and the target-lesion with the aid of the Gamaprobe noise. After having the parts and the surgical margins analyzed by the pathologist, the surgical wound is closed, and the patient is discharged at the appropriate time, remaining in ambulatory supervision until complete healing. Since it contains radioactive material, the seed must be handled with special attention in order to avoid being lost when wrapped in compresses, gauze or by suction of the aspirator.

Surgical part

In cases of previously confirmed malignancy, the excision of the sentinel lymph nodes may be carried out at the same time as the removal of the mammary lesion, due to Gamaprobe's ability to differ low-energy radiation released by ^{125}I seeds (27 KeV) from high-energy radiation (140 Kev) released by $^{99\text{m}}\text{Tc}$ -technetium phytate. In these cases, the seed is implanted into the lesion, followed by an injection of $^{99\text{m}}\text{Tc}$ -technetium phytate in the same region or in the periareolar area, noting the surgery must be performed within 12 hours, at most, once the half-life of the phytate is of only 6 hours.

RESULTS

This analysis included 284 patients, and a total of 338 seeds of ^{125}I were implanted. Patients were referred by 20 different mastologists, and the complete acquisition of data was not possible in all cases. However, the material collected allow the surveying of clinically important results, capable of making this method an effective alternative for intraoperative localization of clinically impalpable breast lesions.

All breast lesions were successfully resected, with no records of pre- or perioperative incidents caused directly by the presence of the seeds.

The age of patients ranged from 25 to 85 years old, with average 56 years of age and confidence interval of 95% (95%CI) 54.4–59.0.

According to the radiological aspect of the lesions, the images were classified as a nodule in 110 cases, and as microcalcification in 49 of them.

Pathologists did not report any damage to the processing of the operative specimen, and the surgical parts were considered malignant in 90 patients, and benign in 50 patients. The search for sentinel lymph nodes was performed in 57 patients, being metastatic in 8 and not compromised in 49.

As definition of appropriate free margins, the value of 2 mm was adopted as the minimum distance between lesion and the borders of the surgical specimen. Based on this concept, the margin was considered insufficient in only one case, in which the patient only remained in observation, once it was a benign lesion.

The number of seed implanted in each patient ranged from 1 to 4 (Table 1), being applied to both breasts in 20 cases.

The ultrasonography was the radiological method used in 167 implants and the mammography, in 66. All implants performed with the aid of ultrasonography were immediately submitted to a mammography in two orthogonal incidences, in order to confirm the perfect positioning of the seed.

Although the half-life of ^{125}I (60 days) allows the surgery to be performed up to 6 to 8 weeks after the implant, 97 patients were submitted to surgery within 24 hours, 66 of them on the same day of the implant. Only 6 patients were operated 14 to 28 days after positioning the seed, due to their being on neoadjuvant chemotherapy.

In one patient, a seed was used to mark a right axillary lymphadenomegaly, later resected by surgery; and two patients received neoadjuvant chemotherapy in order to reduce the size of the tumor, aiming for a more conservative surgery.

Table 1. Seeds per patient.

| Number of seeds | Number of patients |
|-----------------|--------------------|
| 1 | 239 |
| 2 | 38 |
| 3 | 5 |
| 4 | 2 |

Adverse events recorded consisted of: accidental movement of the needle plunger by a patient while being positioned at the mammography, thus injecting the seed other than in the planned site; and implantation of a seed far from the lesion due to failure in evaluating the coordinates of the mammograph.

Although no procedure for millimetric evaluation of seed positioning was adopted, surgeons did not record significant displacement of the radioactive source, confirming its presence within or close to the lesions, despite free movements and manipulation of the patients.

No influence of the learning curve was observed in this method, with consistent and reproducible results obtained from its beginning, in July 2012, to 2017, proving it to be easily understood and applied.

The total financial cost of this procedure, including material and staff, was somewhat higher when compared to traditional methods, without, however, causing any objection from paying sources.

DISCUSSION

This work analyzes the feasibility and efficacy of a new method of intraoperative localization of radiologically visible, but clinically impalpable, mammary lesions, using 125Iodine seeds, implanted with the aid of ultrasonography and/or mammography. Survey made of material provided by 20 mastologists allowed the analysis of histopathological aspects of surgical parts and their complications, enabling the comparison of this technique to the traditional methods of metallic wire and 99m-technetium. From July 2012 to September 2016, 338 seeds were implanted in 284 patients, in ambulatories in different radiological services in the city of Rio de Janeiro. In order to facilitate the presentation of the evidence, the comparison of the seed technique (ROLLIS) with the metallic wire will be presented first, and next, the 99m-technetium (ROLL) comparison will be described.

The literature shows that the metallic wire has high levels of compromised surgical margins, ranging from 20 to 70%¹⁴. A review of the pathological reports provided by the laboratories showed appropriate surgical margins in almost 100% of the cases, with only one exception. It should be noted that the histological evaluation of lesions and margins is a routine procedure performed by a pathologist during the surgery in order to ensure the quality of the surgical specimen. Testimonies from surgeons prove seeds were within or close to the lesions in all cases, which is not the case with the metallic wire, which may be displaced and even migrate to further areas, hampering the complete removal of the target-lesion⁵⁻⁸. The difficulty in identifying the tip of the wire by palpation during surgery is widely known, which may compromise the safety of the surgical margins and the complete excision of

the lesion. This difficulty is not a reality with the use of radioactive seeds, which are easily located thanks to the detection, by Gamaprobe, of the radiation released¹¹. Another disadvantage of the wire regards its insertion point in the breast, sometimes positioned far from the lesion, resulting in extensive operative area and surgical trauma, compromising the final cosmetic result. This does not happen in ROLLIS, once the seed is introduced directly into or next to the lesion, being easily visible in the mammography and/or ultrasound carried out at the moment of the implant, due to its radiopacity¹¹. Patients who receive the wire as pre-surgical marker should be operated as soon as possible, due to the presence of dressings and movement limitation, which may cause unpleasant discomfort. With the use of seeds, these inconvenients do not happen, since there is no need for dressings nor restrictions to routine activities, so patients may return immediately to their daily activities. Studies show complications such as pain, bruises and infection in 8 to 10% of the cases using metallic wire¹², which was not reported, to date, by any patient submitted to the seed technique.

Due to the drawbacks mentioned, the metallic wire is being progressively replaced by the 99m-technetium, which had some advantages and better results¹⁴⁻¹⁶, but which also does not fully satisfy the needs of surgeons and their clientele. Unfortunately, the 99m-technetium is not radiopaque, and thus, its visibility is hindered during mammography and ultrasound, making it rather difficult to ensure its perfect positioning within or close to the lesion. The 125Iodine seeds are coated by titanium, which makes them easily identifiable in any of the radiological methods used, allowing for high precision during implantation. Due to its liquid state, the 99m-technetium diffuses through neighboring tissues, making it difficult to identify their borders and forcing the surgeon to extend the resection limits, with excessive removal and unnecessary amount of mammary parenchyma. On the other hand, the seed are solid and have small dimensions (5 x 0.8 mm), constituting a source of radiation with well-defined limits, facilitating the intraoperative location of the lesion, contributing to more rewarding cosmetic results¹⁷. Another advantage of the seed, when compared to the 99m-technetium, is related to the half-life of these elements. The technetium has a half-life of only six hours, which forces the surgery to be carried out shortly, inputting great psychological pressure upon the whole medical staff, the surgical center and the patient, allowing no space for unforeseen events which would require the postponement of the surgery. Since the half-life of 125Iodine is very long (60 days), this urgency is unnecessary, allowing the surgeon to schedule the intervention according to their own availability, the surgical center's as well as the patients themselves' availability. In case of unforeseen circumstances, the operation may be postponed to any given date within 60 days, free of pressure and distress of the personnel involved. The half-life of the seed also

allows it to be used as a marker of malignant tumors to be treated with neoadjuvant chemotherapy for the reduction of tumor volume, allowing a more economical surgery. If, by any chance, there is a complete tumoral response, the surgeon will have no parameters to guide them during surgery, forcing more extensive resections²². Thus, two patients in this sample were under chemotherapeutical treatment, having received seed implants weeks before the surgery, in order to mark the area to be removed in case there was full response of the tumor to the neoadjuvant chemotherapy. Thanks to the different gamma radiation emitted by iodine (27 Kev) and by technetium (140 Kev), it is possible to perform a lesion excision, marked with seeds, and of a sentinel lymph node, marked by technetium, in the same operation, which is of hard execution when using only the technetium as a radiomarker, for the detector cannot distinguish the radiation originated in the lesion from the one emitted by the lymph node.

There are no significant differences in the financial cost of the three marking methods evaluated in this work, being accepted without further questioning by the paying sources.

No model of evaluation for cosmetic results was used in order to form a scientifically based opinion, however, both doctors and patients seemed satisfied with the aesthetic result achieved by the use of seeds. It was not possible to find, in the literature

consulted, a comparison of the cosmetic result between the three processes described in this work.

CONCLUSIONS

The use of radioactive seeds of ¹²⁵Iodine for intraoperative localization of clinically impalpable breast lesions is a safe, efficient and highly accurate alternative method, presenting numerous advantages over the conventional methods of the metallic wire and the ^{99m}-technetium. The seeds may be adopted in the practice of Mastology, once they facilitate the work of surgeons, without any harm to the pathologist and with several benefits for patients.

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SCIENTIFIC PUBLICATIONS OF BRAZILIAN MASTOLOGISTS REGARDING ONCOPLASTIC AND RECONSTRUCTIVE BREAST SURGERY: A BIBLIOMETRIC STUDY

Publicações científicas de mastologistas brasileiros sobre cirurgia oncolástica e reconstrutiva da mama: estudo bibliométrico

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ABSTRACT

Databases available on the Internet are important sources that enable the promotion of knowledge in the health field. **Objective:** To identify the scientific production of Brazilian mastologists on the subject of oncoplastic and reconstructive breast surgery published between January of 2000 and March of 2016, in the LILACS, MedLine, SciELO, PubMed and Cochrane Library databases. **Methods:** The identified publications were analyzed from a bibliometric perspective, and some elements such as type of publication, applied methodology, year of publication, number of job citations, Qualis ranking of the journal, number and professional profile of the authors, in addition to the publication development institution were separated and categorized. **Results:** A total of 631 published papers were analyzed in these databases. 76 publications were included in the final evaluation of bibliometric parameters. More than half of the evaluated publications were from the PubMed database (78.94%) and were original articles (57.89%). The average number of authors per article was 8.48. The largest number of publications included came from the year 2012 (14.47%) followed by 2013 (13.15%) and 2015 (11.84%). A significant percentage of Qualis rated journals were considered very good (A1, A2 or B1). **Conclusion:** The results show an evolution and an upward trend regarding the participation of Brazilian mastologist authors in national and international scientific productions related to oncoplastic and reconstructive breast surgery.

KEYWORDS: Bibliometrics; reconstructive surgical procedures; mammoplasty.

RESUMO

Os bancos de dados disponíveis na internet são importantes fontes que viabilizam a promoção do conhecimento em saúde. **Objetivo:** Identificar a produção científica de mastologistas brasileiros acerca do tema cirurgia oncolástica e reconstrutiva da mama, publicado entre janeiro de 2000 e março de 2016 nas bases de dados LILACS, MedLine, SciELO, PubMed e Cochrane Library. **Métodos:** As publicações identificadas foram analisadas a partir de uma perspectiva bibliométrica, sendo discriminados alguns elementos, tais como tipo de publicação, metodologia aplicada, ano de publicação, número de citações do trabalho, classificação Qualis do periódico de veiculação do trabalho, número e perfil profissional dos autores, bem como a instituição de desenvolvimento das publicações. **Resultados:** Foram analisados 631 trabalhos publicados nos referidos bancos de dados, sendo incluídas para avaliação final dos parâmetros bibliométricos 76 publicações. Mais da metade das publicações avaliadas foram provenientes do banco de dados PubMed (78,94%) e eram artigos originais (57,89%). O número médio de autores por artigo foi de

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8,48. Dois mil e doze foi o ano com maior número de publicações incluídas (14,47%), seguido por 2013 (13,15%) e 2015 (11,84%), e um percentual significativo da estratificação Qualis dos periódicos foi considerado muito bom (A1, A2 ou B1). **Conclusão:** Os resultados demonstraram uma evolução com tendência ascendente da participação de autores mastologistas brasileiros nas produções científicas nacional e internacional relacionadas à cirurgia oncoplástica e reconstrutiva da mama.

PALAVRAS-CHAVE: Bibliometria; procedimentos cirúrgicos reconstrutivos; mamoplastia.

INTRODUCTION

Breast cancer is a highly prevalent neoplasia and occurs increasingly among women worldwide. The diagnostic and therapeutic advances in breast cancer treatment are constant and the number of women who outlive treatment has expressively grown. In this context, in addition to the issues strictly related to survival and oncologic results, the preservation of femininity associated with the breasts after the cancer treatment, has gained importance in the last years, with regard to aesthetic aspects, quality of life and patient satisfaction^{1,2}.

In the last decades, the surgical techniques used for the therapeutic management of breast cancer, have notably evolved, giving preference to procedures which promote both the complete resection of the tumor and the preservation of mammary tissue, which maintains the same oncological safety as other more invasive procedures^{3,4}.

In this context, breast-conserving surgery (BCS) stands out, especially after it was reinforced as a safe and effective oncological procedure⁵. It was affirmed by means of a randomized study that BCS associated with radiotherapy is the treatment of choice for women with early stages of breast cancer, and who have similar oncologic results to those of a radical mastectomy. However, about 30% of traditional BCSs have late aesthetic results, which are considered unsatisfactory by patients. The adoption of preventive measures, along with the association of breast plastic surgery techniques with oncologic surgeries, aims to change this reality. Nowadays, BCSs gain new horizons, with respect to aesthetic principles and quality of life⁶.

Thus emerges oncoplastic breast surgery (OBS), which is defined as the surgical removal of breast tumors followed by reconstructive breast plastic surgery techniques. OBS is based on three pillars:

1. ideal oncological surgery;
2. homolateral reconstruction; and
3. immediate contralateral remodeling.

This new modality allows the patient to incorporate concepts such as integrality and preservation of sexuality into their treatment, as well as the preservation of their body image. Consequently, they will have a less traumatic process of rehabilitation in addition to physical, psychological and social benefits⁶⁻¹⁰.

The OBS allows for many advantages over standard conserving surgeries. It is possible, for example, to extend the

lumpectomy with the preservation of breast tissue, resulting in better aesthetic effects. Also, there is the possibility of performing, in a single session, oncoplastic reduction of the breasts and macromastia in women with breast cancer, which promotes greater patient satisfaction and reduced costs. OBSs allow for a greater range of free margins, reducing the need for surgical enlargements. In addition, no statistically significant increase in complications was observed in relation to standard conserving surgeries, indicating that these procedures should be offered to all patients undergoing surgery for oncological breast treatment^{11,12}.

Since the advent of OBSs, an increase of texts on the results of these techniques was observed. Many discuss the methods for breast remodeling, including simple techniques, with little mobilizations of the breast, in addition to procedures with large breast volume resection. In this regard, the Brazilian Society of Mastology (*Sociedade Brasileira de Mastologia* – SBM) released, in 2015, a practical guidebook of recommendations on oncoplastic and breast reconstructive surgeries, in order to clarify several issues, which remained controversial with respect to the indication of each specific technique¹³.

The participation of mastologists in OBSs has been increasing, with improvements in the frequency of professionals who use this technique in their daily routine, as well as through their production of knowledge on the theme, including the development of new surgical techniques^{14,15}.

Carrying out a bibliometric study about the scientific production of Brazilian mastologists on oncoplastic breast surgery is important, considering that this methodological strategy allows for the verification of scientific production through a quantitative analysis of the publications. It measures the level of scientific production on a given subject and contributes to the management of scientific knowledge¹⁶.

Bibliometric studies allow, for instance, to evaluate the places where the studies are disseminated, the temporal evolution of the scientific production, the number of productions per institution and author, the rates of growth and progress in various scientific fields, as well as the impact of these publications on the scientific community¹⁷.

The objective of this study was to evaluate, from a bibliometric perspective, the scientific production of Brazilian mastologists regarding oncoplastic and reconstructive

breast surgery, investigating both quantitatively and qualitatively the contribution of Brazilian experience to the world's scientific community.

METHODS

A systematic search was conducted in the literature for works dealing with the theme of "oncoplastic breast surgery" in the LILACS, MedLine, SciELO, PubMed and Cochrane Library databases. These databases provide scientific works online for the development of bibliographic research. The following main keywords were used in order to create a databank: oncoplastic breast surgery, breast reconstruction, *cirurgia oncoplástica da mama* and *reconstrução mamária*.

The search in LILACS and MedLine was conducted using the following search strategy: the descriptor in the subject field was the term "*cirurgia*" associated by the connector *and* to "*mama*" or "*breast*" in the words field and, also, the connector *and* to "*oncoplastic*" or "*oncoplástica*" or "*oncoplásticas*" or "*oncoplastics*" or "*oncoplastie*" or "*oncoplastique*" or "*oncoplastische*" or "*oncoplasty*" or "*reconstrução*" or "*reconstrucion*" or "*reconstruction*" or "*reconstructive*", also in the words field. The search in PubMed was performed according to the following method: ("*breast reconstruction*") *and* "*oncoplastic breast surgery*") *and* ("*2000*"[Date-Publication]: "*3000*"[Date-Publication]). Concomitant to the search in these databases, the strategy used in the Cochrane Library was: ("*oncoplastic breast surgery*") or ("*cirurgia oncoplástica da mama*") or ("*reconstrução mamária*") or ("*breast reconstruction*"), delimitating the year with works published from the year 2000 on. In order to avoid occasional losses induced by the use of predetermined descriptors, an empirical search was carried out with 10 authors known to write on oncoplastic surgery in Brazil. This search was based on their historical trajectory regarding scientific events, publications and participation in oncoplastic surgery committees of the SBM.

The inclusion criteria of the studies were: studies published between 2000 and 2016 dealing with the theme of oncoplastic or breast reconstructive surgeries whose authors are Brazilian doctors with the title of Mastologist. All articles published previous to 2000, by foreign authors and/or authors who had no connections to Brazilian institutions, as well as studies whose authors are companies/institutions, were excluded from the present study.

After the initial analysis and quantification of the articles was performed, a file was created in order to catalog them and carry out the bibliometric study of the scientific production. The following data were inventoried:

- database in which the publication was found;
- title of the work;
- type of publication;

- subject matter;
- methodology used;
- year of publication;
- qualis classification of the journal in which it was published;
- number of citations of the work informed by the database itself;
- total number of author in the works;
- professional profile of the authors included; and
- institution in which the work was developed.

The evaluation of this study by the Research Ethics Committee was not necessary.

RESULTS

After the bibliographic search with the proposed methodology, 631 publications were found, 18 of them in LILACS, 267 in Cochrane Library, 30 in MedLine, 169 in PubMed and 147 in SciELO. A total of 555 works were excluded for not meeting the previously established inclusion criteria or for being found more than once among the databases. Only one of the occurrences was considered for the overall count. As such, the sample of this study consisted of 76 articles, and no publications from Medline or Cochrane Library were included (Table 1). Despite the fact that this database provided the largest number of studies for analysis, the vast majority of papers — 246 publications, or 92.13% — were not of Brazilian authorship, and those that were (11 publications), were not written by mastologists.

Of the 76 publications studied, most of them were original articles (44 articles/57.89%). Table 1 presents the relation of the remaining types of studies. The most common methodological approaches used in the articles were retrospective (22 articles/28.94%), prospective (10 articles/13.15%) and cross-sectional (10 articles/13.15%).

All works addressing oncoplastic breast surgery and/or direct or indirect breast reconstruction were considered, focusing on surgical techniques, surgical post-treatment complications, quality of life and oncoplastic postoperative aesthetic evaluation, all of which are depicted in Graphic 1. The majority of the works showed the main subject performing breast reconstruction after mastectomy through many techniques, such as myocutaneous or muscular flaps and the use of expanders and prostheses. Due to the fact that the reconstruction of fat tissue (lipofilling) has great prominence among breast reconstruction techniques, a separate category was created for the subject.

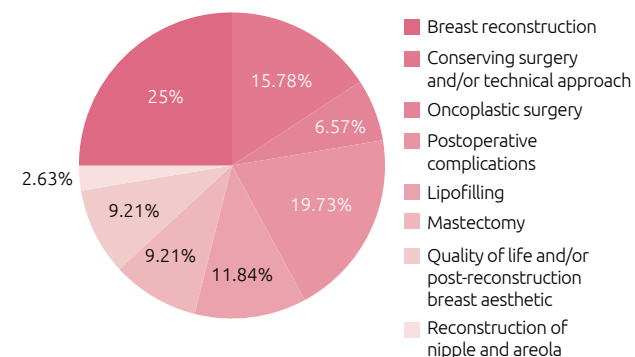
Only the citations of works informed by the databases were included, and as such this number was not found in 28 (36.84%) publications. The maximum number of citations of works included was 20, found in 2 (2.63%) articles (Table 1). As for the Qualis classification of the journals, the interdisciplinary evaluation was

considered, and when it was not available, the greatest categorization in Medicine was considered (Graphic 2).

Regarding the year of publication, it was observed that in the years 2007, 2012, 2013 and 2015 there were a greater number

Table 1. General characteristics of the included articles.

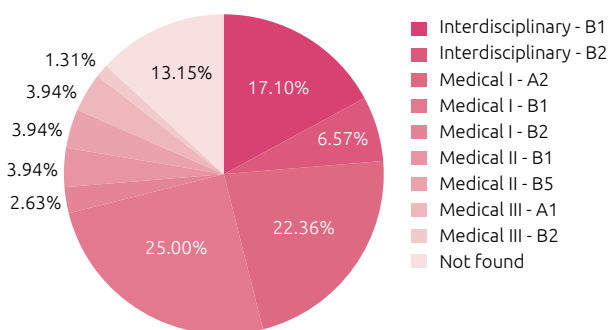
| Number of citations (quantity/percentage) | Type of publication (quantity/percentage) | Articles found in the databases (quantity/percentage) |
|---|---|---|
| 1 citation (15/19.73) | Original article (44/57.89) | Cochrane Library (0/0) |
| 2 citations (9/11.84) | Updated article (5/6.57) | LILACS (1/1.31) |
| 3 citations (8/10.52) | Opinion article (3/3.94) | SciELO (15/19.76) |
| 4 citations (2/2.63) | Response article (1/1.31) | MedLine (0/0) |
| 5 citations (3/3.94) | Review article (8/10.52) | PubMed (60/78.94) |
| 6 citations (2/2.63) | Letter to the editor (5/6.57) | |
| 7 citations (2/2.63) | Editorial (1/1.31) | |
| 8 citations (1/1.31) | Case report (5/6.57) | |
| 11 citations (1/1.31) | Clinical trial (2/2.63) | |
| 12 citations (1/1.31) | Audiovisual (1/1.31) | |
| 13 citations (1/1.31) | Not informed (1/1.31) | |
| 17 citations (1/1.31) | | |
| 20 citations (02/2.63) | | |
| Not found (28/36.84) | | |



Graphic 1. Subjects approached by the publications included.

of productions, with 8 (10.52%), 11 (14.47%), 10 (13.15%) and 9 (11.84%) papers published, respectively. Table 2 describes the amount of publications per year in relation to the database and the overall count.

The maximum number of authors in a single study was 17 (1.31%), the minimum was only 1 (1.31%). The mean number of authors per article was 8.48. A total of 59 different authors were found. Among them, 7 (11.86%) had a PhD, 22 (37.28%) were doctors, 12 (20.33%) held a master's degree and 18 (30.50%) were just specialists. Among the authors found, the



Graphic 2. Qualis classification of the journal.

Table 2. Number of annual publications according to the databases researched.

| Year | PubMed | SciELO | LILACS | Total number of articles quantity/percentage |
|-------|--------|--------|--------|--|
| 2000 | – | – | – | – |
| 2001 | – | 1 | – | 1/1.31 |
| 2002 | 1 | – | – | 1/1.31 |
| 2003 | 2 | – | – | 2/2.63 |
| 2004 | – | – | – | – |
| 2005 | 3 | – | – | 3/3.94 |
| 2006 | 2 | 1 | – | 3/3.94 |
| 2007 | 7 | 1 | – | 8/10.52 |
| 2008 | 2 | 1 | – | 3/3.94 |
| 2009 | 2 | 1 | 1 | 4/5.26 |
| 2010 | 2 | 3 | – | 5/6.57 |
| 2011 | 5 | 1 | – | 6/7.89 |
| 2012 | 8 | 3 | – | 11/14.47 |
| 2013 | 8 | 2 | – | 10/13.15 |
| 2014 | 6 | – | – | 6/7.89 |
| 2015 | 8 | 1 | – | 9/11.84 |
| 2016 | 4 | – | – | 4/5.26 |
| TOTAL | 60 | 15 | 1 | 76/100.00 |

characteristics of five that produced the most are presented in Table 3.

The articles constituting the scope of this study represented 23 institutions, among which include: Brazilian public hospitals (26.08%), private hospitals (8.69%) and philanthropic hospitals (8.69%), and Brazilian public (26.08%) and private (8.69%) universities, in addition to Brazilian (8.69%) and international (13.04%) institutes. Seven articles represented more than one institution, and 21 of them did not inform the institution where the work was carried out. The institution most often represented by the author was the European Institute of Oncology, in Milan, Italy, especially in scientific productions on prevention, early diagnosis and effective treatment of cancer.

DISCUSSION

The increasing interest of specialists and the scientific community as a whole in quantitative and qualitative indicators, justifies the need to create mediums for which scientific production may be managed and attested, especially with the growing emergence of research development and funding agencies. Research in this area is a new niche of work for doctors and other health professionals. The creation of databases has an important role in the gathering, selection and evaluation of journals that disseminate scientific production¹⁸. In this regard, bibliometric analyses are a way to quantify scientific production over time and to evaluate the impact of publications in the scientific community¹⁶.

Despite the various purposes of a bibliometric study, it has been observed that the development of this kind of study is unusual both in Brazilian and international medical literature, particularly when it comes to themes related to the surgical area, such as breast surgery. As an example of this, in the present study, no publications of bibliometric nature were found.

By analyzing the number of productions published per year on the studied theme, a growing tendency in the amount of publications up until 2012 was observed. This was the year with the highest number of articles. From this year on, there was a stabilizing trend in the number of productions, despite the reduction in 2014. This relation denotes a growing appreciation of the theme among Brazilian mastologists.

It should be noted that almost half of the authors who produced the articles reviewed in this study consist of doctors and PhD doctors. This shows that Brazilian mastologists that work with scientific production are increasingly interested in the topic. They are always searching for technical and scientific improvement, which positively interferes and impacts the practical aspects of their specialty. Clear proof of this new way of thinking is the number of productions submitted to the last Goiânia Breast Cancer Symposium, held in the country in May of 2016. When compared to the same event held in 2010, a significantly higher number of works were registered (from 30, in 2010, to 165, in 2016) and participants (from 120, in 2010, to 488, in 2016) were observed¹⁹.

Similar to a bibliometric study on public health and epidemiology carried out between 2000 and 2012 in Germany, most

Table 3. Authors with the highest number of publications on the subject.

| Author | Quantity of publications | Year(s) with the highest production | Current affiliation |
|------------------------------|--------------------------|--|--|
| Mario Rietjens | 45 | 2015 and 2012, with 7 publications each year | European Institute of Oncology; State University of Milan, Italy; European Breast Academy; European School of Abdominopelvic Surgery in Gynecologic Oncology. |
| Angelo Gustavo Zucca Matthes | 9 | 2016, 2013 and 2012, with 2 publications each year | <i>Departamento de Mastologia e Reconstrução do Hospital de Câncer de Barretos, Brazil; Centro de Treinamento em Cirurgia Oncoplástica do Hospital de Câncer de Barretos, Brazil; Fundação Pio XII, Brazil.</i> |
| Cícero de Andrade Urban | 9 | 2016 and 2008, with 2 publications each year | <i>Sociedade Brasileira de Mastologia; Hospital Santa Cruz, Rio de Janeiro, Brazil; Universidade Positivo, Brazil; Conselho Regional de Medicina do Paraná, Brazil; Hospital de Clínicas da Universidade Federal do Paraná, Brazil; Santa Casa de Misericórdia de Curitiba, Brazil; Hospital Nossa Senhora das Graças, Brazil.</i> |
| Fabrcio Palermo Brenelli | 8 | 2011, 2009 and 2007, with 2 publications each year | <i>Universidade Estadual de Campinas, Brazil.</i> |
| Ruffo Freitas- Junior | 6 | No year had a greater number of publications | <i>Hospital Araújo Jorge da Associação de Combate ao Câncer em Goiás, Brazil; Universidade Federal de Goiás, Brazil; Sociedade Brasileira de Mastologia.</i> |

works included in the present study were so-called original articles. In addition, this same study showed that Brazil figures among the five countries with the highest scientific production in the world on the themes analyzed by the authors²⁰.

When analyzing the data in the present study, it was observed that a significant number of articles were published by high quality journals (Qualis classification – A1, A2 and B1), which means the productions considered here are consistent and demonstrate a good performance in the scientific community, despite the low number of citations informed by the databases. Another aspect to be noted is the fact that most articles are from PubMed, a database offered by the National Library of Medicine of the United States, a database which brings together the leading journals worldwide. This allows us to infer that the studies conducted by Brazilian researchers are important in the medical literature relating to oncoplastic and breast reconstruction surgeries.

No similar studies were found with the same research proposal, thus making this a pioneering study, and proving the importance of the contribution that national experience in oncoplastic and breast reconstruction surgeries has given to the world's scientific community in reporting the production levels of Brazilian mastologist authors. Possible limitations

include the fact that many Brazilian authors' resumes found on the Lattes Platform were outdated or incomplete, which may have limited their evaluation. Another limitation regards how the institutions involved were determined, which may have reduced the credibility of the entities that promote the expansion of scientific knowledge.

CONCLUSION

The works that contain a bibliometric methodological approach constitute an important scientific tool that reveal patterns and trends for research, in addition to sources for obtaining data. The present study points toward a constant evolution in the participation of Brazilian mastologists as authors in the development of studies regarding oncoplastic and breast reconstruction surgeries. As for research perspectives, the temporal evolution of publications demonstrates an increasing interest of mastologists in the theme, indicating a possible growth in the area. Thus, the results presented may serve as a stimulus for other mastologists to learn about the subject and to prepare for this procedure which, when performed, is extremely important for the physical, psychological and sexual well-being of women.

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SYSTEMATIC CAVITY SHAVING IN ONCOPLASTIC BREAST SURGERY

Ampliação sistemática das margens cirúrgicas na cirurgia oncológica da mama

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Raffaella Levy de Andrade⁴, Ana Carolina Guglielmelli Mendonça⁶

ABSTRACT

Introduction: Conservative breast surgery has changed considerably in recent decades. Breast remodeling after conservative surgery is a surgical approach that has good oncological and cosmetic results. The surgical margin of oncological breast surgery has been shown to be a limiting factor, because a considerable percentage of patients undergo additional procedures, which increases costs and morbidity. **Objective:** To describe the experience of the establishment of systematic cavity shaving in conservative breast surgery and the benefits of this technique. **Methods:** This is a retrospective study, which evaluated information contained in patient records at the Campinas Breast Institute between 2009 and 2015. Systematic cavity shaving consists of the removal of tissue around the tumor in a thickness of 1 cm, and 2 cm in the other axes. Medial, lateral, cranial, inferior, deep and superficial margins are evaluated. **Results:** In a total of 94 cases with systematic cavity shaving, 18 (20%) reoperations were avoided. Only two patients required further surgery. **Conclusion:** It is a simple and reproducible procedure, which does not affect the final aesthetic result, and aims to provide disease-free surgical margins, avoiding reoperation and delayed adjuvant treatment.

KEYWORDS: Breast neoplasm; margins of excision; mammoplasty.

RESUMO

Introdução: A cirurgia conservadora da mama tem se modificado consideravelmente nas últimas décadas. O remodelamento mamário pós-cirurgia conservadora apresenta-se como uma forma de abordagem cirúrgica com bons resultados oncológicos e cosméticos. A margem cirúrgica das cirurgias oncológicas da mama tem se mostrado um fator limitante, pois um percentual considerável das pacientes é submetido a novos procedimentos, aumentando os custos e a morbidade. **Objetivo:** Descrever a experiência da instituição de ampliação sistemática das margens cirúrgicas na cirurgia conservadora de mama e os benefícios dessa técnica. **Métodos:** Estudo retrospectivo, que avaliou informações contidas em prontuário de pacientes do Instituto de Mama de Campinas, entre os anos de 2009 e 2015. A ampliação sistemática das margens consiste na retirada de tecido em torno do tumor, com espessura de 1 cm e dimensões de 2 cm nos demais eixos. São avaliadas margens medial, lateral, cranial, inferior, profunda e superficial. **Resultados:** Em um total de 94 casos com realização de ampliação sistemática das margens cirúrgicas, foram evitadas 18 (20%) reoperações. Apenas duas pacientes necessitaram de nova cirurgia. **Conclusão:** Trata-se de um procedimento simples e reprodutível, que não prejudica o resultado estético final, e que visa oferecer margens cirúrgicas livres de doença, evitando a reoperação e o atraso do tratamento adjuvante.

PALAVRAS-CHAVE: Neoplasia da mama; margens de excisão; mamoplastia.

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INTRODUCTION

Breast cancer (BC) has been studied extensively in recent decades. These studies have provided a sensitive evolution of diagnostic and therapeutic methods. Among the diagnostic methods, the role of mammography in the screening of the disease is highlighted, as it has acted as an important tool to reduce mortality and offer earlier diagnoses. There is no doubt that the surgical treatment of BC has undergone several modifications. As time goes on, the use of radical surgeries has been replaced by conservative surgeries. Fisher et al. defined BC as a systemic disease, its prognosis established by the tumor's ability to develop metastasis¹. Thus, the radical nature of breast surgery does not have an impact on the prognosis of the disease².

Kaufman et al. demonstrated that an increase in local control in the first 5 years of treatment results in a significant increase in disease-free survival and overall survival 15 years post-treatment³. In this case, it can be affirmed that the patient's initial surgical approach is determinant in their prognosis.

The ideal surgical approach aims to obtain tumor-free margins. However, reoperation rates can reach up to 40% of the cases⁴⁻⁶. The tumor volume versus total breast volume ratio has been presented as a determinant and limiting factor of conservative breast surgery, and it is assumed in most publications that when excision implies 20% or more of breast volume, a deformity after the completion of all local treatment is expected.⁶

The characteristics of the tumor itself—location and relation to breast volume—and the increasing demand for better cosmetic results, means that the breast surgeon must seek to minimize the after-effects of the treatment, considering not only tumor removal, but the location of surgical incisions, deviation from the position of the areola-papillary complex, retractions, asymmetries and possible local effects of radiotherapy⁷⁻⁹.

The different surgical approaches that link oncologic removal surgery to the techniques of plastic and reconstructive surgery are now known as oncoplastic breast surgery. This approach to breast surgery encompasses a range of techniques ranging from the simplest remodeling, which mobilizes breast tissue to techniques that allow the resection of up to almost 50% of the breast volume¹⁰. Oncoplastic breast surgery is associated with a great variability of techniques, which allows an even greater customization of the surgical treatment^{11,12}.

With this type of technique, evaluate surgical margins is even more important, since tissue remodeling hinders the localization of the initial tumor site¹³. Several authors have proposed to mark the surgical margins with metal clips in cases in which reoperation is suggested, as well as to guide radiotherapy¹⁴. However, a new procedure can cause increased morbidity, delayed oncologic treatment and cosmetic damage¹⁵.

Several studies have demonstrated that cavity shaving can reduce the compromised margins indexes, which would further

increase patient safety without cosmetic damage¹⁶. This practice has been adopted for several years in conjunction with oncoplastic techniques, and it seems that there is a positive impact on the surgical breast treatment¹⁷.

METHODS

This was a retrospective study, which evaluated patient records from the Breast Institute of Campinas between 2009 and 2015.

The systematic cavity shaving consists of the removal of tissue around the tumor, with a thickness of 1 cm, and 2 cm in the other axes. The margins evaluated systematically are medial, lateral, cranial, inferior, deep and superficial. In practical terms, after the removal of the primary piece (the breast sector), delicate Allis tweezers lightly grip the additional portion of breast tissue and remove it from the tumor bed as described. That way, an additional margin is obtained and is marked with surgical thread on the side of the tumor in order to guide pathology.

The study included all patients with T1 or T2 BC, undergoing conservative breast surgery using a breast remodeling technique, in which the margins were systematically enlarged according to a surgical description and a histopathological report.

Patients whose breast remodeling technique was not properly described at the time of surgery were excluded from the study, as were those in which the additional surgical margins were not removed in their entirety, i.e., one or more margins were not described in the histopathological study. Patients with a skin impairment, or who had surrounding musculature at the time of surgery or in the analysis of the surgical specimen, were also excluded from the study. Additionally, patients undergoing neo-adjuvant chemotherapy were not evaluated, and neither were patients with stage T3 and T4 tumors.

RESULTS

The study included 94 patients in stages T1 and T2, who underwent conservative breast surgery with the immediate tissue repair technique, from the period of January 2009 to June 2015. The average age of the patients was 56 years old and their ages ranged from 36 to 71 years old. Of the total cases, 88 (93%) were invasive ductal carcinomas, 4 (4.2%) cases were lobular carcinomas, 1 (1%) was a marrow carcinoma and 1 (1%) was a colloid carcinoma. At the end of the study, the average lesion size was 0.9 cm.

All of the patients underwent routine cavity shaving.

Of the 94 patients analyzed, 20 cases of compromised margins were identified. Of these, 12 (60%) had ductal carcinoma in situ and 8 (40%) had invasive ductal carcinoma.

In the serial enlargement of the margins, results showing clear margins were obtained in 18 (90%) cases, with only 2 (10%) patients requiring additional surgery. In specimens that had clear

margins, shaving initially found one (1%) case of a compromised margin, resulting in a subsequent surgery.

DISCUSSION

Conservative breast surgery with the application of oncoplastic techniques is a method that has been increasingly used in clinical practice. Systematic cavity shaving has been shown to be a feasible and low morbidity procedure¹⁷. Mook et al. demonstrated, in a retrospective study, that serial enlargement of the margins allows the surgeon to remove a smaller amount of breast tissue, preventing oncological damages and gaining considerable cosmetic benefits¹⁸.

In the present study, the benefit of the described technique was noteworthy, and reoperation was avoided in 18 patients from the total number of operated cases. This corresponds to 20% of the total and to 90% of the compromised margins cases. Thus, as described by Cao et al., there is benefit in terms of morbidity, costs and time in adjuvant treatment¹⁹.

On the other hand, it was shown that, in certain cases, the use of the technique can lead to the identification of compromised margins in situations where the margin was considered free of disease²⁰, but in a much lower percentage when compared to the benefit of the technique (1%). Tang et al., in their study of

systematic cavity shaving, found an additional positive margin index of 19%, which is an important counterpoint to the data in the present study²¹. It is important to note that, in this study, patients with T1 and T2 tumors were included, and those with neoadjuvant chemotherapy were excluded, which may be the justification for such a difference.

Therefore, it can be concluded that this technique is a procedure that can be reproduced safely, without cosmetic damages, and can lead to the reduction of reoperations in up to 90% of cases²².

The application of cavity shaving demonstrated similar results in the series of patients using oncoplastic techniques and in conventional conservative surgeries.

CONCLUSION

The systematic cavity shaving in breast cancer surgery is a simple and reproducible procedure, which does not detract from the final aesthetic result. It aims to provide clear margins, which reduces the reoperation rate and, consequently, the costs and time of adjuvant treatment. More studies — especially with prospective and randomized designs — should be stimulated, since the benefits of applying systematic cavity shaving in surgeries with oncoplastic techniques in retrospective studies have been very encouraging.

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LOCOREGIONAL FLAPS IN ONCOPLASTIC SURGERY AND BREAST RECONSTRUCTION

Retalhos locorregionais na cirurgia oncoplástica e reconstrutiva da mama

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ABSTRACT

Introduction: Conserving surgery in the treatment of breast cancer, in association with radiotherapy, has replaced mastectomy in most cases. However, depending on the location and size of tumor, the classic conservative surgery can present unfavourable aesthetic results and high levels of commitment of the surgical margins. The oncoplastic breast surgery can have high local control rates and cause minimum breast deformities, leading to a better aesthetic result. **Objective:** To report cases of 30 patients with primary unilateral breast carcinoma who underwent oncoplastic surgery between 2013 and 2015. **Methods:** We used local and regional dermo-glandular rotation techniques. The average age of patients was 58.9 years. The average tumor size was 2.53 cm. Three patients had close or positive surgical margins and underwent a new surgical procedure. **Results:** The aesthetic result was evaluated by the BCCT.core program and was considered excellent in 11 cases, good in 12 cases and regular in 7 cases. Six patients had postoperative complications. **Conclusion:** The use of local and regional dermo-glandular rotation techniques allows extensive resections in breast conserving surgery, leading to a satisfying symmetry and a good aesthetic result without the need of symmetrization, with low postoperative complication rates and high rates of free surgical margins.

KEYWORDS: Breast cancer; breast reconstruction; surgical flaps; surgical margins; cosmetic techniques.

RESUMO

Introdução: A cirurgia conservadora no tratamento do câncer de mama, associada à radioterapia, tem substituído a mastectomia na maioria dos casos. Entretanto, dependendo da localização e do tamanho do tumor, a cirurgia conservadora clássica pode resultar em um resultado estético insatisfatório e em altos índices de comprometimento de margens cirúrgicas. A cirurgia oncoplástica da mama pode apresentar altas taxas de controle local, causando deformidades mamárias mínimas, levando a um melhor resultado estético. **Objetivo:** Relatar casos de 30 pacientes com carcinoma mamário unilateral que foram submetidas à cirurgia oncoplástica da mama entre 2013 e 2015. **Métodos:** Foram utilizadas técnicas de rotação dermoglandular local e regional. A idade média das pacientes foi de 58,9 anos. O tamanho médio do tumor foi 2,53 cm. Três pacientes apresentaram margens cirúrgicas exíguas ou comprometidas, sendo submetidas a novo procedimento cirúrgico. **Resultados:** O resultado estético foi avaliado pelo programa BCCT.core, sendo considerado excelente em 11 casos, bom em 12 casos e regular em 7 casos. Seis pacientes apresentaram complicações pós-operatórias. **Conclusão:** A utilização de técnicas de rotação dermoglandular local e regional permite ressecções extensas na cirurgia conservadora da mama, permitindo uma simetria satisfatória e um bom resultado estético sem a necessidade de simetrização, com baixos índices de complicação pós-operatória e altas taxas de margens cirúrgicas livres.

PALAVRAS-CHAVE: Câncer de mama; reconstrução da mama; retalhos cirúrgicos; margens cirúrgicas; técnicas cosméticas.

Study carried out at the Santa Casa de Misericórdia de Belo Horizonte – Belo Horizonte (MG), Brazil.

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Conflict of interests: nothing to declare.

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INTRODUCTION

Breast conserving surgery associated with radiation therapy in the treatment of breast cancer results in a long-term survival similar to those of mastectomy, whenever tumor-free surgical margins are obtained. However, depending on the volume of tumor and the volume of resection required for adequate cancer control, a negative aesthetic result may be obtained¹.

The criteria for breast conservation have expanded in recent years and have included larger tumors, traditionally treated by mastectomy. Thus, more than half of women currently diagnosed with breast cancer may have their breast preserved². One way to attenuate the conflict between obtaining a good locoregional control without compromising the aesthetic result is the application of plastic surgery techniques to mammary oncologic surgery, called mammary oncoplastic surgery. This concept is based on three fundamental points: ideal oncologic surgery, homolateral reconstruction and immediate contralateral remodeling (when necessary). Thus, it is possible to perform more extensive resections in conserving surgery without significantly compromise the final aesthetic results^{2,3}.

The techniques of oncoplastic breast surgery offer some advantages over the classic conservative treatment: oncologic safety with resection of voluminous tumors, higher index of free surgical margins, lower rates of reoperation and better aesthetic result^{1,2}. The techniques used in oncoplastic surgery can be involving volume displacement or volume replacement⁴. The volume displacement techniques are used for immediate repair in breast-conserving treatment and generally have a lower risk of complications than the techniques used for volume replacement after radical mastectomy¹.

The objective of this study is to show the results of oncoplastic techniques used in the conservative treatment of breast cancer, considering oncologic safety, free surgical margins rates and reoperation rates as well as postoperative mammary symmetry and final aesthetic results.

METHODOLOGY

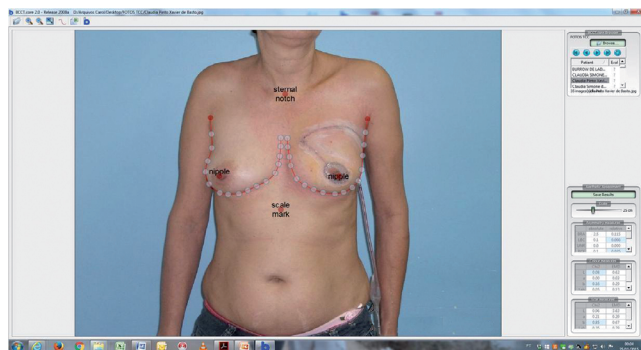
Thirty patients were included in the study between October 2013 and November 2015 at *Santa Casa de Misericórdia* in Belo Horizonte. All patients had unilateral, relatively voluminous malignant tumors in relation to their breast size (tumor/breast ratio greater than 20%) and close to the skin, requiring resection of the skin above the tumor in most cases.

Inclusion criteria were: unilateral carcinoma, tumor/breast ratio >20% and patient's desire to avoid symmetrization. Exclusion criteria were: skin involvement, tumor/breast ratio >50% and the patient's desire to perform associated contralateral mammoplasty.

The evaluated factors were: patient age, tumor's size and location, resected breast volume, surgical margins, reoperation rate for surgical margin enlargement, mastectomy rate after conservative treatment, resection or not of the nipple-areola complex (NAC), neoadjuvant chemotherapy, postoperative complications, body mass index (BMI), comorbidities and smoking.

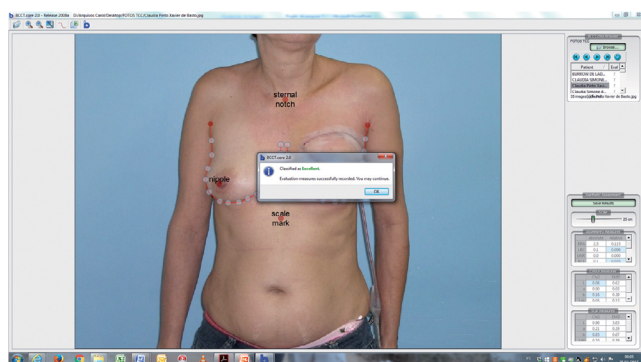
The choice of surgical technique was based on tumor location and tumor/breast ratio. Volume displacement techniques with local and regional dermo-glandular rotation were used. The techniques of local rotation were: dermo-glandular rotation flap and Burow's Triangle. On the other hand, regional rotation techniques were: lateral thoracic flap and thoraco-epigastric flap.

All surgeries were performed unilaterally, only in the breast affected by the tumor. The axilla was managed as appropriate in each case. The aesthetic result was evaluated using the BCCT.core program (Breast Cancer Conservation Treatment Cosmetics Results), an objective method of evaluating the aesthetic result in breast-conserving surgery. This software simplifies and standardizes aesthetic evaluation in the conservative treatment of breast cancer, as it consists of a tool to quantify aesthetic results in breast-conserving surgery, discriminating them between four categories: excellent, good, regular and fair. BCCT.core issues its evaluation from an image database (Figures 1 and 2).



Source: BCCT.core 2.0.

Figure 1. BCCT.core software.



Source: BCCT.core 2.0.

Figure 2. BCCT.core software – excellent result.

Statistical methodology

For the characterization of the sample, frequency tables were constructed for the qualitative variables and the descriptive measures for the quantitative variables were calculated. The χ^2 test was used in order to identify possible associations of systemic arterial hypertension (SAH), *diabetes mellitus* (DM), smoking, axillary dissection (AD), NAC resection and surgical technique with aesthetic result, tested for normality (Table 1).

As the data presented normal distribution, parametric analyses were used. The comparisons of means of variables age, tumor size, part volume and BMI in relation to aesthetic

result were performed using the ANOVA (Variance Analysis) test (Table 2).

For all the statistical tests used, we will consider a significance level of 5%. Thus, statistically significant associations are those whose p-value was less than 0.05. The analyses were performed in the Statistical Package for Social Sciences (SPSS) software, version 20.0, 2012.

RESULTS

Thirty patients underwent oncoplastic breast surgery between October 2013 and November 2015, using the previously described

Table 1. Association of variables with aesthetic result – Test χ^2 .

| | | | SAH | | Total | P-value |
|------------------|-----------|---|---------------|-------|-------|---------|
| | | | No | Yes | | |
| Aesthetic result | Excellent | n | 6 | 5 | 11 | 0.299 |
| | | % | 54.5 | 26.3 | 36.7 | |
| | Good | n | 3 | 9 | 12 | |
| | | % | 27.3 | 47.4 | 40.0 | |
| | Regular | n | 2 | 5 | 7 | |
| | | % | 18.2 | 26.3 | 23.3 | |
| Total | | n | 11 | 19 | 30 | |
| | | % | 100.0 | 100.0 | 100.0 | |
| | | | DM | | Total | P-value |
| | | | No | Yes | | |
| Aesthetic result | Excellent | n | 7 | 4 | 11 | 0.160 |
| | | % | 38.9 | 33.3 | 36.7 | |
| | Good | n | 5 | 7 | 12 | |
| | | % | 27.8 | 58.3 | 40.0 | |
| | Regular | n | 6 | 1 | 7 | |
| | | % | 33.3 | 8.3 | 23.3 | |
| Total | | n | 18 | 12 | 30 | |
| | | % | 100.0 | 100.0 | 100.0 | |
| | | | Smoking | | Total | P-value |
| | | | No | Yes | | |
| Aesthetic result | Excellent | n | 8 | 3 | 11 | 0.203 |
| | | % | 30.8 | 75.0 | 36.7 | |
| | Good | n | 11 | 1 | 12 | |
| | | % | 42.3 | 25.0 | 40.0 | |
| | Regular | n | 7 | 0 | 7 | |
| | | % | 26.9 | 0.0 | 23.3 | |
| Total | | n | 26 | 4 | 30 | |
| | | % | 100.0 | 100.0 | 100.0 | |
| | | | NAC resection | | Total | P-value |
| | | | No | Yes | | |
| Aesthetic result | Excellent | n | 9 | 2 | 11 | 0.514 |
| | | % | 36.0 | 40.0 | 36.7 | |
| | Good | n | 11 | 1 | 12 | |
| | | % | 44.0 | 20.0 | 40.0 | |
| | Regular | n | 5 | 2 | 7 | |
| | | % | 20.0 | 40.0 | 23.3 | |
| Total | | n | 25 | 5 | 30 | |
| | | % | 100.0 | 100.0 | 100.0 | |

Continue...

Table 1. Continuation.

| | | | AD | | Total | P-value |
|------------------|-----------|---|-------|-------|-------|---------|
| | | | No | Yes | | |
| Aesthetic result | Excellent | n | 3 | 8 | 11 | 0.246 |
| | | % | 25.0 | 44.4 | 36.7 | |
| | Good | n | 7 | 5 | 12 | |
| | | % | 58.3 | 27.8 | 40.0 | |
| | Regular | n | 2 | 5 | 7 | |
| | | % | 16.7 | 27.8 | 23.3 | |
| Total | | n | 12 | 18 | 30 | |
| | | % | 100.0 | 100.0 | 100.0 | |

| | | | Surgical technique | | | | Total | P-value |
|------------------|-----------|---|--------------------|----------|------------------|-------------------|-------|---------|
| | | | Burow | Rotation | Lateral thoracic | Thoracoepigastric | | |
| Aesthetic result | Excellent | n | 6 | 3 | 1 | 1 | 11 | 0.336 |
| | | % | 40.0 | 27.3 | 33.3 | 100.0 | 36.7 | |
| | Good | n | 7 | 3 | 2 | 0 | 12 | |
| | | % | 46.7 | 27.3 | 66.7 | 0.0 | 40.0 | |
| | Regular | n | 2 | 5 | 0 | 0 | 7 | |
| | | % | 13.3 | 45.5 | 0.0 | 0.0 | 23.3 | |
| Total | | n | 15 | 11 | 3 | 1 | 30 | |
| | | % | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | |

SAH: systemic arterial hypertension; DM: diabetes mellitus; NAC: nipple-areola complex; AD: axillary dissection.

Table 2. Comparisons – Anova Test.

| Comparisons: aesthetic result | | N | Mean | Standard deviation | 95% CI | | Minimum | Maximum | P-value |
|-------------------------------|-----------|----|-------|--------------------|--------|-------|---------|---------|---------|
| Age | Excellent | 11 | 57.4 | 13.0 | 48.6 | 66.1 | 41.0 | 76.0 | 0.742 |
| | Good | 12 | 60.7 | 9.2 | 54.8 | 66.5 | 44.0 | 74.0 | |
| | Regular | 7 | 58.3 | 7.5 | 51.3 | 65.2 | 50.0 | 71.0 | |
| | Total | 30 | 58.9 | 10.2 | 55.1 | 62.7 | 41.0 | 76.0 | |
| Tumor size (in cm) | Excellent | 11 | 2.7 | 0.7 | 2.2 | 3.1 | 1.5 | 3.5 | 0.648 |
| | Good | 12 | 2.4 | 0.9 | 1.8 | 2.9 | 1.0 | 3.5 | |
| | Regular | 7 | 2.6 | 1.0 | 1.6 | 3.5 | 1.2 | 4.0 | |
| | Total | 30 | 2.5 | 0.8 | 2.2 | 2.8 | 1.0 | 4.0 | |
| Part volume (in g) | Excellent | 11 | 148.9 | 88.0 | 89.8 | 208.0 | 52.0 | 385.0 | 0.991 |
| | Good | 12 | 145.2 | 104.4 | 78.9 | 211.5 | 38.0 | 431.0 | |
| | Regular | 7 | 150.9 | 76.4 | 80.2 | 221.5 | 53.0 | 268.0 | |
| | Total | 30 | 147.9 | 89.5 | 114.4 | 181.3 | 38.0 | 431.0 | |
| BMI | Excellent | 11 | 27.2 | 6.3 | 23.0 | 31.5 | 18.5 | 39.6 | 0.414 |
| | Good | 12 | 29.9 | 6.1 | 26.0 | 33.8 | 19.9 | 41.7 | |
| | Regular | 7 | 26.7 | 3.9 | 23.2 | 30.3 | 22.1 | 33.7 | |
| | Total | 30 | 28.2 | 5.7 | 26.0 | 30.3 | 18.5 | 41.7 | |

BMI: body mass index; 95%CI: 95% confidence interval.

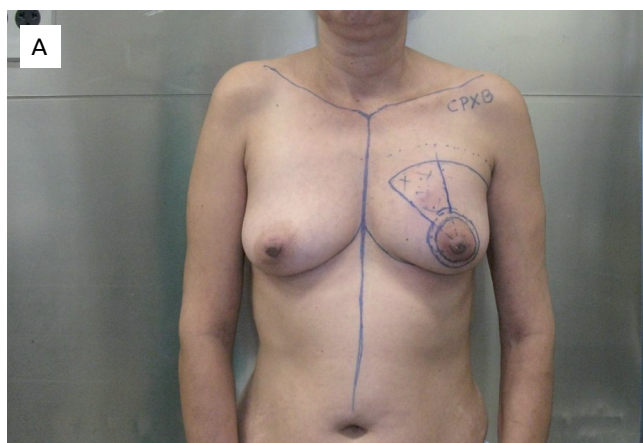
techniques. The mean age of the patients in this study was 58.9 years. The mean pathological tumor size was 2.53 cm. Twelve patients had tumors located in upper inner quadrant, two in lower inner quadrant, eight in upper outer quadrant, two in lower outer quadrant, four at 12 o'clock, one at 3 o'clock and one at 9 o'clock. The NAC was resected in five cases. Twenty-eight patients had invasive ductal carcinoma (IDC); one patient presented invasive mucinous carcinoma of the breast and one patient presented ductal carcinoma in situ

(DCIS). The mean volume of resection of breast tissue was 147.87 g. The mean BMI was 28.18 kg/m². Twenty-six patients underwent breast reconstruction with local flaps, fifteen of which were submitted to the Burow's Triangle (Figure 3) and eleven to the dermo-glandular rotation flap (Figure 4). Four patients underwent regional flap reconstruction, three of which were submitted to the lateral thoracic flap (Figure 5) and one to the thoracoepigastric flap (Figure 6). Only one patient was submitted to neoadjuvant chemotherapy. Three women

had undergone previous tumor resection by classic breast conserving surgery, without obtaining free surgical margins, and were referred for oncoplastic surgery. Surgical margins were free of neoplasia in 27 cases (90%). Two patients had close surgical margins and one had positive surgical margins. These three women underwent surgical reintervention for margin enlargement, with only one being submitted to subsequent total mastectomy. None of these patients presented residual neoplasia in the surgical specimen after margin enlargement or mastectomy. Twenty-four patients did not present postoperative complications (80%). Six women had a postoperative complication: one had epidermolysis, one had partial dehiscence of surgery incision, three had partial necrosis of the flap, and one had infection of surgery incision and subsequent fibrosis. Four patients were smokers. Twenty women were hypertensive, eleven had DM, two had cardiopathy, two had hypercholesterolemia, and four had hypothyroidism. Only six

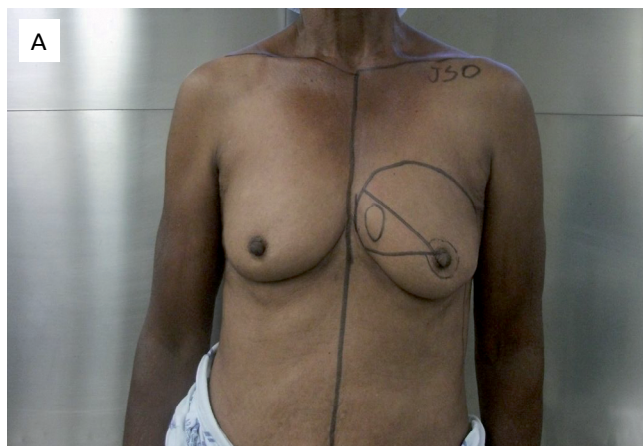
of the patients had no associated comorbidity. All six patients who presented postoperative complications were hypertensives. Three of them had DM, two had hypothyroidism and two had associated heart diseases. Sentinel lymph node biopsy was performed in fifteen patients. Four women underwent AD due to sentinel lymph node positivity, and fifteen, to AD for clinically positive nodes in the initial clinical staging. Adjuvant radiotherapy was indicated in all cases. The final aesthetic result was evaluated by the BCCT.core program. According to the software, the results were rated "excellent" in 11 cases, "good" in 12 cases and "regular" in 7 cases. No results were classified as "fair" (Table 3).

In the present study, the contralateral breast was not approached in any case. Oncoplastic surgery was performed to maintain the patient's initial shape and aesthetics, with the lowest asymmetry rate possible, avoiding the need for symmetrization. In the statistical analysis used, there was



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Figure 3. Patient submitted to the Burow Triangle technique. (A) Preoperative and (B) postoperative.



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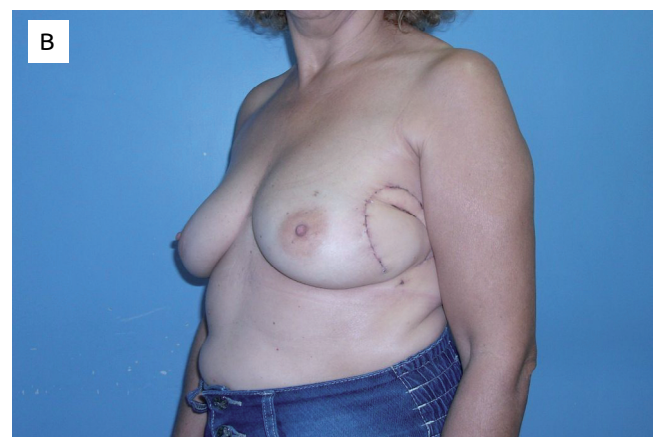
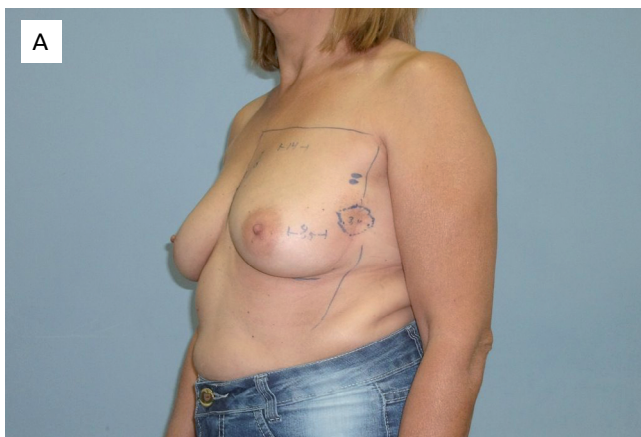
Figure 4. Patient submitted to the dermo-glandular rotation technique. (A) Preoperative and (B) postoperative.

no statistically significant difference between the possible associations of the variables SAH, DM, smoking, AD, NAC resection and surgical technique with aesthetic result. The comparison of means of variables also did not present statistically significant difference when evaluated age, size of the tumor, volume of resection of breast tissue and the BMI in relation to the aesthetic result. One theory to explain the absence of difference between the groups could be the sample size (N) analyzed.

DISCUSSION

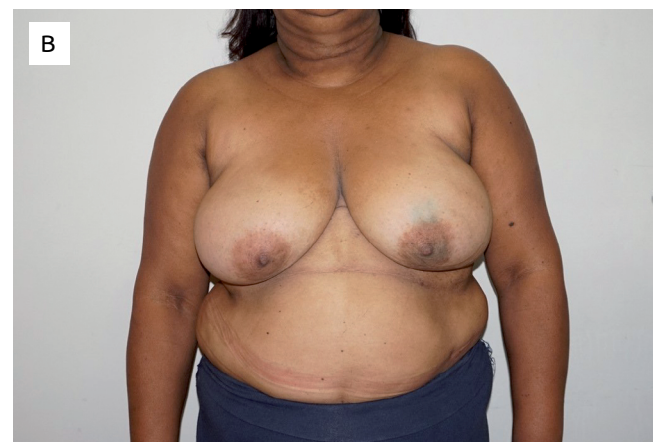
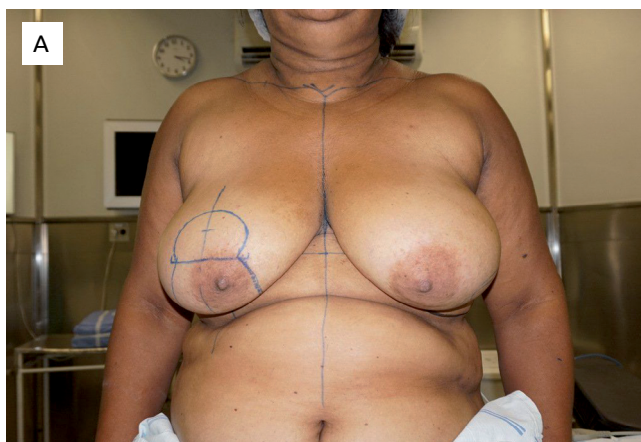
Indications for conservative surgery in the treatment of breast cancer are becoming more frequent. Randomized clinical trials show that breast conserving surgery associated with

radiotherapy has overall survival rates similar to total mastectomy. Starting from this premise, there is a greater tendency to treat large tumors conservatively. However, the greatest limitation is to perform large resections without compromising the cosmetic result^{5,6,7}. Oncoplastic breast surgery, which consists of the combination of plastic surgery techniques and oncologically safe surgical techniques in the treatment of breast cancer, is widely accepted as the alternative that allows for greater resections and less aesthetic damage, even in voluminous tumors. Increasingly indicated, it provides significant advantages, since it minimizes the psychological damage of a possible mutilating treatment^{3,6,8,9}. Thus, it is possible to perform a greater number of breast conserving surgeries in patients who would usually undergo total mastectomy, with a lower rate of postoperative complications and a higher rate



Source: own file.

Figure 5. Patient submitted to the lateral thoracic flap. (A) Preoperative and (B) postoperative.



Source: own file.

Figure 6. Patient submitted to the thoracoepigastric flap. (A) Preoperative and (B) postoperative.

of local disease control^{1,3,4,5,10}. In the classic breast conserving surgery, resections of more than 20% of the breast tissue affected by the disease generates both breast deconfiguration

and contralateral asymmetry. Thus, the use of some oncoplastic techniques is convenient to minimize undesirable aesthetic results³. Extensive defects after breast conserving

Table 3. Clinical and treatment characteristics of the patients (n = 30).

| Tumor localization | | |
|--------------------|----|-------|
| | n | % |
| LOQ | 2 | 6.7 |
| LIQ | 2 | 6.7 |
| UOQ | 8 | 26.7 |
| UIQ | 12 | 40.0 |
| 9 o'clock | 1 | 3.3 |
| 3 o'clock | 1 | 3.3 |
| 12 o'clock | 4 | 13.3 |
| Total | 30 | 100.0 |

| Surgical technique | | |
|---------------------|----|-------|
| | n | % |
| Burow | 15 | 50.0 |
| Rotation | 11 | 36.7 |
| Lateral thoracic | 3 | 10.0 |
| Thoracocephigastric | 1 | 3.3 |
| Total | 30 | 100.0 |

| Type of tumor | | |
|-----------------------------|----|-------|
| | n | % |
| Invasive mucinous carcinoma | 1 | 3.3 |
| IDC | 28 | 93.4 |
| DCIS | 1 | 3.3 |
| Total | 30 | 100.0 |

| Expansion of surgical margins | | |
|-------------------------------|----|-------|
| | n | % |
| No | 27 | 90.0 |
| Yes | 3 | 10.0 |
| Total | 30 | 100.0 |

| Mastectomy | | |
|------------|----|-------|
| | n | % |
| No | 29 | 96.7 |
| Yes | 1 | 3.3 |
| Total | 30 | 100.0 |

| Lymph node biopsy | | |
|-------------------|----|-------|
| | n | % |
| No | 15 | 50.0 |
| Yes | 15 | 50.0 |
| Total | 30 | 100.0 |

| Axillary dissection | | |
|---------------------|----|-------|
| | n | % |
| No | 12 | 40.0 |
| Yes | 18 | 60.0 |
| Total | 30 | 100.0 |

| Postoperative complications | | |
|-----------------------------|----|-------|
| | n | % |
| No | 26 | 86.7 |
| Yes | 4 | 13.3 |
| Total | 30 | 100.0 |

| Aesthetic result | | |
|------------------|----|-------|
| | n | % |
| Good | 12 | 40.0 |
| Excellent | 11 | 36.7 |
| Regular | 7 | 23.3 |
| Total | 30 | 100.0 |

| NAC resection | | |
|---------------|----|-------|
| | n | % |
| No | 25 | 83.3 |
| Yes | 5 | 16.7 |
| Total | 30 | 100.0 |

| SAH | | |
|-------|----|-------|
| | n | % |
| No | 11 | 36.7 |
| Yes | 19 | 63.3 |
| Total | 30 | 100.0 |

| DM | | |
|-------|----|-------|
| | n | % |
| No | 18 | 60.0 |
| Yes | 12 | 40.0 |
| Total | 30 | 100.0 |

| Neoadjuvant chemotherapy | | |
|--------------------------|----|-------|
| | n | % |
| No | 29 | 96.7 |
| Yes | 1 | 3.3 |
| Total | 30 | 100.0 |

| Smoking | | |
|---------|----|-------|
| | n | % |
| No | 26 | 86.7 |
| Yes | 4 | 13.3 |
| Total | 30 | 100.0 |

| | Descriptive measures | | | | | | | |
|--------------------|----------------------|---------|--------|--------------------|---------|---------|------------|-------|
| | n | Average | Median | Standard deviation | Minimum | Maximum | Percentils | |
| | | | | | | | 25 | 75 |
| Age | 30 | 58.9 | 57.0 | 10.2 | 41.0 | 76.0 | 51.0 | 69.0 |
| Tumor size (in cm) | 30 | 2.5 | 2.6 | 0.8 | 1.0 | 4.0 | 2.0 | 3.0 |
| Part volume (in g) | 30 | 147.9 | 132.0 | 89.5 | 38.0 | 431.0 | 93.5 | 177.0 |
| BMI | 30 | 28.2 | 27.6 | 5.7 | 18.5 | 41.7 | 23.7 | 31.5 |

Source: Research data.

LOQ: lower outer quadrant; LIQ: lower inner quadrant; UOQ: upper outer quadrant; UIQ: upper inner quadrant; 9 o'clock: union of lateral quadrants; 3 o'clock: union of inner quadrants; 12 o'clock: union of upper quadrants; IDC: invasive ductal carcinoma; DCIS: ductal carcinoma *in situ*; NAC: nipple-areola complex; SAH: systemic arterial hypertension; DM: diabetes *melittus*; BMI: Body mass index.

surgery tend to require local or regional flap rotations. Due to radiotherapy, deformities tend to become more pronounced over time, as well as technical difficulties and limitations. The consequence is that the aesthetic results of a late reconstruction are more limited. Immediate reconstruction may reduce these risks and provide better results³, although the deleterious action of radiotherapy, from the aesthetic point of view, may reduce success rates after the treatment. Dermo-glandular rotation flaps are a safe locoregional alternative to repair eventual defects caused by conservative breast treatment. In the present study, local and regional rotation flaps were used to mobilize the dermo-glandular flap toward the defect caused by quadrantectomy, aiming to repair it completely. These techniques are called volume displacement techniques, and are used in immediate repair in the conservative treatment of the breast^{4,11}. They generally present a lower risk of complications than volume replacement techniques after total mastectomy^{1,11}.

Surgical margins free of neoplasia correspond to a reduction in the risk of local recurrence, independently of margin size^{4,8}. In breast oncoplastic surgery, the surgical margins are larger than in conservative surgery, and its enlargement is rarely necessary³. In this study, the surgical margins were free of neoplasia in 27 cases (90%). Two patients had close surgical margins and one, positive surgical margins, which needed surgical reinterventions: two margins enlargements and a subsequent total mastectomy. None of these patients presented residual neoplasia in the surgical specimen, demonstrating the effectiveness of oncoplastic surgery in the local control of breast cancer. The focus of oncoplastic breast surgery is to improve the quality of life of patients with treatments that may be more effective from an oncological point of view without compromising the aesthetic-functional result. It represents the major advance in the conservative treatment of breast cancer in the last decades³. Studies have shown a higher satisfaction rate with aesthetic result when using oncoplastic techniques, independently of the extent of resected breast volume tissue¹².

Thus, oncoplastic breast surgery allows the patient to leave the operating room with little or no breast asymmetry and no deformities of the breast treated by cancer^{1,4}. This study used locoregional dermo-glandular rotation flap techniques for immediate breast repair in all patients. These techniques allowed good local oncological control, with satisfactory symmetry and good aesthetic result. No contralateral breast symmetrization was indicated in any case. The rates of free surgical margins were high and the rates of postoperative complications were low, and no complications were severe or required a surgical approach to correction. No variables analyzed in relation to the characteristics of the patient seemed to influence the aesthetic result obtained.

CONCLUSION

Oncoplastic surgery represents an important evolution for breast conserving surgery, since it is an excellent option to approach breast cancer, allowing more extensive resections without compromise the final aesthetic result. Also, it contributes to the improvement of the psychological aspects of the patients with breast cancer.

The focus of oncoplastic breast surgery is to improve the quality of life of patients with treatments that may be more effective and, at the same time, less aggressive. The greatest benefit is the patients themselves, who enjoy a safe oncological treatment and a suitable aesthetic-functional treatment. The various existing techniques for immediate repair must be individualized in each specific case in order to achieve the best results in oncological-plastic integration. Immediate repair surgery usually shows better results when compared to late reconstruction. The use of local dermo-glandular rotation flap techniques allows extensive resections in breast conserving surgery. In addition, they allow good local oncological control, satisfactory symmetry and aesthetic results, without the need for contralateral breast symmetrization, with low rates of postoperative complications and high rates of free surgical margins.

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A CLINICAL-PATHOLOGICAL CORRELATION IN THE DIAGNOSIS OF BREAST SARCOMA

Correlação clinicopatológica no diagnóstico de sarcoma de mama

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Nicolas Silva Lazaretti², Rubens Rodriguez^{1,3}, Rafael Ribeiro Martini^{1,4}

ABSTRACT

Breast sarcomas are rare tumors that are difficult to diagnose. They are characterized by a mobile and painless mass with accelerated growth. This neoplasm represents less than 1% of all breasts malignancies and less than 5% of all soft tissues sarcomas. The present publication reports the case of a 78 year old patient, who was referred to the Hospital da Cidade de Passo Fundo's Mastology Ambulatory due to a suspicious mass occupying almost the entire right breast (BI-RADS[®]5). The diagnosis of breast sarcoma was made through the correlation between a clinical evaluation and an anatomopathological exam, and was supplemented by an immunohistochemistry and oncologic evaluation. The patient developed lung and liver metastasis three months after surgery. This paper aimed to report an unusual case of a breast tumor and the difficulty in performing its diagnosis, even after surgery. In the end, a multidisciplinary evaluation was needed.

KEYWORDS: Sarcoma; breast; immunohistochemistry; breast neoplasms; neoplasms.

RESUMO

Sarcomas de mama são tumores raros e de difícil diagnóstico, que se apresentam como uma massa indolor, móvel e de crescimento acelerado. Essa neoplasia representa menos de 1% de todas as malignidades da mama e menos de 5% de todos os sarcomas de tecidos moles. Relata-se nesta publicação o caso de uma paciente de 78 anos, encaminhada ao Ambulatório de Mastologia do Hospital da Cidade de Passo Fundo em razão de uma massa suspeita ocupando quase a totalidade da mama direita (BI-RADS[®]5), que teve diagnóstico de sarcoma de mama, o qual foi obtido por meio da correlação entre avaliação clínica, exame anatomopatológico complementado por estudo imuno-histoquímico e avaliação oncológica. A paciente evoluiu com metástase pulmonar e hepática três meses após a intervenção cirúrgica. O objetivo deste trabalho foi relatar um caso inusitado de tumor de mama e a dificuldade em realizar o diagnóstico, mesmo após intervenção cirúrgica, tendo sido necessária uma avaliação multidisciplinar.

PALAVRAS-CHAVE: Sarcoma; mama; imuno-histoquímica; neoplasias da mama; neoplasias.

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INTRODUCTION

Breast sarcomas are rare and low-frequency tumors. The first case of breast sarcoma was described in the literature in 1828, by Chelius¹. This tumor seems to affect both pre- and post-menopausal women¹. Its low incidence and the lack of a specific pattern of how it presents itself make it so that, at the time of diagnosis, it is often unsuspected. As such, only 50% of cases are diagnosed properly¹. We present here the case of a patient with an extensive neoplastic lesion in the right breast, whose diagnosis was defined by the correlation of clinical, macroscopic and histological information of the lesion, which is considered to be a primary breast sarcoma.

CASE REPORT

PPSM, female, 78 years old, was referred to the Ambulatory of the Hospital da Cidade de Passo Fundo (HCPF), Rio Grande do Sul, for a change in the image examination (breast ultrasound) performed on October 2, 2015. She is a former smoker (smoked for 6 years, 8 straw cigarettes/day, and stopped 59 years ago). She was in treatment for systemic arterial hypertension for 10 years and congestive heart failure. The patient has a previous history of breast cancer in the left breast, and had a radical mastectomy performed 22 years ago. There is no information about adjuvant treatment. One year ago, she underwent a biopsy of the right breast, in her city of origin, and had a benign anatomopathological examination.

Upon physical examination, a tumor was felt occupying the entire right breast, with a clinically negative axilla (Figure 1).

Regarding the examinations brought in by the patient, the US revealed the right breast node, which measured 5.7 cm, BI-RADS[®] 5 report; the core-biopsy showed evidence of the proliferation of oval cells with an extensive area of necrosis; and the



Figure 1. Right breast, preoperative aspect.

following immunohistochemistry inferred atypical lymphoid infiltrate with extensive areas of necrosis. From this information, surgical intervention with a transoperative examination was planned. At the time of admission, the lesion occupied the entire right breast and showed no evidence of lymphadenomegaly. In view of this, and because the previous biopsies showed no clear pathology, the tumor excision was characterized in the mastectomy itself. The definitive anatomopathology revealed oval and giant multinucleated cells neoplasia with vascular proliferation and extensive tumor necrosis, measuring 10.5 × 9.5 cm. The immunohistochemical study revealed positive neoplastic cells with a vimentin antibody (Figure 2). There was no positivity with the pancytokeratin, Melan A, CD31, S100 and desmin antibodies. The immunohistochemical study identified a pleomorphic malignant neoplasm that had an undefined histogenesis. Through process of elimination, it was considered a primary breast sarcoma.

Systemic staging did not show metastasis from a distance. The patient followed up with clinical oncology and developed pulmonary and hepatic metastasis three months after surgery, and thus remained on doxorubicin chemotherapy.

DISCUSSION

Primary breast sarcoma is a rare tumor that accounts for 1% of all breast cancers and has an approximate incidence of 4.6 new cases per million women²⁻⁴. In this group of neoplasias, we also found malignant phylloid tumors, carcinosarcomas, liposarcomas, osteosarcomas, angiosarcomas, malignant histiocytobromas and leiomyosarcomas². The main diagnosis of breast sarcoma that is different from the others, is that of metaplastic carcinoma, which should always be discarded^{2,5}. An immunohistochemical study may help differentiate these entities. Negativity to pancytokeratin excludes the possibility of metaplastic carcinoma, and negativity to Melan A, CD31, S-100 and desmin removes the possibility of melanoma, angiosarcoma, liposarcoma and leiomyosarcoma, respectively. Vimentin is positive in sarcomas.

The main clinical display of breast sarcoma is of a painless, mobile, fast-growing and diffuse mass, with an average size of 5 cm. It occurs in an increased incidence in people in their 50s and 60s. Bilateral and axillary involvement are rarely described². Diagnosis is often difficult, and is usually done by histopathology after surgical removal of the lesion², since mammography and US are non-specific^{3,6}. The tumor tends to have a reserved prognosis. Because size of the lesion is the most important variable, it is related, in addition to the long-term prognosis, to the local recurrence.

Given the rarity of breast sarcomas, there are no prospective randomized trials that guide treatment⁷. A multidisciplinary approach in a referral center, involving surgery,

radiotherapy and oncological evaluation, is indicated. In general, the choice of treatment is influenced by the stage of the tumor, its histological grade and its size⁷. Axillary lymph node metastasis hardly occurs. To treat it, the preferred method is resection with wide margins and without axillary emptying^{1-3,5,6}. For tumors larger than 5 cm, a simple mastectomy is recommended, since local resection, in these cases, is associated with a considerable relapse rate. Axillary lymph node resection is only recommended when clinically compromised¹. The most common sites of metastases described in the literature are the lungs and the liver.

Chemotherapy is not effective in this type of neoplasia, although in combination with another treatment method, there may be some clinical improvement. Adjunctive radiotherapy is associated with a decreased likelihood of local recurrence. Retrospective studies have shown that the use of radiotherapy may influence disease-free survival¹, especially in cases of high-grade sarcoma².

Early diagnosis is considered difficult, since the tumor grows rapidly and its histopathological classification is difficult to determine, causing the treatment to be extended and harming the prognosis².

In the immunohistochemical examination, there are several markers that can be applied - one is the vimentin antibody, a cell marker of mesenchymal origin, such as sarcomas.

CONCLUSION

In the present case reported, we have a rare tumor - breast sarcoma - whose diagnosis was made possible by correlating clinical signs and symptoms, macroscopy, histology, preoperative and post-operative immunohistochemical studies, and an evolution with short-term systemic metastasis. This wide range of information open to investigation makes the early diagnosis very difficult, increasing the medical team's concern to treat an aggressive, fast-growing tumor. As such, the prognosis is affected by the prolongation of the treatment.

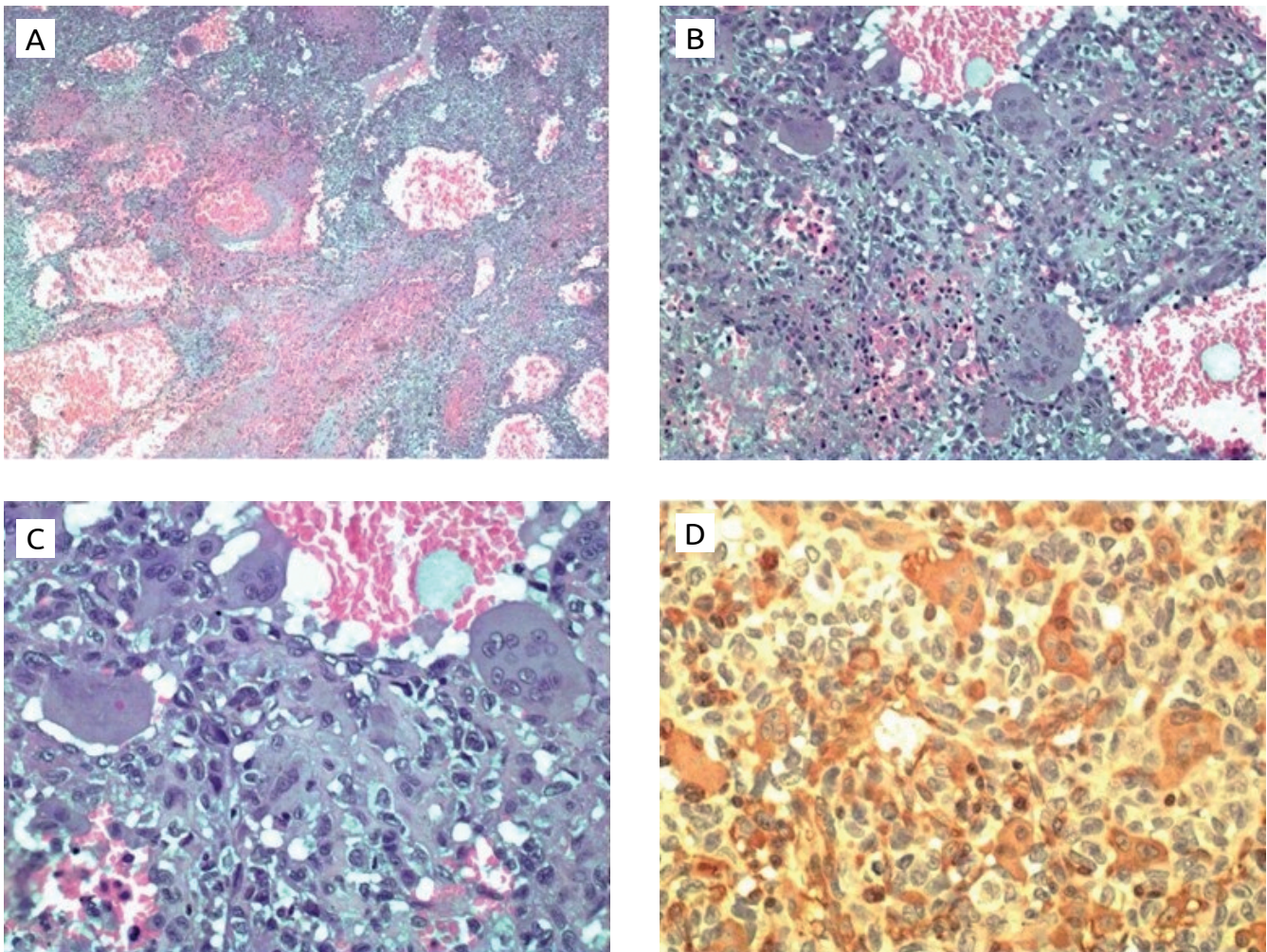


Figure 2. (A) Area of necrosis and tumor hemorrhage. HE-25x; (B) multinucleated giant tumor cells. HE-100x; (C) pleomorphic tumor cells and giant multinucleated cells HE-200x; (D) positive neoplastic cells with vimentin antibody, 200x.

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UNILATERAL BREAST EDEMA DUE TO SUBCLAVIAN VEIN COMPRESSION

Edema mamário unilateral resultante de compressão da veia subclávia

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ABSTRACT

Unilateral breast edema may have different causes that vary from malignant to benign diseases. The knowledge of the main etiologies, associated to a detailed clinical examination and to radiological findings, is important in order to establish the correct diagnosis and determine the appropriate management of the patient. This article will report the case of a patient with lung cancer who developed unilateral breast edema; the main differential diagnoses will also be discussed.

KEYWORDS: Lung neoplasms; subclavian vein; ultrasonography, mammary; mammography; inflammatory breast neoplasms.

RESUMO

O edema mamário unilateral pode ter diferentes causas, que variam desde doenças malignas até benignas. O conhecimento das principais etiologias, associado ao exame clínico detalhado e aos achados radiológicos, é importante para que se estabeleça o diagnóstico correto, e para que se determine o manejo adequado do paciente. Neste artigo, será relatado o caso de uma paciente com câncer de pulmão que desenvolveu edema mamário unilateral; também serão discutidos os principais diagnósticos diferenciais.

PALAVRAS-CHAVE: Neoplasias pulmonares; veia subclávia; ultrassonografia mamária; mamografia; neoplasias da mama.

INTRODUCTION

Unilateral breast edema may occur due to different etiologies ranging from malignant — such as inflammatory breast carcinoma and metastasis — to benign conditions — such as mastitis, alteration after surgeries or radiotherapy procedures and lymphatic or central venous obstruction¹. The knowledge of these etiologies, in association with a detailed clinical examination and radiological findings, is important in order to establish the correct diagnosis, and to determine the appropriate management of the patient.

Thus, this study aimed to report a not-so-frequent cause for unilateral breast edema — determined by pulmonary lesion causing the obstruction of the subclavian vein and subsequent damage to the lymphatic drainage of the breast —, as well as to discuss the main differential diagnoses of the case.

CASE REPORT

Female patient, 48 years of age, with a 10 pack-year smoking history, having quit ten years ago. At the end of 2013, she had a typical clinical case of cholelithiasis, confirmed by an ultrasound study. During preoperative evaluation, a simple chest X-ray identified an ill-defined right paramediastinal opacity. Complementary investigation, with computed tomography (CT) scan of the thorax, detected a right peri-hilar mass, with infiltrative aspect and subcarinal lymph node enlargement. A CT guided biopsy was carried out, with anatomopathological results of an invasive muco-secretory adenocarcinoma of primary acinar pattern of the lung. Imaging tests for staging — magnetic resonance of the skull, abdomen and pelvis CT and bone scintigraphy — showed no metastases; however, the mediastinoscopy revealed the involvement of the upper mediastinal lymph

Study carried out at the Imaging Department of AC Camargo Cancer Center – São Paulo (SP), Brazil.

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nodes, reaching stage III A. The treatment with carboplatin and paclitaxel chemotherapy, and radiotherapy with irradiation field, started for the right peri-hilar mass and mediastinal lymph nodes, with chemoradiotherapy ending in July 2014. In July 2015, during follow-up, the disease progressed into pleura, and a pleurodesis was performed; there was also involvement of high mediastinal and supraclavicular lymph nodes, forming conglomerated, and metastases in the central nervous system. New chemotherapy cycles were performed, this time with docetaxel, and radiotherapy with irradiation of the mediastinum and right bronchus and radiosurgery of the lesion in the brain and cerebellum.

In April 2016, the patient was hospitalized with worsening respiratory complaints and enlargement of the right breast, a few days before.

At physical examination, the patient was afebrile, with edema in the lateral quadrants of the right breast and minimal erythema, without local temperature increase. Also, there was hardened and palpable lymphadenopathy in the right supraclavicular chain, and the right axilla was free. Laboratory exams did not evidence infectious conditions, with C-reactive protein (CRP) ranging from 2 to 10 mg/L and leukocytes from 6,000 to 8,000/mm³. The main diagnosis hypothesis were mastitis, metastasis and new breast cancer. New imaging exams were requested for further investigation, the mammography (Figure 1) and ultrasonography (Figure 2) demonstrated non-specific signs of edema, with no solid lesions, malignant microcalcifications and collections. Given the situation, empirical antibiotic therapy was started, with no improvement. An x-ray of the chest, requested in order to evaluate respiratory complaints, detected a veiling opacity of the right hemithorax. In the sequence, a chest angiogram was performed (Figures 3 and 4), which showed an extensive solid mass in the apical segment of the right superior lobe extending to the right hilum, infiltrating the mediastinum and invading the right pulmonary artery and segmental bronchi causing partial pulmonary collapse, in addition to a significant caliber reduction of the right subclavian vein at the outlet to the superior vena cava.

Subsequently, a vascular endoprosthesis was placed in the right subclavian vein, resulting in improvement in venous circulation and breast edema. The patient had no recurrence of symptoms of breast congestion within the following months, and carried on with her cancer treatment, using a new chemotherapy regimen with nevelbine. After four months, due to the lack of response to the new treatment and considering the requests of family members, only palliative measures were continued and, in December 2016, the patient passed away.

DISCUSSION

The clinical manifestation of breast edema, translated by cutaneous thickening and volumetric tissue enlargement, is

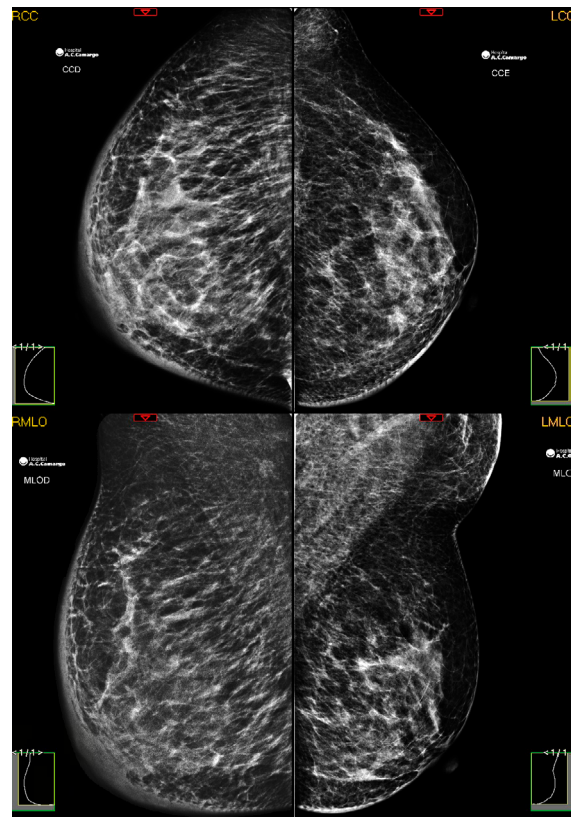


Figure 1. Mammography of craniocaudal (CC) and mediolateral oblique (MLO) incidences – dense breasts, with cutaneous thickening and slight increased trabeculation of the right breast, suggesting edema.

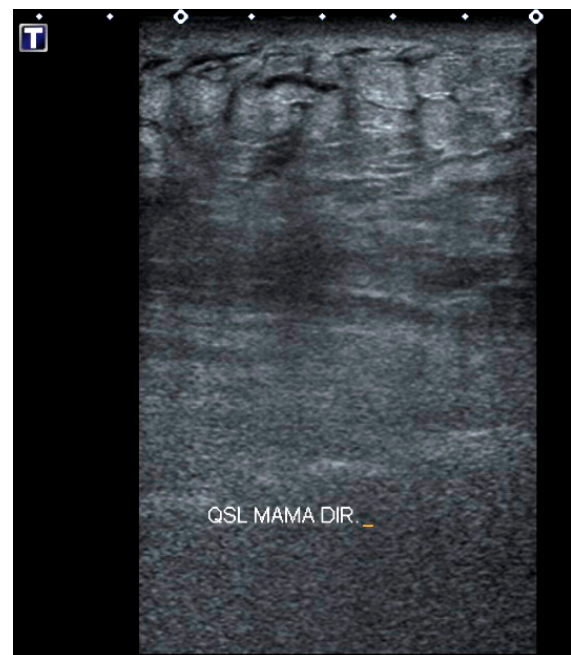


Figure 2. Ultrasonography – cutaneous thickening and hyperechogenicity of the subcutaneous cellular tissue, with anechoic serpiginous images of permeation (edema).

nonspecific. However, there are imaging characteristics which may be present and useful in etiological differentiation. In the mammography, breast edema is characterized by cutaneous thickening, increased parenchyma density and prominence of the interstitium, characterized by trabecular thickening^{1,2}. The identification of nodules and/or microcalcifications may be of help in diagnosing malignancy². Ultrasonography shows cutaneous thickening associated with hyperechogenicity of the subcutaneous tissue and the mammary parenchyma, with lymphatic engorgement. Ultrasonography may assist the detection and characterization of nodules and collections, as well as guide biopsies³. In magnetic resonance, breast



Figure 3. Chest CT – extensive involvement of the right pulmonary parenchyma and homolateral breast edema.

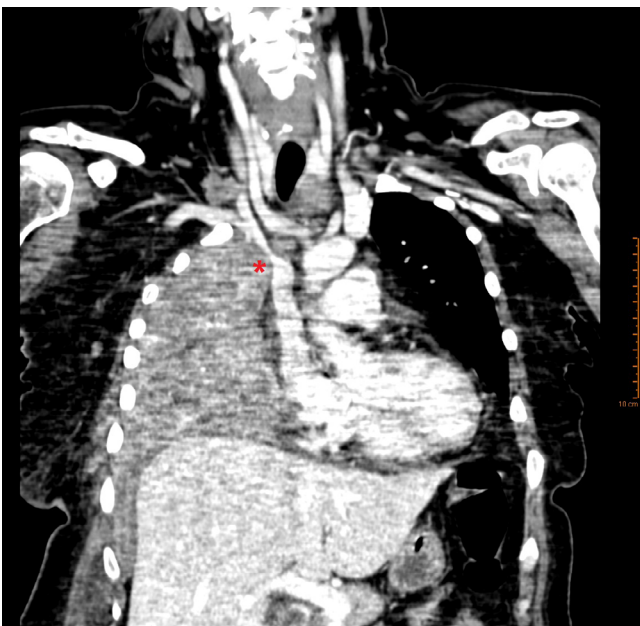


Figure 4. Chest CT scan (coronal reconstruction) – mass in the right pulmonary Apex, which caused compression and important reduction of caliber of the right subclavian vein at the opening to the superior vena cava (asterisk).

edema is manifested by cutaneous and interstitial thickening, which come along with hypersignaling of T2 images, and if breast edema is the only finding, there is no post-contrast enhancement.

Breast inflammatory carcinoma — a relatively uncommon form of breast cancer of rapid progression, which affects women between their fourth and fifth decade of life — in general is locally advanced when diagnosed, and is manifested with edema and erythema, which may be associated with sensation of warmth in the affected breast, in addition to orange-peel-like skin. There may or may not be a palpable nodule and, usually, the patient has no fever^{1,3-5}. Histologically, there is an invasion and obstruction of the lymphatics of the dermis and capillaries and of subepidermal venules, resulting in mammographic findings of edema and cutaneous retraction. Malignant nodule and calcifications may be present; axillary lymph node disease is a common occurrence^{1,3-5}. Ultrasonography may evidence an irregular hypoechoic nodule with speculated or indistinct margins and posterior acoustic shadow; the nodule may be obscured in the mammography due to the increased breast density, in addition to the possibility of showing an invasion of pectoral muscles and lymph node involvement³.

Metastasis to the breast may be lymphatic or hematogenous. The former usually occurs transthoracically or by dissemination of the contralateral primary breast cancer. The latter, the hematogenous spread of extramammary cancer, is uncommon, and suggests advanced systemic disease. In these cases, both lymphoma and melanoma are the most common sources of metastases. In general, they do not cause cutaneous nor papillary retraction and tend to be more frequently multiple or bilateral in relation to primary breast neoplasms. The radiographic appearance is of one or more round and well-defined nodules, without microcalcifications in the subcutaneous tissue — except for rare exception, as in cases of ovarian cancer^{1,3,6,7}.

Mastitis usually occurs among young women and breastfed infants, but may also affect immunosuppressed women. The most common agents are *Staphylococcus sp.* and *Streptococcus sp.* although *Mycobacterium tuberculosis* may also be found. In general, it presents erythema, pain, heat, fever, reactionary lymph node disease and leukocytosis, which respond to antibiotic therapy. If inflammatory symptoms are not improved with treatment, a biopsy may be required in order to rule out the possibility of inflammatory carcinoma. The most common mammographic aspect of mastitis is an ill-defined area, with increased density and cutaneous thickening, whereas the diffuse edema is seen only in a minority of cases. In the ultrasonography, there is an ill-defined area, with heterogeneous echotexture, presenting areas of hyperechogenicity, due to inflamed fat lobes,

and hypoechogenicity in glandular parenchyma, in addition to cutaneous thickening. Occasional abscesses may be identified. Mastitis may present a mammographic pattern similar to that of inflammatory carcinoma, though without malignant-like calcifications^{1-3,8}.

Tissue response after partial mastectomy or radiotherapy, with cutaneous thickening and breast edema, is more pronounced 6 to 12 months after treatment, being gradually solved within 1 to 3 years. The clinical history is essential in order to differentiate this kind of edema and other causes. The changes after radiotherapy may be focal or diffuse, and with typical non-anatomic linear configuration borders^{1,9}.

Less commonly, mechanical problems, such as vascular obstruction, may also be presented along with unilateral breast edema. Unilateral dilation of breast veins may be observed due to the obstruction of the axillary and subclavian veins. Superficial collateral veins may drain to the contralateral breast and even to the contralateral axillary or subclavian veins; however, they might not be seen if they form gradually^{1,10}.

The understanding of breast venous drainage is important, once this may be a route of neoplastic dissemination, in addition to their intimate relation to lymphatic drainage. The main venous drainage routes are: internal mammary vein (inner thoracic), drained to the pulmonary capillary network; axillary vein; and intercostal veins. Lymphatic drainage is typically unidirectional, with approximately 75% of the lymphatic flow through the axillary lymph nodes; the rest flows

to internal mammary and parasternal chains, which may even present anastomosis with the contralateral network¹⁰.

In the case presented, an uncommon cause for unilateral breast edema was diagnosed, determined by a pulmonary lesion that damaged the vascular drainage. The patient was under treatment for pulmonary adenocarcinoma, which, despite therapy, evolved with a significant progression regarding its size, leading to the involvement of the right lymphatic duct and the right subclavian vein proximal to the inner mammary vein, determining increased venous and lymphatic pressure, with the leakage of fluid into the interstitial space, resulting in breast congestion.

The breast presented edema, of fast progression, in its lateral quadrants, a location outside the field of previous irradiations. However, there were no other signs to corroborate an infection. Nevertheless, the main diagnostic hypothesis, prior to the CT, was of acute mastitis, and a treatment with broad-spectrum antibiotics was initiated, with no clinical response.

CONCLUSION

Unilateral breast edema is a condition with different etiologies, most often related to benign diseases such as infections. However, the attending physician should be aware of and analyze the range of available clinical and radiological information, which may suggest the hypothesis of potentially more severe conditions, such as malignant neoplasms, or rarer causes, such as vascular obstruction.

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PRIMARY BREAST LYMPHOMA PRESENTING AS LOCALLY ADVANCED BREAST CANCER: A CASE REPORT

Linfoma primário apresentando-se como um câncer de mama localmente avançado: relato de caso

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ABSTRACT

Hematopoietic diseases can be found in the breast and mimic a mammary neoplasm, such as leukemia and/or lymphoma. Although lymphomas are considered lymph node tumors, 25-40% have extranodal sites. Primary lymphomas of the breast represent 0.1-0.5% of all breast neoplasms and may have primary or secondary origin. Primary lymphomas normally start in the breast without involvement of other sites. The diagnosis is made through physical and pathological examination. We report a 77-year-old female who had a locally advanced mass in the right breast associated with inflammatory signs and symptoms and with palpable axillary lymph nodes. The imaging tests were non-specific and didn't help the diagnosis. The pathology report revealed a diffuse, B-cell lymphoma infiltrating the breast (lymphoma non-Hodgkin's). Due to the rarity of the case, and the unknown pathogenesis systemic chemotherapy with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) regime were performed. The use of rituximab, as well as radiotherapy, remain controversial in the literature, but for some authors the radiotherapy is indicated with a total dose of 30 to 45 GY. Our patient performed radiotherapy of the breast and axilla. Because of total remission of the disease, it was not necessary complementary treatment or breast surgery.

KEYWORDS: Lymphoma; Breast cancer; Non-Hodgkin lymphoma.

RESUMO

Doenças hematopoiéticas podem ser encontradas na mama e simular uma neoplasia mamária, como leucemia e/ou linfoma. Apesar de os linfomas serem considerados tumores linfonodais, 25-40% acometem sítios extranodais, sendo um deles a mama. Os linfomas primários da mama representam 0,1-0,5% de todas as neoplasias da mama. Podem ter origem primária ou secundária. Os primários normalmente iniciam-se na mama sem acometimento de outros sítios linfonodais. O diagnóstico é feito através do exame físico e anatomopatológico. Relatamos um caso de uma paciente, idosa, de 77 anos, que compareceu em nosso serviço com uma massa progressiva envolvendo toda a mama direita, ulcerada e associada a sinais e sintomas inflamatórios com linfonodos axilares palpáveis. Os exames de imagem foram inespecíficos e não ajudaram no diagnóstico, não tendo sido recomendados para o rastreamento dessa neoplasia. O exame anatomopatológico revelou um linfoma de células B difuso infiltrando a mama (linfoma não Hodgkin). Devido à raridade do caso, a etiopatogenia é desconhecida, e o tratamento foi realizado com os esquemas quimioterápicos para linfoma segundo o consenso para linfomas de células B, sendo a base o tratamento com antraciclina. A paciente realizou seis ciclos de CHOP (ciclofosfamida, doxorubicina, vincristina e prednisona), com a regressão total da lesão. O uso do rituximabe, bem como a radioterapia, permanecem controversos na literatura, mas a radioterapia é indicada por alguns autores na dose de 30 a 45 GY. Nossa paciente realizou radioterapia da mama e da axila com ausência de remissão da doença, não tendo sido necessário tratamento complementar ou cirurgia da mama.

PALAVRAS-CHAVE: Linfoma; Neoplasias da mama; Linfoma não Hodgkin.

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INTRODUCTION

Hematopoietic diseases can be found in breast and mimic breast cancer, like leukemia and/or lymphoma. Although lymphomas are considered lymph node tumors, 25–40% involve extranodal sites. By definition, extranodal diseases refer to any lymph node involvement of the lymphatic system in other tissues, such as the central nervous system, Waldeyer ring, lungs, bones, skin and stomach¹⁻³. We report a case of breast lymphoma presenting as a locally advanced breast cancer.

CASE DESCRIPTION

We describe a 77-year-old female patient, without comorbidities. She was referred to our hospital due to a progressive lump growth in the right breast noticed four months before. The contralateral mammography (left breast) showed a category BI-RADS 2. The patient had no family history of cancer, except for an aunt who died of intestinal cancer. Physical examination revealed a large mass involving the entire right breast. The mass was ulcerated and associated with inflammatory signs and palpable ipsilateral axillary lymph node (cT4bN2) (Figure 1). Histopathologic investigation with core biopsy was performed. The pathology findings confirmed the diagnosis as diffuse B-cell lymphoma infiltrating the breast tissue (diffuse non-Hodgkin lymphoma) (Figure 2). The patient had a Karnofsky performance status of 90 and an ECOG 1. The treatment recommended was chemotherapy with six cycles of CHOP (cyclophosphamide, hydroxy doxorubicin, vincristine, Prednisone). A complete clinical response

with regression of the mammary lesion after the fifth cycle was observed. The treatment was complemented with breast radiotherapy of the right axilla. Currently, the patient is under regular monitoring, without signs of recurrence or progression of the disease as of her last visit (Figure 3).

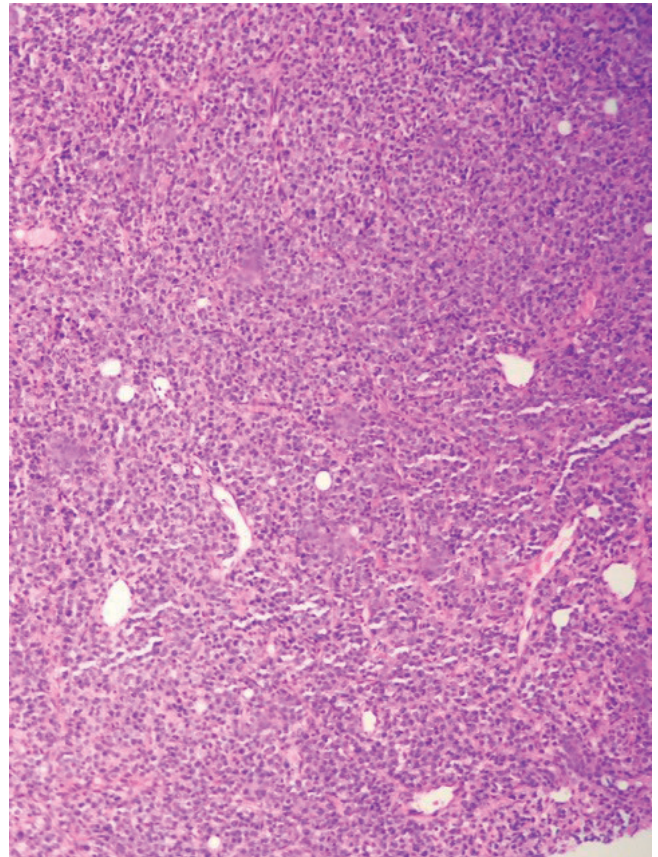


Figure 2. Diffuse B-cell lymphoma.



Figure 1. Large mass involving the entire right breast.



Figure 3. Resolution after chemotherapy.

DISCUSSION

Primary breast lymphomas are rare tumors, accounting for 0.85 to 2.20% of all extranodal lymphomas and 0.1 to 0.5% of all breast tumors. The World Health Organization (WHO) subdivides breast lymphomas into large cell lymphoma, Burkitt's lymphoma, and mucosa-associated lymphoid tissue (MALT) follicular lymphoma. Their origin may be primary or secondary and the distinction is often very difficult. The primary tumor is first manifested in the breast, without history or evidence of lymph node disease elsewhere, except in the ipsilateral axilla and supraclavicular lymph nodes. Primary breast lymphomas are usually B-cell non-Hodgkin lymphomas, but there are reports of some forms of T-cell lymphoma, common in Asia^{4,5}. This pathology was first described in 1972 by Liao and Wiseman⁶. They proposed four diagnostic criteria that are still used:

1. Presence of lymphoma and breast tissue, very close anatomically.
2. Previous diagnosis of lymphoma.
3. Absence of another disseminated disease.
4. Lack of adequate and quality histopathological sample^{1,2,6}.

Due to its rarity, the natural history of the disease and pathogenesis remains unknown. As there are few reports of men with this involvement, some hypotheses suggest the role of sex hormones². The natural history of breast lymphoma is known to be different from other extranodal lymphomas, due to its rapid progression and poor prognosis¹. The diagnosis is made by clinical examination and pathology, and the disease usually occurs in women in their 50s or 60s⁴. The most common symptom is a lump or a palpable, unilateral and painless mass in the breast. Although rare, there are some reports of bilateral lymphomas⁷. Other diagnoses are made through incidental findings in mammography screening or computed tomography (CT) scans^{1,4}. Less frequent symptoms are shrinking or papillary flow, thinning of the skin and swelling, simulating an inflammatory carcinoma and B symptoms (fever, weight loss and sweating), which are more common in patients with secondary origin^{1,2,4}. Aviv et al. showed that only 5% of 906 patients studied had B symptoms, and suggest that the absence of these symptoms may be because the vast majority of patients are pre-selected for diagnostic criteria². Imaging tests are nonspecific and do not provide a diagnosis. In mammography images, the lesion can be present as a circumscribed lesion⁵ without calcifications or a desmoplastic reaction

and on ultrasound, usually as a hypoechoic mass^{8,9}. Glazebrook showed that half of all cases of breast lymphoma present an irregular mass with indistinct margins, a third circumscribed margin, four cases of breast asymmetry, and one case as an architectural distortion⁴. According to Domchek et al., a mammogram does not increase its detection rate¹⁰. Although there are few reports, magnetic resonance imaging (MRI) appears to have a role in establishing the extent of disease and response to therapy. Positron emission tomography (PET/CT) proved to be a good test for staging lymphoma, with sensitivity and specificity close to 100%. This technique is useful for evaluating therapeutic response, demonstrating residual metabolic activity of the tumor and areas of necrosis and fibrosis. It may be useful in female patients with dense breasts where mammography shows a dark mass^{1,4}. The patient is classified in stages for diagnostic criteria based on the staging for lymphomas (Ann Arbor classification). The Ann Arbor staging system is indicated by the tumor localization. Breast lymphoma comprises only stage I and II. This means that, when only one extra lymphatic site is involved, stage IE is indicated, or when lymph nodes with local extension extra lymphatic on the same side of the diaphragm are involved stage IIE is indicated. The letter E is used when the disease is extranodal. The distinction in staging is important because it entails a difference of 5 years survival, with a survival rate of 78-83% in the IE stage against 20-57% in stage IIE. Prognostic factors: Ann Arbor stage greater than IE, increased lactate dehydrogenase (DHL) and, according to some authors, tumor size greater than 4-5 cm². As a rare condition, most of the processing is carried out on the basis of trials to diffuse B-cell lymphomas, the main system based on treatments with anthracycline, the most common being the CHOP regimen (cyclophosphamide, hydroxy doxorubicin, vincristine, Prednisone). A few studies show that adding rituximab improves the effectiveness of treatment, therefore many authors recommend its use with a view to a greater chance of eradicating lymphoma and decreasing disease recurrence. Hosein et al. showed no impact on survival levels with rituximab^{2,4,5}. The role of radiotherapy is still controversial, but it is believed that it has a positive impact on the outcome. Most patients receiving radiation dose of 30 to 45 Gy. Jennings et al., in a meta-analysis, demonstrated that radical surgery has no benefit for this disease and should be performed only for diagnosis⁶.

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MANAGEMENT OF COMPLICATIONS IN RECONSTRUCTIVE MAMMOPLASTIES WITH PROSTHESES: SYSTEMATIC REVIEW

Conduas em complicações de mastectomias reconstruídas com próteses: revisão sistemática

Rafael Amin Menezes Hassan^{1*}, Cícero de Andrade Urban¹

ABSTRACT

Objective: The aims of this study were to determine the main managements of surgical complications in reconstructive mammoplasties with prostheses through a systematic literature review, and to evaluate the effectiveness in preserving the reconstruction. The secondary objective was to analyze factors regarding prosthetic loss. **Methods:** We used the MedLine database through the following expressions: “breast cancer” or “breast neoplasm” or “breast and neoplasm” or “breast and cancer” and “implants complications” or “implants and complications”. The reference period for these studies comprised January 2000 to July 2016. **Results:** Of the 856 articles found, seven were included to analyze the applied protocols. The rate of saved prostheses after stratification of complications and use of managements varied from 45 to 100%, depending on the degree of complication. Other 12 articles that evaluated the factors associated with prosthetic loss were secondarily chosen. Radiotherapy was considered the most frequent factor and was found in seven studies. The number of lost prostheses varied from 0.9 to 22.7% in such studies. **Conclusion:** There is still no agreement on how to manage complications of reconstructive mammoplasties with prostheses. The decision remains a challenge, and therefore surgeons need to know the possible conducts in order to establish the most appropriate treatment.

KEYWORDS: Breast cancer; mastectomy; mammoplasty; breast implantation.

RESUMO

Objetivos: O objetivo principal deste estudo foi determinar, por meio de revisão sistemática da literatura, as principais condutas nas complicações cirúrgicas de mastectomias reconstruídas com próteses, bem como avaliar a eficácia em preservar a reconstrução. O objetivo secundário foi analisar fatores relacionados à perda da prótese. **Métodos:** Foi empregado o banco de dados do MedLine, utilizando as expressões: *breast cancer*, ou *breast neoplasm* ou *breast and neoplasm* ou *breast and cancer* e *implants complications* ou *implants and complications*. O período de referência desses estudos foi de janeiro de 2000 até julho de 2016. **Resultados:** Dos 856 artigos encontrados, 7 foram incluídos para análise dos protocolos de condutas aplicados. A taxa de próteses salvas após estratificação das complicações e aplicação das condutas variou de 45 a 100%, a depender do grau de complexidade. Foram selecionados, secundariamente, outros 12 artigos que avaliaram fatores associados à perda da prótese. A mais frequente foi a radioterapia com 7 estudos. O número de próteses perdidas variou entre 0,9 e 22,7% nesses estudos. **Conclusão:** Ainda não existe unanimidade no manejo das complicações de mastectomias reconstruídas com próteses. Portanto, a decisão permanece desafiadora e o cirurgião necessita conhecer as possíveis condutas para definir a mais apropriada.

PALAVRAS-CHAVE: Câncer de mama; mastectomia; reconstrução da mama; implante de mama.

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INTRODUCTION

Breast cancer surgical treatment is divided into two great groups: conservative surgeries and mastectomies. Both of them have similar and well-established oncological safety defined in medical literature^{1,2}. The improvement of reconstructive techniques, concomitant to the technological prosthetic evolution, enabled less morbid surgeries, without changing survival³⁻⁶. The choice for mastectomies became more popular in the last decades because they have been assuming a less damaging character throughout time⁷.

The cosmetic advantages of reconstruction with prosthesis provide the patient a positive impact on psychosocial aspects, organ functionality, and quality of life^{8,9}. They explain the increasing number of indications, even after the increased costs attributed to post-mastectomy reconstruction^{10,11}.

Although patients' satisfaction is above 85% in reconstructive surgeries with implants¹², no managements protocols regarding its complications have been established yet. Understanding the mechanisms associated with reconstructive failures and establishing criteria may lead to better cosmetic results.

The main purpose of this study was to review, in the medical literature, the protocols of managements of surgical complications in reconstructive mammoplasties with permanent implants and/or tissue expanders.

METHODS

The study evaluated, through the literature systematic review, women who underwent reconstructive mastectomy with temporary or permanent implants. The two authors selected the studies in MedLine database. The terms used were:

1. "breast cancer" or "breast neoplasm" or "breast and neoplasm" or "breast and cancer"; and
2. "implants complications" or "implants and complications".

Inclusion criteria were:

- studies presenting their own results;
- patients who underwent mastectomy and reconstructive surgery with implants;
- papers published between January 2000 to July 2016;
- investigations carried out only in humans;
- female participants;
- 18 years old or older; and
- papers written in English.

The preliminary research was carried out in July 2016 and resulted in 854 articles. After applying the inclusion criteria, only 330 articles were left for title evaluation. Papers with disagreement between the authors were separated for discussion until a consensus was achieved, which was divided into refusal or inclusion. Then, irrelevant or doubled articles were excluded,

resulting in 62 studies for complete text analysis. From then on, the studies were separated into three groups:

1. excluded: if it did not approach the complications and losses of prostheses;
2. data direct extraction: if it presents management protocols for treatment of reconstructions complications and prosthesis outcomes;
3. data indirect analysis: if it did not satisfy any of the two previous criteria.

Forty-five studies were excluded, in which 6 were chosen for data direct analysis and 11 for data indirect extraction. A study that was mentioned in the reviewed studies was later included in the direct analysis group due to its relevance for the theme, resulting in 7 papers for direct analysis and 11 papers for indirect ones.

RESULTS

Seven studies had their management protocols evaluated on different kinds of complications, mainly prosthesis infection and exposure. Published between 2003 and 2013, they were all retrospective studies. The isolation of *staphylococcus* and *streptococcus* cultures in breast wounds was the most common factor found in prosthetic complications. This fact was associated with surgical failure in three of seven studies and then with radiotherapy (two studies). The classification of the infection degree was performed in all seven studies; and even though this stratification was not uniform, the advanced level was among the main causes of prosthetic loss. In four studies, the severity of infection implicated in removal of the prosthesis and late reconstruction, in case the patient desired so¹³⁻¹⁹. The rate of saved prostheses after stratification of complications — including the use of the same prosthesis or its replacement by another device — varied from 45 to 100%. Differences in complications' stratification are included in Table 1. The suggested managements and rates of "saved" prostheses are seen in Table 2.

The eleven studies chosen for indirect analysis did not present a specific management protocol for patients with surgical complications; however, they evaluated the relation between surgical complication and prosthetic loss. Two of these studies were prospective and assessed complications during a six-week period of follow-up while the others evaluated from postoperative 30 days to 3 years. The total "n" of patients who underwent a reconstructive surgery, either with prosthesis or expander, in the indirect analysis studies was 15,353. The main factors associated with prosthetic loss were:

- radiotherapy (7 studies);
- lymph node condition (2 studies); and
- surgeon's experience (2 studies).

The number of prostheses lost ranged between 0.9 and 22.7% in the studies (Table 3)²⁰⁻³⁰.

DISCUSSION

Mastectomies reconstructed with prostheses preserve the patients' quality of life. However, we need to understand the mechanisms associated with reconstruction failures in order to increase the number of excellent results³¹. The main kinds of early complications include infection, exposure, and extrusion.

Their consequences vary from simple local dressings to the need of antibiotic administration, hospitalization or even prosthetic removal, compromising the expected result and afflictions due to an additional morbidity to the previous oncological disease. The threshold separating several managements in these situations is not unanimous, considering it is very influenced by their complication degree and the experience of each surgeon¹².

Spear et al.¹⁸ have created a management protocol divided according to the kind of complication. In 2010, the same authors published an update with a larger number of cases¹⁷. In both

Table 1. Stratification of complications.

| First author, reference, and year of publication* | Title | Study type | Review period | Stratification of complications |
|---|--|---------------|---------------|---|
| Reish ¹³ , 2013 | Infection following implant-based reconstruction in 1952 consecutive breast reconstructions: salvage rates and predictors of success. | Retrospective | 2004 to 2010 | Clinical opinion on the infection degree (erythema, fever degree, leukocytes, and use of acellular matrix), of the quality of remaining flap and patient's desire. |
| Peled ¹⁴ , 2012 | Long-term reconstructive outcomes after expander-implant breast reconstruction with serious infectious or wound-healing complications. | Retrospective | 2005 to 2007 | Infection regardless the level of any healing problem of the operative wound that requires unplanned surgical intervention. |
| Prince ¹⁵ , 2012 | Prosthesis salvage in breast reconstruction patients with periprosthetic infection and exposure | Retrospective | 2002 to 2008 | Severe infection (free pus with bad smell or signs and symptoms of local or systemic severe inflammation) versus without severe infection. Exposed prostheses were analyzed according to the infection degree or associated contamination. |
| Bennett ¹⁶ , 2011 | Management of exposed, infected implant-based breast reconstruction and strategies for salvage | Retrospective | 1989 to 2009 | Severe infection (edema, heat and erythema and progressive systemic signals or culture microorganisms); versus mild infection. The exposure condition was classified in intact skin, exposure risk, and exposed implant. |
| Spear ¹⁷ , 2010 | Management of the infected or exposed breast prosthesis: a single surgeon's 15-year experience with 69 patients | Retrospective | 1993 to 2008 | Division into 7 groups: G1. Mild infection (edema, heat and cellulitis, without pus drainage and with antibiotic response); G2. Severe infection (edema, heat and cellulitis that do not respond to antibiotics, pus drainage, positive culture or severe systemic signs); G3. Exposure threat; G4. Exposure threat with mild infection; G5. Exposure threat with severe infection; G6. Exposed prosthesis with or without mild infection. G7. Exposed prosthesis and severe infection. |
| Spear ¹⁸ , 2004 | The infected or exposed breast implant: management and treatment strategies. | Retrospective | 1990 to 2002 | Division into 7 groups: G1. Mild infection (edema, heat and cellulitis, without pus drainage and with antibiotic response); G2. Severe infection (edema, heat and cellulitis that do not respond to antibiotics, pus drainage, positive culture or severe systemic signs); G3. Threat exposure; G4. Threat exposure with mild infection; G5. Threat exposure with severe infection; G6. Exposed prosthesis with or without mild infection. G7. Exposed prosthesis and severe infection. |
| Yii ¹⁹ , 2003 | Salvage of infected expander prostheses in breast reconstruction. | Retrospective | 1995 to 2000 | Implant infection of was defined as the presence of purulent secretion around the prosthesis and/or bacteria growth in wound cultures. All the suspected cases underwent antibiotic therapy with exclusion of those with improvement. |

*Associated with recurrent infection; G: Degree.

studies, the complications were divided into seven groups based on the infection severity and the degree of prosthetic exposure. It presented the most precise management criteria of the reviewed studies. Stratification began with mild infection without prosthetic exposure and evolved to severe infection with exposed prosthetic, which was the only situation resulting in immediate removal of the device and reconstruction postponing. The use of specific management protocol by these authors was able to save the prostheses in 76.9% of the cases in the first publication and 64.4% in the second one. However, the case selection of authors included breast enlargement (aesthetics) surgeries, performed in the majority

of the population in both studies, and the reconstruction with prosthesis (repair). It is known that complication incidences are different between these two kinds of surgery. Breast reconstructive surgeries with prosthesis have higher rates of complications (around 21%)³² if compared with breast enlargement surgeries of purely aesthetical nature, in which the rates vary from 1 to 2%^{33,34}. The study's "n" was not enough for a significant statistical analysis and varied from 1 to 8 patients per analyzed subgroup, with a total of 26 patients in the first study and 87 in the following one.

Reish et al.¹³ have developed the study with the largest selection of cases, in which 1,952 patients who had their breasts

Table 2. Synthesis of management protocols.

| First author, reference, and year of publication* | Therapeutic Plan | Rate of saved implants | Factors associated with failure (p<0.05) |
|---|---|--|--|
| Reish ¹³ , 2013 | If the quality of the remaining skin was poor, then the prosthesis was removed, the infection was controlled, and late reconstruction was performed. Managements to save the prosthesis include washing with antibiotics, capsulectomy, change of device, and primary or combined closure with muscular flap. | 13 (72.2%) | Leukocytosis during admission and cultures with methicillin-resistant <i>Staphylococcus Aureus</i> |
| Peled ¹⁴ , 2012 | All the patients were candidate to one or more attempts of salvage implants, unless they refused | 15 (62%) | Radiotherapy |
| Prince ¹⁵ , 2012 | In patients with severe infection, the implant was removed. In patients without severe infection, attempts of saving the implant: antibiotics, cultures, prosthetic removal, capsule curettage, site washing with 3 liters of physiological solution and 3 liters containing antibiotics, placement of new prostheses and drain, removal of the inviable skin and closure according to each type of incision. | 33 (76.7%) | <i>Staphylococcus Epidermidis</i> |
| Bennett ¹⁶ , 2011 | In patients with severe infection, the implant was removed. In other situations, we tried to save the implant, which was divided into four possible approaches: 1. Change of implant and primary suture; 2. Change for a smaller implant and primary suture; 3. Development of thoracoabdominal skin and change of implant; 4. Great dorsal flat and implant change. | 9 (45%) | No factors associated with failure were seen. |
| Spear ¹⁷ , 2010 | G1: Antibiotic; G2: Antibiotic, capsulectomy, device modification with possible site change; G3: Antibiotic, coating with local tissues; G4: Antibiotics, capsulectomy, debridement, washing, change of device, primary closure and/or local flaps; G5: Antibiotics, in case of improvements, G4 managements, in case of no improvements, prosthesis removal; G6: Antibiotics, capsulectomy, debridement, washing, change of device, primary closure and/or with local flaps or implant removal; G7: Antibiotics, implant removal and late reconstruction assessment. | G1=34 (100%), G2=8 (30.8%); G3=6 (100%); G4=2 (66.7%); G5=2 (40%); G6=4 (66.7%); G7=0 (0%) | <i>Staphylococcus Aureus</i> in cultures and radiotherapy* |
| Spear ¹⁸ , 2004 | G1: Antibiotic; G2: Antibiotic, capsulectomy, change of device with possible site change; G3: Antibiotic, coating with local tissues; G4: Antibiotics, capsulectomy, debridement, washing, change of device, primary closure and/or local flaps; G5: Antibiotics, in case of improvements, G4 managements, in case of no improvements, prosthesis removal; G6: Antibiotics, capsulectomy, debridement, washing, change of device, primary closure and/or with local flaps or implant removal; G7: Antibiotics, implant removal and late reconstruction assessment. | G1=8 (100%), G2=2 (50%); G3=3 (100%); G4=3 (100%); G5=0 (0%); G6=4 (80%); G7=0 (0%) | Severe infection |
| Yii ¹⁹ , 2003 | All the patients with suspicion of periprostheses infection who did not get better after using antibiotics were candidates to attempting to use salvage implants, unless they refused to. | 9 (64%) | <i>Staphylococcus Aureus</i> in cultures. |

*Associated with recurrent infection; G: Degree.

Table 3. Indirect data on complication stratification and prosthetic loss factors.

| First author and reference | Year | Study type | Review period | Amount of patients reconstructed with implant or expander | Evaluated complications | Number of lost prosthesis (%) | Factors associated with prosthesis loss (p<0.05) |
|----------------------------|------|---------------|---------------|---|--|-------------------------------|---|
| Jagsi ²⁰ | 2016 | Retrospective | 1998 to 2007 | 3007 | New hospitalization in 30 days, operative wound complications and infection. | 442 (14.7%) | Radiotherapy |
| Wang ²¹ | 2016 | Retrospective | 2006 to 2013 | 489 | Operative wound dehiscence that required surgical intervention; infection was divided into those needing oral, intravenous antibiotics or surgery; exposure of expander/implant; expander/implant removal. | 33 (4.3%) | Radiotherapy and axillary emptying |
| Kearney ²² | 2015 | Retrospective | 2007 to 2013 | 210 | Complications of greater impacts including implant/expander removal; hematoma or seroma with the need of surgery; cellulitis with the need of antibiotics; expander/implant removal (without placement of a new device). | 26 (9.8%) | Radiotherapy |
| Anker ²³ | 2015 | Retrospective | 1998 to 2009 | 218 | Any complications requiring surgical intervention: asymmetry, poor cosmetic result and contracture; pain; necrosis, dehiscence and extrusion; infection; seroma or hematoma; papillary problems; and disease recurrence. | 20 (9%)* | Radiotherapy |
| Cordeiro ²⁴ | 2014 | Retrospective | 1998 to 2010 | 1415 | Any complications resulting in implant loss: infection, extrusion, contracture, seroma, deflation, cosmesis, asymmetry and rippling. | 160 (7.5%)** | Radiotherapy |
| Fischer ²⁵ | 2013 | Retrospective | 2005 to 2010 | 9305 | Perioperative complications (30 days); dehiscence, infection (superficial or deep) | 85 (0.9%) | Severe infection |
| Petersen ²⁶ | 2012 | Retrospective | 2002 to 2009 | 141 | Epidermolysis (skin superficial necrosis), skin necrosis (reaches the entire thickness), infection (clinical diagnosis), prosthetic removal. | 26 (12.5%) | Age >44 years old and smoking |
| Kobraei ²⁷ | 2012 | Retrospective | 2005 to 2010 | 102 | Greater complications (requiring hospitalization or return to the operating room); smaller complications: flap necrosis, hematoma, seroma, healing issues, and infection. | 22 (14%) | Radiotherapy |
| Cowen ²⁸ | 2010 | Prospective | 1998 to 2006 | 141 | Any complications requiring other surgical intervention. | 32 (22.7%) | Smoking, initial size of the tumor and lymph node condition |
| Radovanovic ²⁹ | 2010 | Prospective | 2004 to 2008 | 205 | Greater complications: necrosis of flap larger than 2 cm, infection requiring intravenous antibiotics; lower complications: necrosis of flap smaller than 2 cm, infection that may be treated with oral antibiotics. | 12 (5.6%) | Experience of surgeons |
| Woerdeman ³⁰ | 2006 | Retrospective | 1996 to 2000 | 120 | Seroma, hematoma, skin issue or infection. Divided into greater (in case of prosthesis loss) or smaller complications. | 19 (11%) | Experience of surgeons |

*Data taken after analysis of the article; **Data regarding the period before the expander change.

reconstructed with prosthesis were retrospectively evaluated. The progression of complications followed the:

- clinical opinion on the infection severity;
- evaluation of the remaining tissue; and
- patient's desire on trying to keep their prosthesis.

Based on the conducts outlined in the study (Table 1), only if the skin quality remained poor, the prosthesis would not be saved. The rate of overall complication of this study was 5.1%. There has been success among the attempts to preserve the implants in 72.2% of the complicated cases.

Peled et al.¹⁴ defined the complications of patients as any infection or problem in the operative wound which required surgical intervention. Based on this situation, the initial management plan was to try and save the prosthesis in all the cases, provided the patient would not refuse it. Of the 29 patients presenting complications with indication for surgical intervention, 5 underwent a reconstructive surgery with abdominal flap, and only 24 cases had the intent to save the prosthesis; of which 15 were successful (62.5%). Yii and Khoo¹⁹ applied similar criteria in 17 cases, of which 3 patients refused the conduct and 14 were approached with the objective of saving the prosthesis; 9 of them (64%) were successful. Although the rates of saved prostheses in these two studies were lower than those of other ones, the complication criterion was more restricted and only the most severe patients were chosen, considering that cases with conservative management did not enter the selection. The managements established by these authors are simple, considering that all the cases are indicative of saved prosthesis. Therefore, they are objective and have great reproducibility, in addition to being challenging, once that for several decades, on an imminent risk situation, the irrefutable procedure was to remove the prosthesis³⁵.

For Prince et al.¹⁵, cases of severe infection (pus associated with signs of local or systemic severe inflammation) consisted in the only situation where there was not an attempt of saving the prosthesis. Among the 60 patients with complications and indication of surgical approach, 43 received recommendations for trying to save the prosthesis. Success was achieved in 76.7% of these cases. Indications for surgical intervention were similar to those presented in the study of Peled et al.¹⁴. However, in Prince et al.¹⁵, removing the most severe cases presented higher rates of saved prostheses. Stratification of postoperative complications, in Bennet et al.¹⁶, is similar to Prince et al.¹⁵ and Peled et al.¹⁴, in which the management of severe infection cases consisted in

prosthetic removal and late reconstruction. In the other cases, there was an attempt to save the prostheses, with or without the support of myocutaneous flaps, depending on the quality of the remaining skin. Of the 68 patients with complications, 45 of them underwent immediate removal of the prosthesis, 3 underwent immediate reconstructive surgery with autologous tissue, and 20 underwent an attempt to save the implant, of which only 9 (45%) cases were successful. The rates of saved prostheses showed in these seven studies do not allow establishing means or comparative analyses, considering they refer to different stratifications of specific complications and managements of each team.

Three of the seven studies with direct data presented positive Gram-bacteria of the skin as a statistically significant factor of non-success among the attempts of saving the prostheses^{13,15,19}, and *Staphylococcus Aureus* was the most responsible one for it. Radiotherapy appears in second place as the cause of implant loss. Spear and Seruya¹⁷ concluded that both the presence of *S. Aureus* in wound culture and radiotherapy were associated with recurrent infection and prosthetic exposure, without impact on the rate of saved prostheses. Agreement on the adversities of reconstruction with prostheses has not yet been achieved, whether due to the heterogeneity of managements, whether by the selection of cases; therefore, we need prospective studies with higher "n", as well as uniform and reproducible managements.

Reconstruction of breasts that had undergone radiotherapy still remains a great challenge. Among the studies with indirect data analysis, radiotherapy was the main factor associated with implant loss, which was shown in seven papers^{20-24,27,30}. According to a metaanalysis published in 2015, the relative risk of reconstructive surgery failure in irradiated patients is 2.58 (95% confidence interval – 95%CI 1.86–3.57). The main management to minimize this situation is the reconstructive surgery with autologous tissue alone or together with prosthesis, thus decreasing such risk in 92 and 72%, respectively³⁶.

CONCLUSION

Breast reconstructions with the use of prostheses have high rates of complications and therefore increase the relevance of researches that might help defining and improving managements in these situations. Among the several existing management protocols, there is not an agreement between the authors; therefore, the choice for the most adequate procedure remains a challenge.

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TRAINING IN ONCOPLASTIC AND RECONSTRUCTIVE BREAST SURGERY: ANALYSIS OF TRAINING IN AMERICA AND IN THE EUROPEAN UNION WITH THE BRAZILIAN REALITY

Formação em cirurgia oncoplástica e reconstrutiva da mama: análise da formação na América e na União Europeia com a realidade brasileira

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ABSTRACT

The reconstructive and aesthetic breast surgery is a major breakthrough for the treatment of women fighting cancer. An advantage for the patient is the reduction of surgical treatment to one professional, besides the psychological and aesthetic relief of having her breast comfortably reconstructed by the doctor who is already accompanying her in the treatment of the disease. Considering the advances in oncological breast surgery, the ideal surgical procedure is one that achieves local control of the disease by maintaining the symmetry of the breast with immediate reconstruction. Plastic surgery techniques can be used in breast cancer surgery. The original focus is on improving the quality of life of oncological patients undergoing treatments that may be more effective in the aesthetic and functional point of view from the perspective of traditional techniques of breast conservation. Formation and training of professionals able to treat breast cancer is an innovative concept that brings discussions to the scientific community. Specific studies are required to standardize oncoplastic training. Training in reconstructive and aesthetic breast surgery also brings about new perspectives of surgical research related to aesthetic results, quality of life and local control, as well as the optimization of operative time, reducing adverse effects and costs. This study aimed to evaluate the main existing techniques, the training time for specialization in the context of Brazilian reality and whether it is necessary to change the current training model. This review is based on the conviction shown in other publishing studies (in press), which demonstrate the best way and the best work load for the improvement of the mastologist regarding oncoplastic and reconstructive breast surgeries.

KEYWORDS: Breast neoplasm; mammoplasty; education.

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RESUMO

A cirurgia reparadora e estética da mama representa um grande avanço para o tratamento de mulheres que lutam contra o câncer. Uma das vantagens para a paciente é a diminuição de procedimentos cirúrgicos e tratamentos com mais de um profissional, além do alívio psicológico e estético de ter sua mama reconstruída de forma confortável pelo médico que já a acompanha no tratamento da doença. No que diz respeito aos avanços das cirurgias oncológicas da mama, deve-se levar em consideração o procedimento ideal com margens livres e o controle local adequado da doença, a reconstrução imediata da mama de forma simétrica e, por fim, a transposição de técnicas da cirurgia plástica para a cirurgia de câncer de mama. O foco original é a melhoria da qualidade de vida das pacientes oncológicas submetidas a tratamentos que podem ser mais eficazes do ponto de vista estético-funcional sob a ótica das técnicas tradicionais de conservação mamária. A formação e a capacitação de todos os profissionais aptos ao tratamento do câncer de mama é um conceito inovador e trará discussões e novos desafios ao meio científico, o que instiga a possibilidade de criar estudos específicos que levem em consideração a opinião da sociedade no intuito de padronizar a formação em oncoplastia. A pesquisa científica é necessária para avaliar muitos outros aspectos relacionados à oncoplastia, como o resultado estético, a qualidade de vida das pacientes e o controle local da doença, bem como a otimização do tempo operatório e a redução de efeitos adversos e custos. O presente estudo visou avaliar as principais técnicas existentes, o tempo para formação dessa especialização no contexto da realidade brasileira e se há necessidade de mudanças no modelo de formação dos profissionais que optarem por segui-la. Esta revisão baseia-se na convicção mostrada em trabalhos em editoração (*in press*) que demonstram a melhor forma e a melhor carga horária para aprimoramento do mastologista em técnicas de cirurgia oncoplástica e reconstrutiva da mama referendada em observação.

PALAVRAS-CHAVE: Neoplasia da mama; mamoplastia; educação.

INTRODUCTION

Oncoplastic surgery in the treatment of breast cancer favors breast surgeons in the contexts of breast reconstruction and patient care, providing better aesthetic results without sacrificing the oncological treatment. The interaction between plastic surgery and mastology techniques originated a new approach to surgical training that aims to facilitate the treatment of this neoplasm. Technological advancements and benefits provided have already been discussed and presented in various global scenarios¹.

Professionals from different fields came together to share experiences and confront basic principles and techniques involved. Oncoplastic and reconstructive surgery of the breast was introduced in postgraduate course programs in 2010, during the Annual Clinical Congress of the American College of Surgeons (ACS), in San Francisco, California, with the participation of 120 professionals specializing in breast surgery, general surgery and plastic surgery. In this event, well-known oncoplastic surgeons, such as Dr. Elizabeth Beahn and Prof. Melvin Silverstein, brought to light a number of relevant aspects of oncoplasty, such as indications, contraindications, postoperative radiotherapy, cost-effectiveness and variations in surgical time¹.

Most patients diagnosed with breast cancer in the United States are currently treated by a general surgeon specialized in cancer surgery. This scenario is different in Brazil, where most of the surgeries are performed by breast surgeons with training in general surgery, oncologic surgery and/or gynecology and obstetrics².

The objective of this study was to analyze the discussions about the different formations of the breast surgeons in the studies published in the European Union and the works published by their direct collaborators to contrast and compare the different views put forward by each professional. The present study evaluated the different models for the training of breast reconstruction worldwide and their results. We focused our assessment on the essential criteria for candidates to participate in the training and performed a curricular analysis in the oncology field. Finally, we assessed whether significant changes in the current model of breast reconstruction surgery training in Brazil are required.

METHODS

The present study is a review of the scientific literature on the training of surgeons to perform oncoplastic and reconstructive breast surgeries. According to Gil³, a bibliographical research is carried out using publications that are already prepared, especially books and scientific papers. The present bibliographic work is a literature review of published works, master's thesis, electronic magazines and federal council bulletins. Our search terms included oncoplastic, surgeon training, reconstructive surgery of the breast and their equivalent in Portuguese (*oncoplastia, formação do cirurgião* and *cirurgia reparadora da mama*) with no period limits. In the result section, we discussed different points of view that form the training base considering time and number of patients adequate to oncoplastic surgery referral, as well as the amplitude of the clinical situation.

OBJECTIVES

General Objectives

To discuss methodological, operational and training aspects of professionals in oncoplastic and reconstructive breast surgery in Brazil.

Specific objectives

- To identify the time required for the training of medical professionals in oncoplastic and reconstructive breast surgery;
- To know and define the methodology applicable to the training of oncoplastic and reconstructive breast surgery (postgraduate programs, specialization courses, extension courses, continuing education, modular courses);
- To establish the professional practice time in oncoplastic and reconstructive breast surgery; and
- To identify the professional profile indicated for the performance of oncoplastic and reconstructive breast surgery.

RESULTS

Oncoplastic and reconstructive breast surgery scenario in several continents

The oncoplastic and reconstructive surgery of the breast techniques discussed worldwide seem to have parameterization with the Brazilian reality. The basis of reconstructive surgeries applied both in the US and in the European Union has the same basic surgical features for tumor removal and reconstitutions by flaps or breast implants. In relation to basic training, not many differences have been observed, since most professionals are surgeons — breast surgeons, plastic surgeons or oncologists. It should be emphasized that, although reconstructive surgeries are performed mostly by professionals of various specializations, the aesthetic part is almost entirely reserved for breast surgeons with training in oncoplastic and reconstructive breast surgeries⁴.

According to Mazzei⁵, mastology, oncology and general surgery professionals should have mastery over oncoplastic and reconstructive breast surgery techniques in order to plan and customize the treatment for each patient. This, undoubtedly, has led to protests by plastic surgeons who advocate oncoplastic surgery is an exclusive practice for professionals in this field. This medical progress can aggregate plastic surgery techniques, adapting them to the oncological profile. The various Brazilian institutions that offer training in this specialty train residents to perform and develop the process correctly. Several international health centers find difficulties in adding plastic surgeons to teams for different reasons, which forces breast surgeons to acquire more experience in the reconstructive area⁵.

Baidam⁶ analyzes that the legacy of historical surgical training meant that, until recently, few surgeons were equipped to offer this surgical approach to cancer, which simultaneously involves aesthetics and reconstruction. The author states that the change in the training of these professionals came to definitively change this reality. According to him, in the United Kingdom, only in the last decade, about 90 surgeons were awarded with high level scholarships. The basic course consists of 12 months of oncoplastic surgery training in 9 training centers performed by breast surgeons and plastic surgeons in an integrated manner. This approach seems to improve the quality of surgical care for the benefit of women, in addition to indicating a renovation in the field of breast surgery, far from the procedures based purely on resection techniques that remained unchanged for many decades.

Therefore, the outcome of the process in the UK has been marked by the interest in training among surgeons, so as to continue investing in a career in the breast surgery field, thus encouraging national scholarships and making them highly competitive. Some countries are already prepared to absorb this new medical specialty and have strategies in a partnership with the government to support the benefits of this type of surgery. The psychological impact on the patient and the increase in survival rates are numerically enthusiastic. Table 1 shows the training requirements to complete specialization in different countries⁷⁻¹¹.

Oncoplastic Surgery in Brazil

According to Brazilian Law n. 12,802, sanctioned on April 24, 2013, when there are technical conditions, reconstruction shall be performed in the same surgery. In case of the immediate reconstruction is impossible, the patient shall be referred for follow-up and submitted to surgery soon after reaching the required clinical conditions¹². This law was elaborated by Congresswoman Rebecca Garcia, who fought for more than five years for this service to be offered by the Brazilian public unified health system (SUS). The deputy reports that this law originated from feminist movements that believed the mutilation left by a tumor removal surgery would cause psychological damage as an effect of low self-esteem¹³.






After the law passed, some medical societies — such as the Brazilian Society of Mastology (SBM), the Brazilian Society of Plastic Surgery (SBCP) and the National Cancer Institute (INCA) — took actions to include oncoplasty as a medical complement in academic and extensive training for different specialties, graduating and training professionals who work in the fight against breast cancer to perform the reconstructive treatment in the early stages of diagnosis. According to Ruffo¹⁴, in an interview with Onconews, oncology safety must be aligned with aesthetic results to promote the better quality of life of patients. In addition, there seems to be the need

for more intensive training of our professionals. The SBM has identified this gap even among residency graduates who have recently undergone medical licensing examination. In this sample, it is possible to see that 20% of these medical residency programs still offer very little or almost no oncoplastic training¹⁴. In 2010, in Brazil, five courses in oncoplasty were started

(post-graduation, specialization or continuing or modular education), which are described in Table 2.

In Brazil, the requirements to apply for these courses are medical specialty in oncology, breast surgery or plastic surgery. The selection process includes curricular analysis, specific test and interview.

Table 1. Basic training for oncoplastic specialization in Brazil and in other countries.

| Country | Attending physician | Base | Future actions |
|---|---------------------|---|--|
|  | Dick Rainsbury | General surgeons Breast surgeons | Encourage training through scholarships Introduce plastic surgery techniques to postgraduate training |
|  | Belen Maerck | Gynecologist General Surgeons with postgraduate degrees in Mastology | Create a new surgical specialty Implement intensive training courses on breast reconstruction |
|  | Maria João Cardoso | Gynecologists Oncologists Plastic surgeons | Certification Centers Design appropriate curriculum to train professionals |
|  | Cícero Urban | Mastologists Gynecologists Plastic Surgeons Oncologists | Train professionals with a specialty in Mastology Grant scholarships to multiply professionals |
|  | Breast Surgeon | General surgeons | Introduce programs for breast reconstruction techniques combined with plastic surgery techniques |

Source: Cardoso MJ, et al.²⁷

Table 2. Training centers in oncoplasty in Brazil.

| Institution | City | Physician in charge | Certification | Workload |
|--|----------------|-----------------------|-----------------------|----------------------|
| Santa Casa de Belo Horizonte | Belo Horizonte | Douglas Pires | Graduate diploma | 540 h (15 months) |
| Hospital do Câncer de Barretos | Barretos | Gustavo Zucca Matthes | Specialization course | 380 h (19 months) |
| Hospital Araújo Jorge de Goiânia | Goiânia | Régis Paulinelli | Continuing education | 240 h (10 months) |
| Beneficência Portuguesa de São Paulo | São Paulo | Vilmar Marques | Extension course | 240 h (10 months) |
| Hospital das Clínicas da Universidade Federal do Rio Grande do Sul | Porto Alegre | Jorge Biazús | Modular course | 60 h Module |

Source: Pires DM. Tcc - Orivaldo Gazoto Jr. [personal message] Message received on April 13, 2016.

Oncoplasty development

Today's medical career requires specific refinements in each area. Patients are aware that specialized care is available for certain types of diseases, and realize that the care provided by a specialist is better than the service provided by a general surgeon. Thus, medical specialists who provide this type of care will, in great demand, be a byproduct of a well-informed society¹⁵.

Physicians who graduated in general surgery seem to respond well to these demands, seeking professional distinction in record numbers. It is estimated that half of the general surgeons acquire, each year, a certificate in some subspecialty recognized by the American Board of Medical Specialties¹⁶. Although the data show high volume of mortality by the hands of general surgeons, physicians who seek training are more assertive in complex surgical procedures such as oncology surgery. Oncoplasty came as an aggregating byproduct that, in addition to generating good results against breast cancer, promotes an increase in the quality of life of the patient. Oncoplasty also provides improvements in self-esteem by preserving a part of the body that, for a long time during the fight against this type of cancer, used to be mutilated¹⁷.

The emergence of oncoplasty and fundamental techniques

In the 1990s, the German surgeon Audretsch coined the term oncoplastic surgery to name the procedures that allowed tumor resection followed by immediate breast reconstruction, with restorative techniques that applied the principles of cosmetic surgery and its variations (considering tumor location in the different quadrants of the breast and the relationship between breast volume and tumor size). After that, this new technique for the handling of breast cancer spread in Europe and the United States. Multidisciplinary work with the integration of oncologists and plastic surgeons began with excellent results. The immediate reconstruction of the breast was consecrated as a routine practice of major importance. Oncoplasty or oncoplastic surgery is the union of plastic surgery techniques directed to the reconstruction of the breast in the treatment against mammary tumors. From the 1980s and especially in the 1990s, part of the breast started to be preserved in cases of initial cancer. Some studies have shown that breast conservation enhances the quality of life and the self-esteem, and the fear of disease recurrence is not different between patients undergoing conservative breast therapy and mastectomy. However, there are still insufficient studies regarding the impact of oncoplastic surgery on local recurrences and overall disease-free survival. In addition, data regarding their aesthetic results are also limited. Thus, everything should be done to increase the breast conservation rate. However, the aesthetic result may vary between the different conservative procedures. It is extremely important to follow the surgical guidelines and to use oncoplastic techniques

when indicated, especially in patients with larger tumors⁴. Partial breast reconstruction techniques were also developed using the same principles of breast aesthetic surgeries, such as suspension, reduction and placement of silicone prostheses¹. In 1994, a division of the breast into quadrants was instituted, which allowed the prior and planned analysis of the oncoplastic techniques to be used¹⁷.

Breast oncoplastic surgery is based on some fundamental techniques: reconstructions with and without flaps and breast implants¹⁹ (Tables 3-5).

Oncoplastic surgery and the Brazilian public service

In 2016, 57,960 new cases of breast cancer were estimated in Brazil²⁰. Oncoplasty may be able to improve the outcome in the treatment of most patients, including those treated by the SUS. In this context, the diffusion of professionals specialized in oncoplasty is essential, aiming at the benefit to patients submitted to breast surgery for cancer treatment. Currently, the number of Brazilian professionals qualified in oncoplasty is limited, especially those in the public health sector²¹. In Brazil, breast surgeons are the target audience in oncoplasty training, which is an excellent starting point for defining the purpose of this

Table 3. Types of techniques without flaps.

| Type | Breast size | Tumor location |
|---------------|-------------------------|---|
| Lower pedicle | Small, medium and large | Lateral and medial and superior quadrants |
| Upper pedicle | Medium and large | Lower quadrants |
| Round block | Small and medium | Periareolar and central quadrant |

Source: Mesquita M²⁸.

Table 4. Types of techniques with flaps.

| Type | Correction type | Risks |
|----------------------------------|-------------------------|---------|
| TRAM flap | Post-mastectomy defects | High |
| Latissimus dorsi muscle rotation | Post-quadrant defects | Reduced |

TRAM: transverse abdominal muscle.

Source: Mesquita M²⁸.

Table 5. Flap reconstruction.

| Breast type | Indication |
|-----------------------|---|
| Implants or expanders | All sizes but more appropriate to small, medium or absent breasts |

Source: Mesquita M²⁸.

study. The emphasis of oncoplastic specialization courses is the improvement of existing surgical techniques towards aesthetic breast reconstruction⁵.

In a publication of the SBM magazine, from São Paulo, Mazzei (2010) states: "Our surgical practice underwent major and important modifications in the last years with conservative and less mutilating techniques, which allow us to preserve more of the cutaneous tissue, the nipple-areolar complex, the mammary gland and the axilla"⁵. Today, breast surgeons must have mastery over oncoplastic surgery techniques in order to plan and provide the most appropriate treatment for patients. This undoubtedly has created protests on the part of plastic surgeons, who consider themselves to be exclusive for this specialty. It is a fact that the interaction between teams allows knowledge sharing and the adaptation of plastic surgery techniques to the oncological profile. Therefore, institutions that offer training in this specialty certainly cover some of the oncoplastic techniques and must increasingly improve this approach⁵. The point defended by Mazzei portrays that oncoplastic surgeons must have a curriculum in oncology⁵ in order to provide the most appropriate treatment for their patients. The data in Table 6 were published by SUS and refer to the medical actions for breast repair surgery. The figures reveal that the number of procedures is growing, which is encouraging. However, the rate of repair surgery does not exceed 10% in the states analyzed.

DISCUSSION

After evaluating some authors of oncoplasty worldwide, we observed that three specialties have greater demand for oncoplastic certification: breast surgery, plastic surgery and oncology surgery. Most of these specialties are based both in the United States and in the European Union. These professionals seek certification as a process of medical career improvement, aiming to combine treatment with psychological and aesthetic features. Although Brazil is a country of continental dimensions, not all its regions have multidisciplinary teams.

Table 6. Number of reparative surgeries in some Brazilian states.

| State | Procedures | Repair surgery | % |
|----------------|------------|----------------|-----|
| São Paulo | 8,058 | 386 | 4.8 |
| Rio de Janeiro | 3,951 | 220 | 5.6 |
| Minas Gerais | 2,429 | 88 | 3.6 |
| Ceará | 2,242 | 15 | 0.7 |
| Pernambuco | 2,155 | 54 | 2.5 |
| Brasil | 32,548 | 1074 | 3.3 |

Source: Resende MA²⁹.

Some regions are faced with the shortage of specialized physicians, which forces patients to travel in order to seek breast cancer treatment, consequently reducing survival rates. A trained oncoplastic practitioner, by having support material, will considerably reduce the number of deaths due to late treatment or absence of treatment, contributing to an effective public health program.

Mastology point of view

The surgical treatment of benign and malignant mammary neoplasias, as well as the approach of hypertrophies and mammary asymmetries, requires mastologists to have the technical knowledge previously applied by plastic surgeons. The contralateral breast symmetry among patients undergoing conservative surgical treatments should be considered. Oncological mammoplasty adapts mammoplasty to the surgical treatment of breast cancer. It is a well-defined surgical strategy to treat selected cases that promotes an increase in conservative surgery indications²². Reduction mammoplasty techniques appear to be safe for treating neoplasms in any mammary region with satisfactory aesthetic results. They are based on original techniques that preserve the ascending and perfusing features of the nipple-areolar complex²². For conservative surgical treatments, breast cancer surgeons should take the following into consideration: local recurrence, survival rates and patient satisfaction. The application of mammoplasty techniques in the treatment of breast cancer offers an improvement in patient satisfaction, without compromising oncological outcomes²³. In relation to relapses, tumors larger than 2 cm appear to have an increased risk of local recurrence²⁴.

The results of oncological mammoplasty are similar to those obtained in purely esthetic reductions.²² The proper preoperative planning should consider tumor location and the relation of the area to be resected with the total mammary volume. That will determine the technique to be applied and the location of the incisions for a satisfactory outcome both from the oncological and the aesthetic points of view. Patients affected by mammary neoplasia and with very large breasts, when submitted to oncological mammoplasty, will, in addition to the treatment of the disease, benefit from an improvement in overall quality of life. Although these patients could have a good outcome with simple conservative surgery, they constitute the group with the highest morbidity in postoperative radiotherapy, which is usually very uncomfortable due to the volume and shape of their breasts. In addition, dose homogeneity is more difficult to obtain in large breasts²².

A good preoperative evaluation (with emphasis on the resection area, incision design, possibility of immediate silhouette repair and mammary symmetry), besides providing treatment of malignant neoplasms, improves the patients' quality of life²². The basis of mastology requires the current

professional to master surgical techniques of reductive mamoplasty, to provide a treatment with oncological safety associated with excellence in aesthetic results for a greater number of patients.

Plastic surgery's point of view

According to Sampaio²⁵, the approach of plastic surgeons to breast surgeons, radiologists, pathologists, clinical oncologists and radiotherapists, when aiming to exchange knowledge, contributes with the multidisciplinary understanding of breast cancer. According to clinical oncology and oncoplastic breast surgery experience, the concerns that a plastic surgeon should have when performing oncoplastic surgery include:

1. awareness of the extent of the disease;
2. oncologic surgical programming and possibilities of intraoperative changes;
3. anatomopathological diagnosis and margin control;
4. radiotherapy and breast reconstruction;
5. adjuvant chemotherapy and neoadjuvant chemotherapy;
6. reconstruction aesthetic results; and
7. clinical and imaging follow-up²⁵.

The plastic surgery principles indicate that oncological or mastological follow-up is of extreme importance for a better treatment strategy. The plastic surgeon should also be concerned about the aesthetic implications of radiotherapy treatment (which may be compromised²⁶) or chemotherapy, which should start within 12 weeks after the surgical procedure²⁵.

Oncology Overview

It is the responsibility of the surgeon to diagnose breast cancer and ensure that there is a multidisciplinary team to approach the treatment before introducing the patient in the process. Another essential component is the inclusion of the patient in the multidisciplinary team, since a consensus among professionals will result in a common agreement on the guidelines and will have an impact on the quality of care. The absence of guidelines will result in different ways of treating patients within the same team, generating lack of clarity and variability in outcomes. A database on breast cancer is essential for auditing and for surgical quality control in individual units. The objective of this database is to define standards of care towards the cure of the patient. The presence of combined protocols allows the deficiencies to be clearly identified. It is a fundamental auditing principle to change and improve the surgical practice. Delayed diagnosis of breast cancer due to poor quality of care can alter the disease stage and impact patients' survival. The oncology practitioner is, for the most part, the first point of contact for patients with symptomatic disease, who has the responsibility to adequately refer the patient to the diagnostic service. Finally, oncology advocates that it should be the basis

for the oncoplastic surgeon, in order to guarantee better survival and, especially, the quality of the treatment from beginning to end. This is justified by the fact that, in the middle of their studies, oncoplastic surgeons study techniques of treatment for all types of cancer and have contact with a multidisciplinary team of professions, including radiology, radiography, pathology, surgery, nursing and medical physics.

CONCLUSION

Considering the time invested in training and thesis defense of each specialty, it is relevant that all areas involved have a minimum knowledge of cancer treatment and undergo a selective process related to a multidisciplinary surgery team before handling the neoplasia. Mastology and oncology already have an extensive curriculum, with no need for selections to be eligible for sub-specialization in oncoplasty. However, the plastic surgeon needs to perform a curricular test of medical activities directly or indirectly connected with the treatment of cancer in general, or specifically breast cancer. An additional period should be introduced in the plastic surgeon's curriculum to approach oncological theories and techniques. The commitment of oncoplasty with patients favored less invasive surgical procedures. Many of the oncoplastic techniques can be performed by other medical specialties, but, without proper professional training, they can lead to inappropriate harm to patients. According to Simmons⁷, it is extremely important to be flexible and adaptable to these changes in the way we care for our cancer patients.

Table 1 shows that, in Brazil, in the United States and in Europe, the specialties do not differ from each other in relation to the surgical basis of breast reconstruction or in relation to initial or advanced treatment of breast cancer. Based on these conclusions, we can suggest the following design for the formation of oncoplastic breast professionals:

1. type of training: postgraduate program, in which the graduate student will receive academic background proved by a thesis presentation;
2. training time: which can vary between 12 and 24 months, depending on the previous training;
3. number of procedures: at least 4 patients for each of the basic themes of oncoplastic training, including changes in breast volume;
4. target audience: plastic surgeons, breast surgeons and oncologists.

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