

TRENDS IN BREAST CANCER SURGERY IN PRIVATE PATIENTS UNDER OPPORTUNISTIC SCREENING

Tendências na cirurgia de câncer de mama em pacientes de um serviço privado sob rastreamento oportunístico

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ABSTRACT

Objective: This study aims to determine the evolution of staging and surgical treatment in patients with breast cancer in a private clinic over the last 40 years. **Methods:** Retrospective descriptive observational study, through statistical analysis of the medical records of 2105 patients treated at a private clinic in Curitiba, Paraná, between 1977 and 2017. **Results:** Data analyzed from 2,105 patients diagnosed with breast cancer revealed that, over time, radical surgeries predominated when compared to conservative ones. However, when analyzed proportionally over the years, it is possible to observe an inversion of the surgical modalities. It was demonstrated that from 1977 to 2017, there was a 273% increase in the number of conservative surgeries and a 45.5% decrease in mastectomies. In addition to this data, there was a decrease in the number of axillary emptying and, consequently, of positive sentinel lymph nodes. In addition, tumors diagnosed early (T1) have increased over the years. **Conclusion:** Patients had an early diagnosis of the disease, resulting in less invasive surgical treatments and, consequently, lower morbidity and mortality.

KEYWORDS: Breast neoplasms, sentinel lymph node, lymph node excision, segmental mastectomy, simple mastectomy.

RESUMO

Objetivo: A pesquisa visa determinar a evolução do estadiamento e do tratamento cirúrgico em pacientes com câncer de mama em uma clínica privada, nos últimos 40 anos. **Métodos:** Estudo observacional descritivo retrospectivo, por meio da análise estatística dos prontuários de 2105 pacientes atendidas em clínica privada em Curitiba, Paraná, entre 1977 e 2017. **Resultados:** Dados analisados de 2.105 pacientes diagnosticadas com câncer de mama revelaram que, ao longo do tempo, as cirurgias radicais predominaram quando comparadas às cirurgias conservadoras. No entanto, quando analisadas proporcionalmente ao longo dos anos, é possível constatar uma inversão das modalidades cirúrgicas. Demonstrou-se que de 1977 a 2017, houve aumento de 273% do número das cirurgias conservadoras e queda de 45,5% das mastectomias. Associado a esse dado, notou-se diminuição do número de esvaziamento axilar e consequentemente de linfonodos sentinela positivos. Além disso, os tumores diagnosticados em fase inicial (T1) aumentaram ao longo dos anos. **Conclusão:** As pacientes tiveram um diagnóstico em estadiamento mais precoce da doença, proporcionando tratamentos cirúrgicos menos invasivos e, consequentemente, menor morbidade.

PALAVRAS-CHAVE: neoplasias de mama; linfonodo sentinela; excisão de linfonodo; mastectomia segmentar; mastectomia simples.

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INTRODUCTION

Breast cancer is the most common malignant cancer among women second to non-melanoma skin cancer, accounting for 2,088,849 new cases worldwide¹. In Brazil, it is estimated that 59,700 new cases will occur in 2018, which corresponds to 28% of all cases of cancer in women². Every year, more than 1.5 million women die from the disease¹. Although it is considered a disease found in developed countries, more than half (52%) of new breast cancer cases and the majority of deaths (62%) occur in developing countries³.

Breast cancer treatment has evolved substantially in recent decades. Extensive surgeries have resulted in more conservative management and oncoplasty. One of the factors that contributed to the modification and evolution of the surgical treatment was the introduction of mammographic screening, making the diagnosis of smaller tumors possible⁴⁻⁷. In addition, randomized, controlled trials have demonstrated that conservative surgery followed by radiotherapy presents results equivalent to those of mastectomy⁸⁻¹⁰. Improved patient survival, both early diagnosis and the improvement of systemic and locoregional treatment, led physicians to also consider aesthetic and psychological aspects in breast cancer management. Oncoplastic surgery combines plastic and oncologic surgery techniques, resulting in multiple benefits for patients: it allows for larger resections, lower rates of positive margins and reoperations, and better results regarding aesthetics and quality of life¹¹⁻¹³.

Surgical management of the axilla has also undergone significant changes over the years. The concept of lymphatic drainage mapping, introduced in 1991, led to the replacement of axillary emptying by sentinel lymph node biopsy for the treatment of early breast cancer¹⁴⁻¹⁶. More recently, randomized and controlled studies have demonstrated the oncological safety of not performing axillary emptying in patients with early tumors and up to two positive sentinel lymph nodes, submitted to conservative surgery¹⁷ or axillary radiotherapy¹⁸.

Understanding the trends in surgical treatment of breast cancer is extremely valuable. In addition to training new specialists, this knowledge can identify areas for further research. The objective of this study was to evaluate the patients diagnosed with breast cancer who underwent surgical treatment in a private health system in Brazil, in order to map the management tendency in relation to time.

METHODS

A descriptive and retrospective observational study. The information was obtained in the medical records of patients attending a private referral service, located in Curitiba, Paraná, Brazil. Approval was obtained from the Research Ethics Committee (opinion no. 2,115,700).

The study evaluated a sample of 2,105 patients treated between 1977 and 2017. Women with breast cancer treated at a

private referral service in Curitiba were included in the study. Regarding exclusion criteria, the following were considered: male patients, women who did not receive treatment at the service in question, and unavailable or incomplete medical records.

Statistical analysis

The SPSS program was used for statistical analysis. Continuous variables were expressed as means and standard deviation. Categorical variables were expressed as percentages and compared with the χ^2 test. P values less than 0.05 were considered statistically significant.

RESULTS

Between January 1977 and May 2017, 2,105 women with breast cancer who were treated with surgery were evaluated in a private care service, located in the city of Curitiba, Paraná.

The patients' ages ranged from 22 to 95 years, with a mean of 54.67 years, a median of 54 years and a standard deviation of 13.2 years. In the period between 1998 and 2002, the mean age at the time of surgery was 57.67 years, representing the highest mean between all the periods. In the last 5 years of research (2013-2017) the average was 53.85 years (Figure 1).

Family history of cancer was analyzed according to first degree relatives (father, mother, siblings and children), such as breast, endometrial, ovary, thyroid and prostate cancer. Among the total of 1,891 patients, 405 had family history for cancer (21.41%). Among the 2,105 included patients, 71 (3.37%) were evaluated for mutations associated with breast cancer. Among these, 24 (33.8%) had mutations in the BRCA1 or 2 genes. The most frequent histological subtype among the patients

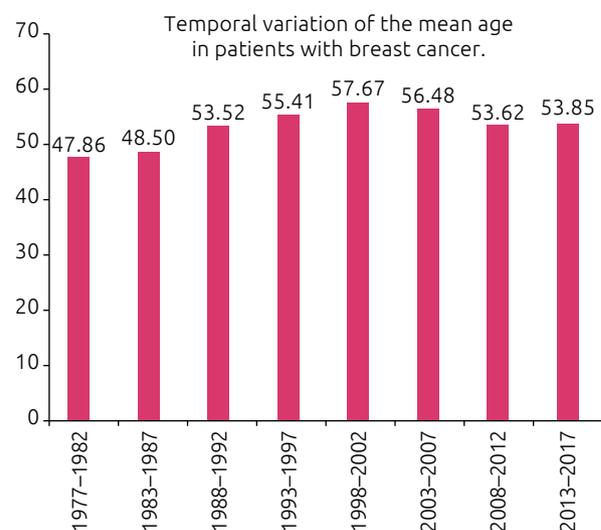


Figure 1. Temporal variation of the mean age in patients with breast cancer.

was invasive ductal carcinoma, corresponding to 1,413 cases (67.12%). Lobular carcinoma appeared as the second most prevalent, in 6.36% (134) of the cases. The rest of the patients presented other histological subtypes such as: mucinous, papillary, tubular, micropapillary, tubular duct, lobular duct and lobular tubule. The HER-2 oncogene was positive in 331 of the 1,650 analyzed cases (78.4%).

Regarding surgeries, 48.2% (1,000) of the patients were submitted to conservative surgeries and the remaining patients were submitted to radical surgical treatments. For the purpose of classification, we considered centralectomies, wide excisions, local excisions, simple excisions, segmental resections, quadrantectomies, sectionectomy and lumpectomy. Among the radical surgical treatments, the Horsted surgery, Patey surgery, mastectomiatotal simplese mastectomy were listed. In absolute numbers, radical surgeries predominated when compared to conservative surgeries. However, when analyzed proportionally over the years, it is possible to observe an inversion of the surgical modalities, as observed in Figure 2. In the comparative analysis at five-year intervals, it was found that the number of conservative surgeries is increasing, and the number of radical surgeries is decreasing. In the period from 1977 to 2017, there was a 273% increase in the number of conservative surgeries and a 45.5% decrease in mastectomies.

As for axillary surgery, there was a decrease in the number of patients submitted to axillary emptying (Figure 3). In the last analyzed interval, only 21.34% needed to undergo this procedure, contrary to what is observed in the first 5 years, during which period 71.43% performed lymph nodes emptying.

At the same time of this inversion, the number of patients with positive lymph nodes decreased, going from 57.14 to 21.25% between 1977 and 2017 (Figure 4).

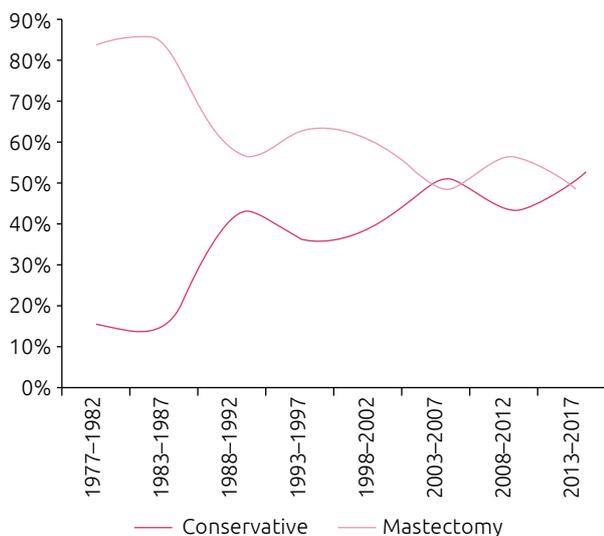


Figure 2. Types of surgery performed between 1977 and 2017 in 5-year intervals ($p < 0.001$).

The staging at the time of diagnosis was stratified into Tis, T1, T2, T3 and T4. Tumors with up to 2.0 cm (T1) increased over the 40 years analyzed. Between 1977 and 1982, T1 corresponded to 40.0% of the tumors, increasing to 60.41% from 2013 to 2017. At the same time, T2, T3 and T4 staging declined, as Figure 5 demonstrates. Thus, T1 reached the highest prevalence between the stages.

DISCUSSION

The present retrospective data analysis from a private center in Brazil showed a significant decrease in the number of mastectomies and axillary emptying and the consequent increase in

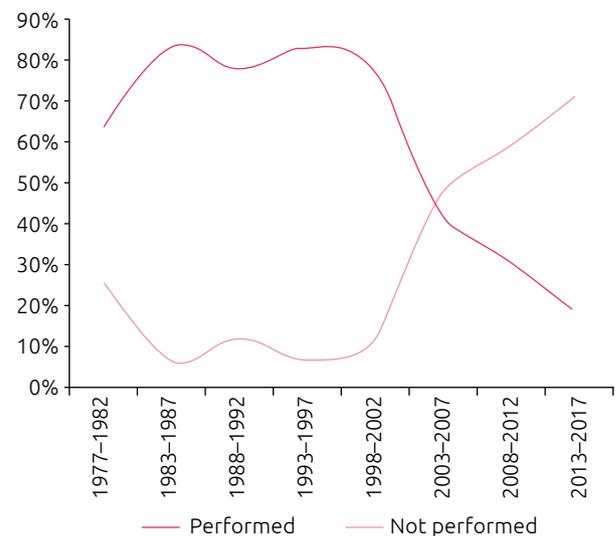


Figure 3. Proportion of axillary emptying performed between 1977 and 2017 in 5-year intervals ($p < 0.01$).

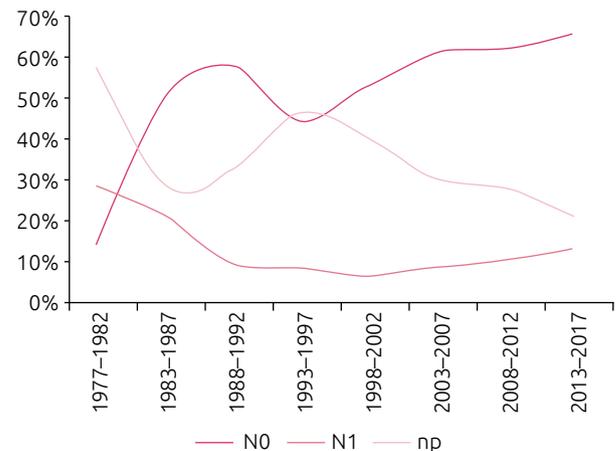


Figure 4. Proportion of patients with positive lymph node between 1977 and 2017 at 5-year intervals ($p < 0.001$).

the number of conservative surgeries and biopsies of the sentinel lymph node. These results show the history of mastology in the last forty years.

Between 1977 and 1982, only 14.29% of the surgeries were conservative; in the period between 2013-2017, 53.31% of the patients received this treatment. This increase is in agreement with the worldwide tendency and approach for this type of cancer^{19,20} and with the recommendation of the National Accreditation Program for Breast Centers, which states that at least 50% of patients with early breast cancer (clinical stages 0, I or II) are treated with conservative surgery²¹. This conservative movement began in the 1980s with clinical studies demonstrating that conservative post-therapy survival, defined as surgical excision of the primary tumor with adjacent normal tissue margin followed by radiotherapy, is equivalent to mastectomy for the treatment of stages I and II of invasive breast cancer⁸⁻¹⁰

Regarding the axillary approach, sentinel lymph node biopsy revolutionized the management of patients with early breast cancer. Several studies published since the late 1990s were able to demonstrate the oncological safety of sentinel lymph node biopsy when compared to axillary emptying^{15,16,22,23}. Our data show a gradual reduction in the number of lymphadenectomies in the five-year period between 1998-2002, which is in agreement with the publication of the randomized studies in the literature. Subsequently, new studies have shown no need to perform axillary emptying for patients with lymph nodes containing micrometastases²⁴; or for those with T1 or T2 tumors and up to two positive lymph nodes submitted to conservative surgery¹⁷. These new data further reduced the indication for lymphadenectomy in breast cancer treatment. In addition, the increasing use of neoadjuvant chemotherapy reduces the number of patients with positive lymph nodes and, consequently, the number of performed lymphadenectomies²⁵. Another factor that may influence the

reduction of lymphadenectomies is the introduction of mammographic screening and the early diagnosis of breast cancer. In the present study, between 1977 and 1982, tumors up to 2.0 cm were responsible for 40% of all treated patients, increasing to 60.41% between 2013 and 2017.

In order to increase the survival of patients with breast cancer and reduce the aggressiveness of the treatment, the early detection of the disease is extremely important. Meta-analyses and randomized controlled trials have shown a 20-35% reduction in mortality from breast cancer due to mammographic screening^{4,7,26,27}. Around 8 to 11 deaths from breast cancer will be avoided for every 1,000 women who undergo mammographic screening every two years⁷. Recommendations as to when to start and how to track it vary from country to country. In Brazil, the Ministry of Health recommends mammography for women between 50 and 69 years old, every two years²⁸. The Brazilian Society of Mastology recommends that mammographic screening should be performed annually, starting at 40 years of age²⁹.

The present study has several limitations. Firstly, as it is a retrospective analysis, the study is subject to some biases, mainly due to the lack of information in the medical records. Secondly, some important information, such as the performance of neoadjuvant chemotherapy, hormone receptor status of the tumors and the performance of radiotherapy were not investigated in the present analysis. Thirdly, the fact that the study population comes from a single private center in Brazil means that the data reported here can not be generalized to the whole country or to the patients of the Unified Health System (SUS).

The disparity between the public health system in Brazil and the private system is still quite large. A prospective study conducted by the Brazilian Breast Cancer Study Group (GBECAM) collected data from 28 public and private centers in the country and showed that 36.9% of the women treated in the SUS were diagnosed with stage III or IV breast cancer, compared to 16.2% in private services³⁰. Another study that evaluated breast cancer surgeries performed at the Hospital das Clínicas of the Federal University of Goiás between 2002 and 2009 showed a significant increase in tumor size at diagnosis and a consequent increase in indications for neoadjuvant chemotherapy (54.5%) and mastectomies (53%). In this study, only 9.1% of the patients had a clinical stage I at diagnosis, as opposed to 60.4% in our service³¹.

One of the explanations for this disparity is the low mammographic coverage for SUS patients. In 2010, throughout Brazil, 3,126,283 mammograms (with diagnostic or screening indication) were performed by SUS, in women aged 40 years or older, which corresponds to 12.4% of women in this age group. In the target age groups of the screening, the ratio of examinations / target population was 32.2% for women aged 50-59 years and 25% for those aged 60-69 years. These values are lower than those observed in countries where population-based screening

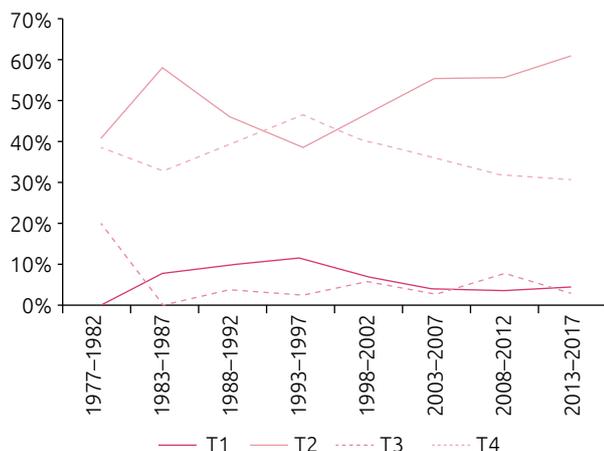


Figure 5. Proportion of tumor sizes diagnosed between 1977 and 2017 at 5 year intervals ($p = 0.0017$).

programs have been organized, such as in England, where coverage was 73% in 2010/2011³².

With an earlier diagnosis, patients from the private system are submitted to less invasive procedures and have a better prognosis. An analysis performed in a retrospective study of 193,596 patients treated in the Brazilian public health system between 2008 and 2014 revealed different trends than those found in the private health system³³. In SUS, there was stabilization of conservative surgical treatment, and reduction of simple mastectomies. In contrast, in the private system, the surgical approach has become more conservative over the years, reflecting the benefits of early diagnosis and demonstrating the lack of access to health services by SUS patients.

A large part of the world has an increasing incidence of breast cancer but limited resources to treat it³⁴. The offer of health insurance plans to clients is significantly higher than made available by SUS regarding medium and high complexity care, from mammography screening, magnetic resonance staging, to access to mastologists for diagnostic confirmation of the suspected cases

identified in mammography and access to specialized treatment³⁵. In view of this, the need for greater investments in public health in Brazil is visible compared to other public and universal health systems such as the United Kingdom and Canada. From our study and from other studies it is obvious that early diagnosis is inversely proportional to morbidity in the treatment of breast cancer.

Although the present study reveals part of the reality of breast cancer in Brazil, future analyzes are necessary in order to improve breast cancer treatment.

CONCLUSION

During the 40 years analyzed, we demonstrated a reduction in the number of axillary mastectomies and lymphadenectomies in the treatment of women with breast cancer treated in a private service in Brazil. These data demonstrate the increasingly conservative trend in the treatment of this disease, seeking the patients' quality of life in addition to survival.

REFERENCES

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* [Internet]. 2018 [acessado em 2 nov. 2018];68(6):394-424. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/30207593>. <https://doi.org/10.3322/caac.21492>
2. Instituto Nacional de Câncer. Ministério da Saúde. Tipos de câncer [Internet]. Instituto Nacional de Câncer; 2018 [acessado em 31 maio 2018]. Disponível em: http://www2.inca.gov.br/wps/wcm/connect/tiposdecancer/site/home/mama/cancer_mama
3. World Health Organization. Diagnosis and screening [Internet]. World Health Organization [acessado em 01 nov. 2018]. Disponível em: <http://www.who.int/cancer/prevention/diagnosis-screening/breast-cancer/en/>
4. Alexander FE, Anderson TJ, Brown HK, Forrest AP, Hepburn W, Kirkpatrick AE, et al. 14 years of follow-up from the Edinburgh randomised trial of breast-cancer screening. *Lancet* [Internet]. 1999 [acessado em 26 nov. 2017];353(9168):1903-8. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/10371567>. [https://doi.org/10.1016/s0140-6736\(98\)07413-3](https://doi.org/10.1016/s0140-6736(98)07413-3)
5. Shapiro S. Periodic screening for breast cancer: the HIP Randomized Controlled Trial. *Health Insurance Plan. J Natl Cancer Inst Monogr* [Internet]. 1997 [acessado em 26 nov. 2017];(22):27-30. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/9709271>. <https://doi.org/10.1093/jncimono/1997.22.27>
6. Myers ER, Moorman P, Gierisch JM, Havrilesky LJ, Grimm LJ, Ghate S, et al. Benefits and Harms of Breast Cancer Screening - A systematic review. *JAMA* [Internet]. 2015 [acessado em 21 out. 2015];314(15):1615-34. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/26501537>. <https://doi.org/10.1001/jama.2015.13183>
7. Tabár L, Vitak B, Chen TH, Yen AM, Cohen A, Tot T, et al. Swedish two-county trial: impact of mammographic screening on breast cancer mortality during 3 decades - with comments. *Radiology* [Internet]. 2011 [acessado em 02 nov. 2018];260(3):658-63. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/21712474>
8. Fisher B, Anderson S, Bryant J, Margolese R, Deutsch M, Fisher ER, et al. Twenty-Year Follow-Up of a Randomized Trial Comparing Total for the Treatment of Invasive Breast Cancer. *N Engl J Med*. 2002;347(16):1233-41. <https://doi.org/10.1056/NEJMoa022152>
9. Veronesi U, Cascinelli N, Mariani L, Greco M, Saccozzi R, Luini A, et al. Twenty-year follow-up of a randomized study comparing breast-conserving surgery with radical mastectomy for early breast cancer. *N Engl J Med* [Internet]. 2002 [acessado em 2 nov. 2018];347(16):1227-32. Disponível em: <http://www.nejm.org/doi/abs/10.1056/NEJMoa020989>. <https://doi.org/10.1056/NEJMoa020989>
10. van Dongen JA, Voogd AC, Fentiman IS, Legrand C, Sylvester RJ, Tong D, et al. Long-term results of a randomized trial comparing breast-conserving therapy with mastectomy: European Organization for Research and Treatment of Cancer 10801 trial. *J Natl Cancer Inst* [Internet]. 2000 [acessado em 2 nov. 2018];92(14):1143-50. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/10904087>. <https://doi.org/10.1093/jnci/92.14.1143>
11. Urban C, Rietjens M. *Oncoplastic and Reconstructive Breast Surgery*. 1ª ed. Itália: Springer-Verlag; 2013. p. 13-21.
12. Kuroda F, Urban C, Zucca-Matthes G, de Oliveira VM, Arana GH, Iera M, et al. Evaluation of Aesthetic and Quality-of-Life Results after Immediate Breast Reconstruction with Definitive Form-Stable Anatomical Implants. *Plast Reconstr Surg* [Internet]. 2016 [acessado em 7 jul. 2018];137(2):278e-86e. Disponível em: <http://content.wkhealth.com/linkback/openurl?sid=WKPTLP:landingpage&an=00006534-201602000-00005>. <https://doi.org/10.1097/01.prs.0000475746.17968.f4>

13. Peiris L, Olson D, Kelly D. Oncoplastic and reconstructive breast surgery in Canada: breaking new ground in general surgical training. *Can J Surg* [Internet]. 2018 [acessado em 1º nov. 2018];61(5):294-9. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/30246974>. <https://doi.org/10.1503/cjs.016717>
14. Giuliano AE, Kirgan DM, Guenther JM, Morton DL. Lymphatic mapping and sentinel lymphadenectomy for breast cancer. *Ann Surg* [Internet]. 1994 [acessado em 2 nov. 2018];220(3):391-8; discussion 398-401. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/8092905>. <https://doi.org/10.1097/00000658-199409000-00015>
15. Krag DN, Anderson SJ, Julian TB, Brown AM, Harlow SP, Costantino JP, et al. Sentinel-lymph-node resection compared with conventional axillary-lymph-node dissection in clinically node-negative patients with breast cancer: overall survival findings from the NSABP B-32 randomised phase 3 trial. *Lancet Oncol* [Internet]. 2010 [acessado em 2 nov. 2018];11(10):927-33. Disponível em: <http://linkinghub.elsevier.com/retrieve/pii/S1470204510702072>. [https://doi.org/10.1016/S1470-2045\(10\)70207-2](https://doi.org/10.1016/S1470-2045(10)70207-2)
16. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, et al. Randomized Multicenter Trial of Sentinel Node Biopsy Versus Standard Axillary Treatment in Operable Breast Cancer: The ALMANAC Trial. *JNCI Natl Cancer Inst* [Internet]. 2006 [acessado em 2 nov. 2018];98(9):599-609. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/16670385>. <https://doi.org/10.1093/jnci/djj158>
17. Giuliano AE, Hunt KK, Ballman KV, Beitsch PD, Whitworth PW, Blumencranz PW, et al. Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis. *JAMA* [Internet]. 2011 [acessado em 2 nov. 2018];305(6):569-75. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/21304082>. <https://doi.org/10.1001/jama.2011.90>
18. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJH, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol* [Internet]. 2014 [acessado em 2 nov. 2018];15(12):1303-10. Disponível em: <https://linkinghub.elsevier.com/retrieve/pii/S1470204514704607>. [https://doi.org/10.1016/S1470-2045\(14\)70460-7](https://doi.org/10.1016/S1470-2045(14)70460-7)
19. Yu K-D, Di G-H, Wu J, Lu J-S, Shen K-W, Shen Z-Z, et al. Development and trends of surgical modalities for breast cancer in China: a review of 16-year data. *Ann Surg Oncol* [Internet]. 2007 [acessado em 2 nov. 2018];14(9):2502-9. Disponível em: <http://www.springerlink.com/index/10.1245/s10434-007-9436-2>. <https://doi.org/10.1245/s10434-007-9436-2>
20. Kang SY, Kim YS, Kim Z, Kim H-Y, Lee SK, Jung K-W, et al. Basic Findings Regarding Breast Cancer in Korea in 2015: Data from a Breast Cancer Registry. *J Breast Cancer* [Internet]. 2018 [acessado em 1º nov. 2018];21(1):1-10. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/29628978>. <https://doi.org/10.4048/jbc.2018.21.1.1>
21. National Accreditation Program for Breast Centers. 2018 Breast Cancer Standards Manual. Chicago: National Accreditation Program for Breast Centers; 2018.
22. Veronesi U, Paganelli G, Viale G, Luini A, Zurrada S, Galimberti V, et al. A Randomized Comparison of Sentinel-Node Biopsy with Routine Axillary Dissection in Breast Cancer. *N Engl J Med* [Internet]. 2003 [acessado em 4 nov. 2018];349(6):546-53. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/12904519>. <https://doi.org/10.1056/NEJMoa012782>
23. Zavagno G, De Salvo GL, Scalco G, Bozza F, Barutta L, Del Bianco P, et al. A Randomized clinical trial on sentinel lymph node biopsy versus axillary lymph node dissection in breast cancer: results of the Sentinella/GIVOM trial. *Ann Surg* [Internet]. 2008 [acessado em 4 nov. 2018];247(2):207-13. Disponível em: <https://insights.ovid.com/crossref?an=00000658-200802000-00001>. <https://doi.org/10.1097/SLA.0b013e31812e6a73>
24. Galimberti V, Cole BF, Zurrada S, Viale G, Luini A, Veronesi P, et al. Axillary dissection versus no axillary dissection in patients with sentinel-node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial. *Lancet Oncol* [Internet]. 2013 [acessado em 4 nov. 2018];14(4):297-305. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/23491275>. [https://doi.org/10.1016/S1470-2045\(13\)70035-4](https://doi.org/10.1016/S1470-2045(13)70035-4)
25. Hunt KK, Yi M, Mittendorf EA, Guerrero C, Babiera GV, Bedrosian I, et al. Sentinel Lymph Node Surgery After Neoadjuvant Chemotherapy is Accurate and Reduces the Need for Axillary Dissection in Breast Cancer Patients. *Ann Surg* [Internet]. 2009 [acessado em 4 nov. 2018];250(4):558-66. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/19730235>. <https://doi.org/10.1097/SLA.0b013e3181b8fd5e>
26. Bjurstam NG, Björneld LM, Duffy SW. Updated results of the Gothenburg Trial of Mammographic Screening. *Cancer* [Internet]. 2016 [acessado em 26 nov. 2017];122(12):1832-5. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/27061821>. <https://doi.org/10.1002/cncr.29975>
27. Oeffinger KC, Fontham ETH, Etzioni R, Herzig A, Michaelson JS, Shih Y-CT, et al. Breast Cancer Screening for Women at Average Risk: 2015 Guideline Update From the American Cancer Society. *JAMA* [Internet]. 2015 [acessado em 26 nov. 2017];314(15):1599-614. Disponível em: <http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2015.12783>. <https://doi.org/10.1001/jama.2015.12783>
28. Instituto Nacional de Câncer. Diretrizes para a detecção precoce do câncer de mama no Brasil. Rio de Janeiro: Instituto Nacional de Câncer; 2015.
29. Urban LABD, Chala LF, Di Pace Bauab S, Schaefer MB, dos Santos RP, Maranhão NMDA, et al. Recomendações do Colégio Brasileiro de Radiologia e Diagnóstico por Imagem, da Sociedade Brasileira de Mastologia e da Federação Brasileira das Associações de Ginecologia e Obstetrícia para o rastreamento do câncer de mama. *Radiol Bras* [Internet]. 2017 [acessado em 4 nov. 2018];50(4):244-9. Disponível em: <http://dx.doi.org/10.1590/0100-3984.2017-0069>
30. Simon S, Bines J, Barrios C, Nunes J, Gomes E, Pacheco F, et al. Clinical Characteristics and Outcome of Treatment of Brazilian Women with Breast Cancer Treated at Public and Private Institutions – The AMAZON Project of the Brazilian Breast Cancer Study Group (GBECAM). *Cancer Res* [Internet]. 2009 [acessado em 4 nov. 2018];69(24 Supl.):3082. Disponível em: <http://cancerres.aacrjournals.org/lookup/doi/10.1158/0008-5472.SABCS-09-3082>. <http://dx.doi.org/10.1158/0008-5472.SABCS-09-3082>

31. Freitas R Jr., Siqueira LB, Carrijo EN dos A, Lacerda RP, Paulinelli RR, Rahal RMS, et al. Temporal variation of breast cancer surgical treatment in a university hospital in Brazil's Central West region. *Rev Col Bras Cir* [Internet]. 2013 [acessado em 4 nov. 2018];40(3):180-5. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/23912363>
32. NHS Digital. NHS Breast screening programme, England 2010-11. Inglaterra: NHS Digital; 2012.
33. Freitas-Júnior R, Gagliato DM, Moura Filho JWC, Gouveia PA, Rahal RMS, Paulinelli RR, et al. Trends in breast cancer surgery at Brazil's public health system. *J Surg Oncol* [Internet]. 2017 [acessado em 28 jul. 2018];115(5):544-9. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/28168857>. <https://doi.org/10.1002/jso.24572>
34. Nyström L, Rutqvist LE, Wall S, Lindgren A, Lindqvist M, Rydén S, et al. Breast cancer screening with mammography: overview of Swedish randomised trials. *Lancet* (London, England) [Internet]. 1993 [acessado em 4 nov. 2018];341(8851):973-8. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/8096941>. [https://doi.org/10.1016/0140-6736\(93\)91067-v](https://doi.org/10.1016/0140-6736(93)91067-v)
35. DeSantis CE, Bray F, Ferlay J, Lortet-Tieulent J, Anderson BO, Jemal A. International Variation in Female Breast Cancer Incidence and Mortality Rates. *Cancer Epidemiol Biomarkers Prev* [Internet]. 2015 [acessado em 4 nov. 2018];24(10):1495-506. Disponível em: <http://www.ncbi.nlm.nih.gov/pubmed/26359465>. <https://doi.org/10.1158/1055-9965.EPI-15-0535>