A Produção do Conhecimento **nas Ciências da Saúde 5**

Benedito Rodrigues da Silva Neto
(Organizador)

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APRESENTAÇÃO

Encerramos nesse quinto volume a coleção “A Produção do Conhecimento nas Ciências da Saúde”, com um sentimento de gratidão e dever cumprido ao apresentar uma diversidade de pesquisas sólidas e de amplo espectro fomentando o conhecimento na área das Ciências da Saúde.

Tendo em vista todo conhecimento apresentado nesta coleção, finalizamos o trabalho apresentando de forma mais multidisciplinar possível trabalhos científicos na interface de estudos ligados à saúde.

Apresentamos de forma ampla conceitos atuais em pesquisas desenvolvidas com os temas psico-oncologia, qualidade de vida biopsicosocial, perfis epidemiológicos, práticas integrativas, automedicação, novos tratamentos, promoção e educação em saúde, biotecnologias em saúde, diagnóstico, sistema de saúde pública, fatores de risco, nanotecnologia, além de revisões e estudos de caso, que poderão contribuir com o público de graduação e pós graduação das áreas da saúde.

O profissional da saúde atual precisa cada vez mais estar conectado com as evoluções e avanços tecnológicos. Além disso é necessário um comprometimento com o conhecimento, pois esse avança à passos largos dentro das pesquisas em saúde, já que descobertas e publicações de alto impacto são diárias e trazem conteúdo aprimorado e de relevância, assim a leitura de fontes que possam ir além da área específica de atuação são extremamente importantes. Como objetivo central deste volume desejamos que o leitor tenha essa possibilidade em um único volume podendo transitar de diversas formas nas áreas afins.

Assim, reforçamos a importância do aprendizado contínuo do profissional da saúde, e desejamos fortemente que esse material contribua para isso. O conteúdo de todos os volumes é significante não apenas pela teoria bem fundamentada aliada à resultados promissores, mas também pela capacidade de professores, acadêmicos, pesquisadores, cientistas e da Atena Editora em produzir conhecimento em saúde nas condições ainda inconstantes do contexto brasileiro. Desejamos que este contexto possa ser transformado a cada dia, e o trabalho aqui presente pode ser um agente transformador por gerar conhecimento em uma área fundamental do desenvolvimento como a saúde.

Dr. Benedito Rodrigues da Silva Neto

SUMÁRIO

CAPÍTULO 30

REAL-WORLD DATA IN VERY YOUNG NON-METASTATIC BREAST CANCER: SINGLE INSTITUTION EXPERIENCE

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ABSTRACT: Breast cancer is the leading cause of cancer-related deaths in women aged 20 to 59 years old. Young women usually have more aggressive tumors and more advanced disease with larger size and axillary nodal involvement. There are few studies assessing the characteristics of breast cancer in very young women. **Method:** We performed a retrospective analysis to evaluate the epidemiological and clinical profile of non-metastatic breast cancer patients with 30 years of age and younger treated between 1993 and 2011 at the Brazilian National Cancer Institute (INCA). **Results:** From the 196 patients evaluated, 181 patients (90%) had ductal carcinoma, 79 (40%) high-grade tumors, and 102 (52%) were HR positive. 117 patients (60%) were classified as stage III at diagnosis. The median age was 29 y (range: 17-30y). Of 185 patients who underwent surgery, 156 (84.3%) had total mastectomy, and 171 (92%) had axillary node dissection. 119 patients received neoadjuvant chemotherapy, and 14 patients (9.3%) underwent neoadjuvant radiotherapy. After a median follow-up of 81.5 months, there were 109 relapses (55%) and 81 deaths (41%). Median RFS and OS was 49.5 months and 134 months, respectively. Positive node involvement and neoadjuvant chemotherapy were associated with shorter RFS and OS. **Conclusion:** Breast cancer is not frequent in young patients, especially under 31 years of age. We found more locally advanced disease and worse prognostic pathological characteristics. Despite the aggressive treatment, our patients had worse outcomes than reported by other authors.

KEYWORDS: Breast Neoplasms; Young Adult; Health Services Research.

1 I INTRODUCTION

Breast cancer remains the leading cause of cancer-related deaths in women aged 20 to 59 years old in the United States. In 2015, the American Cancer Society estimated that 231.840 women would be diagnosed and 40.290 patients would die[25]. Accordingly to the Information System of Breast Cancer (SISMAMA) and the Unified Health System Data (DATASUS) of Brazilian Ministry of Health, from 2009 to 2012, in Brazil, 31.195 cases of breast cancer were identified, 10.6% occurred in women under 40 years of age[11].

Generally, the diagnosis is due to the perception of a palpable mass, since young women have rarely undergone previous screening mammograms[14]. The Brazilian recommendation for breast cancer screening is annual clinical breast examination starting at age 40 and biennial mammography between the ages of 50–69 years old. For high-risk women, it is recommended an annual clinical breast examination and mammography starting at 35 years of age[9].

Young women usually have more aggressive tumors — poorly differentiated, hormone receptor-negative and HER2 overexpression tumors — and more advanced disease with larger size and axillary nodal involvement[29]. They often need and receive more aggressive multimodal treatment.

Breast cancer at any age has great psychological, functional and social impacts. Women face both the treatment of a potentially fatal disease, the effects of an aggressive treatment, and the destruction of their self-image. In this age group, there is an associated impact on motherhood plans and professional career goals.

Currently, there are few studies assessing the characteristics of breast cancer in this specific population of women in Brazil. We performed a retrospective analysis to evaluate the epidemiological and clinical profile of non-metastatic very young patients with breast cancer treated at the Brazilian National Cancer Institute (INCA).

2 I METHOD

This study was approved by the ethics in human research committee of the Brazilian National Cancer Institute (INCA), Rio de Janeiro, Brazil in November 2014 (Protocol number: 37517314.5.0000.5274), and was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The informed consent was dispensed.

Two hundred forty-nine very young women treated at INCA with breast cancer between 1993 and 2011 were identified through internal database. We considered “very young women” those less than 31 years of age at diagnosis. We retrospectively

reviewed the medical records and collected data about clinicopathological and treatment characteristics.

All the patients had a biopsy performed or had tumor samples reviewed at our institution. Pathological variables such as histological grade (Bloom and Richardson score[2]), estrogen-receptor (ER) and progesterone-receptor (PR) status had always been evaluated, whereas we began evaluation of HER2 status since 2007. The tumors with > 1% nuclear-stained cells were considered positive for ER or PR. The histological grade was reported by Bloom and Richardson grade: well-differentiated (low grade-G1), moderately differentiated (intermediate grade – G2) and poorly differentiated (high grade-G3)[2]. The HER2 immunohistochemical staining (Herceptest; Dako A/S, Glostrup, Denmark was scored from 0 to 3+: score 0 and 1+ were considered negative; score 3+ was considered positive; and score 2+ needed additional fluorescent in situ hybridization test (FISH; PathVision Her2 DNA probe kit, Vysis Inc., Downers Grove, IL, USA).

The tumor stage was based on the seventh American Joint Committee on Cancer[7]. We defined Pathological complete response (pCR) as ypT0/is ypN0: no invasive residual in breast or nodes. Weight and height information was collected at the first visit with medical oncology. BMI categories were selected according to the World Health Organization definition: underweight, <18.5 kg/m2; normal range between 18.5 and 25 kg/m2; overweight between 25 and 30 kg/m2; and obese ≥30.0 kg/m2[28].

3 I STATISTICAL ANALYSIS

The relapse-free survival (RFS) was defined as the interval from the histological diagnosis to relapse, death or the last follow-up. The overall survival (OS) was defined as the interval from the histological diagnosis to death or the last follow-up. The RFS and OS analysis were estimate using the Kaplan-Meier method and compared by log-rank test.

We used the COX proportional regression to estimate hazard ratios and the 95% confidence interval. The variables with p-value<0.05 in the univariate analysis were included in multivariate analysis. We conducted multivariate analysis through manual selection based on hierarchical model, beginning with demographic characteristics, then tumor characteristics and treatment. In each block, the non-significant variables were excluded. Baseline characteristics was compared using Fisher's exact test or the chi-square test, as appropriate. P-value were considered significant if less than 0.05. All analyses were performed with the SPSS software, version 18.0.

4 I RESULTS

Between January 1993 and July 2011, 249 patients aged 30 years or younger

were diagnosed with breast cancer at INCA hospital. Of this group, 53 patients were excluded (41 had metastasis upon diagnosis and 21 were treated elsewhere).

Patients, tumor and treatment characteristics are summarized in table 1. The median age was 29 years old (range: 17-30 years old). From the 196 patients evaluated, 181 patients (92.3%) had ductal carcinoma, 4 patients (2%) had lobular carcinoma, and 10 patients (5.1%) had other histological subtypes (metaplastic, sarcomas). High-grade tumors were presented in 79 patients (40%). As for the imunohistochemical assay, 102 patients (52%) had hormone receptor positive. The HER2 status were evaluated only on 79 patients (40%) and enriched in 19 patients (24%). There were 27 patients (34 %) with triple negative tumors. One hundred and seventeen patients (60%) were classified as stage III upon diagnosis, 55 patients (28%) were stage II, and 23 patients (12%) were stage I.

As shown in Table 1, a total of 185 patients (94.5%) underwent surgery, 156 patients (84.3%) had total mastectomy, 29 patients (15%) had breast-conserving surgery, and 171 patients (92%) underwent axillary node dissection.

Of the 119 patients who received neoadjuvant chemotherapy, 21 patients (17.5%) were diagnosed with clinical stage II and 98 patients (81.6%) were diagnosed with clinical stage III, 103 patients (85.8%) underwent radical mastectomy and 106 patients (88.3%) underwent axillary dissection. Only three patients (2.5%) had complete pathological response, 2 patients were initially diagnosed with stage II and I patient with stage III. Eleven patients (9.2%) who received neoadjuvant therapy did not undergo surgery as they remained inoperable or developed metastasis (stage III at diagnosis). Fourteen patients (9.3%) underwent neoadjuvant radiotherapy as second-line neoadjuvant treatment.

Anthracycline-based was the most applied regimen, with or without taxane. Sixty patients (31.5%) received sequential anthracyclines plus taxane regimen (total: 6 to 8 cycles), 119 patients (62.6%) received anthracycline-based regimen without taxane (total: 4 to 6 cycles), and 11 patients (5.7%) received others chemotherapy regimen (CMF) (Table 2). One hundred and fifty patients (76%) had radiotherapy, more often as adjuvant treatment. Ninety-five hormone receptor-positive patients (94.1%) received adjuvant tamoxifen, and 1 patient received neoadjuvant endocrine therapy. Six hormone receptor-positive patients did not receive any hormone therapy: one patient missed follow-up, and five had relapsed before starting adjuvant treatment.

After a median follow-up of 81.5 months, there were 109 relapses (55%) and 81 deaths (41%). The median relapse-free survival (RFS) was 49.5 months; the 5-year and 10-year relapse rate was 50% and 37%, respectively (Figure 1). Univariate analysis identified younger than 29 years of age (p: 0.016 - HR 1.54; 95% CI 1.09-2.32), neoadjuvant chemotherapy (p<0.001 – HR 3.35; 95% CI 2.11-5.31), positive node involvement (p<0.001 – HR 3.01; 95% CI 1.88-4.82), and stage III at diagnosis (p<0.001 – HR 2.77; 95% CI 1.80-4.25) as significantly associated with relapse. Positive node involvement (p<0.001 – HR 2.45; 95% CI 1.52-3.94) and neoadjuvant chemotherapy

(p<0.001 – HR 2.88; 95% CI 1.79-4.69) remained an independent prognostic factor for relapse (Table 3 and Figure 2).

The median OS was 134 months, the 5-year survival rate was 63.4%, and the 10-year survival rate was 52.6% (figure 1). In the univariate analysis, younger than 29 years of age (p:0.016– HR 1.70; 95% CI 1.09-2.65), negative hormone receptor (p<0.001 – HR: 2.21; 95% CI 1.40-3.47), neoadjuvant chemotherapy (p<0.001 – HR 3.84; 95% CI 2.20 -6.70), positive node involvement (p<0.001 – HR:2.72; 95% CI 1.57-4.71), and stage III at diagnosis (p<0.001 – HR 3.71; 95% CI 2.17-6.36), were significantly associated with overall survival. Only negative hormone receptor (p<0.001 – HR2.1; 95% CI 1.28-3.44), positive node involvement (p<0.001 – HR:2.71; 95% CI 1.51-4.87), and neoadjuvant chemotherapy (p<0.001 – HR:2.95; 95% CI 1.63-5.32) remained an independent prognostic factor for survival (Table 3 and Figure 2).

We were not able to evaluate neither the use of Trastuzumab nor the receipt of radiotherapy as prognostic factors due the small sample size.

5 I DISCUSSION

Breast cancer is not frequent in young patients, especially 30 years or younger. However, it has been the leading cause of cancer death in women over the age of 20[25]. Previous studies evaluated breast cancer in young women (under 40 years of age), but there has not been much research on very young patients (under 31 years of age).

In our study, of the 196 very young breast cancer patients analyzed, half were hormone receptor-positive. Of the patients who had their HER2 status evaluated, a quarter was diagnosed with HER2 overexpression and 34% with triple negative tumors. In previously published analyses, immunohistochemical findings vary widely: HR-positive (48-77%), HER2 positive status (19-33%), triple-negative (15-24%), and high histological grade (34-50%)[29,19]. When compared to older women, there were higher grade, more HER2-enriched, and triple-negative tumors. Therefore, our sample appears to have even more aggressive features: more triple-negatives and fewer positive hormone-receptors.

Patients with HER2-positive and triple-negative subtypes have shorter survival regardless of age at diagnosis[19]. We also found that positive hormone receptor was associated with longer overall survival. Although Early Breast Cancer Trialists' Collaborative Group (EBCTCG) showed in a meta-analysis 29% reduction in cancer-related mortality in women less than 45 years of age with 5 years receiving tamoxifen[6], young age seems to be associated with worse outcomes in positive hormone-receptor patients, even with adjuvant endocrine therapy[19,20]. This age-related distinct benefit could be explained by lower adherence to endocrine therapy, less occurrence of chemotherapy-related amenorrhea[27], tamoxifen resistance, the need for incremental ovarian suppression, or the combination of any of these factors[8]. In 2011, Hershman

showed that both early discontinuation and non-adherence to hormonal therapy (below 80% of dose) were common and associated with increased mortality[13]. Furthermore, SOFT trial reported the benefit of the addition of ovarian suppression with aromatase inhibitor in premenopausal patients at high risk when compared to tamoxifen with or without ovarian suppression[8].

In Brazil, the patients have more advanced tumors at diagnosis than those reported in others countries, probably due the delay on diagnosis and health service disparity[16,22]. We found 60% of stage III patients at diagnosis and 60% other patients with nodal involvement, whereas the international literature describes 20% of patients with stage III tumors[20], 20% other patients with T3 / T4 lesions[12], and 35-50% of patients with nodal involvement[29]. In our study, node involvement was an independent poor prognostic factor for both relapse and death, as found in previous trials[12,29].

Anthracycline-based plus taxane or higher-cumulative-dosage anthracycline-based regimens were the most applied regimens. There was no significant difference in relapse or survival between chemotherapy regimen. It is in line with Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis findings, suggesting that suggesting that extra cycles of a taxane could be counterbalanced by extra cycles of other cytotoxic drugs[5].

At our institution, 60% of our patients received neoadjuvant chemotherapy, usually to ensure operability. Currently, neoadjuvant treatment is widely used to allow more conservative surgery,[15] which leads to lower morbidity and offers better cosmetic results[4]. However, it was initially applied to patients with locally advanced tumors in an attempt to make these tumors resectable. Randomized studies have shown that timing of chemotherapy has no impact on survival[26], but allows for the evaluation of tumor response, more conservative surgeries[15], and the early treatment of micrometastasis.

The achievement of complete pathological response (pCR) on the other hand is an important prognostic factor[15], especially in triple negative and HER2 positive tumors. In 2005, the HERA trial showed that Trastuzumab increased disease-free survival in HER2 positive patients[21]. This drug was approved in 2006 by the U. S. Food and Drug Administration for the adjuvant treatment of breast cancer in patients with HER2-positive tumors. However, the HER2 evaluation at INCA was not possible until 2007 and was applied in only 40% of patients. Despite the HERA results in 2005, Trastuzumab was available at our institution after 2008, and only 12 patients received this anti-HER2 drug. We could not evaluate the use of anti-HER2 drug as a prognostic factor, due to the small number of patients.

Neoadjuvant chemotherapy is the standard of care for locally advanced breast cancer treatment, with objective clinical response in 80-90% of patients[24] and complete pathological response in 20-40% of patients[15]. We found complete pathological response rates of 2.5% and twenty-one patients (17.6%) remained with unresectable tumors after neoadjuvant chemotherapy. Fourteen patients (11.7%) received neoadjuvant radiotherapy with or without chemotherapy, and 10 patients (71.4%) could undergo

surgery afterwards. This approach has been tested in chemotherapy-refractory tumors. It was well-tolerated and showed good clinical response[10]. In 2007, Gaui reported that 23 of the 28 patients could be submitted to surgery after this approach[10]. However, Coelho et al reported frequent surgical complications, with no deaths related to procedure[3].

The BRCA1 mutation was also associated with higher pCR compared to noncarriers or BRCA2 carriers[1]. Although choosing the chemotherapy regimen based on genetic findings is not recommended, genetic counseling should be considered for all patients under 40 years old, especially in case of family history or triple-negative tumor[18]. We did not have genetic counseling available nor genetic testing for all patients during this trial period.

Conservative breast surgery in young patients is a controversial issue in the literature, with conflicting findings regarding the increased risk of local relapse. Randomized trials from 1980s and 1990s showed equivalence between treatments[18], but they offered outdated chemotherapy and radiotherapy treatments, with few young patients in their sample. The most recent trials showed that despite the fact that conservative surgery increases the risk of local relapse, there are no survival differences in such young patients[17]. Actually, young age alone is not a contraindication to breast conserving therapy. In this trial, almost 90% underwent mastectomy and / or axillary dissection because the locally advanced disease.

This is a retrospective study which raises the possibility of missing clinical data in patients' records. Other possible limitations are the very few HER2 status evaluation in our samples, the lack of comparison with other age groups or control population, and the relatively short follow-up period, especially for positive-hormone receptor patients. However, it is one of the largest trials to date including such young patients, and reflects the real-world in developing countries.

6 I CONCLUSION

In summary, this analysis showed a very young population with more locally advanced disease and worse prognostic pathological characteristics. Despite the aggressive treatment, our patients had worse outcomes than reported by other authors.

7 I CONTRIBUIÇÕES

Juliana Cunha e Silva Ominelli de Souza e Jesse Lopes da Silva contribuíram na concepção, no desenho do trabalho; na aquisição de dados, na análise e interpretação dos dados da pesquisa; na redação e na aprovação final da versão para publicação. Andrew Sá Nunes contribuiu na aquisição de dados, na análise e interpretação dos dados da pesquisa; na redação e na aprovação final da versão para publicação. Aline Coelho Gonçalves e Susanne Crocamo Ventilari da Costa contribuíram na concepção,

no desenho do trabalho; na interpretação dos dados da pesquisa; na redação e na aprovação final da versão para publicação.

Declaração de conflitos de interesse: Nada a Declarar

REFERENCES

Arun B, Bayraktar S, Liu DD, et al. **Response to Neoadjuvant Systemic Therapy for Breast Cancer in BRCA Mutation Carriers and Noncarriers: A Single-Institution Experience.** J Clin Oncol. 2011;29(28):3739-46.

Bloom HJ, Richardson WW. **Histological grading and prognosis in breast cancer; A study of 1409 cases of which 359 have been followed for 15 years**. Br J Cancer. 1957;11(3):359-77.

Coelho RC, Silva FML, Carmo IML, et al. **Is there a role for salvage radiotherapy in locally advanced breast cancer refractory to neoadjuvant chemotherapy?** Breast. 2016;31:192-6.

Curran D, van Dongen JP, Aaronson NK, et al. **Quality of life of early-stage breast cancer patients treated with radical mastectomy or breast-conserving procedures: results of EORTC Trial 10801.** Eur J Cancer. 1998;34(3)307-14.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG). **Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials.** Lancet. 2012;379(9814):432-44.

Early Breast Cancer Trialists' Collaborative Group. **Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials**. Lancet. 2011;378(9793):771-84.

Edge SB, Byrd DR, Compton CC, et al. **AJCC cancer staging manual. 7th ed**. New York: Springer; 2010.

Francis PA, Regan MM, Fleming GF, et al. **Adjuvant Ovarian Suppression in Premenopausal Breast Cancer.** N Engl J Med. 2015;372(5)436-46.

Gajdos C, Tartter PI, Bleiweiss IJ, et al**. Stage 0 to stage III breast cancer in young women**. J Am Coll Surg. 2000;190(5)523-9.

Gaui MF, Amorim G, Arcuri RA, et al. **A phase II study of second-line neoadjuvant chemotherapy with capecitabine and radiation therapy for anthracycline-resistant locally advanced breast cancer**. Am J Clin Oncol. 2007;30(1):78-81.

Gravena AAF, Agnolo CMD, Lopes TCR, et al. **Breast Cancer in Young Brazilian Women: Challenge for the Oncology Care**. Epidemiology Research International; 2014.

Han W, Kang SY. **Relationship between age at diagnosis and outcome of premenopausal breast cancer: age less than 35 years is a reasonable cut-off for defining young age-onset breast cancer.** Breast Cancer Res Treat. 2010; 119(1):193-200.

Hershman DL, Shao T, Kushi LH, et al. **Early discontinuation and non-adherence to adjuvant hormonal therapy are associated with increased mortality in women with breast cancer.** Breast Cancer Res Treat. 2011;126(2)529-37.

Instituto Nacional de Câncer José Alencar Gomes da Silva**. Estimativa 2016: Incidência de Câncer no Brasil.** INCA; 2015.

Killelea BK, Yang VQ, Mougalian S, et al. **Neoadjuvant chemotherapy for breast cancer increases the rate of breast conservation: results from the National Cancer Database**. J Am Coll Surg. 2015;220(6):1063-9.

Lee BL, Liedke PE, Barrios CH, et al. **Breast cancer in Brazil: present status and future goals.** Lancet Oncol. 2012;13(3):e95-e102.

Mahmood U, Morris C, Neuner G, et al. **Similar survival with breast conservation therapy or mastectomy in the management of young women with early-stage breast cancer**. Int J Radiat Oncol Biol Phys. 2012;83(5):1387-93.

Paluch-Shimon S, Pagani O, Partridge AH, et al. **Second international consensus guidelines for breast cancer in young women (BCY2).** Breast. 2016;26:87-99.

Park YH, Lee SJ, Jung HA et al. **Prevalence and clinical outcomes of young breast cancer (YBC) patients according to intrinsic breast cancer subtypes: Single institutional experience in Korea**. Breast. 2015;24(3):213-7.

Partridge AH, Hughes ME, Warner ET, et al. **Subtype-Dependent Relationship Between Young Age at Diagnosis and Breast Cancer Survival**. J Clin Oncol. 2016;34(27):3308-14.

Piccart-Gebhart MJ, Procter M, Leyland-Jones B, et al. **Trastuzumab after Adjuvant Chemotherapy in HER2-Positive Breast Cancer**. N Engl J Med. 2005;353(16):1659-72.

Pinheiro AB, Lauter DS, Medeiros GC, et al. **Câncer de mama em mulheres jovens: análise de 12.689 casos.** Rev Bras Cancerol. 2013;59(3):351-9.

Poggi MM, Danforth DN, Sciuto LC, et al. **Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy.** Cancer. 2003;98(4):697-702.

Rastogi P, Anderson SJ, Bear HD, et al. **Preoperative Chemotherapy: Updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27.** J Clin Oncol. 2008;26(5):778-85.

Siegel RL, Miller KD, Jemal A. **Cancer Statistics, 2016**. CA Cancer J Clin. 2016;66(1):7-30.

van der Hage JA, van de Velde CJ, Julien JP, et al. **Preoperative chemotherapy in primary operable breast cancer: results from the European Organization for Research and Treatment of Cancer trial 10902**. J Clin Oncol. 2001;19(22):4224-37.

Walshe JM, Denduluri N, Swain S.M. **Amenorrhea in premenopausal women after adjuvant chemotherapy for breast cancer**. J Clin Oncol. 2006;24(36):5769-79.

World Health Organization (WHO). **Physical status: the use and interpretation of anthropometry.** Geneva: WHO; 1995.

Zhao Y, Xiaoqiu D, Li R, Song J, Zhang D. **Correlation Between Clinical-Pathologic Factors and Long-Term Follow-Up in Young Breast Cancer Patients**. Transl Oncol. 2015;8(4):265-72.

Characteristics	OVERALL	Stage I	Stage II	Stage III	p-value*
	N: 196	N: 23	N: 55	N:117	
Age (years)					
-Median (range)	29 (17 - 30)	29 (19-30)	29 (17-30)	28 (20-30)	P:0.34
Body Mass Index					

- Median (range)	24 (16-41.9)	24 (19-42)	22.8 (16-42)	24 (17-36)	P:0.09
Race					
- White	94 (48%)	13 (56%)	28 (51%)	53 (45%)	P:0.72
- Non – White	59 (30%)	5 (21%)	18 (32%)	36 (30%)	
- Missing	43 (22%)	5 (21%)	9 (16%)	28 (23%)	
Receptor status					
-Positive	102 (52%)	16 (70%)	27 (50%)	59 (50%)	P:0.17
-Negative	86 (44%)	6 (26%)	26 (47%)	54 (46%)	
- Missing	8 (4%)	1 (4%)	2 (3%)	4 (4%)	
HER2 status					
- Positive	19 (24%)	1 (5%)	4 (7%)	14 (12%)	P:0.17
- Negative	58 (73%)	8 (35%)	19 (35%)	31 (26%)	
- Triple negative	27 (34%)	-	11 (47%)	14 (31%)	
- Missing	117 (60%)	14 (60%)	32 (58%)	72 (62%)	
Histological grade					
-1 and 2	76 (38%)	11 (48%)	20 (36%)	45 (39%)	P:0.36
- 3	79 (40%)	6 (26%)	25 (46%)	47 (40%)	
- Missing	41 (21%)	6 (26%)	10 (18%)	25 (21%)	
Pathological Lymph node involvement					
- Positive	110 (56%)	3 (13%)	28 (51%)	79 (67%)	P<0.01
- Negative	72 (37%)	20 (86%)	27 (49%)	25 (21%)	
- Missing	14 (7%)		0	13 (11%)	
Chemotherapy					
- Neoadjuvant	120 (61%)	0	21 (38%)	98 (84%)	P<0.01
- Adjuvant	70 (35%)	20 (87%)	33 (60%)	17 (14%)	
- Not done	6 (3%)	3 (13%)	1 (2%)	2 (2%)	
Hormonal therapy					
- Neoadjuvant	2 (1%)	0	0	2 (2%)	P:0.17
- Adjuvant	102 (52%)	16 (70%)	28 (51%)	58 (49%)	
- Not done	92 (46%)	7 (30%)	27(49%)	57 (49%)	
Radiotherapy					P<0.01
- Neoadjuvant	14 (7%)	0	0	14 (12%)	
- Adjuvant	136 (69%)	15 (65%)	42 (76%)	79 (67%)	
- Not done	46 (23%)	8 (34%)	13 (23%)	24 (20%)	

Type of surgery					
- Breast conserving	29 (14%)	13 (56%)	10 (18%)	6 (5%)	P<0.01
- Total mastectomy	156 (79%)	10 (44%)	45 (82%)	101 (86%)	
- Not done	11 (5%)	0	0	10 (9%)	
Nodal treatment					
- Axillary dissection	171 (87%)	17 (74%)	48 (87%)	106 (90%)	P<0.01
- Sentinel node biopsy	14 (7%)	6 (26%)	7 (13%)	1 (1%)	
- Missing	11 (5%)	0	0	10 (9%)	

Table 1. Patient, tumor and treatment's characteristics according to presentation status

*p- value from chi-square test.

The sum of patients per stage was 195 because 1 patient had no information on stage at diagnosis

	Neoadjuvant	Adjuvant
Anthracycline	69 (57%)	50 (71%)
Anthracycline + taxane	46 (38%)	14 (20%)
Others	5 (4%)	6 (8%)

Table 2. Chemotherapy regimen

p: 0.014

Parameter		Relapse-free survival		Overall Survival	
		HR (95%CI)	P value	HR (95%CI)	P value
Age	≤28y vs >28y	1.43 (0.96-2.13)	0.077	1.39 (0.86-2.25)	0.175
Hormone receptor	Negative vs Positive	1.450 (0.98-2.13)	0.061	2.1 (1.28-3.44)	0.001
Node involvement	Positive vs negative	2.45 (1.52-3.94)	0.001	2.7 (1.51-4.80)	0.001
Stage at diagnosis	III vs I + II	1.21 (0.74-1.99)	0.433	1.96 (0.98-3.91)	0.055
Chemotherapy	Neoadjuvant vs adjuvant	2.884 (1.79-4.69)	0.001	2.95 (1.63-5.32)	0.001

Table 3. Multivariate analysis for relapse-free survival and overall survival

Abbreviations: HR, Hazard Ratio; CI, Confidence Interval.

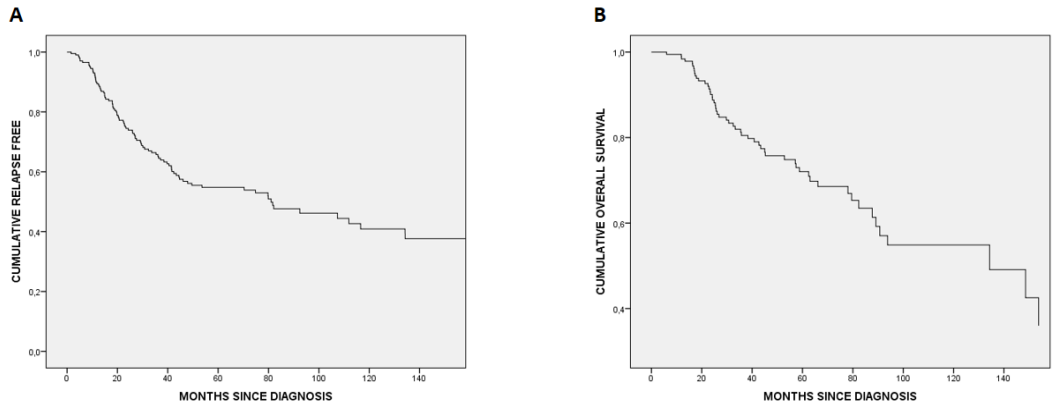

Figure 1. Kaplan Meier Curve for (A) Relapse-free Survival (B) Overall Survival

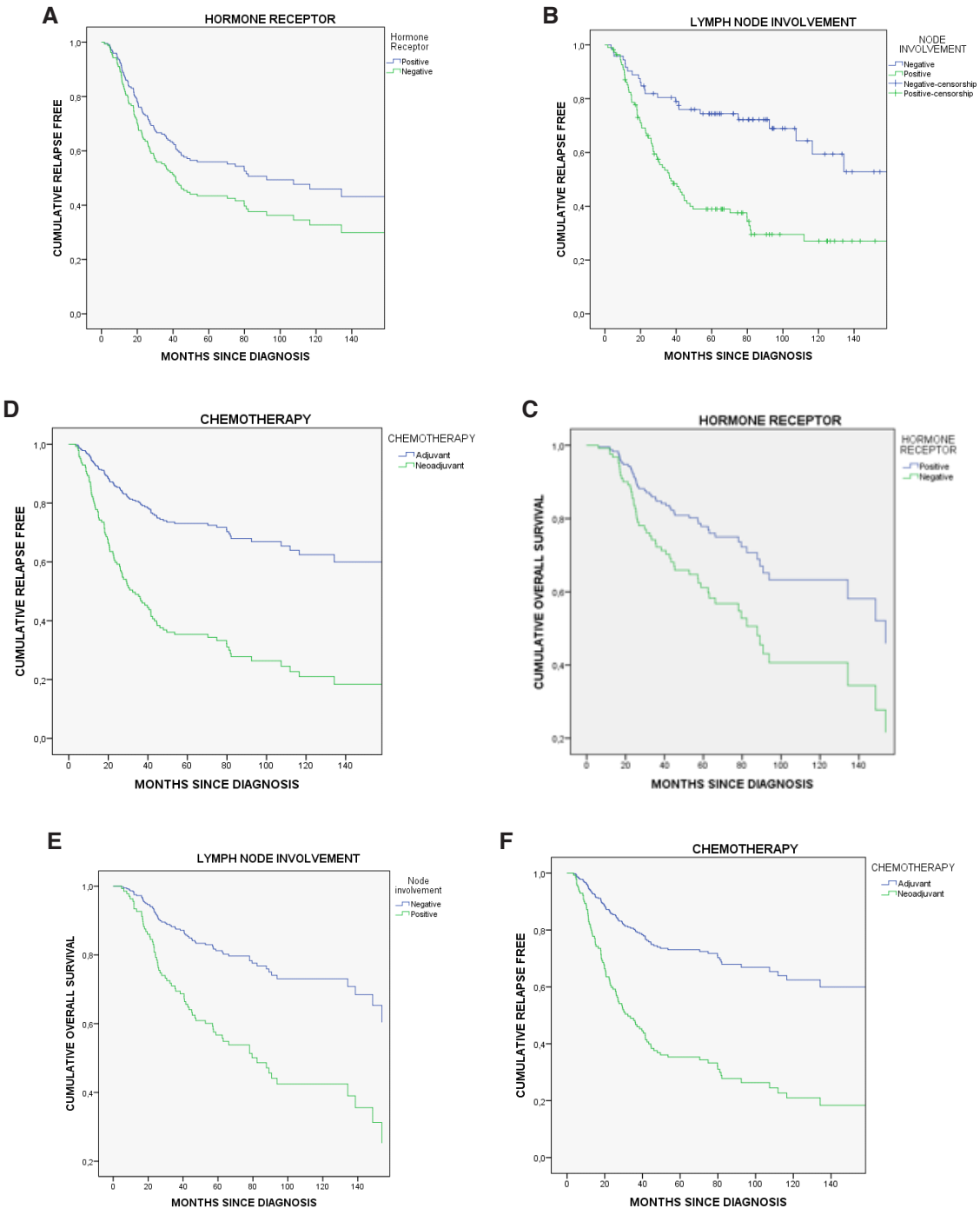

Figure 2. Kaplan-Meier relapse-free survival curves according to: (A) Hormone receptor; (B) Axillary lymph node involvement; (C) Chemotherapy timing; Kaplan-Meier overall survival curves

according to: (D) Hormone receptor; (E) Axillary lymph node involvement; (F) Chemotherapy timing

SOBRE O ORGANIZADOR

Dr. Benedito Rodrigues da Silva Neto

Possui graduação em Ciências Biológicas pela Universidade do Estado de Mato Grosso (2005), com especialização na modalidade médica em Análises Clínicas e Microbiologia. Em 2006 se especializou em Educação no Instituto Araguaia de Pós graduação Pesquisa e Extensão. Obteve seu Mestrado em Biologia Celular e Molecular pelo Instituto de Ciências Biológicas (2009) e o Doutorado em Medicina Tropical e Saúde Pública pelo Instituto de Patologia Tropical e Saúde Pública (2013) da Universidade Federal de Goiás. Pós-Doutorado em Genética Molecular com concentração em Proteômica e Bioinformática. Também possui seu segundo Pós doutoramento pelo Programa de Pós-Graduação Stricto Sensu em Ciências Aplicadas a Produtos para a Saúde da Universidade Estadual de Goiás (2015), trabalhando com Análise Global da Genômica Funcional e aperfeiçoamento no Institute of Transfusion Medicine at the Hospital Universitatsklinikum Essen, Germany.

Palestrante internacional nas áreas de inovações em saúde com experiência nas áreas de Microbiologia, Micologia Médica, Biotecnologia aplicada a Genômica, Engenharia Genética e Proteômica, Bioinformática Funcional, Biologia Molecular, Genética de microrganismos. É Sócio fundador da “Sociedade Brasileira de Ciências aplicadas à Saúde” (SBCSaúde) onde exerce o cargo de Diretor Executivo, e idealizador do projeto “Congresso Nacional Multidisciplinar da Saúde” (CoNMSaúde) realizado anualmente no centro-oeste do país. Atua como Pesquisador consultor da Fundação de Amparo e Pesquisa do Estado de Goiás - FAPEG. Coordenador do curso de Especialização em Medicina Genômica e do curso de Biotecnologia e Inovações em Saúde no Instituto Nacional de Cursos. Como pesquisador, ligado ao Instituto de Patologia Tropical e Saúde Pública da Universidade Federal de Goiás (IPTSP-UFG), o autor tem se dedicado à medicina tropical desenvolvendo estudos na área da micologia médica com publicações relevantes em periódicos nacionais e internacionais.