

Oral health after breast cancer treatment in postmenopausal women

Juliana Amódio,¹ Daniela Bazan Palioto,¹¹ Helio Humberto Angotti Carrara,¹ Daniel Guimaraes Tiezzi,¹ Jurandyr Moreira de Andrade,¹ Francisco José Candido dos Reis¹

¹ Universidade de São Paulo, Faculdade de Medicina de Ribeirão Preto, Departamento de Ginecologia e Obstetrícia, Ribeirão Preto/SP, Brazil.

¹¹ Universidade de São Paulo, Faculdade de Odontologia de Ribeirão Preto, Departamento de Cirurgia e Traumatologia Buco-Maxilo-Facial e Periodontia, Ribeirão Preto/SP, Brazil.

OBJECTIVE: Oral health can affect a patient's general health and quality of life. Given the increase in breast cancer survival rates, investigations of factors influencing the quality of life of survivors have gained importance. Therefore, the objective of our study was to characterize oral health in postmenopausal breast cancer survivors.

METHODS: We conducted a matched case-control study. Forty-eight women who survived breast cancer (age 62.1 ± 9.1 years) and 48 healthy controls (age 61.8 ± 8.6 years) were included. For each case and control, a complete oral evaluation chart was completed.

RESULTS: The prevalence of chronic periodontal disease was 98% in breast cancer survivors and 87% in controls. The breast cancer survivors had a median of 16 remaining teeth, whereas controls had a median of 22 remaining teeth ($p = 0.03$). The percentage of sites with gingival bleeding was 16.05% (0-100%) in breast cancer survivors and 0% (0-72%) in controls ($p = 0.04$).

CONCLUSION: Chronic periodontal disease and tooth loss were highly prevalent in postmenopausal breast cancer survivors. To improve survivors' quality of life, a preventive oral health evaluation should be available prior to cancer treatment.

KEYWORDS: Breast Cancer; Periodontal Disease; Tooth Loss.

Amódio J, Palioto DB, Carrara HH, Tiezzi DG, Andrade JM, Candido dos Reis FJ. Oral health after breast cancer treatment in postmenopausal women. *Clinics*. 2014;69(10):706-708.

Received for publication on February 2, 2014; First review completed on February 28, 2014; Accepted for publication on March 18, 2014

E-mail: fjcrcis@fmrp.usp.br

Tel.: 55 16 3602-2589

INTRODUCTION

Breast cancer mortality has declined dramatically since 1990 (1). In the U.S., breast cancer death rates have decreased by 34% (2). This epidemiological change can be attributed to a combination of screening programs and improvements in adjuvant therapy (3). In this context, an important issue faced by clinicians caring for these women is how to improve their long-term quality of life. Many latent clinical disorders can emerge during or after cancer treatment that eventually may attenuate the survival gains obtained via recent advances in curative-intent therapies (4).

Good oral health is important to quality of life and overall health. Chronic periodontal disease (CPD) is associated with low flow-mediated dilation of the brachial artery and high levels of systemic inflammation markers (5). CPD is also

associated with atherogenesis (6) and a risk of myocardial infarction and stroke (7). Oral care during cancer treatment primarily focuses on the management of acute complications, such as mucositis, oral pain and infection (8). Chronic oral diseases have the potential to impair survivors' quality of life after oncological treatment and are frequently neglected.

In this study, we report the results of a systematic oral evaluation after breast cancer treatment in postmenopausal women. Our objective was to characterize the oral health in breast cancer survivors treated in the public health system.

MATERIALS AND METHODS

Subjects

This case-control study included 48 voluntary postmenopausal breast cancer survivors and 48 age-matched healthy women volunteers. The cases and matched controls were recruited from the public health system in Brazil.

Oral examination

The oral examinations were conducted by a single calibrated dental examiner who collected the complete clinical history of the patients and performed the clinical

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

No potential conflict of interest was reported.

DOI: 10.6061/clinics/2014(10)10



oral examination. The oral examinations were performed after the end of oncological treatment for all breast cancer survivors. The data included the following: the total number of teeth, full-mouth plaque score (the number of sites with detectable dental plaque divided by the total number of sites per mouth, multiplied by 100), full-mouth gingival bleeding on probing score (the number of sites with gingival bleeding on probing divided by the total number of sites per mouth, multiplied by 100), full-mouth periodontal lesion score (the number of sites with a probing depth ≥ 4 mm divided by the total number of sites per mouth, multiplied by 100) and the mean probing attachment level.

Statistics

The data for each variable were tested using the D' Agostino & Pearson normality test. The mean and standard deviation or median and range were determined. Student's t test or the Mann-Whitney test was performed as appropriate. All analyses were performed using GraphPad Software® 5.0 for Windows (GraphPad Software Inc, La Jolla, CA, USA).

Ethics

The study was approved by the local institutional review board, and all subjects signed a written informed consent form. All procedures were in accordance with the Helsinki Declaration.

■ RESULTS

The medical parameters associated with breast cancer are presented in Table 1. The mean age was 62.1 ± 9.1 years for breast cancer survivors and 61.8 ± 8.6 years for controls.

Oral health data are presented in Table 2. CPD was identified in 98% of breast cancer survivors (mild periodontitis: 30 cases; moderate periodontitis: 11 cases; severe periodontitis: 6 cases) and 87% of controls (mild periodontitis: 23 cases; moderate periodontitis: 12 cases; severe periodontitis: 7 cases).

The median number of teeth was 16 (3-28) for breast cancer survivors and 22 (4-31) for controls ($p=0.03$, Mann-Whitney test). The median full-mouth plaque score was 50 (0-100) for cancer survivors and 36.57 (0-100) for controls ($p=NS$, Mann-Whitney test). The median full-mouth gingival bleeding on probing score was 16.05 (0-100) for the cases and 0 (0-72) for the controls ($p=0.04$, Mann-Whitney test).

Table 1 - Medical parameters of breast cancer survivors.

Parameter	N (%)
Tumor histology	
Ductal	46 (95.8)
Lobular	2 (4.2)
Tumor stage	
I	10 (20.8)
II	25 (52.1)
III	12 (25.0)
IV	1 (2.3)
Chemotherapy	33 (66.43)
Radiotherapy	41 (85.4)
Tamoxifen	40 (83.3)
Aromatase inhibitor	8 (16.7)
Surgery	
Radical	18 (37.5)
Conservative	30 (62.5)

Table 2 - Oral health parameters in breast cancer survivors and controls.

Parameter	Cases	Controls	p
Chronic periodontitis (%)	47 (98)	42 (87)	NS
Total number of teeth	16 (3-28)	22 (4-30)	0.03
% of sites with detectable plaque	50 (0-100)	36.57 (0-100)	NS
% of sites with gingival bleeding	16.05 (0-100)	0 (0-72)	0.04
% of sites with a depth ≥ 4 mm	3.3 (0.0-46.7)	3.6 (0.0-51.6)	NS
Probing attachment level	2.8 (1.3-5.9)	3.1 (1.5-5.2)	NS

Data are presented as the median (range).

The median full-mouth periodontal lesion score was 3.3 (0.0-46.7) for breast cancer survivors and 3.6 (0.0-51.6) for controls. The probing attachment level was 2.8 (1.3-5.9) in breast cancer survivors and 3.1 (1.5-5.2) in controls ($p=NS$, Mann-Whitney test).

■ DISCUSSION

We identified a very high prevalence of CPD in postmenopausal breast cancer survivors; only one of our patients did not exhibit signs of the disease. The controls also presented a high prevalence of CPD; however, breast cancer survivors had significantly higher indices of gingival bleeding and tooth loss. These findings are highly relevant for the multidisciplinary management of breast cancer.

The quality of life and long-term survival of breast cancer survivors may be affected by lack of oral health care. CPD is associated with several unpleasant symptoms that can range from mild to severe, including swelling, bluish purple discoloration of the gingiva, bleeding after eating or brushing and halitosis. CPD can also induce loss of supportive connective tissues, including alveolar bone, thereby resulting in loss of attachment of the periodontal ligament to the cementum and eventual tooth loss (mainly among older individuals) (9).

The prevalence of CPD increased significantly with age and remained constant after the 50–59 age group (10). The prevalence of CPD in postmenopausal women not taking hormonal replacement is approximately 64.4%, whereas the prevalence is 46.3% in postmenopausal women taking hormonal replacement (11). Overall, 87% of the individuals in our control group had CPD; this prevalence is comparable to that observed in Germany (10) and higher than that observed in the U.S. (12). The association between breast cancer treatment and oral health has not previously been explored, but it is well known that “potentially complicating oral disease should be identified and corrected as early as possible before commencement of anticancer therapy” (13). A comprehensive dental examination performed prior to treatment can identify approximately 80% of the patients with chronic odontogenic pathology who should receive treatment to prevent local exacerbation or systemic spread of ongoing infection while avoiding long-term oral complications, such as tooth loss (14).

On the other hand, the association between CPD and cardiac morbidity is well established. Cardiac complications have a serious impact on the life expectancy and quality of life of breast cancer survivors. The risk for cardiac disease may be increased in breast cancer survivors due to various reasons other than CPD. Data from The Late Effects Breast Cancer Cohort have revealed that 62.9 excess cases of cardiovascular events per 10,000 patient-years are asso-



ciated with long-term breast cancer treatment and the main risk factors are associated with radiotherapy of the internal mammary chain, radiation with adjuvant chemotherapy and smoking (15). After breast conservation treatment for early stage disease, the subsequent development of cardiac disease is more frequent in women with cancer of the left breast (16). Anthracyclines, which are largely used in breast cancer chemotherapy, have long been recognized as a cause of cardiac dysfunctions, such as cardiomyopathy and heart failure. These side effects are dose-dependent (17) and occur more frequently in older patients (18). Trastuzumab, a monoclonal antibody that blocks the HER-2 receptor and improves the survival of women with HER-2-positive breast cancer, is also associated with an increased risk of cardiac dysfunction (19).

High-quality management of breast cancer patients should include strategies for identifying patients who are at high risk for cardiac disease and developing effective interventions to prevent the development of late toxicities and minimize their effects on quality of life (20). Epidemiological (7) and experimental (5,21) evidence indicates that periodontal disease is linked to an increased risk of cardiovascular disease. Despite the limitations of our case-control design and a lack of diversity in the therapeutic methods employed, our data consistently revealed a high prevalence of periodontal disease and tooth loss after breast cancer treatment in post-menopausal women. We believe that the current evidence warrants the inclusion of a recommendation for a comprehensive oral examination and treatment of identified lesions in the breast cancer management protocols in the public health system. Efforts have been made to screen for and reduce or eliminate risk factors for cardiac disease, such as smoking, elevated lipid levels and hypertension, in patients who have breast cancer after menopause. However, these efforts should also include the prevention and treatment of oral diseases.

AUTHOR CONTRIBUTIONS

Amodio J, Palioto DB and Candido dos Reis FJ conceived and designed the study, performed data collection, analyzed data, interpreted data, wrote and critically reviewed the manuscript. Carrara HH, Tiezzi DG and Andrade JM participated in writing and critically reviewed the manuscript.

REFERENCES

1. Parkin DM, Bray FI, Devesa SS. Cancer burden in the year 2000. The global picture. *Eur J Cancer*. 2001;37(Suppl 8):S4-66.
2. DeSantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. *CA Cancer J Clin* 2014;64(1):52-62.
3. Berry DA, Cronin KA, Plevritis SK, Fryback DG, Clarke L, Zelen M, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med*. 2005;353(17):1784-92.

4. Jones LW, Haykowsky MJ, Swartz JJ, Douglas PS, Mackey JR. Early breast cancer therapy and cardiovascular injury. *J Am Coll Cardiol*. 2007;50(15):1435-41, <http://dx.doi.org/10.1016/j.jacc.2007.06.037>.
5. Amar S, Gokce N, Morgan S, Loukideli M, Van Dyke TE, Vita JA. Periodontal disease is associated with brachial artery endothelial dysfunction and systemic inflammation. *Arterioscler Thromb Vasc Biol*. 2003;23(7):1245-9, <http://dx.doi.org/10.1161/01.ATV.0000078603.90302.4A>.
6. Beck JD, Elter JR, Heiss G, Couper D, Mauriello SM, Offenbacher S. Relationship of periodontal disease to carotid artery intima-media wall thickness: The atherosclerosis risk in communities (aric) study. *Arterioscler Thromb Vasc Biol*. 2001;21(11):1816-22, <http://dx.doi.org/10.1161/hq1101.097803>.
7. Scannapieco FA, Bush RB, Paju S. Associations between periodontal disease and risk for atherosclerosis, cardiovascular disease, and stroke. A systematic review. *Ann Periodontol*. 2003;8(1):38-53, <http://dx.doi.org/10.1902/annals.2003.8.1.38>.
8. Mosel DD, Bauer RL, Lynch DP, Hwang ST. Oral complications in the treatment of cancer patients. *Oral Dis*. 2011;17(6):550-9, <http://dx.doi.org/10.1111/j.1601-0825.2011.01788.x>.
9. Murray Thomson W. Epidemiology of oral health conditions in older people. *Gerodontology*. 2014;31 Suppl 1:9-16, <http://dx.doi.org/10.1111/ger.12085>.
10. Holtfreter B, Schwahn C, Biffar R, Kocher T. Epidemiology of periodontal diseases in the study of health in pomerania. *J Clin Periodontol*. 2009;36(2):114-23, <http://dx.doi.org/10.1111/j.1600-051X.2008.01361.x>.
11. Haas AN, Rosing CK, Oppermann RV, Albandar JM, Susin C. Association among menopause, hormone replacement therapy, and periodontal attachment loss in southern brazilian women. *J Periodontol*. 2009;80(9):1380-7, <http://dx.doi.org/10.1902/jop.2009.090082>.
12. Dye BA, Tan S, Smith V, Lewis BG, Barker LK, Thornton-Evans G, et al. Trends in oral health status: United states, 1988-1994 and 1999-2004. *Vital Health Stat* 11. 2007(248):1-92.
13. Consensus statement: Oral complications of cancer therapies. National institutes of health consensus development panel. *NCI Monogr*. 1990(9):3-8.
14. Toljanic JA, Bedard JF, Larson RA, Fox JP. A prospective pilot study to evaluate a new dental assessment and treatment paradigm for patients scheduled to undergo intensive chemotherapy for cancer. *Cancer*. 1999;85(8):1843-8, [http://dx.doi.org/10.1002/\(SICI\)1097-0142\(19990415\)85:8<1843::AID-CNCR26>3.0.CO;2-R](http://dx.doi.org/10.1002/(SICI)1097-0142(19990415)85:8<1843::AID-CNCR26>3.0.CO;2-R).
15. Hooning MJ, Botma A, Aleman BM, Baaijens MH, Bartelink H, Klijn JG, et al. Long-term risk of cardiovascular disease in 10-year survivors of breast cancer. *J Natl Cancer Inst*. 2007;99(5):365-75, <http://dx.doi.org/10.1093/jnci/djk064>.
16. Harris EE, Correa C, Hwang WT, Liao J, Litt HI, Ferrari VA, et al. Late cardiac mortality and morbidity in early-stage breast cancer patients after breast-conservation treatment. *J Clin Oncol*. 2006;24(25):4100-6, <http://dx.doi.org/10.1200/JCO.2005.05.1037>.
17. Von Hoff DD, Layard MW, Basa P, Davis HL, Jr., Von Hoff AL, Rozencweig M, et al. Risk factors for doxorubicin-induced congestive heart failure. *Ann Intern Med*. 1979;91(5):710-7, <http://dx.doi.org/10.7326/0003-4819-91-5-710>.
18. Pinder MC, Duan Z, Goodwin JS, Hortobagyi GN, Giordano SH. Congestive heart failure in older women treated with adjuvant anthracycline chemotherapy for breast cancer. *J Clin Oncol*. 2007;25(25):3808-15, <http://dx.doi.org/10.1200/JCO.2006.10.4976>.
19. Seidman A, Hudis C, Pierri MK, Shak S, Paton V, Ashby M, et al. Cardiac dysfunction in the trastuzumab clinical trials experience. *J Clin Oncol*. 2002;20(5):1215-21, <http://dx.doi.org/10.1200/JCO.20.5.1215>.
20. Giordano SH, Hortobagyi GN. Local recurrence or cardiovascular disease: Pay now or later. *J Natl Cancer Inst*. 2007;99(5):340-1, <http://dx.doi.org/10.1093/jnci/djk085>.
21. Tonetti MS, D'Aiuto F, Nibali L, Donald A, Storry C, Parkar M, et al. Treatment of periodontitis and endothelial function. *N Engl J Med*. 2007;356(9):911-20.